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Contents

Original Articles

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Immunoinflammatory mechanism of severe pneumonia and the application of inflammatory markers in clinical practice

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Abstract: Pneumonia is a common disease and one of the leading causes of morbidity and mortality worldwide. [1] Severe pneumonia is a unique clinical disease that is highly life-threatening, characterized by severe sepsis, septic shock, or respiratory failure. Usually, treatment is required in the intensive care unit (ICU). Approximately 10% of community-acquired pneumonia (CAP) patients require hospitalization, with a mortality rate of 21% -47%. Most patients with severe community-acquired pneumonia have complications, including chronic obstructive pulmonary disease, diabetes and coronary heart disease. Streptococcus pneumoniae, Staphylococcus aureus, Mycoplasma pneumoniae, aaLegionella, Klebsiella pneumoniae, Haemophilus influenzae, novel coronavirus, respiratory virus and Pseudomonas aeruginosa are important pathogenic microorganisms for severe CAP. [2] Host autoimmune factors, patient clinical manifestations, and laboratory and imaging examination results at admission can help identify high-risk populations for this disease. Early identification and timely empirical application of antibiotics are particularly important for the prognosis of patients.

Keywords: Severe Pneumonia; Immune Inflammation; Inflammatory Markers

1. Immunoinflammatory mechanisms in severe pneumonia

The strength of the immune function of the lungs determines the severity of the disease following infection with pathogenic bacteria. Innate and adaptive immune responses to lung microorganisms play a crucial role in maintaining a healthy respiratory system and preventing lung disease. Initiation of antimicrobial defenses and mitigation of the risk of lung injury during acute infections, and the shaping of lung immunity by respiratory infections also helps to improve autoimmune function, and a small number of less virulent pathogenic microorganisms can be eliminated by physical defenses in the respiratory tract, such as the ciliary system and alveolar macrophages in the airways. [3]

The role of T cells in the immune system is particularly important, as CD4-positive (CD4+) T cells, also known as helper T cells, aid in the production of antibody responses by B cells and provide feedback to dendritic cells (DCs) through the production of cytokines and co-stimulatory molecules, as well as augmenting and sustaining the responses of CD8-positive (CD8+) T cells, also known as cytotoxic T cells.CD8+ T cells CD8+ T cells contribute to cytokine production and, more importantly, directly kill virus-infected cells. Invariant natural killer T (iNKT) cells and γδ T cells and and the newly discovered innate lymphoid cells (ILCs) also play a key role in the early response to many lung infections. cD4+ T cells and cD8+ T cells can form an immune memory that can benefit the host when it encounters a secondary attack from a related or the same pathogen.[4] CD4+ T cells and CD8+ T cells are also known as cytotoxic T cells, and are also known as cytotoxic T cells. [4] Inadequate T cell responses during persistent infections increase the likelihood that the body will become infected and delay pathogen clearance. In addition to this, insufficient T cell immunity may also increase the likelihood of pathogen transmission through the lungs.

2. Severe pneumonia and immune cells

2.1 Severe pneumonia and macrophages

Alveolar macrophages are key sensors and effectors of the lung's innate immune response to infection,[5] roaming the lumen of the alveolar ducts, are the first line of defense of the respiratory tract, and are also referred to as dust cells because of their ability to clear and digest relatively inert inhaled material. They send warning signals like the body when the lungs are infected and secrete a variety of cytokines and chemokines to regulate pulmonary innate and adaptive immunity. [6,7]

2.2 Severe pneumonia and neutrophils

During lung infections, neutrophils migrate from the pulmonary capillaries into the airspace. It has been suggested that neutrophils are excellent microbial defense cells. After exerting phagocytosis, neutrophils destroy microorganisms with reactive oxygen species (e.g., hypochlorite), antimicrobial proteins (e.g., bactericidal permeability-inducing proteins and lactoferrin), and degradative enzymes (e.g., elastase). [8]

Inadequate numbers of neutrophils (neutropenia) and defective quality (e.g., chronic granulomatousdisease) predispose patients to opportunistic lung infections, as do complement and immunoglobulin deficiencies. Since neutrophils and plasma proteins mediate innate immune function and are necessary to prevent lung infections, acute inflammation can be considered an essential innate immune response in the lung.

2.3 Severe pneumonia and lymphocytes

Lymphocytes not only exert immune effects in the human body, but also participate in immunoregulation, among which T cells play a key role in the immune system and are of interest in lung host defense against bacterial, viral, and fungal pathogens.T-lymphoid progenitor cells can differentiate into CD4+ and CD8+ T cells in the thymus, and then migrate to peripheral immune organs, such as the spleen, and the lymph nodes, to become primitive T cells.When the organism is infected by a When the organism is infected by a pathogen, the cellular antigen receptor (TCR) complex binds to peptide antigens presented to them by antigen-presenting cells (APCs), and T cells can be activated through cell-cell interactions.APCs present antigens through major histocompatibility complexes I or II (MHCI and MHCII), which interact with the two major subpopulations of T cells, the CD8+ and CD4+ T cells, respectively.CD8+ T cells are known as CD4+ and CD4+ T cells, and CD8+ T cells are known as CD8+ T cells. CD8+ T cells are called cytotoxic T lymphocytes (CTL), while CD4+ T cells are referred to as T helper cells (Th). [9,10]

CD4+ T cells are a major T cell subset that play a central role in immune system function when naïve CD4+ T cells differentiate into effector and or memory cells after encountering cognate antigens via antigen-presenting cells (APCs).CD4+ T cells are an important component of the lung host's defense against a variety of pathogens, as can be demonstrated in HIV.CD4+ T cells can be categorized as helper T cells (Th)1 (Th1), Th2, Th9, Th17, Th22 as well as follicular helper T (Tfh) cells and regulatory T cells (Treg). [11,12,13] Th1 cells are characterized by the production of their signature cytokine, interferon gamma (IFN-γ), which is primarily involved in intracellular immune responses to viruses and bacteria. Th2 immune responses are characterized by the production of interleukin-4 (IL-4), which can act as an autocrine factor for Th2 differentiation, and can stimulate activated B cells to promote the differentiation of B cells into plasma cells. Th2 cells are involved in worm-induced immunopathology and are responsible for the initiation and maintenance of allergic diseases. [14,15]

Treg cell production depends on productive antigen presentation by APC in a microenvironment enriched with tumor necrosis factor-β (TGF-β) and interleukin-2 (IL-2). [16] Depending on the type and stage of infection, inhibition of the inflammatory response by Treg cells can be both beneficial and detrimental to host defense. In the lung, these cells play an important role in mediating the response to inhaled antiplays a key role in the tolerance of the original. [17]

3. Severe pneumonia and inflammatory markers

Localized inflammation in pneumonia is caused by pathogen infection and organism reactivity. Entry of infectious agents into the lungs can stimulate alveolar macrophages, produce large amounts of inflammatory factors, mediate the migration of inflammatory cells in the peripheral circulation, and exacerbate the severity of pneumonia. Inflammatory mediators are closely related to lung inflammation, and their roles in disease exacerbation and progression are critical. Interleukin-6 (IL-6) and C-reactive protein (CRP) are widely recognized as typical inflammatory factors, which contribute significantly to the pathogenesis of a variety of inflammatory diseases,[18] and have been associated with the development of pneumonia. [19,20] Recent studies have shown that calcitoninogen is also of value in the diagnosis of severe pneumonia. [21] The combined detection of multiple inflammatory markers shows promising applications.

3.1 Severe pneumonia and C-reactive protein

CRP is considered a valuable marker of inflammation, and CRP has an important role in host defense against pathogen invasion as

well as in the inflammatory response.CRP consists of five identical subunits arranged to form a cyclic pentamer.CRP currently exists in at least two different conformational forms, including the natural pentameric CRP (pCRP) and the modified/monomeric CRP (mCRP). These isoforms bind to different lipid rafts and receptors while exhibiting different functional properties. In the inflammatory microenvironment pCRP dissociates into subunits and the newly formed mCRP may help to localize the inflammatory response. [21] Recent studies have shown that early identification of patients with poor prognosis in moderate to severe pneumonia can be achieved by measurement of CRP sequential ratios. [22]

3.2 Severe pneumonia and interleukin-6

IL-6, an inflammatory interleukin, is produced primarily by T lymphocytes and macrophages in response to pathogens and is critical for the control of many viral infections. Although steady state values of IL-6 contribute to the regression of infections and tissue lesions, its exacerbated production is decisive for cytokine storm. [23] It has been found that in patients with severe neocoronary pneumonia, its levels are negatively correlated with peripheral oxygen saturation (SpO2) and partial pressure of arterial oxygen (PaO2), which are associated with respiratory failure, and that there is a positive correlation between IL-6 and C-reactive protein (CRP.) IL-6 behaves as a predictor of disease progression.

3.3 Severe pneumonia and calcitoninogen

Calcitonin (PCT) is a calcitonin hormone produced by C cells in the thyroid gland. The calcitonin 1 gene (CALC-11) on chromosome 11 controls its production. The product of this gene, precalcitoninogen precursor (prePCT), undergoes proteolytic cleavage to produce PCT, which is further processed into the mature calcitonin molecule.Transcription and translation of the CALC-1 gene is usually restricted to thyroid C cells and, to a lesser extent, to other neuroendocrine cells. Production is activated in all parenchymal tissues under bacterial infection mediated by the cytokines IL-6, TNF-α, and interleukin-1β (IL-β). Other tissues lack the ability to cleave PCT into the mature form of calcitonin, resulting in the accumulation of PCT. [26] In contrast, interferon gamma, which is secreted primarily in response to viral infection, attenuates PCT production. Therefore, plasma PCT concentrations, which are low in healthy individuals and elevated during bacterial, parasitic, or fungal infections and remain at normal levels during viral infections or noninfectious inflammatory responses, have been used as a biomarker to aid in the diagnosis of bacterial infections or sepsis, (as well as to differentiate between bacterial versus viral pneumonia and chronic obstructive pulmonary disease (COPD). Although elevated serum concentrations of PCT are not specific to infection, PCT is still considered one of the best biomarkers for the diagnosis of sepsis. Early diagnosis facilitates timely initiation of therapeutic measures, whereas delays result in severe infection-related morbidity and mortality.

Summary and Outlook

Severe pneumonia is an increasing incidence worldwide in recent years, which starts as a localized infection of the lungs and can easily lead to serious complications such as respiratory failure and circulatory failure if the initial antimicrobial therapy is inappropriate and the infection is not controlled in a timely manner. Early, rapid, and accurate diagnosis is essential for the treatment of severe pneumonia and for improving survival and prognosis. Immunity and inflammation are present throughout the pathogenesis of severe pneumonia, leading to extensive lung damage. The strength of the pulmonary immune response is closely related to the severity of the disease following infection with the pathogenic organisms; an under-response can lead to life-threatening infections, but an over-response can lead to life-threatening inflammatory damage.

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Research progress of embryonic stem cells in treatment of spinal cord injury

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Abstract: Spinal Cord Injury (SCI) refers to the structural and functional injury of the spinal cord under external forces. The spinal cord is an important part of the human nervous system, responsible for transmitting information between the brain and the rest of the body. Spinal cord injury may lead to varying degrees of neurological dysfunction, including impaired sensory, motor, autonomic, and vesical and intestinal functions [1]. Traditional treatments for patients often fail to fully restore their function, so it is particularly important to find a new treatment [2]. As a kind of cell with the ability of self-replication and multidirectional differentiation, stem cells have been widely used in the treatment of spinal cord injury, showing great potential in the treatment of spinal cord injury and achieving certain clinical effects [3]. This article reviews the research progress of embryonic stem cells in spinal cord injury, aiming to explore the application status, mechanism and prospect of stem cells in the treatment of spinal cord injury, and provide scientific basis for clinical treatment.

Keywords: Stem Cells; Spinal Cord Injury; Transplantation; Repair; Treatment

1. Characteristics of embryonic stem cells

Embryonic stem cells are formed during early embryonic development and have the characteristics of self-renewal and pluripotency. They can replicate themselves without limit and are able to differentiate into various cell types in the body. [4] Human embryonic stem cells (hESCs) are stable in terms of pluripotency, karyotype, global gene expression, ability to repair DNA and maintain telomerase levels, and growth characteristics. hESCs provide a renewable source of multiple cell types for research and cell-based therapies to treat disease. This makes embryonic stem cells a potential option for treating a variety of diseases. Embryonic stem cells can be transplanted into the damaged spinal cord area to promote nerve regeneration. Once transplanted, these cells can differentiate into nerve cells, replace damaged nerve cells, and rebuild damaged neural networks. [5] Research has shown that cell replacement therapy using stem cells or their derivatives has become a very promising approach to promoting motor recovery in this regard. Embryonic stem cell transplantation can improve motor and sensory function in patients and improve quality of life. [6]Jones I, et al transplanted embryonic stem cells into acute and chronic rat models of cervical spinal cord injury, promoting remodeling of descending spinal projection and contributing to partial recovery of forelimb motor function. The results obtained in this proof-of-concept study suggest that human embryonic stem cell-derived neural crest cells warrant further investigation as cell-based therapeutic candidates for spinal cord injury. Second, embryonic stem cells have the ability to secrete a variety of growth factors and cytokines, which can promote the regenerative environment of the damaged spinal cord. [7] Stem cells are induced by nutritional factors in vivo and in vitro to differentiate into other types of cells, including neurons. Scientists have isolated various stem cells from different organs and tissues in the human body and demonstrated that these cells are effective in regenerative medicine. The use of these cells offers a non-surgical approach to treating neurological disorders such as neurological defects. These molecules can stimulate the growth and connections of nerve cells, promoting repair and regeneration of damaged areas. The study found that embryonic stem cells can promote nerve cell regeneration and improve functional recovery after spinal cord injury.

2. Mechanism of stem cells promoting spinal cord injury repair

The mechanism by which stem cells promote spinal cord injury repair is an area of great interest. Research has shown that stem cells can promote spinal cord injury repair in a variety of ways, including promoting neuronal regeneration, reducing inflammation, promoting neuronal regeneration and forming new synaptic connections. These mechanisms provide a theoretical basis for the application of stem cells in the treatment of spinal cord injury, and also provide an important research direction for future clinical treatment.

Release of secretory factors: Stem cells can release a variety of growth factors, neurotrophic factors and neuroprotective factors, such as nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neuron-oriented factor (NT-3), etc. These factors can promote the growth, regeneration and connectivity of nerve cells, provide nutrition and support, and improve the environment of damaged areas. [8]Luo H et al. transplanted RADA16-PRG self-assembled nanopeptide scaffolds (SAPNSs), bone mesenchymal stem cells (BMSCs), and brain-derived neurotrophic factor (BDNF) expressing adeno-associated virus (AAV) into rats with acute spinal cord injury (SCI). To investigate the effects of these transplants on acute spinal cord injury (SCI) repair and explore the mechanisms, results showed: Co-transplantation of RADA16-PRG-SAPNS with BMSCs and BDNF-AAV can prolong the survival time of BMSCs in rats, reduce postoperative scar formation caused by glial cell proliferation, promote the migration and proliferation of neurons in the injured area, and promote functional repair after acute spinal cord injury.

Immune regulation: Stem cells have the function of immune regulation, which can inhibit the inflammatory response, reduce the infiltration and activation of immune cells, reduce the release of inflammatory factors, reduce the inflammatory damage in the injured area, and promote repair and regeneration [9].

Spinal cord environmental regulation: Stem cells can change the environment at the site of spinal cord injury, including improving blood circulation, increasing angiogenesis, promoting the migration and localization of neurons and glial cells, and providing suitable growth environment and support [10].

These mechanisms interact to promote the repair and functional recovery of spinal cord injury. However, there are still some controversies and unanswered questions about the specific mechanism, and further research and experiments are needed to further understand it.

3. Application of embryonic stem cells in spinal cord injury

Spinal cord injury (SCI) is one of the serious neurological diseases that occur in young people with high rates of morbidity and disability. However, effective treatments are still lacking. Stem cell (SC) therapy for SCI has gradually become a new research hotspot in the past decades. [11]Zeb H, Khan IN, et al., mention that in the last century, scientific advances have created a new paradigm for the medical treatment of SCI. Basic and translational research has flourished, so much so that a variety of protective and regenerative therapies can be used in clinical trials. In particular, the mechanisms underlying the pluripotent state of human embryonic stem cells (hESCs) proved crucial in identifying the intended role of SCI in regenerative medicine. Knowledge of SCI related neurogenesis and hESC is essential for critical evaluation of existing translational therapy strategies for SCI. [12] To date, more than 200 clinical studies have been registered applying various stem cell approaches to treat neurological disorders (Clinicaltrials.gov), most of them for multiple sclerosis, stroke, and spinal cord injury. In total, we identified 17 neurological indications that are in clinical development. By transplanting embryonic stem cells into damaged areas of the spinal cord in the hope that they will differentiate into nerve cells and repair the damage, [13] A large number of studies have focused on SCI treatment of SCI, most of which have shown good results with both in vivo and in vitro induction. The transplantation routes include intravenous, transarterial, nasal, intraperitoneal, intrathecal and intramedullary injection. Most SC treatments for SCI use many cells, ranging from tens of thousands to millions. Researchers can do this by taking a patient's own adult stem cells, differentiating them into nerve cells, and transplanting them to the site of the spinal cord injury. [14]Dalamagkas K et al mentioned NeuralStem Inc. Phase I clinical trials are currently underway using human spinal cord stem cells (NSI-566) derived from the spinal cord of a single 8-week-old fetus and continuously expanded by epigenetic means only. Although no publicly available data is available, the company reports that no serious adverse events have occurred, that stem cell implantation is feasible in patients with chronic SCI, and that implantation of NSI-566 FSC in patients with SCI is safe and well-tolerated. The last surgery was completed in June 2015, and the patient recently completed the 2015 month post-observation period (NeuralStem Inc., 566). [15]Tsuji O et al. found that when ES cells are applied to the treatment of SCI, it is preferred to transplant ES derived cells that have formed nerve stem/progenitor cells, which can produce glial cells and neurons, rather than nerve stem/progenitor cells that almost only produce neurons. These findings are therefore extremely important for future attempts to implement ES cell and iPS cell transplantation therapies. This approach avoids the problem of immune rejection;

4. Challenges and prospects of embryonic stem cells in clinical application

Although embryonic stem cells have made some progress in the treatment of spinal cord injury, there are still some challenges. Such as cell transplantation survival and differentiation efficiency, cell source selection, immune rejection and safety. In response to these problems, researchers are constantly working to find solutions to improve the effectiveness and safety of stem cell therapy. Embryonic stem cells face several challenges in clinical applications, including the following:

Safety concerns: [16] Heng BC et al mentioned indirect evidence that the observed therapeutic effect was due to various secretory factors produced by transplanted cells. This therefore raises the exciting prospect of using human embryonic stem cells as a "catalyst" to promote bioremediation and regeneration in transplant therapy. However, the immune barrier against allotransplantation and the teratogenic potential of human embryonic stem cells present significant technical challenges. Stem cell transplantation may trigger safety issues such as immune rejection or tumor formation after xenotransplantation, and these potential risks need to be addressed to ensure the safety of treatment. 2. Quality control: [17] Hashii N et al mentioned the limited availability of cell therapy products and the need for more sensitive and specific quality testing methods. Quality control of cell therapy products requires a more sensitive and specific approach, as in many cases only a small number of cell products, approximately 1×106 to 1× 108, should be available for quality testing. Quality control of stem cells is an important challenge to ensure that the source, culture, differentiation and quality of stem cells meet clinical requirements. 3. Ethical issues: Due to ethical and legal restrictions on the use of embryonic stem cells, their clinical application still needs further research and discussion.

Despite the challenges, stem cells still hold great promise in clinical applications:

Therapeutic potential: [18]Gazdic M et al. mentioned that hESC is pluripotent both in vitro and in vivo. Since hESC can differentiate into ectodermal cells such as neurons and glial cells, it has been used as a new treatment option for SCI in many clinical studies. Transplantation of HESC-derived oligodendrocyte progenitor cells into SCI models in this paper resulted in cell survival and clinically relevant recovery of neural function without evidence of harmful effects. Embryonic stem cells are pluripotent and self-renewing, can differentiate into a variety of cell types, has a wide range of therapeutic potential, can be used to treat a variety of diseases and injuries, such as cardiovascular and cerebrovascular diseases, neurodegenerative diseases, tissue damage and so on. 2. Individualized treatment: Embryonic stem cells can be derived from patients themselves, which has a low risk of immune rejection, and can realize individualized treatment strategies and improve treatment effects.

Tissue Engineering and regenerative medicine: Embryonic stem cells can be used in tissue engineering and regenerative medicine to help repair and regenerate damaged tissues and organs, offering new possibilities for clinical treatment. 4. Innovative therapies: Embryonic stem cell therapy is an innovative treatment method that can develop new therapeutic strategies and drugs and promote the progress of medical science.

To sum up, stem cells face some challenges in clinical application, but they still have broad prospects and application value, and are a field of concern and research. With the continuous progress of science and technology, these challenges will gradually be overcome, and stem cell therapy is expected to bring more well-being to human health.

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Application Analysis of Combining Scenario Simulation with the Problem-Based Learning (PBL) Model in Orthopedic Teaching

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Abstract: The development of medical expertise demands a meticulous and scientific approach, relying not solely on extensive theoretical foundations but also on ample practical experience to reinforce theoretical applications. This is particularly evident in orthopedic teaching, where an understanding of the skeletal system, analysis of pathogenesis, and treatment are essential. Practicality becomes crucial in this context. To augment teaching effectiveness, it is imperative to employ effective teaching methods and strategies. Integrating scenario simulation with the Problem-Based Learning (PBL) model allows for a more intuitive presentation of pathological knowledge to students. This method aids students in better absorbing theoretical content, fostering deeper communication and learning during scenario simulation, and ultimately achieving superior learning outcomes.

Keywords: Scenario Simulation; PBL Model; Orthopedic Teaching; Application Strategies

Introduction

Given the specificity and complexity of orthopedic learning, advancing the training of applied and compound medical talents necessitates active innovation in teaching methods and models. By amalgamating scenario simulation with the PBL model, a more authentic situational atmosphere is created. This enables students to embark on practical exploration and problem-solving under specific scenarios, emphasizing their subjectivity and initiative. Consequently, this approach deepens students' understanding and enhances their learning outcomes. This paper begins by analyzing the significance of combining scenario simulation with the PBL model in orthopedic teaching and subsequently briefly discusses relevant application strategies for reference [1].

1. Importance of Integrating Scenario Simulation and PBL Model in Orthopedic Teaching

Orthopedics plays a crucial role in the human body's structural organization, involving a wide range of content with strong cross-disciplinary knowledge. Given the dynamic nature of orthopedic knowledge and its frequent clinical applications, high-level orthopedic treatment and rehabilitation require robust support from quality medical education. To enhance the effectiveness of combining theory and practice for students, it is essential to actively explore feasible paths and effective methods in orthopedic teaching methods and models. Based on the unique characteristics of orthopedic learning, employing a teaching model that combines scenario simulation with the Problem-Based Learning (PBL) model proves valuable in elevating the quality and efficiency of orthopedic education.

By integrating the scenario simulation and PBL model, a more realistic setting can be created for students. The human body exhibits variations in skeletal characteristics, functionality, and distribution across different areas. Additionally, patients' specific manifestations and clinical representations differ, leading to variations in treatment methods. To reflect the specificity and scientific nature of orthopedic teaching, combining scenario simulation with the PBL model meets the diverse needs of students in theoretical knowledge learning, practical training, and assessment. This approach places theoretical learning in a more realistic context, facilitating more intuitive teaching. With the support of content, scenarios, and tangible materials, students can better comprehend abstract medical terms. In particular, for surgical teaching, the absence of scenario simulation hampers the transformation of surgical procedures into observable phenomena, hindering the effective improvement of students' practical skills. In the context of combining scenario simulation with the PBL model, students can repeatedly practice certain procedures without trauma, overcoming the limitations of theoretical explanations and translating theoretical knowledge into practical application. This method helps students master specific requirements and steps proficiently. Moreover, under the combined scenario

simulation and PBL model, students can engage in simultaneous operations, discussions, practices, and explorations. This facilitates effective problem-solving, providing answers to questions and uncertainties, reinforcing knowledge impressions during interaction and communication.

2. Application of Integrating Scenario Simulation and PBL Model in Orthopedic Teaching

2.1 Effective Design of Integrating Scenario Simulation and PBL Model

In orthopedic teaching, enhancing teaching quality by integrating scenario simulation with the PBL model requires thorough design and preparation. This involves selecting specific teaching content resources, and preparing for scenario simulations, such as constructing a realistic clinical setting with necessary equipment and auxiliary materials like orthopedic images and surgical tools. Simultaneously, during the simulation and reenactment process, relevant questions need to be designed to stimulate students' enthusiasm for learning and exploration. Through the presentation of questions, students are encouraged to immerse themselves in the scenarios, identify key clues, and solve problems, realizing the initial purpose of integrating scenario simulation with the PBL model.

2.2 Implementation of Scenario Simulation

Orthopedic knowledge covers a wide range and exhibits strong interconnections and logical coherence. To achieve better teaching outcomes and help students grasp theoretical concepts while reinforcing practical skills, it is essential to integrate scenarios with case studies. This combined approach of integrating situations with problems guides students to absorb and consolidate knowledge effectively. The integration of scenario simulation with Problem-Based Learning (PBL) serves this purpose and plays a crucial role, contingent upon several foundational elements. Apart from meticulous planning and thorough preparation, the implementation process of scenario simulation is equally significant. Successful scenario simulation relies not only on the preparatory groundwork but also on the execution of simulations and guidance provided to students during the process. Particularly in the context of complex orthopedic treatments, which involve not only orthopedic knowledge but also the application of interdisciplinary knowledge from fields such as anatomy and anesthesia, the need for comprehensive preparation becomes even more pronounced. To further enhance the quality of teaching, especially in the simulated implementation of surgical scenarios, significant coordination of personnel and instruments is required. Establishing a well-constructed setting and context is crucial for students to immerse themselves effectively in the scenario. This approach allows students to comprehend the significance of different roles and the positive impact each role contributes to the treatment process. Furthermore, students can assume various roles such as doctors, nurses, or patients, based on scenario simulation cases, engaging in performances that require the application of their learned theoretical knowledge through practical operations and communication [4].

2.3 Guidance Through Problem-Based Learning

The integration of scenario simulation with the PBL model in orthopedic teaching aims to immerse students in real situations and guide them through in-depth exploration, understanding, and cognition based on changing scenarios. Therefore, guidance through well-crafted problems is crucial. As mentioned earlier, in scenario simulation, students can play different roles and be assigned corresponding tasks. Students, according to their roles and tasks, can pose questions and uncertainties. Teachers and other students can engage in discussions and provide answers collaboratively. During this process, teachers play a guiding role, helping students discover, analyze, and solve problems. Students are encouraged to propose questions and uncertainties, and using their acquired knowledge and skills, conduct in-depth analysis and research on these questions. Teachers guide students in contemplating the essence of problems, exploring solutions, and providing necessary assistance.

2.4 Timely Summation and Evaluation

While employing the scenario simulation and PBL model in orthopedic teaching, it is imperative to not only focus on the process but

also to promptly summarize and evaluate the teaching results. This provides insights into students' specific situations and their absorption of professional knowledge. In the summarization and evaluation process, perspectives from both students and teachers are considered. It involves analyzing and explaining issues that arose during the process, identifying their root causes, and making improvements accordingly.

3. Conclusion

In conclusion, under modern teaching philosophies, cultivating high-caliber orthopedic talents necessitates active exploration in teaching methods. By integrating scenario simulation with the PBL model and using diverse scenario-based practical activities, the integration of theoretical and practical aspects is promoted, stimulating students' subjectivity and enhancing their professional competence.

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Reperfusion Combined with Neuroprotective Agents Treatment in Acute Ischemic Stroke: a Literature Review of Current Progress

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Abstract: Acute ischemic stroke remains to be a heavy burden causing serious mortality and disability. Clinical studies of neuroprotective agents produced disappointing results in the treatment, and recanalization may be a precondition for it to be successful. By searching for relevant randomized controlled trials concerning combination therapy in the online databases and analyzing them, this literature review investigated the therapeutic effect of reperfusion combined with neuroprotective agents treatment in acute ischemic stroke. We found that reported trials specifically designed to investigate the efficacy of combination treatment are scarce. Overall, use of uric acid and nerinetide in the combination therapy exhibited positive results. These results indicate a high potential for clinical use with further confirmation. Future studies are still needed. They should focus on (1) designing clinical trials that investigate combination therapy specifically or include prespecified subgroup analyses for different types of recanalization, (2) reaffirming previous positive clinical trials with more patients of different characteristics or geographical locations, (3) employing multitarget neuroprotectant combinative therapy (cocktail therapy) to target multiple targets of ischemia-reperfusion injury instead of the currently prevalent single neuroprotectant with recanalization therapy.

Keywords: Stroke; Reperfusion; Neuroprotective; Combination Therapy

Introduction

A stroke is a severe emergency that the circulation to certain region of the brain is suspended. Stroke is an international health issue requiring worldwide attention. Stroke has two main types: ischemic and hemorrhagic. In the U.S., ischemic stroke accounts for 87% of strokes[1]. The damage caused by cerebral ischemia is not only the reduced supply of oxygen and glucose. Oxidative injury brought by the ischemia and recanalization treatment after is also critical. The two intertwine and contribute to the most part of the damage done by ischemic stroke[1].

As claimed by the American Stroke Association, clot removal is the predominant treatment for ischemic stroke, which can be accomplished by either medication or surgical means. Of all treatments, tissue plasminogen activator, r-tPA, (known as alteplase) is considered the gold standard. Some patients will receive mechanical thrombectomy especially when they have a large vessel occlusion[2].

Although restoration of blood flow to the occluded region as soon as possible remains to be the gold standard for acute ischemia stroke, considerable studies have shown that rapid recanalization could cause a cascade of complications[1]. The bleak outcome of current single therapy strategy and complexity of stroke pathophysiology call for additional treatment or combined treatment to help with the rehabilitation of acute ischemia stroke patients. This review intends to review the literature of reperfusion combined with neuroprotective agents treatment in acute ischemic stroke.

Main body

1. Existing treatment

1.1 Existing treatment: thrombolytics

Thrombolytics is the conventional treatment for stroke. Thrombolytics are clot-busting drugs that dissolve dangerous blood clots in the blood vessel. Thrombolytic agents can convert plasminogen into plasmin, which leads to blood clots lysis. Up till now, no less than three generations of thrombolytics with varying effectiveness, tolerability, and convenience are available[3].

Thrombolytics treatment is a tradeoff between the complication of hemorrhage and the possible recovery. The heterogeneity of the patients and lack of reliable approach to measure the treatment response make the quest for an ideal agent even harder. So far, despite the ever-improving therapeutic effect of new thrombolytics, the risk of hemorrhage is still an alarming side effect to be addressed[4].

1.2 Existing treatment: endovascular thrombectomy

Endovascular thrombectomy is a mechanical intervention that the blood clot is removed directly under image guidance. After the publication of five positive randomized controlled trials of thrombectomy in 2015, it became the new standard of treatment for stroke, especially for patients with large vessel occlusion[5,6].

Endovascular thrombectomy is performed most often by the use of stent-like thrombectomy devices. Retrievable stents are elastic stent-like devices that can be retrieved. The procedure has high recanalization rates with shorter time and fewer risk. However, there are some clinical situations that cannot be solved by stent retrievers. That's when the aspiration technique is employed. Overall, endovascular thrombectomy improve the recanalization rates, functional outcome, and reduce the disability of patients. The benefits apply to patients with different age and initial stroke severity and the overall therapeutic effect is better than the thrombolytics[1,2].

1.3 Existing treatment: neuroprotective treatment

Neuroprotection treatments have the potential to prevent or reverse the devastating cascade of acute ischemia stroke. It is generally accepted that their targets can be classified into four parts: excitotoxicity, reactive oxygen species, cellular apoptosis, and inflammation[3].

1.3.1Excitotoxicity

Acute ischemia stroke causes the decrease of energy and oxygen supply to the cell. The depletion of adenosine triphosphate (ATP) resulting from ischemia render the sodium/potassium (Na/K) transporter inoperable, thus increasing the intracellular calcium level. There is increased excitatory neurotransmitters level and activation of N-methyl-D-aspartic acid (NMDA) and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors. Neuroprotective drugs targeting the calcium channel or NMDA and AMPA receptors may promote neuroprotection. Such drugs include clomethiazole, magnesium, repinotan, nerinetide, and so on[3].

1.3.2 Reactive oxygen species

Ischemia induced energy depletion renders the energy-dependent scavenger enzymes inactive. Then the reactive oxygen species build up in the affected area. Neuroprotective drugs that can degrade free radicals have the potential of neuroprotection. Such drugs include NXY-059, cerebrolysin, simvastatin, albumin, uric acid, and so on[3].

1.3.3 Cellular apoptosis

The ischemic conditions cause a cascade of signaling change. The downstream messengers ultimately induce cell apoptosis. Neuroprotective drugs that counter the apoptosis process have the potential of neuroprotection. Such drugs include imatinib and so on[3].

1.3.4 Inflammation

Cytokine released after the ischemia attract the resident microglia and immune cells from elsewhere which can destroy blood brain barrier and cause tissue damage. Neuroprotective drugs that have anti-inflammatory effect or immune suppressing effect have the potential of neuroprotection. Such drugs include erythropoietin, otaplimastat, and so on[3].

2. Combination therapy

This literature review reviewed the literature of reperfusion combined with neuroprotective agents treatment in stroke and investigate the therapeutic effect of combination therapy. This literature review primarily focused on random controlled trials research journals focusing on neuroprotection combined with reperfusion treatment in acute ischemic stroke. Studies were selected by searching electronic databases, i.e., Web of Science, PubMed, and so on. The search included studies up to March 10, 2023.

Reported trials specifically designed to investigate the combination treatment are scarce. Many of the reviewed literature were originally designed to test specific neuroprotective agents, yet some patients received thrombolytics, thrombectomy, or both as part of the standard

treatment during the process. Overall, use of uric acid and nerinetide in the combination therapy exhibited positive results. These results indicate a high potential for clinical use with further confirmation.

3. Discussion

Despite the bleak past of neuroprotection and the challenging road toward successful combination therapy, combination therapy is one of the most promising directions to improve the management of stroke. Future studies should focus on (1) designing clinical trials that investigate combination therapy specifically or include prespecified subgroup analyses for different types of recanalization, (2) reaffirming previous positive clinical trials with more patients of different characteristics or geographical locations, (3) employing multitarget neuroprotectant combinative therapy (cocktail therapy) to target multiple targets of ischemia-reperfusion injury instead of the currently prevalent single neuroprotectant with recanalization therapy.

This literature review is not without limitation. Despite rigorous literature collection process, not all studies investigating combination therapy for stroke can be acquired and analyzed. Plus, the available time for the research and writing is restricted. Further research encompassing larger sample size with more comprehensive analysis can be done to improve the review.

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The Impact of Energy Level Zoning Nursing Mode on the Emergency Response Effect of Critically Ill Patients

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Abstract: Objective: To improve the emergency response effect of critically ill patients, and to implement a level zoning nursing model in clinical practice to clarify its impact on critically ill patients. Methods: A total of 95 critically ill patients who received diagnosis and treatment in the hospital during the period of January 2023 to December 2023 were analyzed. They were divided into a control group (49 cases) and an observation group (46 cases) in order of diagnosis and treatment. Two groups of nursing interventions were implemented using conventional methods and level based nursing models, and the intervention situation was analyzed. In terms of the incidence of complications, the observation group had a lower total value (P<0.05) compared to the two groups. In terms of clinical indicators, the observation group had lower values (P<0.05) compared to the two groups. In terms of nursing quality, the observation group had higher values (P<0.05) compared to the two groups. Conclusion: Implementing a level zoning nursing model in clinical practice can have a positive impact on emergency treatment of critically ill patients, and can help control related complications, improve clinical indicators, and enhance nursing quality.

Keywords: Critical Illness; First Aid; Energy Level Zoning Nursing Mode

From the perspective of clinical development, critically ill patients have a more emergency condition and need to take corresponding measures in a timely manner to ensure the effectiveness of emergency treatment and reduce the risk of death. When carrying out emergency treatment for critically ill patients in clinical practice, conventional methods are mainly adopted. Although they can help patients control their condition, they cannot guarantee the maximum effectiveness of emergency treatment[1]. With the continuous development of modern medical and health care, various new nursing models have been gradually applied to clinical nursing, effectively improving nursing effectiveness, which provides a new direction for research on emergency nursing for critically ill patients[2]. The article analyzes the impact of energy level zoning nursing mode on the emergency response effect of critically ill patients, as follows.

1. Materials and methods

1.1 General information

A total of 95 critically ill patients who received diagnosis and treatment in the hospital during the period of January 2023 to December 2023 were analyzed. They were divided into a control group (49 cases) and an observation group (46 cases) in order of diagnosis and treatment. In terms of age range, the two groups had an age range of 23 years ≤ 74 years, with a mean of (47.43 ± 4.33) years in the observation group and (47.45 ± 4.31) years in the control group. In terms of gender, there were 28 males and 18 females in the observation group, and 29 males and 20 females in the control group. After processing the relevant data information of two sets of basic data through statistical systems, it was confirmed that the comparability was high (P>0.05). This study was approved and approved by the hospital ethics committee. Selection requirements: All are critically ill patients; The information material is complete. Exclusion requirement: Missing data.

1.2 Methods

1.2.1 Routine nursing measures for the control group

Monitor various vital signs of patients according to conventional standards, and provide measures such as maintaining blood pressure, correcting water and electrolyte imbalances, anti infection, and nutritional support.

1.2.2 Observation group level zoning nursing mode means

(1) In terms of skill level positions: ① To organize meetings and discussions with medical and nursing leaders to determine relevant

skill level positions, improve and perfect the competition mechanism according to the requirements of skill level positions, and require the nursing staff involved in nursing work to meet the relevant standard requirements in terms of years of service, nursing professional abilities, and professional title qualifications; Dividing nursing staff levels accordingly to ensure that their abilities match the requirements of job positions, and determine the actual work content and scope of each position. To strengthen daily training and learning on job skills, and in the process of formulating nursing plans, it is required to combine the specific nursing needs of patients, relevant job functions, etc. At the same time, organizing nursing staff to conduct professional learning, regularly assessing their professional knowledge and practical operations, and maximizing the professional level of nursing staff.

(2) In terms of skill level allocation: When arranging the working hours of various nursing staff in the emergency department, it is necessary to take the work content of different skill level positions and the working conditions of the department as the basis, to ensure the rationality of scheduling and work content arrangement to the greatest extent possible, and to ensure the cooperation and cooperation among staff in various positions to ensure the quality of nursing. To control the quality of nursing in all aspects, and maintain a good working condition in the emergency green channel area for 24 hours. Reasonably arrange job changes and provide green channels for patients at any time. Regularly inspect the emergency room equipment and devices, and nursing staff need to master the operation and daily maintenance methods of various devices to ensure that the emergency equipment and devices are in a safe and stable state. They are required to complete examination preparation work in a short period of time, understand the examination process, and improve examination efficiency; Regularly inspect first aid supplies, replenish and replace them in a timely manner to avoid shortages or expiration of first aid supplies during the first aid process. Nursing staff are required to have rich clinical experience, be proficient in using emergency tools and nursing skills, be able to effectively cooperate with physicians in carrying out rescue work, and be able to calmly handle emergencies. Master relevant communication skills, promptly inform family members of the situation, and guide them to handle relevant procedures. Nursing staff are required to master various nursing measures such as health education, psychological counseling, nutritional support, and specialized disease care techniques, and be able to independently complete them.

(3) In terms of zoning management: Intensive Care Area: It is equipped with complete equipment and personnel, providing advanced nursing measures such as intensive care and emergency treatment, mechanical ventilation, and critical disease treatment, with high requirements for professional operation skills of nursing staff. Moderate Monitoring Area: After the patient's condition stabilizes, closely monitor vital signs, have corresponding nursing techniques, and can assist doctors in completing treatment measures. General Ward Area: It mainly manages patients with stable conditions and can provide basic medical care for patients, such as monitoring vital signs, medication administration, wound care, etc.

1.3 Judgment criteria

(1) Calculate the incidence of complications in two groups, including cardiac arrest, acute respiratory distress, and hypovolemic shock. (2) Statistically analyze two sets of clinical indicators, including the duration of emergency examination procedures, duration of venous channel opening, duration of rescue, and duration of hospitalization. (3) Evaluate the nursing quality before and after intervention in two groups, using the hospital orthopedic nursing quality survey scale as a survey tool. The survey content includes nursing attitude (0-25 points), nursing skills (0-25 points), nursing cognition (0-25 points), and nursing profession (0-25 points). The lower the score, the worse the nursing quality.

1.4 Statistical methods

Using SPSS 20.0 software to analyze the data, t and x±s are measures of compliance with normal distribution in continuous variables, chi square and% are count data, and $P<0.05$ indicating the data is statistically significant or valuable.

2. Results

2.1 Analysis of complications

In terms of the incidence of complications, the observation group had a lower total value ($P<0.05$) compared to the two groups. As

shown in Table 1.

Table 1 Comparison of incidence of complications between two groups（n,%）

Groups	Cardiac arrest	Acute respiratory distress	Hypovolemic shock	Total complications
Observation group（n=46）	0	0	1	1（2.17）
Control group（n=49）	2	2	2	6（12.24）
X2				7.812
P				0.005

2.2 Clinical indicator analysis

In terms of clinical indicators, the observation group had lower values (P<0.05) compared to the two groups. As shown in Table 2.

Table 2 Comparison of clinical indicators between two groups（`x±s）

Groups	Emergency examination operation duration（min）	Duration of venous channel opening（min）	Duration of rescue（min）	Duration of hospitalization（d）
Observation group（n=46）	25.01±2.12	3.41±1.10	32.52±2.69	14.01±1.02
Control group（n=49）	36.45±5.65	4.99±1.28	45.85±4.57	20.23±2.13
t	12.903	6.433	17.181	17.962
P	0.001	0.001	0.001	0.001

2.3 Analysis of nursing quality

In terms of nursing quality, compared to the two groups, the observation group had higher values in all aspects (P<0.05):

The scores for nursing attitude, nursing skills, nursing cognition, and nursing profession were (10.28±1.22, 10.32±1.04, 11.03±1.04, 10.57±1.21) in the observation group before intervention, and (10.30±1.24, 10.35±1.02, 11.05±1.06, 10.60±1.19) in the control group. The results were (t=0.079, 0.141, 0.092, 0.121, P=0.937, 0.887, 0.926, 0.903). After intervention, the observation group was (23.34 ± 6.63, 23.58 ± 7.02, 23.69 ± 7.01, 23.60 ± 6.99) (points), while the control group was (18.12 ± 3.20, 18.21 ± 3.33, 17.97 ± 4.10, 17.99 ± 4.03) (points). The results were (t=4.934, 4.810, 4.890, 4.828, P=0.001, 0.001, 0.001, 0.001).

3. Discussion

When carrying out emergency work for critically ill patients, it is necessary to pay attention to the control of complications, minimize the time of emergency examinations and the opening of venous channels, improve emergency efficiency, and provide certain guarantees for the patient's life and health. The energy level zoning nursing model, as a new type of nursing method, can allocate resources according to the patient's condition, provide personalized and professional nursing, and effectively manage and arrange nursing staff, improving work efficiency[3].

Compared with conventional nursing models, the energy level zoning nursing model has the following advantages in clinical application. Firstly, the level zoning nursing model allocates patients to corresponding nursing areas based on their severity, thereby providing more personalized and specialized care. For example, critically ill patients can receive closer monitoring and treatment in the intensive care unit, and after their condition stabilizes, they can receive corresponding care in the general care area. Secondly, after the classification and zoning, the requirements for nursing staff in different areas may vary. Corresponding training management and competitive measures will be taken for different nursing staff, requiring them to have corresponding job abilities and improve nursing quality[4]. Thirdly, under the level zoning nursing model, it is conducive to strengthening the management of nursing staff, allowing nursing staff with different abilities to be responsible for corresponding nursing areas, improving work efficiency, and avoiding waste of nursing resources[5]. At the same time, it will also strengthen nursing management in various stages, control the quality of nursing in each stage, ensure that the emergency green channel area is in good working condition 24 hours a day, ensure that emergency equipment and devices are in a safe and stable state, improve emergency examination efficiency, ensure sufficient emergency supplies, improve the professional level of nursing staff, effectively cooperate with physicians to complete emergency operations, do a good job in family communication, and orderly carry out post emergency nursing work, so as to improve the efficiency of first aid, shorten the time of first aid, enable patients to recover as soon as possible, shorten hospital stay,

and facilitate the control of complications[6]. Based on the research results in the article, in terms of the incidence of complications, the observation group had a lower total value (P<0.05) compared to the two groups. In terms of clinical indicators, the observation group had lower values (P<0.05) compared to the two groups. In terms of nursing quality, the observation group had higher values (P<0.05) compared to the two groups. Reminder: Providing a level zoning nursing model to critically ill patients can improve emergency efficiency and nursing quality. However, the number of research cases in the article is limited, and further analysis of its application value is needed.

In summary, implementing the level zoning nursing model in clinical practice can have a positive impact on emergency treatment of critically ill patients, help control related complications, improve clinical indicators, and enhance nursing quality.

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Study on the application of CBCT in the diagnosis of chronic periapical periodontitis with different depth of periodontal pocket

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Abstract: Objective To investigate the application of conical beam CT(CBCT) in the diagnosis of VRF with chronic periapical inflammation and different depth of periodontal exploration. Methods 40 teeth with chronic periapical inflammation suspected of VRF in 39 patients were examined by X-ray apical film, CBCT and periodontal examination respectively. Diagnosis and statistical analysis were performed for each affected tooth by two specialists, and subgroup analysis was performed according to the influence of the depth of the peridental pocket on the diagnosis results of CBCT. Results The sensitivity, missed diagnosis rate and consistency rate of CBCT in the diagnosis of VRF were 78.8%, 21.2% and 82.5%, respectively, which were significantly different from that of X-ray root tip film (54.8%, 45.2% and 60.0%) ($P<0.05$). The sensitivity and missed diagnosis rate of CBCT in the deep periodontal pocket group (probing depth ≥5mm) were significantly different from those in the non-deep periodontal pocket group (probing depth <5mm) ($P<0.05$). Conclusion CBCT is superior to X-ray apical film in the diagnosis of VRF. The presence of deep periodontal pocket has influence on sensitivity and missed diagnosis rate.

Keywords: CBCT; Chronic Periapical Inflammation; Longitudinal Root Cleft; Periodontal Pocket Depth

Vertical Root Fracture (VRF), also known as vertical root fracture (VRF), is a noncaries disease of hard tissue of teeth with complex etiology. It refers to longitudinal fracture occurring in the root of teeth, which can spread to the tooth body, pulp and periodontal tissue, and can be clinically manifested as spontaneous pain, knock pain and deep periodontal pocket, etc. [1]. Therefore, the clinical symptoms of VRF teeth often lack specificity, and the site of onset is deep root, which increases the difficulty of early diagnosis [2]. X-ray apical radiography and conical beam CT (CBCT) are often used to assist the diagnosis of VRF in clinic. Previous studies [3] have shown that conical beam CT (CBCT) has the advantages of good image quality, non-trauma and high precision, and has higher sensitivity and accuracy in the diagnosis of VRF. However, it is not clear whether CBCT is different in the diagnosis of VRF with different depth of periodontal exploration. The purpose of this study was to investigate the application of conical beam CT(CBCT) in the diagnosis of VRF with chronic periapical inflammation and different depth of periodontal probe.

1. Object of study

Choose materials and methods from January 2021 to August 2022 in the First Affiliated Hospital of Bengbu Medical University of dental patients with suspected type VRF (variable refrigerant flowrate) as the research object. Inclusion criteria [4]: The chief complaint of the affected tooth has obvious clinical symptoms, and there is percussion or palpable pain; Deep isolated periodontal pockets (reduced bone mass) with one or more sinuses; X-ray apical film and CBCT were performed. The ability to track the final treatment outcome. Exclusion criteria: VRF can be directly observed in clinic; Patients with contraindications such as tooth extraction and periodontal flap exploration; No treatment or clinical absence; Into standard with a total of 39 cases, teeth 40, age 28 ~ 69, the average age of 51.3 years. The basic information of the patients is as follows (Table 1).

Table 1 Basic situation

	39 patients (40 teeth)
Year	
＜ 45 years old	13 (32.7%)
≥45 years old	27 (67.5%)
Gender	
Man	23 (57.5%)
Woman	17 (42.5%)
Tooth Position	
Dentes premolares	12 (30.0%)
Molar teeth	28 (70.0%)
Probing depth of periodontal pocket	
＜ 5mm	15 (37.5%)
≥5mm	25 (62.5%)

1.1 Research methods

X-ray affected tooth root, CBCT examination and periodontal examination, examination results by the physician, and a mouth of an oral cavity radiation image doctor diagnosis analysis together, and record the results.

1.1.1 Radiography of root tips

Instrument parameters:

the X-ray diagnostic criteria [5] root slices: periodontal membrane lacuna broadening; Tooth root linear projection; Periapical transmission area showed root fracture segments. Displacement of root cleft; The defect of root bifurcation was obvious.

1.1.2 CBCT inspection

Instrument parameters:

diagnostic criteria [6] of CBCT: observe the linear projection, parallel to the root fracture of periodontal membrane to root canal; Obvious displacement of root fracture lobes; Fracture images appear on at least two consecutive fault images and two coordinate planes; Eliminate artifacts from adjacent tissues, such as adjacent metals and dental filling materials.

1.1.3 VRF diagnostic gold Standard [7] :

Reference CBCT test results, the CBCT diagnosed as type VRF (variable refrigerant flowrate) and not to pull out the tooth, signed in patients after informed consent, for regular one-time root canal therapy and root canal treatment, again in oral microscope the existence of root crack, and to develop Asia periodontal flap surgical exploration or half tooth resection; For patients diagnosed with VRF who could not undergo endodontic treatment or had a poor prognosis, extraction, root-amputation, semi-resection, periapical curettage, etc., were also performed after signing the informed consent. VRF was observed during operation as the diagnostic criterion. For patients diagnosed as VRF negative by CBCT, if there are no symptoms after clinical follow-up after corresponding treatment, they are diagnosed as non-VRF.

1.1.4 Periodontal charting

Periodontal pocket depth was measured at six sites of buccal distal, buccal central, buccal mesial, lingual mesial, lingual central and lingual distal, respectively, and periodontal probing depth (PD) was recorded. The affected teeth were divided into two groups according to the depth of periodontal probing (PD < 5mm; PD≥5mm).

1.2 Accounting-based measures

According to the gold standard of VRF diagnosis, the diagnostic results of the two methods were compared, and the true positive, false positive, true negative and false negative were recorded. The sensitivity, specificity, missed diagnosis rate, Jorden index and agreement rate of the diagnosis of VRF by X-ray apical film and CBCT were calculated. Then, the affected teeth were grouped according to the depth of perio-

dontal pocket, and the CBCT diagnostic analysis was performed. The results were recorded and sensitivity, specificity, missed diagnosis rate, Jorden index and consistency rate were calculated. Sensitivity = true positive/(true positive + false negative), specificity = true negative/(true negative + false positive), missed diagnosis rate = false negative/(true positive + false negative), Jordan index = (sensitivity + specificity) -1, agreement rate = (true positive + true negative)/(true positive + true negative + false positive + false negative).

1.3 statistical analysis

By SPSS 25.0 statistical software for data analysis, data classification powerusageeffectiveness (%), using χ squared inspection and Fisher's exact probability method, inspection standard of alpha = 0.05, $P < 0.05$, the difference was statistically significant.

2. Results

2.1 Diagnostic results

The gold standard for diagnosis: Of 40 affected teeth, 33 were VRF positive and 7 were VRF negative. X-ray apical radiography showed that 19 affected teeth were diagnosed as VRF positive and 21 affected teeth were diagnosed as VRF negative. CBCT showed that 26 teeth were VRF positive and 14 were VRF negative. According to the depth of periodontal exploration, 15 affected teeth with PD < 5mm were grouped, of which 10 were confirmed VRF positive and 5 were confirmed VRF negative. CBCT diagnosis showed that 5 were VRF positive and 10 were negative. Of the 25 affected teeth with PD≥5mm, 23 were confirmed VRF positive and 2 VRF negative. CBCT diagnosis showed that 21 were VRF positive and 4 were VRF negative. The diagnosis results are shown in Table 2:

Table 2 Diagnostic results

diagnostic method	VRF（+）	VRF（-）	true positive	false positive	true negative	false negative
X-ray apical film	19	21	17	2	7	14
CBCT	26	14	26	0	7	7
CBCT(PD ＜ 5mm)	5	10	5	0	5	5
CBCT(PD≥5mm)	21	4	21	0	2	2

2.2 Diagnostic analysis

The sensitivity, specificity, consistency and Jorden index of CBCT in the diagnosis of VRF were 78.8%, 100%, 82.5% and 78.8%, respectively, which were higher than 54.8%, 77.8%, 60.0% and 32.6% of X-ray root tip film, and there were statistical differences in sensitivity and consistency. The missed diagnosis rate of CBCT was 21.2%, which was lower than 45.2% of X-ray root tip film, and the difference was statistically significant. The diagnosis results were analyzed as shown in Table 3. According to periodontal probing depth of diagnosis group, CBCT diagnosis of PD group 5 mm or higher sensitivity, consistent rate, about an index were 91.3%, 92.0%, 91.3% were greater than PD < 5 mm group, of which the sensitivity statistically difference; The missed diagnosis rate of CBCT in the PD≥5mm group was 8.7%, which was lower than 50.0% in the PD < 5mm group, and the difference was statistically significant, as shown in Table 3:

Table 3 X-ray and CBCT diagnostic results

	Sensitivity	Specificity	Rate of missed diagnosis	Concordance rate	Jordan index
Apical radiogram	54.8%	77.8%	45.2%	60.0%	32.6%
CBCT	78.8%	100%	21.2%	82.5%	78.8%
P 值	0.041*	0.475	0.041*	0.026*	-
CBCT PD ＜ 5mm	50.0%	100%	50.0%	66.7%	50.0%
CBCT PD≥5mm	91.3%	100%	8.7%	92.0%	91.3%
P 值	0.028*	-	0.028*	0.107	-

* : $P < 0.05$, the difference was statistically significant

3. Discussion

The longitudinal root crack can occur at any position of the tooth root and extend longitudinally to form a complete or incomplete crack. Once it occurs, the prognosis is poor and often requires complex treatment, with severe cases even removal [8]. VRF is more common in middle-aged and elderly people, and patients often have a history or habit of biting hard objects [9], and the incidence rate is highest in the first molar. Its clinical symptoms lack specificity and can be manifested as pulp, periapical and periodontal symptoms, which increases the difficulty in the diagnosis of VRF. Clinically, imaging methods such as X-ray apical film and CBCT are often used to assist in the diagnosis of VRF[10].

In this study, the diagnostic effect of CBCT and X-ray apical film on VRF was compared. The results showed that the diagnostic sensitivity and consistency rate of CBCT were higher than those of the latter, while the rate of missed diagnosis was lower, with statistical significance ($P < 0.05$). In the study, there were 2 cases of false positives in the diagnosis of X-ray apical film, and artifact interference from root canal contents was found after examination. The image of the X-ray apical film is a two-dimensional plane, which is difficult to display due to the influence of the overlapping image or artifact of the shooting Angle or adjacent tissues [11]. When the fractured lobes of VRF teeth do not shift significantly, it is also difficult to observe the fractured lines through the two-dimensional image, and the diagnosis cannot be made. Compared with X-ray apical film, CBCT can observe the fracture line from multiple angles and levels to avoid the occurrence of overlapping images. The imaging accuracy is high, and the broken line image is clearer; Doctors can freely choose the examination area and conduct three-dimensional analysis, which has higher flexibility [12].

Clinically, VRF is often accompanied by periodontal symptoms, including recurrent swelling of the gums and discharge of pus, persistent fistula, and deep and narrow periodontal pockets. Studies have shown [13] that periodontal tissue damage is more likely to be secondary to root fractures, and the periodontal tissue damage is aggravated with the extension of root fractures. In this study, suspected VRF cases were grouped according to different periodontal pocket depth to observe whether the diagnostic results of CBCT were different. The results showed that the diagnosis sensitivity of the deep periodontal pocket group was higher, the rate of missed diagnosis was lower, and the difference was statistically significant ($P < 0.05$). In the shallow periodontal pocket group, the diagnostic sensitivity was only 50.0%, while the rate of missed diagnosis was as high as 50%, which may be related to the degree of VRF lesions. Wen Lingying et al. believed that the destruction of periodontal bone was aggravated with the extension of fracture, so when the destruction of periodontal tissue was light, the degree of VRF was light, and the difficulty of CBCT diagnosis was increased. There are also studies [14-15] that long-term periodontal tissue inflammation and alveolar bone absorption will change the tooth stress point and form occlusal trauma, thus increasing the risk of VRF. VRF and periodontal tissue damage promote each other, periodontal damage will increase the probability of VRF, VRF will aggravate the periodontal tissue damage. Therefore, when the CBCT image of the affected tooth shows complex periodontal destruction, periapical bone destruction combined with vertical bone resorption, the occurrence of VRF can be considered [16]. For those with shallow periodontal pockets and light periodontal destruction, CBCT has low diagnostic sensitivity and can be combined with periodontal endoscopy to improve the diagnostic accuracy [17].

In this study, the diagnostic results of 39 patients and 40 teeth suspected to be VRF were statistically analyzed, and it was concluded that the diagnostic effect of CBCT was better than that of X-ray apical film. CBCT has different diagnostic results for VRF teeth with different periodontal probing depths: when $PD \geq 5mm$, the diagnostic sensitivity is higher; when $PD < 5mm$, it should be combined with other examination methods, such as periodontal endoscopy, to further diagnose and improve the diagnostic accuracy. In addition, this study also has some limitations, such as a small sample size.

To sum up, the diagnostic effect of CBCT is better than that of X-ray apical film. CBCT has different diagnostic results for VRF teeth with different periodontal probing depths: when $PD \geq 5mm$, the diagnostic sensitivity is higher; when $PD < 5mm$, it should be combined with other examination methods, such as periodontal endoscopy, to further diagnose and improve the diagnostic accuracy.

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Research Progress on the effect of High altitude and hypoxia on Mitochondrial function in Obesity

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Abstract: Obesity is one of the diseases that threaten human health at present, and it can lead to the increasing prevalence of related complications, such as Insulin resistance, Non-alcoholic fatty liver diseases NAFLD and Type 2 diabetes mellitus and so on. In the whole world, the prevalence rate of obesity is on the rise. Insulin resistance is one of the most common complications of obesity. More and more studies have shown that there is a close relationship between mitochondrial dysfunction and insulin resistance. Skeletal muscle is an important target organ of insulin. Skeletal muscle mitochondrial dysfunction can lead to abnormal glucose and lipid metabolism and further affect the signal pathway of energy metabolism. The new epidemiological survey shows that the prevalence of obesity in high altitude areas is significantly lower than that in plain areas, and the prevalence of overweight and obesity is negatively correlated with altitude. This paper discusses the relationship between high altitude hypoxia and mitochondrial metabolism.

Keywords: High Altitude; Hypoxia; Obesity; Insulin; Skeletal Muscle; Mitochondrial Metabolism

1. Introduction

Obesity has become one of the diseases affecting public health. It increases the risk of insulin resistance (IR), Non-alcoholic fatty liver diseases (NAFLD), Type 2 diabetes mellitus(T2DM), cardiovascular disease, hypertension and some malignant tumors such as breast cancer, rectal cancer and renal cancer [1-3]. Obesity refers to the accumulation of excessive fat in organisms, which is affected by many factors, such as behavioral factors, socio-economic factors, environmental factors, heredity, metabolism and microbiota. In contemporary society, changes in people's lifestyle, such as long-term intake of high-calorie foods, sedentary inactivity and other factors are the most common causes of obesity[4-5]. Sherpa L Y et al. [6] found that there was a negative correlation between BMI and sea pull by comparing the body mass index (Body weight index, BMI) of residents living at different elevations of 1200 m, 2900 m and 3600 m (Nepal and Qinghai-Tibet Plateau). Lippel et al. [7] scholars have shown that living at high school altitude can reduce the weight of obese patients and improve their metabolic function.

2. Effects of High altitude hypoxia on body weight, Insulin sensitivity and Lipid Metabolism in obese mice

IR is one of the metabolic characteristics of obesity[8]. IR is a response to the weakening of the effect of insulin, which can lead to a decrease in glucose uptake by muscle and adipose tissue fine cells, a decrease in liver glycogen production, and an increase in intrahepatic glucose production[9-10]. Obesity seriously affects the biological function and function of insulin target tissues including skeletal muscle, liver and adipose tissue. Obesity is considered to be the main risk factor for IR, and IR is the most common metabolic disorder of obesity. They interact and influence each other. The long-term interaction of genetic and environmental factors leads to the occurrence of IR. Genetic factors refer to the susceptibility to insulin resistance. At present, studies are mainly focused on gene mutations, such as insulin receptor, glucose transporter 4 (GLUT-4) and insulin signal pathway. At the same time, aging, nutritional imbalance, lack of exercise and stress are all environmental factors that cause IR, among which overnutrition, especially high-fat diet is one of the most common causes of IR in daily life.

Hill NE et al. [11] showed that insulin resistance improved gradually with the increase of altitude (3600-5120m). Nirmal Aryal et al. [12] reported that with the increase of altitude, triglyceride and low density lipoprotein decreased, while the content of high density lipoprotein

increased.

Compared with residents living below 500m above sea level, healthy residents living between 3000 m and 4500 m above sea level had lower fasting blood glucose [13]. The related literature reports further suggest that the median fasting plasma glucose concentration of healthy male residents living above 3000 m is 81.6 mg/dl, while the median fasting plasma glucose concentration of non-pregnant women at low altitude is 91.2 mg/dl; above 3000 m, the median fasting plasma glucose concentration is 71.7 mg/dl, while the blood glucose concentration of low altitude is 85.9 mg/dl [14]. Compared with people living at sea level, the analysis of blood glucose in 12 hours found that people living at 3200 m above sea level had lower blood sugar [15].

3. Effects of hypoxia at high altitude on mitochondria and insulin signal pathway in obese skeletal muscle

One of the recognized metabolic characteristics. Skeletal muscle is an important target organ of insulin, and skeletal muscle plays a central role in systemic insulin resistance and metabolic syndrome related to high-fat diet, obesity and aging [16-17]. Skeletal muscle accounts for about 45% of the human body, and is an important tissue involved in human glucose metabolism. Under normal circumstances, 60-70% of the glucose in the blood is metabolized in the skeletal muscle and stored in the form of glycogen, and when needed, the body decomposes into glucose for the benefit of the machine, forming a dynamic balance [18]. When obesity, the balance is broken, in order to control elevated blood sugar, the body will secrete more islet, aggravating IR [19].

Mitochondrial dysfunction is associated with the occurrence of insulin resistance [16,20-22]. Mitochondria are the platform for the production and supply of cellular energy ATP[23]. Mitochondrial function can be evaluated by changes in mitochondrial-related m-RNA levels, protein levels, activities of key mitochondrial enzymes, mitochondrial size and shape, and substrate oxidation levels. When mitochondrial dysfunction occurs, it can affect glucose metabolism and lipid metabolism and induce glycolipid toxicity [24]. Aging is accompanied by the decrease of mitochondrial biomass function, which leads to the decrease of glucose and lipid metabolism, and glycolipid accumulation induces glycolipid toxicity further affect the energy metabolism signal pathway and cause mitochondrial function damage. Increased ROS production, decreased mitochondrial biosynthesis or changes in some mitochondrial-related proteins may impair mitochondrial function, and these factors are also the inducements of insulin resistance[25-26].

Adenosine monophosphate activated protein kinase (AMPK) is a serine / threonine protein kinase in eukaryotic cells. Its function is to regulate energy metabolism and maintain mitochondrial homeostasis as an energy sensor[27]. According to the literature, the biological function of mitochondria in skeletal muscle decreased after the knockout of AMPK genes in mice [28]. A large number of studies have shown that lipid accumulation in skeletal muscle can reduce insulin sensitivity. Intracellular lipid adenosine monophosphate activated protein kinase (AMPK) is a serine / threonine protein kinase in eukaryotic cells. Its function is to regulate energy metabolism and maintain mitochondrial homeostasis as an energy sensor[27].

Previous studies have confirmed that in the skeletal muscle tissue of patients with IR, the expression of PGC-1 protein decreased significantly, and the number of mitochondria in muscle tissue decreased. The increase of NRFs and Tfam can promote the transcription and replication of mitochondrial DNA and improve the function of mitochondrial biosynthesis[29-30]. A large number of studies have shown that lipid accumulation in skeletal muscle can reduce insulin sensitivity. Intracellular lipid adenosine monophosphate activated protein kinase (AMPK) is a serine / threonine protease in eukaryotic cells. Its function is to regulate energy metabolism and maintain mitochondrial homeostasis as an energy sensor[27].

4. Conclusion

To sum up, high altitude hypoxia can reduce the body weight of obese mice induced by high fat diet, enhance insulin sensitivity, and reduce the contents of free fatty acids and triglycerides in serum. Mitochondria are the main place of energy metabolism. Skeletal muscle and liver contain a large amount of mitochondria. Under high altitude and hypoxia environment, by improving the biosynthesis function of skeletal muscle mitochondria, the content of mitochondria and the level of mitochondrial oxidized phosphate, it can reduce the deposition of lipids in skeletal muscle cells, improve fat decomposition, decrease the content of ceramide and improve the expression of AKT in insulin signal

pathway.

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The clinical effection of thoracoscopic subsegmentectomy in the treatment of peripheral lung cancer

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Abstract: Objective: To investigate the clinical effect of thoracoscopic subsegmentectomy in the treatment of patients with early lung cancer. Methods: A retrospective analysis was performed between January 2021 and December 2022 The clinical data of 121 patients with early lung cancer admitted to the hospital were collected. According to different surgical methods, they were divided into control group (n=59) and observation group (n=62). The observation group was given thoracoscopic subsegmentectomy, and the control group was given thoracoscopic segmentectomy. The perioperative indicators, inflammatory factors and complications were compared between the two groups. Results: The number of resected subsegments in the observation group was less than that in the control group.The levels of CRP and PCT in the observation group were lower than those in the control group. There was no significant difference in the incidence of complications, operation time, intraoperative blood loss, width of lesion margin, and length of hospital stay between the two groups. Conclusions: Thoracoscopic subsegmentectomy and thoracoscopic subsegmentectomy have the same surgical effect in the treatment of early stage lung cancer, but thoracoscopic subsegmentectomy can reduce the number of resected subsegments and reduce the inflammatory response after operation.

Keywords: VATS; Subsegmentectomy; Lung Cancer

Lung cancer is a relatively common cancer in clinical practice, with the highest mortality rate among all cancers [1- 2] . Therefore, timely treatment is of great significance for patients with early lung cancer [3]. Pulmonary segmentectomy is a useful surgical treatment of early peripheral lung cancer with tumor diameter ≤2 cm (tumor is located in the outer third of the lung) can not only ensure adequate resection margin, but also maintain the morphology of the residual lung. With the continuous maturity of technology such as thoracoscopy, clinical segmentectomy has been extended to the subsegmental level of the lung [4]. In clinical practice, it has been found that for small pulmonary nodules located at the edge of a lung segment or between adjacent lung segments, pulmonary subsegmentectomy can reduce the damage of normal lung tissue to a greater extent and retain more lung function, thereby realizing the "internal minimally invasive" of reducing tissue damage. The aim of this study is to retrospectively analyze the clinical effects of thoracoscopic segmentectomy and thoracoscopic subsegmentectomy in the treatment of patients with early stage lung cancer.

1. Data and Methods

1.1 General Information

From 2021 and December 2022, the clinical data of 94 patients with early lung cancer admitted to our hospital were analyzed. Inclusion criteria: located in the outer third of the lung; Single pulmonary nodule; Maximum tumor diameter ≤2.0 cm and solid ratio ≤0.5 [7]; Aged 18-70 years; Primary adenocarcinoma; Complete clinical data. Exclusion criteria: combined with other system tumors; Acute infection or chronic infection; Combined with other immune or endocrine diseases; Conversion to extended resection or thoracotomy; Pregnancy or lactation. According to different surgical methods, they were divided into control group (n=59) and observation group

(n= 62).

1.2 Methods

The two groups of patients underwent chest CT, electrocardiogram, abdominal ultrasound and other examinations before operation. At the same time, in order to quickly find the lesion and ensure the resection margin, the two groups of patients were planned according to three-dimensional reconstruction of CT images before operation.

The observation group was treated with thoracoscopic subsegmentectomy. The subsegmental pulmonary arteries, bronchi and veins were separated under thoracoscopy using electric coagulation hook. The subsegmental pulmonary arteries, bronchi and veins were separated by linear cutting and stapler. Extent of pulmonary subsegmental resection was determined by tissue ventilation inflation and the natural collapse of the affected lung. Then the lung tissue in the target area was resected with staplers. The control group was treated with thoracoscopic segmentectomy, and the segmental pulmonary arteries, bronchi and veins were separated and the intersegmental plane was determined as the observation group.

1.3 Observation indexes and evaluation criteria

(1) Perioperative indicators: the operation time, intraoperative blood loss, number of resected subsegments, width of lesion resection margin, and length of hospital stay were compared between the two groups. (2) Inflammatory factors: the blood Serum C-reactive protein (CRP) and procalcitonin (PCT) levels of the two groups before operation and at 1 and 3 days after operation were compared. (3) Complications: the postoperative complications including atelectasis, pulmonary air leakage, respiratory failure, arrhythmia, pulmonary infection and other complications were compared between the two groups.

1.4 Statistical Processing

Data in this study were analyzed and processed by SPSS 23.0 statistical software. Measurement data conforming to normal distribution were represented by (x-±s) and t test, while measurement data non-conforming to normal distribution were represented by M (P25, P75) and Mann-Whitney U test. The count data were expressed as rate (%), $\chi 2$ test was used, and $P<0.05$ was considered statistically significant.

2. Results

2.1 Comparison of perioperative indexes between the two groups

There was no significant difference in operation time, intraoperative blood loss, incisal margin width and hospital stay between the two groups ($P<0.05$), the number of resection subsegments in observation group was less than that in control group, and the difference was statistically significant($P<0.05$), Table 1.

2.2 Comparison of the levels of inflammatory factors between the two groups

The levels of CRP and PCT in the two groups were higher than those before surgery 1 and 3 days after surgery, and the levels of CRP and PCT in the two groups were lower than those in the control group 3 and 3 days after surgery, and the levels of CRP and PCT in the observation group were lower than those in the control group, the differences were statistically significant ($P<0.05$), Table 2.

2.3 Comparison of complications between the two groups

There was no significant difference in the incidence of complications between the two groups ($P>0.05$).

Table 1 Comparison of perioperative indicators between the two groups

Group	Operation time,min	Intraoperative blood	The number of resected subsegments	Width of lesion	Hospital stay,day
Observation group (n=62)	133.24±23.44	22.72±11.75	2(1,4)	2.21±0.18	5.22±1.12
Control group (n=59)	131.26±23.11	23.12±12.78	3(2,5)	2.26±0.27	5.45±1.28
t/U	1.344	1.373	4.454	1.134	1.232
P	0.113	0.212	<0.001	0.213	0.233

Table 2. Comparison of the level of inflammation factor in the preoperative and postoperative 1 dam 3 d.

Group	CRP(mg/L)		
	preoperative	postoperative1 day	postoperative 3 days
Observation group (n=62)	3.6(1.9,4.8)	17.6(11.4,36.7)	8.5(3.6,11.3)
Control group (n=59)	3.6(1.9,4.8)	25.6(17.2,46.5)	11.9(5.2,15.7)
U	0.656	4.364	3.324
P	0.676	<0.001	<0.001

Group	PCT(ng/mL)		
	preoperative	postoperative1 day	postoperative 3 days
Observation group (n=62)	0.026(0.018, 0.030)	0.126(0.091, 0.176)	0.055(0.028, 0.086)
Control group (n=59)	0.024(0.016, 0.037)	0.161(0.09, 0.193)	0.077(0.043, 0.094)
U	1.283	3.283	3.377
P	0.676	0.002	0.004

3. Discussion

Lung cancer has become the highest rate of malignancies in our country, which seriously affect people's life and health. The thoracic surgery is a hot topic in thoracic surgery in recent years, and for early lung cancer, it can effectively keep the lung normal tissue.

In recent years, with the development of minimally invasive surgery, the subsegmentectomy has been applied to clinical practice. Before surgery, the area of lung removal was planned through 3d reconstruction, and the location of the lesion was accurately identified. Removing the lung segment accurately, and protect the normal lung, can reduce the impact on lung function. Preoperative operation path planning can minimize damage to the intersegment artery and subsegment[8]. In this study, surgical time, the incidence of blood volume, the width of the lesion and the amount of hospitalization was no obvious difference. In the case of the lung loss, the observation group was less than the control group. The cause may be a three-dimensional technical plan for the laparoscopic subsection of the thoracoscopy, which can be removed by precision, and can keep normal lung tissue as much as possible while removing the lesion.[9].

The CRP is an acute phase protein, which is able to reflect the inflammatory state of the body in the inflammation, trauma and infection of inflammation, trauma and infection[10-11]. The PCT is mainly concentrated in the thyroid gland, which is found in the thyroid gland, which is a common detection indicator for early lung bacterial infections, which directly stimulates the synthesis and secretion of PCTS in thyroid c cells, and increases the level of serum expression in the chest, and increases the level of the serum expression[12-13]. The study showed that the PCT level of the two groups of CRPCT was higher than before surgery, and the PCT level was lower than in the control group, and both of these surgery could cause different degree of inflammation, but the laparoscopic subsection ectomy was more invasive and less damaged, and the degree of postoperative inflammation was relatively light. In addition, there was no significant difference in the incidence of complications of the two groups, indicating that the laparoscopic subsection of the case was better safe for patients with early lung cancer. Above all, the thoracoscopic subsection resection and pulmonary resection treatment for early lung cancer surgery were fairly safe.

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Analysis of therapeutic effect of extracorporeal shock wave on tennis elbow

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Abstract: Extracorporeal shock wave therapy plays an important role in the prevention and treatment of musculoskeletal diseases due to its advantages of convenient operation, safety, high efficiency and no drug intervention. In recent years, extracorporeal shock wave therapy has been widely used in the treatment of external humeral epicondylitis, such as through extracorporeal shock wave combined with ultrashort wave therapy and other physical factors. As people become more accepting of exercise, the frequency of some musculoskeletal disorders is also increasing. For such diseases, the effect of drug treatment is often reflected in the alleviation of symptoms, and the radical cure of the disease is not obvious. Under this premise, the advantages of the physical factor therapy approach appear. By performing extracorporeal shock wave therapy, the pain can be relieved in a short period of time, and the patient's normal activities and symptoms can be significantly improved after the treatment cycle.

Keywords: Extracorporeal Shock Wave; Tennis Elbow; External Humerus Epicondylitis

1. Concept of tennis elbow

1.1The origin of the name tennis elbow

Tennis elbow is another name for humeral epicondylitis, a common musculoskeletal disorder. This disease is also known as humeroradial joint bursitis, humeroradial periostitis is also a clinical name for him. The above is the name of Western medicine, in Chinese medicine, tennis elbow is called "arm impediment" [1]. External humerus epicondylitis first entered people's field of vision is because of tennis players, many tennis players have pain in the external humerus epicondyle, so it is called tennis elbow.

1.2Concept of external humeral epicondylitis

The pain site of external humerus epicondylitis is located on the lateral side of the elbow joint, where the extensor muscle of the forearm starts. It is a disease caused by chronic fasciitis in the common extensor tendon of the forearm [2]. On the one hand, the patient presented with pain on the external epicondyle of the humerus, and on the other hand, the patient presented with significant discomfort when performing gripping movements, wrist extension movements, and combined movements. Tennis, table tennis, badminton and other sports require the athlete to grasp the hand at the same time to stretch the wrist joint. The most classic action is reflected in the backhand stroke, which needs to be completed in a short time, such as grasping, wrist extension, acceleration, power and other actions. Repeated operations of this kind tend to increase the load on the extensor carpi radialis short, resulting in injury and tearing. This is also the cause of the currently widely recognized external humeral epicondylitis [3].

2. Research status of external humeral epicondylitis

With the in-depth study, people found that although the humerus epicondylitis is called tennis elbow, but the incidence of the population is not limited to tennis players. Many people who work in handicrafts have a higher incidence of tennis elbow [4]. Moreover, there is anatomical evidence that humerus epicondylitis is not an inflammation in the traditional sense, but a degenerative disease caused by tendon damage and other reasons. In addition, the disease course of external humeral epicondylitis is long and the onset is slow. The tendon is subjected to heavy load for a long time, resulting in injury, which gradually accumulates over time, and calcium salt deposit may exist [5]. After reaching a certain level, symptoms of gripping, wrist extension, forearm rotation, and external epicondyle tenderness of the humerus are shown. Tennis elbow has a certain degree of self-healing, some patients can be cured without treatment, but there are still a considerable

number of patients with persistent disease, need systematic treatment, such as drug therapy, physical therapy, etc., more serious patients also need surgical treatment [6].

3.Extracorporeal shock wave therapy

3.1 Working principle of extracorporeal shock wave

Extracorporeal shock wave is a kind of mechanical pulse pressure wave, which converts the energetic and dynamic characteristic pulse sound wave into the airway pressure type shock wave through the device [7]. During the treatment process, the probe of the device needs to be attached to the patient's skin through a certain medium, so that the shock wave can be better transmitted, and prevent the shock wave from being unable to be transmitted due to the probe being empty, resulting in damage to the device. Since extracorporeal shock wave therapy only needs to fit closely with the treatment site in the treatment process, it is not invasive treatment, and it has little damage to its own tissues in the treatment process, and its safety is guaranteed. And the operation of the equipment is rapid and efficient, and the effect is rapid. It is widely used in the design of departments related to musculoskeletal diseases, such as rehabilitation departments [8].

3.2 Therapeutic effects of extracorporeal shock wave

At present, extracorporeal shock wave has been widely used by domestic and foreign researchers in the treatment of shoulder periarthritis, humerus epicondylitis, plantar fasciitis and other diseases [9], but there is no exact conclusion on its therapeutic mechanism. Professor Huang Guozhi [10] believes that the treatment principle is mainly reflected in the following three aspects. First, mechanical stress effect. Therapeutic high energy shock waves exert different forces on different tissues, which is mainly due to the different density of different tissues. Because this difference in force can loosen the adhesive tissue, the fundamental treatment of musculoskeletal diseases. Second, the piezoelectric effect. Piezoelectric effect refers to the effect of high energy shock wave on the body. Due to the pressure action of the shock wave, the potential of neurons at the treatment site changes, thus affecting the transmission of nerve impulse and achieving the analgesic effect [11]. Third, cavitation effect. Cavitation effect means that under the action of shock wave, part of the cell membrane at the treatment site is destroyed, changing the environment here, and releasing factors that promote tissue repair and anti-inflammatory and analgesic pain. Fourth, nerve blocking effect. The stimulation of pain receptors at the treatment site by high-energy shock wave can raise the threshold value, and the intuitive clinical response is that patients report significant pain relief after treatment.

4. Effect of extracorporeal shock wave on external humeral epicondylitis

In the Chinese Guidelines for Extracorporeal Shock Wave Therapy for Osteomuscular Diseases (2023 edition) [12], it is clearly pointed out that extracorporeal shock wave therapy for external humeral epicondylitis is A grade A recommendation, and its evidence level reaches 1a. Therefore, the use of extracorporeal shock wave in the treatment of external humeral epicondylitis has theoretical basis. Hong Xiping et al. [13] conducted extracorporeal shock wave therapy for 1 to 3 times on 18 patients with external humeral epicondylitis, and the frequency, number of shocks and the number of shock wave therapy were determined according to the actual conditions of the patients. After the treatment, the effective rate of the treatment reached 94.4%. The effect of extracorporeal shock wave therapy is rapid and long-lasting. Li Fulin et al. [14] followed up patients who underwent extracorporeal shock wave therapy for external humerus epicondylitis and patients who underwent block therapy, and the long-term follow-up results showed that both treatments had therapeutic effects on external humerus epicondylitis. However, the short and medium follow-up showed that the mode of using extracorporeal shock wave therapy was superior to the mode of using block therapy in terms of the duration of treatment effect and the probability of disease recurrence. Qiao Baoguang et al. [15] intended to study whether extracorporeal shock wave pressure had an impact on the treatment of the external epigondyle of humerus. They divided the pressure into three medium levels of 1.2.3bar and divided the patients into groups based on this, and compared the treatment effect, pain score and adverse reactions of the three groups of patients. It was found that the treatment effect of 2bar pressure on patients was significantly better than that of the other two groups. This study focused on extracorporeal shock wave pressure, and due to the equipment and sample size, it was not possible to further refine the pressure range more suitable for the treatment of external humeral epicondylitis. However, it is

also beneficial to further study the therapeutic effect of extracorporeal shock wave.

5. Summary and prospect

With the development of research and application, extracorporeal shock wave therapy has become one of the preferred options for the treatment of musculoskeletal diseases. For patients with external humeral epicondylitis, extracorporeal shock wave therapy can relieve pain and release adhesions. However, the frequency of extracorporeal shock wave therapy and the time interval before multiple treatments still need to be supported by a large amount of experimental data. And extracorporeal shock wave therapy can be combined with other treatment methods, such as combined exercise rehabilitation training, intramuscular adhesive treatment and so on.

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The value and application of project teaching method in higher vocational nursing teaching

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Abstract: Project teaching is of great value in higher vocational nursing teaching, which can improve students' practical ability and comprehensive quality. The application of project teaching method can stimulate students' interest in learning, cultivate students' teamwork ability and problem-solving ability. In addition, project teaching can promote students' independent learning and innovative thinking, so that students can better adapt to the actual work environment. Therefore, project teaching method should be actively applied in nursing teaching in higher vocational colleges to improve teaching effect.

Keywords: Higher Vocational Nursing Teaching; Project Teaching Method; Value and Application

Introduction

Project teaching method is an important teaching method in higher vocational nursing teaching, which combines theoretical knowledge with practical operation to cultivate students' practical operation ability and problem-solving ability. This paper will summarize the value and application of project teaching method in order to provide reference for nursing teaching in higher vocational colleges.

1. The value of project teaching method in nursing teaching in higher vocational colleges

Project teaching method has important value in nursing teaching in higher vocational colleges. First of all, project teaching method can improve students' learning interest and participation, and stimulate students' learning motivation. Secondly, the project approach cultivates students' practical ability and problem-solving ability, enabling students to apply theoretical knowledge to practical operations. In addition, project teaching method can also promote students' cooperation and communication, and cultivate students' teamwork spirit and communication skills. Finally, project teaching method improves students' comprehensive quality and innovation ability, and cultivates students' independent thinking and problem-solving ability. To sum up, project teaching is of great value in nursing teaching in higher vocational colleges, which significantly improves students' learning interest and participation, strengthens students' practical ability and problem-solving ability, promotes students' cooperation and communication, and improves students' comprehensive quality and innovation ability [1].

2. The application strategy of project teaching method in nursing teaching in higher vocational colleges

2.1 Determine project objectives and learning content

In higher vocational nursing teaching, the first step of project teaching method is to determine the project goal and learning content. According to the curriculum requirements and the actual needs of students, the teacher chooses the appropriate project theme, and defines the project objectives and learning content. Project objectives are defined in order to clarify the expected results that students should achieve in the project learning. Goals should be specific, clear, measurable, and match course requirements and student needs. For example, one program goal is for students to master specific nursing skills, such as intravenous fluid operation or wound management skills. Another project goal is to develop students' teamwork and communication skills by simulating real nursing scenarios, allowing students to work together in a team to solve problems. The purpose of determining the learning content is to clarify the knowledge, skills and attitudes that students need to learn and master in the project learning. The learning content should be consistent with the project objectives and be able to meet the learning needs of the students [2].For example, in an intravenous infusion operation project, the learning content includes the steps and precautions of venipuncture, the use and maintenance of infusion equipment, possible problems in the infusion process and countermeasures. In a team

project, the learning content includes the principles and skills of teamwork, communication and coordination methods, problem solving and decision-making strategies, etc. By defining the objectives and learning content of the project, teachers provide students with a clear learning direction and goals to help them better understand and master the acquired knowledge and skills. At the same time, project teaching method can also stimulate students' learning interest and initiative, improve their learning motivation and participation. Therefore, in higher vocational nursing teaching, determining the project goal and learning content is an important step of project teaching method, which is of great significance for promoting the cultivation of students' comprehensive quality and professional ability.

2.2 Design project tasks and activities

In project teaching, teachers design the following tasks and activities to promote the cultivation of students' active learning and practical ability:

Project tasks require students to select a practical problem or topic, investigate and analyze it, and then design a solution or propose improvement measures. Students are expected to work in teams and work together to complete all stages of a project, including problem definition, needs analysis, solution design, implementation and evaluation. Field trip activities, organize students to relevant field trips, let them personally experience and observe the actual situation, collect relevant data and information. Students are expected to apply their knowledge and skills in the study, analyze problems, and propose solutions. Case analysis tasks, which provide a series of real-world cases, ask students to analyze and evaluate. Students are required to apply their knowledge and skills to analyze problems and challenges in cases and propose solutions or improvements. Team work projects require students to form teams and work together to complete a project task. Students need to work in teams, coordinate and communicate, solve problems, and ultimately accomplish project objectives. Make a physical activity, guide students to make a physical object or prototype according to the project needs. Students are required to apply their knowledge and skills to design, build and test, and ultimately present and evaluate their results. Simulate practical activities. Let students do practical activities by simulating real situations. For example, simulate business operations, simulate market research, etc. Students need to apply their knowledge and skills in the simulation, solve problems, and make decisions accordingly. Expert lectures and interviews: Experts in related fields are invited to give lectures or interviews, so that students can understand practical applications and industry trends, and students can take the initiative to ask questions and participate in discussions to deepen their understanding and application of relevant knowledge and skills.

2.3 Provide project resources and support

Teachers need to provide necessary project resources and support in project teaching, including relevant literature, experimental equipment, internship opportunities and other resources. In addition, teachers need to provide the necessary guidance and support to help students solve problems and overcome difficulties. The teacher provides students with relevant literature materials, including academic papers, research reports, case studies, etc., to help students understand the project background and relevant theoretical knowledge. Provide experimental equipment, teachers provide students with necessary experimental equipment, such as computers, sensors, experimental instruments, etc., to support students to conduct experiments and data collection. Providing internships, teachers provide internships for students, giving them the opportunity to apply what they have learned in real projects to improve their practical skills and problem-solving skills. Provide guidance and support. Teachers provide necessary guidance and support to students through individual guidance, group discussions, project meetings, etc., to help students clarify project objectives, develop project plans, and solve technical problems.Provide feedback and evaluation, teachers regularly evaluate and feedback students' project progress, help students find problems and timely adjust the project direction and strategy. Provide opportunities for cooperation, encourage cooperation among students, promote the development of teamwork and collaboration skills, organize students to conduct group projects, solve problems and complete tasks together.

2.4 Evaluate project results and learning effects

In project teaching, teachers use a variety of evaluation methods to evaluate students' project results and learning effects. First, students are asked to submit a project report. By reading students' project reports, we can understand students' thinking process, problem-solving

methods and project implementation. According to the content of the report, students' project results and learning effects are evaluated. Secondly, students are asked to present their projects. Students show their work and learning results in the project to teachers and other students by displaying their project results. Teachers observe the process and results of students' display and evaluate the project results and learning effects of students. In addition, students are required to give a project presentation, through which students demonstrate their work and learning results in the project. When evaluating students' project results and learning effects, teachers need to give timely feedback and guidance, and put forward specific suggestions and improvement suggestions for students' project results and learning effects to help students further improve.

3.Conclusion

Project teaching method has important value and application in higher vocational nursing teaching. Through the project teaching method, students are able to learn and master nursing skills in practical operation, improve practical ability and problem solving ability. Project teaching method can cultivate students' teamwork spirit and communication ability, so that students can cooperate with each other in a team and complete project tasks together. In addition, project teaching method can stimulate students' learning interest and initiative, improve learning effect and motivation. Therefore, project teaching method is a very effective teaching method in higher vocational nursing teaching, which is worthy of wide application.

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Application of novel oral anticoagulants for the antithrombotic effect of cardiovascular system diseases

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Abstract: Long-term oral anticoagulant is one of the methods for the treatment of cardiovascular system diseases, and the most widely used anticoagulant drug is warfarin, but its clinical application has been greatly limited due to its slow onset, easy to affect by various factors, and difficult dose control. In recent years, with the continuous in-depth research on cardiovascular system diseases, the emergence of new oral anticoagulants (NOAC) has greatly impacted the status of traditional anticoagulant warfarin because of its safety, stability and convenience of consumption. The purpose of this article is to review the classification and application of novel oral anticoagulants.

Keywords: Warfarin; Novel Oral Anticoagulants; Anticoagulant Therapy; Cardiovascular Disease

Thromboembolic disease seriously threatens the life and health of patients, especially elderly patients, and has become the main cardiovascular disease faced by Chinese and Western countries. The use of anticoagulants is an indispensable step in the treatment of many cardiovascular diseases such as atherosclerosis, pulmonary embolism, atrial fibrillation and thrombosis.

1. Warfarin and novel oral anticoagulants

Warfarin, as a classic traditional anticoagulant drug, is often used clinically for the treatment of thromboembolism, but the drug has a slow onset, generally 3~4 days after medication, and the treatment window is narrow, the dose of medication varies greatly, and there is a risk of bleeding, so its clinical application is limited [1]. In recent years, through in-depth research on the coagulation mechanism in clinical practice, new oral anticoagulants (NOAC) are gradually replacing warfarin as the preferred drug for anticoagulation therapy.

2. Pharmacological characteristics of warfarin

Vitamin K as a procoagulant substance, has the effect of activating II., VII., IX., X. coagulation factors, warfarin structure is similar to vitamin K, can be used as a non-competitive inhibitor of vitamin K to inhibit vitamin K epoxide reductase, prevent its reduction to hydroquinone vitamin K, and then hinder the recycling of vitamin K in the body, thereby preventing the carboxylation of coagulation factors and coagulation proteins, producing anticoagulant effect [2], but has no effect on coagulation factors that have been carboxylated. Warfarin oral absorption in the gastrointestinal tract is fast and complete, mainly combined with albumin in the blood, plasma protein binding rate is about 99%, the apparent volume of distribution is very small, and the plasma half-life is about 40 hours. Warfarin is mainly metabolized by the liver, and its anticoagulant effect is easily affected by many factors, such as liver enzyme inhibitors can enhance its anticoagulant effect, liver enzyme inducers can inhibit its anticoagulant effect; Combined with drugs with high plasma protein binding rate can increase its anticoagulant effect, which is easy to cause bleeding; It can have a synergistic effect with antibacterial drugs, platelet inhibitors, etc. Although warfarin lasts for a long time, factors such as slow onset of action and difficult dose control may put patients at risk of bleeding or thrombosis, endangering life, health and safety.

3.Novel oral anticoagulants

(NOAC), i.e. non-vitamin K antagonists, including factor Xa inhibitors such as apixaban, rivaroxaban, edoxaban, and factor IIA inhibitors such as dabigatran. NOAC are increasingly used in anticoagulation therapy because of their good anticoagulant efficacy, low bleeding risk, predictable efficacy and safety, little genetic and drug interactions, and the need for routine testing of coagulation and dose adjustment [3].

3.1 Dabigatran ester

Dabigatran probiotic drug, dabigatran etexilate, is currently the only factor IIA inhibitor that can be used orally in clinical practice.

Dabigatran ester can be rapidly converted into dabigatran in the body after oral administration to exert its medicinal effect, which can directly inhibit free thrombin and thrombin that has been bound to fibrin, prevent fibrinogen from cleaving into fibrin, prevent coagulation from inducing platelet aggregation, and inhibit III., V., VII., X., XI. coagulation factors. The bioavailability of dabigatran etexilate is about 3%~7%, and the peak plasma concentration is reached after about 1~4h after oral administration, the plasma protein binding rate is about 35%, and the t1/2 is about 12~17h, without being metabolized by the liver drug enzyme CYP3A4. Dabigatran cilexetil biomass availability is low, about 6.5% [5], but the advantage of dabigatran etexilate is that it is not metabolized by the liver drug enzyme CYP450, so the interaction between food and drugs has less impact on it, and the drug is relatively safe [6], and does not cause liver damage.

3.2 Rivaroxaban

Rivaroxaban is the first oral factor Xa inhibitor, which reversibly inhibits factor Xa, which has inhibitory effects on both free and bound factor Xa, thereby inhibiting the conversion of fibrinogen to fibrin [6]. Rivaroxaban can reduce thrombin production, but has no effect on thrombin already produced, so it has little effect on physiologic hemostasis. Rivaroxaban has a rapid onset of action after oral administration, reaching the peak plasma concentration after about 2.5~4h, plasma protein binding rate is about 95%, T1/2 is about 5~9h, and elderly patients are about 11~13h. Rivaroxaban is mainly metabolized in the liver by the liver enzyme CYP3A4 and the liver enzyme CYP450, about 1/3 of the prototype drug is excreted by the kidney through urine, and about 2/3 is metabolized by the liver [7], of which 1/2 of the drug is excreted by the kidney, and the other 1/2 of the drug is excreted through the hepatobiliary route [8]. Experiments [9] have confirmed that rivaroxaban in patients with atrial fibrillation is not inferior to warfarin in preventing various types of stroke, and the safety is better.

3.3 Apixaban

Apixaban is similar to rivaroxaban, is a factor Xa inhibitor, pharmacokinetics and pharmacokinetics are also similar to rivaroxaban, highly selective for Xa coagulation factor, after oral administration about 1~4h after reaching the peak blood concentration, bioavailability is 60%, t1/2 is about 8~14h, plasma protein binding rate is 87%, about 24%-25% is excreted by the kidney, 75%~76% is metabolized by the liver enzyme CYP3A4. Apixaban can be eliminated by multiple metabolic excretion routes, including hepatic metabolism and renal excretion, so patients with mild impairment of liver and kidney function who cannot use other newer oral anticoagulants [10] can be treated with apixaban and are less likely to have a significant effect on their interactions with food and drugs. Apixaban should not be combined with liver enzyme CYP3A4 inhibitors and liver enzyme CYP450 inhibitors.

3.4 Edoxaban

Edoxaban is similar to rivaroxaban and apixaban, also a factor Xa inhibitor, pharmacokinetics and pharmacokinetics are also similar to the two, after oral administration about 1~2h to reach the peak blood concentration, bioavailability is 62%, t1/2 is about 9~10h, plasma protein binding rate is about 50%, about 35% is excreted by the kidneys, drugs entering the human body are rarely metabolized by the liver drug enzyme CYP450, only 4% are metabolized by the liver drug enzyme CYP450 [11]. The relatively low plasma protein binding rate is the more special of the three factor Xa inhibitors and may have implications for patients undergoing hemodialysis. Although edoxaban has certain advantages in the treatment of venous thromboembolism, studies [12] have shown that the probability of bleeding caused by orthopedic major surgery is slightly increased, so there is still controversy about whether edoxaban is suitable for the prevention of venous thromboembolism in orthopedic surgery. However, there are some limitations in this study, and the vast majority of patients in this study are Caucasian and racial differences with Chinese and Asian may cause imaccuracy in the results, so more rigorous randomized controlled trials are needed to further validate its safety.

4. Disadvantages and adverse reactions

Warfarin overdose can lead to vomiting, diarrhea and varying degrees of bleeding, when warfarin overdose, vitamin K antagonism can be given accordingly to inhibit the bleeding reaction of warfarin, if the bleeding is more serious, intravenous vitamin K, or fresh frozen plas-

ma, coagulation factor concentrate should be given to reverse the effect of warfarin. After the bleeding effect of warfarin has been suppressed, if it is necessary to continue warfarin, excessive use of vitamin K should be avoided to reduce resistance to warfarin.

Although dabigatran etexilate is better than warfarin in safety and efficacy, because most of it is excreted through the kidneys, long-term use of dabigatran etexilate will increase the burden on the kidneys, so the elderly and patients with renal insufficiency should consider the use of this drug as appropriate. Testing dabigatran etexilate is not available in most hospitals, and dabigatran etexilate can only be determined by calibrating diluted thrombin time (dTT) and viper venom clotting time (ECT) [13]. Dabigatran etexilate currently has no specific antagonists, and in the event of major bleeding, only prothrombin complex and fresh frozen blood can be relieved. In addition, dabigatran etexilate has a high price, which causes an economic burden for patients who take it for a long time, and the use should consider economic issues.

The half-life of rivaroxaban is short, its anticoagulant effect will be weakened after discontinuation, and its anticoagulant effect basically disappears after 16~24h, and patients need to be closely monitored to prevent excessive fluctuations in blood concentration from causing its anticoagulant effect to be unstable. Because rivaroxaban is mainly metabolized through the liver, it will increase the burden on the liver and affect the efficacy of the drug in patients with hepatic insufficiency.

The dose of apixaban needs to be combined with the patient's liver and kidney function, constitution, age and other factors to develop an appropriate plan, and patients with severe liver function are prohibited from using apixaban.

Only a small amount of edoxaban will be metabolized by CYP450, and the metabolic enzymes in the body have little effect on the metabolism of edoxaban, and the clinical use value is low.

5. Conclusion and outlook

Although the traditional oral anticoagulant warfarin has been used for decades, the efficacy has been clear, but there is still a narrow treatment window, its safety and efficacy are easily affected by the environment and the patient's own factors, and the food and drugs taken together are easy to affect its efficacy. With the clinical use, the insufficiency of warfarin has gradually affected the treatment of thrombosis and embolism. The emergence of new oral anticoagulants can make up for the shortcomings of warfarin to a certain extent, and its advantages are convenient to take, fixed dose, less interaction with food and drugs, higher bioavailability, wide treatment window, clear pharmacokinetics, small individual differences, stable effect, few complications, and can be used for long-term treatment. However, compared with warfarin, the higher price of new oral anticoagulants will bring financial burden to patients, and there is a lack of specific antagonists, and there is a lack of effective methods to reverse the anticoagulant effect of new oral anticoagulants when bleeding occurs. Looking back at the development of anticoagulant drugs, anticoagulant therapy has entered the post-warfarin era from the warfarin era, and the research and development of new drugs seems to be moving towards the goal of "safe, effective and controllable". With the expansion of clinical research, the application prospects of new oral anticoagulants will be more impressive. The era of anticoagulation represented by new oral anticoagulants is coming, although there are still some shortcomings in new oral anticoagulants, but with the further deepening of research, new oral anticoagulants will bring more benefits to patients, and I believe that there will be safer and more effective drugs and more rigorous treatment plans in the future, bringing good news to patients.

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Visual Analysis of The Citespace-based COPD Research On The Stable Care Field

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Abstract: Objective To explore the research hotspot and development frontier of stable care in COPD. Methods The CNKI database was searched, and the search year was set from January 1,2013 to March 31,2023. citespace software was used to visually analyze the distribution of publications, authors and institutions, keyword co-occurrence and clustering. Results A total of 511 articles were included, among which the number of articles showed a significant upward trend from 2013 to 2019;Xiaolei Shang Shang , Guifang Yu and other 21 authors; the school of Nursing of Nanjing Medical University has 3 articles; The research focus focus on quality of **life, extended nursing, compliance, TCM nursing, etc. The research frontier is mainly in exercise endurance. Conclusion Clinical medical staff should establish scientific evidence-based intervention program and establish evidence-based patient care in stable COPD to improve patients' exercise endurance.

Keywords: Copd Stable Period; Nursing; Citespace

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable chronic airway disease characterized by persistent airflow limitation and corresponding respiratory symptoms, which is not completely reversible and progressive [1].According to statistics, the number of COPD patients in China is about 100 million, among which 13.7% are patients over 40 years old. According to the statistics of the World Health Organization, COPD ranked the third in the disease burden in 2020 [2].Clinical studies show that the etiology of chronic obstructive pulmonary disease is complex, long course of disease, and difficult to cure. The treatment in the stable period mainly includes exercise, diet guidance, pulmonary rehabilitation training and drug treatment, which can improve patients' cough, dyspnea and other symptoms, and is also of great significance to improve the quality of life of patients [3,4].Information visualization analysis is an important research method in the field of metrology in recent years, and has been widely used in various fields[5] .With the help of the CiteSpace visualization software [6] developed by Dr. Chen Chaomei, this study analyzed the domestic literature in the field of COPD stable nursing from January 1,2013-March 31,2023,To understand the hotspot and development frontier of COPD stable nursing research in China, in order to provide reference for COPD stable nursing research and development.

1. Data and methods

1.1 Search strategy

CNKI was selected for the literature search, The search strategy: (theme = "chronic pulmonary disease stable and care" or "COPD stable and care"),The search time is limited to January 1,2013-March 31,2023, and the search date is April 5,2023 in Chinese. Include the literature on stable phase care in COPD. Meeting notices, news reports, and inconsistent research literature were excluded. The retrieved documents were exported in refworks format and downloaded in the download.txt file name.

1.2 Literature analysis

The literature was visualized using citespace6.2.2.msi software, The time slice is set from 01 January 2013-31 March 2023, a single time slice (years per slicing) for 1 year; TOP N = 50, the node is set with "Author", "Keyword", "Institution" as the network nodes, to extract the author, keywords, organization and other information, According to the frequency of keywords, the visual co-occurrence map was analyzed, the high frequency keywords were clustered, and the emergence of keywords was analyzed.

2. Results

2.1 Basic characteristics analysis of the literature

2.1.1 Distribution of post volume

In this study, 511 articles were finally included in the annual publication statistics ,This study shows that the number of articles published from 2013 to 2019, the number of documents gradually increased, indicating that this stage is a period of rapid development. From 2019 to 2021, the number of articles published was relatively stable, while the number of articles published in 2022 decreased, and the number of articles published was 39.

2.1.2 Distribution of the authors and the institutions

The results showed 276 nodes, 129 lines and a network density of 0.0034,In this study, the size of the nodes represents the number of the author. The larger the nodes means the more the author posts. The connection between the authors represents the cooperative relationship. The study found that Xiaolei Shang , Guifang Yu , Chao Xia, Shuang Li, Jie Tian and other 21 people had the largest number of articles, with two articles respectively. There have also formed several cooperative networks represented by Ying Zeng , BaolanLi , Qian Liu, Xin Xia and Li Guan respectively, and other published authors have no cooperative relationship with each other; Using the organization as the network node, the study results showed 254 nodes, 32 lines, and a network density of 0.001,In this study, a node represents a publishing agency, and the connection between the nodes represents the cooperation between the publishing agencies, and the thickness of the connection represents the close cooperation between the publishing agencies. The results show that COPD stable care institutions are scattered and less cooperation between institutions. The School of Nursing of Nanjing Medical University published the most articles with 3 articles.

2.2 Keyword co-occurrence and cluster analysis

2.2.1 Keyword co-occurrence analysis

The results show that 224 nodes, 634 attachment, network density 0.0254 , the same keywords, the top 10 high frequency keywords are stable, quality of life, lung function, nursing, extended nursing, nursing intervention, elderly, compliance, COPD, traditional Chinese medicine care.

2.2.2 Keyword cluster analysis

This study generated a keyword cluster map, which formed 10 meaningful clusters, namely, patients with lung function, stable period, quality of life, nursing, respiratory function, nursing intervention, self-management, compliance, rehabilitation and nursing, and stable period. The map shows Q=0.4208, indicating that the cluster structure is significant, S=0.8372, indicating that the cluster structure is reasonable, it can be seen that the cluster structure and high frequency words are basically consistent.

2.3 Prompt word analysis

Emergent words contain two important aspects: mutation strength and duration, the former represents the emergent strength of keywords, and the latter includes [7], the onset of the beginning and end of keywords. In order to understand the frontier progress and development trend of COPD stable nursing research, “Burstness” in keyword analysis is selected, and the top 14 emergent words are obtained. The key word in the recent and still growth stage is exercise endurance, and the emergent intensity is as high as 3.08, and the emergent time is 2021-2023.

3.Discussion

Analysis of the study status: The number of COPD stable nursing research literature showed a ladder upward trend between 2013 and 2019, indicating that this field was valued, which is closely related to the policy at that time. According to the author cooperative map analysis, only 21 authors published more than two articles, indicating that the research of COPD stable care is scattered and has not yet formed a certain scale system. Through institutional cooperation map analysis, Nanjing medical university and Shanghai jiaotong university school

of medicine, Suzhou Kowloon hospital, Lianyungang city first people's hospital, Nanjing university of Chinese medicine nursing college cooperation is better, the second people's hospital of Shandong Dongying city disability rehabilitation center cooperation is better, other institutions are cooperation. Therefore, the cooperation among the various institutions should be strengthened to promote resource sharing and improve the research level.

Analysis of research hotspots: Through the analysis of high-frequency keywords and clusters in cnCNKI database, it is found that the research hotspots of COPD stable nursing in China mainly focus on quality of life, extended nursing, compliance, traditional Chinese medicine nursing, etc. It is now analyzed from the following 4 points. ① Compliance with stable COPD patients: long-term standard inhalation medication is the core of treatment for stable COPD patients, but a considerable number of patients have reduced compliance (such as self-increase / reduction of dose, withdrawal or non-standard inhalation technology), leading to poor prognosis [8].Some studies have shown that the pharmaceutical care intervention [9], health education lecture [10], and comprehensive intervention [11] of the "nurse + pharmacist" medication education model are conducive to the improvement of patients' medication compliance. However, medication compliance is influenced by many factors including patients themselves, disease, family, medical staff and so on [12]. Therefore, the cooperation of society, family, medical staff, patients and other aspects is needed to improve the medication compliance of COPD patients, so as to increase the treatment effect of drugs, reduce the occurrence of adverse reactions, and promote the recovery of patients. ② Extension nursing for COPD patients in stable period: extended nursing is a new nursing mode, which can extend hospital nursing to families, realize the effective connection between in-hospital intervention and out-of-hospital intervention, and play a positive role in stabilizing the patient's condition [13].The COPD treatment cycle is long, and most of the stable patients recuperate at home, so it is difficult for the compliance with their lung function exercise to be effectively guaranteed, so it is necessary to give effective continuous nursing intervention [14].The ways of extended nursing implementation include telephone follow-up, family visit, health education based on network platform, and knowledge lectures. The main contents include health education, respiratory function exercise, dietary guidance, medication guidance, oxygen safety, and psychological nursing [15].There are a large number of studies [16-20] show that quality continuity care can significantly improve the living conditions of COPD patients after returning home, improve the symptoms of dyspnea, delay the development of the disease, improve patients' mobility, improve the quality of life, and reduce the fatality rate, which is an important measure to implement overall nursing and quality nursing. ③ TCM nursing of patients in stable COPD: TCM nursing intervention is guided by the overall concept of TCM, provides disease prevention and syndrome differentiation nursing to patients, takes the patient as the center, evaluates the patient's condition, guides the patient's diet, conducts health education for patients, eases their feelings, and makes them cultivate the TCM health habits, such as [21].The study shows that [22] TCM nursing technology combined with routine nursing has better efficacy compared with routine nursing, it has obvious advantages in lung function and quality of life, and the application of appropriate TCM nursing technology has the advantages of less adverse reactions and higher safety. Clinically, TCM nursing combined with routine nursing for COPD patients can improve the improvement degree of lung function and the quality of life of patients. ④ Quality of life of patients with stable COPD: Quality of life refers to the subjective experience [23] of the survival status related to their expectations, standards and things they care about in different cultures and value systems. COPD has a complex disease, long course and recurrent episodes, and the quality of life of patients during treatment is often low [24].Some studies have shown that disease course, comorbidities, disease perception and self-management are the influencing factors affecting the quality of life of COPD. Therefore, targeted interventions should be developed in the clinic to improve the quality of life of patients [25].

Research frontier analysis: Through the analysis of the emerging keywords in CNKI, it is found that the emerging keyword is exercise endurance. Due to the decline of patients with lung function, exercise endurance is weakened. How to improve the exercise endurance of COPD patients is still the future research direction. Studies are emerging to improve patients' exercise endurance, and in future studies, healthcare professionals should establish scientific evidence-based intervention programs combined with evidence-based interventions for patient care with stable COPD.

In conclusion, based on the visual analysis of citespace software, this study summarizes the research hotspots and development frontiers of stable care for chronic obstructive pulmonary disease in China from 2013 to 2023. This study also has some limitations. The literature data are from China, and comparative research can be conducted in the future. At the same time, the author's subjective judgment may have

an impact on the combination of keywords, so the research results may be biased.

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Risk factors for ventilator-associated pneumonia in ICU mechanically ventilated patients: a meta-analysis

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Abstract: Objective: This study aims to determine the risk factors for the development of ventilator-associated pneumonia (VAP) in ICU mechanically ventilated patients through meta-analysis. Method: Conduct a comprehensive search of multiple domestic and international databases, collect literature on the risk factors of VAP in ICU patients from November 2023, and conduct meta-analysis using RevMan5.4 software. Result: 31 high-quality studies were included, and it was found that age, COPD history, position, APACHE II score, antibiotic combination, repeated tracheal intubation, tracheostomy, indwelling gastric tube, mechanical ventilation time, and ICU hospitalization time were significantly associated with an increased risk of VAP; However, consciousness disorders and hypoalbuminemia do not show a significant correlation with the risk of VAP. Conclusion: Specific patient characteristics and clinical procedures are associated with increased risk of VAP, and clinical attention should be paid to these risk factors in order to intervene early to prevent VAP and improve patient prognosis.

Keywords: Mechanical Ventilation; Ventilator Associated Pneumonia; Risk Factors

1. Background

Mechanical ventilation is a method used in the ICU to treat critically ill patients, which includes both invasive and non-invasive methods aimed at meeting the respiratory needs of patients[1]. However, this treatment can lead to ventilator-associated pneumonia (VAP). VAP is the key cause of high morbidity and mortality in ICU patients. Its incidence rate and mortality have significant international differences. Incidental complications seriously threaten patients' lives [2]. This study discussed the risk factors for VAP in ICU mechanically ventilated patients both domestically and internationally through meta-analysis, aiming to provide data support for nursing practice and clinical decision-making to reduce the incidence of VAP.

2. Materials and Methods

Using meta-analysis method, relevant cohort studies and case-control studies on risk factors for VAP in ICU mechanical ventilation patients were collected by searching domestic and foreign databases. Extract and integrate research data, analyze and merge the data using RevMan 5.4 software.

3. Retrieval strategy

Conduct comprehensive searches on multiple domestic and international databases, including CNKI, Wanfang, VIP, Sinomed, Pubmed, Web of Science, EMbase, and Cochrane. The search period covers the period from database establishment to November 2023.

4. Discharge standards

Literature inclusion and exclusion criteria: ① The research method is cohort study or case-control study; ② The research subjects were ICU mechanically ventilated patients who did not develop pneumonia before admission; ③ The research focuses on the risk factors for VAP in ICU mechanically ventilated patients. Exclusion criteria: ① Non Chinese and English literature; ② Repeated publication; ③ Incomplete data and inability to obtain full text.

5. Literature screening and data extraction

To ensure the reliability and accuracy of the study, a double-blind independent screening method was adopted in this study. If there is any disagreement, it shall be judged by a third party. Extract literature information based on the required content.

6. Literature quality evaluation

To ensure the quality of the literature in the study, a double-blind independent evaluation method was adopted. Specifically, the Newcastle Ottawa Scale (NOS) scale [3] was used to evaluate the risk of bias in the literature.

7. Statistical methods

A meta-analysis was conducted on risk factors using RevMan 5.4 software. Evaluate the homogeneity and heterogeneity of the study. If the number of studies included in the same outcome measure reaches 10 or more, a funnel plot is used to evaluate whether there is publication bias.

8. Literature screening results

By searching domestic and foreign databases, a total of 3102 articles were retrieved. Among them, there are 1231 articles in Chinese and 1871 articles in English, with 31 articles included, 21 in Chinese, and 10 in English. 25 case-control studies and 6 cohort studies are all high-quality studies.

9. Meta analysis results

A publication bias analysis was conducted on risk factors for 10 or more articles on mechanical ventilation time, APACHE II score, antibiotic combination therapy, and age. The scatter plots of the first three risk factors show a basic symmetrical distribution, and the likelihood of publication bias is relatively small. The funnel plot of age risk factors shows an asymmetric distribution, which may lead to publication bias. A meta-analysis was conducted on 13 risk factors mentioned in more than 2 articles. The results of the meta-analysis are shown in Table 1:

Table 1 Meta analysis results of various risk factors

Risk factor	Quantity (piece)	Test for heterogeneity		Effect model	Merger effect			Is it statistically significant
		I2(%)	P value		Effect size	95%CI	P value	
Ventilation time	21	99%	＜0.001	Random	2.25	1.90-2.67	＜0.001	Yes
≥5days	5	50%	0.11	Random	7.09	5.62-8.94	＜0.001	Yes
≥7days	9	93%	＜0.001	Random	1.26	1.12-1.43	＜0.001	Yes
APACHEIIScore	13	98%	＜0.001	Random	3.20	2.27-4.51	＜0.001	Yes
15Score	9	98%	＜0.001	Random	3.73	1.95-7.16	＜0.001	Yes
Combination of antibiotics	11	0%	0.54	Fixation	4.61	3.92-5.42	＜0.001	Yes
Year	11	95%	＜0.001	Random	1.03	1.02-1.05	＜0.01	Yes
60years	6	96%	＜0.001	Random	1.57	1.28-1.94	＜0.001	Yes
COPD history	9	65%	0.006	Random	2.31	1.68-3.17	＜0.001	Yes
Repeated tracheal intubation	8	69%%	＜0.001	Random	5.82	4.21-8.05	＜0.001	Yes
Disturbance of consciousness	7	91%	0.001	Random	1.86	0.93-3.72	0.08	No
Indwelling gastric tube	6	36%	0.18	Fixation	3.70	2.65-5.19	＜0.001	Yes
Hypoproteinemia	5	97%	＜0.001	Random	1.92	0.77-4.75	0.16	No
Tracheotomy	5	30%	0.23	Fixation	1.41	1.21-1.63	＜0.001	Yes
ICU hospitalization time	4	90%	＜0.001	Random	2.67	1.11-6.43	0.03	Yes
position	4	28%	0.25	Fixation	3.88	2.82-5.34	＜0.001	Yes

9.1 Elderly individuals, history of COPD, and long-term supine position are risk factors for VAP

Research has shown through meta-analysis that elderly people over 60 years old are significantly at risk for VAP due to weakened lung function and immunity[4]. Airways should be kept clean, appropriate ventilation strategies should be adopted, and chronic diseases should be managed to reduce risk. COPD patients have a high risk of VAP and need to follow medical advice and receive timely treatment. Long term supine position increases the risk of VAP. It is recommended to change the position, such as prone and 45 ° semi prone positions, to promote lung ventilation and reduce VAP[5-6].

9.2 High APACHE II score and combination of multiple antibiotics are risk factors for VAP

Research analysis shows that a high APACHE II score is a risk factor for VAP[7], and personalized treatment is needed to reduce risk if the score is ≥ 15. The combination of antibiotics may increase drug-resistant bacteria and increase the risk of VAP. It is recommended to assess the risk and consider bacterial spectrum and drug sensitivity when selecting antibiotics to reduce infection[8].

9.3 Invasive airway operations can increase the risk of VAP occurrence

This study conducted a meta-analysis on the impact of invasive airway procedures and found that repeated tracheal intubation, tracheostomy, and indwelling gastric tubes all increased the risk of VAP. These operations may disrupt the respiratory defense structure, impair immune cell function, reduce self-defense ability, and allow bacteria to cause respiratory infections through multiple pathways [9]. It is recommended that medical staff adopt aseptic techniques, optimize operating methods, reduce operating frequency, and minimize the risk of VAP.

9.4 The longer the duration of mechanical ventilation and hospitalization, the higher the risk of VAP occurrence

This study conducted a meta-analysis on "mechanical ventilation time" and "ICU hospitalization time", which showed that prolonged time increased the risk of VAP occurrence, matching the findings of Wu et al. Prolonged ventilation and hospital stay make patients more susceptible to the long-term effects of respiratory equipment and environmental bacteria, and may lower immunity and increase the risk of VAP [10]. Research suggests reducing the occurrence of VAP through strict aseptic procedures, regular replacement of pipelines, shortened ventilation time, and early weaning.

9.5 There is no significant relationship between consciousness disorders, hypoalbuminemia, and the occurrence of VAP

Meta analysis found that consciousness disorders and hypoalbuminemia are not independent risk factors for VAP, although the literature is inconsistent[11]. Research suggests that consciousness disorders reduce patient protection, and hypoalbuminemia affects immunity and tissue repair, which are among the multiple factors of VAP. It is recommended to regularly replace pipelines and clean disinfection equipment, limit the use of sedatives and sleeping pills, and provide nutrition and protein supplementation for patients with hypoalbuminemia to strengthen immunity and repair.

10. Summary

This study used meta-analysis to investigate the risk factors of VAP in ICU mechanically ventilated patients. It was found that aging, history of COPD, long-term lying flat, high APACHE II score, use of multiple antibiotics, and invasive airway procedures were significantly correlated with the risk of VAP. In addition, mechanical ventilation and prolonged hospital stay increase the risk of VAP, while consciousness disorders and hypoalbuminemia are not significantly associated with the occurrence of VAP. It is recommended to conduct clinical interventions targeting risk factors to improve patient outcomes. The results are influenced by differences in literature and require more high-quality research to verify.

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Mesenchymal stem cells secretions for treating neurological diseases and their mechanism of action

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Abstract: Neurological diseases are a class of diseases that seriously affect human health, including stroke, Parkinson's disease, Alzheimer's disease and spinal cord injury. Traditional treatments have some limitations in the treatment of these diseases, such as drug side effects, surgical risks, etc. In recent years, secretions from mesenchymal stem cells (MSCs) have attracted much attention as a new method to treat neurological diseases. The secretions are composed of a variety of bioactive components, which can exert their therapeutic effects by regulating the inflammatory response, promoting the regeneration and repair of nerve cells, and resisting oxidative stress. This review aims to review the application of MSC secretions in the treatment of neurological diseases and explore the mechanism of action.

Keywords: Mesenchymal Stem Cell Secretions; Neurological Diseases; Neuroinflammation; Nerve Repair

1. Introduction

1.1 Background and current status of neurological disorders

Neurological diseases are a large category that contains a wide range of pathological conditions, such as neurodegenerative diseases, stroke, and traumatic brain injury [1]. Globally, neurological diseases have become a major public health problem. The resulting death, disability and socio-economic burden cannot be ignored. Although many traditional treatment modalities exist, new approaches are needed to alleviate the disease process and improve patient quality of life.

1.2 Progress in mesenchymal stem cell secretions

As an important source of mesenchymal stem cells, mesenchymal stem cells (MSCs) have shown promising applications in various tissue repair and disease treatment [2]. Especially in recent years, with the in-depth exploration of MSCs, it was found that a variety of bioactive factors secreted by MSCs show powerful functions in neuroprotection, promoting neuroregeneration, regulating immune response and inhibiting inflammation. Currently, there is extensive research evidence supporting the promising application of MSC secretions in the treatment of neurological diseases [3]. For example, MSC secretions have shown significant effects in the treatment of Parkinson's disease (PD), stroke and traumatic brain injury in experimental animal models. Further studies have found that they mainly achieve neuroprotection through various mechanisms such as inhibiting inflammatory response, and promoting nerve regeneration and cell survival [4-7].

This provides new perspectives and ideas for the application of MSC secretions in the treatment of neurological diseases, and also paves the way for future clinical trials.

2. Components and characteristics of the MSC secretions

2.1 Cytokines and growth factors

MSCs secrete a large number of cytokines and growth factors, such as transforming growth factor-beta (TGF-β), vascular endothelial growth factor (VEGF), tumor necrosis factor-α (TNF-α), stem cell factor (SCF) and other [8]. These factors have the function of regulating cell survival, proliferation and differentiation. For example, VEGF stimulates the formation of new blood vessels to provide sufficient nutrients to the damaged nerve tissue; TNF-α regulates the cellular immune response to help resist infection.

2.2 Exosomes and microcysts

MSCs also release small membrane capsules called exosomes and microcapsules. These membrane vesicles contain abundant bioactive molecules such as RNA, protein. Moreover, these molecules may be passed between cells, thus influencing the function of cells [9]. Recent studies showed that exosomes and microcysts secreted by MSCs show important functions in several aspects, including nerve repair and immune regulation.

2.3 Other bioactive molecules

In addition, MSC secretions contain some other types of bioactive molecules, such as antioxidant enzymes, proteases, and their tissue inhibitory factors [9]. These molecules have important roles in maintaining the stability of the tissue microenvironment, regulating cell behavior, and resisting damage. For example, antioxidant enzymes can remove free radicals in the body and protect cells from oxidative stress; proteases and their inhibitory factors are involved in the constant maintenance of the extracellular matrix.

3. MSC secretions in the treatment of neurological disorders

3.1 Stroke treatment

Studies have shown that the application of MSC secretions has great potential for promoting stroke recovery. MSCs can secrete a variety of growth factors and cytokines, which can help to improve the microenvironment and promote the survival and regeneration of nerve cells. Moreover, their secreted exosomes are enriched in miRNA, which can regulate the expression of target genes and further influence neuroprotection and neural repair [10].

3.2 PD treatment

PD is a refractory neurodegenerative disease. However, MSC secretions have shown some therapeutic effects. Some laboratory studies have found that MSCs can reduce symptoms in PD model animals by secreting neuroprotective factors, such as brain-derived neurotrophic factors (BDNF) and catalase, which can effectively protect dopamine neurons from injury [11].

3.3 Alzheimer's disease (AD) treatment

MSCs have also shown some results in the treatment of AD. It has been reported that mesenchymal stem cells can inhibit neuroinflammatory responses and reduce amyloid beta production, which has the potential to improve cognitive function in AD patients [12-15]. Moreover, exosomes secreted by MSC have some effect on nerve regeneration and regeneration.

3.4 Spinal Cord Injury Treatment

MSCs also have significant advantages in managing spinal cord injury [16,17]. The repair effect of MSC is mainly achieved through mechanisms such as inhibiting the inflammatory response, promoting the regeneration of damaged nerve fibers, and stimulating new blood vessel formation. Studies have shown that coronary intravenous injection of MSC or direct transplantation to the site of SCI can significantly improve motor function recovery.

3.5 Treatment for other neurological diseases

In addition to the above diseases, MSCs are also used in the treatment of several other neurological diseases, such as multiple sclerosis, amyotrophic lateral sclerosis, peripheral nerve diseases, and others [18]. Although the treatment of these diseases is experimental, preliminary results show the therapeutic potential of MSC. Overall, MSCs and their secretions provide a new potential therapeutic strategy for neurological diseases through multiple mechanisms of action including anti-inflammatory, immune regulation, as well as promoting the survival and regeneration of nerve cells.

4.Mechanism analysis of mesenchymal stem cell secretions

4.1 Regulate the inflammatory response

MSCs play an important role in regulating inflammatory responses. They can secrete a range of bioactive factors, including but not limited to inflammatory cytokines, growth factors, chemokines, etc., and the interaction between these factors can regulate the inflammatory response of the body. For example, anti-inflammatory cytokines secreted by MSCs such as IL-10 and TGF-β1 can inhibit the neuroinflammatory response to some extent by inhibiting the evolution of T-inducing factors, thereby reducing the damage in neural tissue [19].

4.2 Promote nerve cell regeneration and repair

Treatment with secretions from MSCs is an effective way to promote nerve cell regeneration and repair. MSCs can promote the survival and regeneration of nerve cells by secreting neurotrophic factors and other bioactive components such as BDNF, nerve growth factor, and VEGF [20]. These factors can protect nerve cells and prevent cell apoptosis, while promoting the differentiation of neural stem cells, eventually reaching the goal of repairing the damaged nervous system.

4.3 Anti-oxidative stress

MSCs have significant anti-oxidative stress ability and can effectively resist the oxidative damage of the nervous system caused by various adverse factors. MSCs regulate the redox balance, reduce the damage of free radicals to nerve cells, and protect the normal function of nerve cells. In addition, MSCs can secrete a series of antioxidant enzymes, such as catalase and glutathione, which can remove excessive free radicals in the body and prevent oxidative damage by free radicals to nerve cells [21].

4.4 Progress in studying other mechanisms of action

Exosomes in the secretions of MSCs have attracted much attention recently, and these small RNA and protein-rich vesicles have key roles in cell-to-cell communication. They can affect neuroprotection and nerve repair by regulating gene expression, and can also be released to damaged areas, thus affecting cell behavior, improving cell survival and functional recovery [22]. For example, miRNAs in the exosomes of MSCs are able to regulate the expression of genes involved in neurological diseases to exert a therapeutic effect. Although the research in this field is still in its initial stage, it has shown great potential for application and provided a new research direction for the diagnosis and treatment of neurological diseases.

5. Clinical application prospects and challenges

Although MSCs secretions have shown positive prospects in the treatment of neurological diseases, there are still some challenges in translating them into clinical applications. First, due to the complex composition of MSC secretions, there is no clear standardized production and storage method, which may cause some difficulty in clinical application. Secondly, although preliminary studies have shown the good safety and efficacy of MSC secretions, further verification of these results should be conducted in clinical trials with large samples. Moreover, since the current understanding of the mechanism of action of MSC secretions is incomplete, determining the optimal treatment options suitable for various neurological diseases is also a problem to be solved. Overall, MSC secretion undoubtedly provides new possibilities for the treatment of neurological diseases, but its clinical application still needs more in-depth research and exploration [23].

6. Conclusion

This review summarizes the application of mesenchymal stem cells (MSCs) in the treatment of neurological diseases. As a kind of stem cells with multidirectional differentiation potential, mesenchymal stem cells can secrete a variety of bioactive substances, such as nerve growth factor, BDNF and VEGF, and play anti-inflammatory, antioxidant and anti-apoptotic roles, thereby improving the symptoms of nervous system diseases. The premise of clinical application is the safety of use, so the secretion of mesenchymal stem cells shows a broad development prospect. However, the mechanism of using secretions instead of cell transplantation is still insufficient, and further exploration and

research are still needed to give full play to its therapeutic effect and better serve patients.

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Anaphylactic shock causing cardiac arrhythmia: A case analysis of successful precordial thump intervention

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Abstract: This article presents a clinical case analysis of cardiac arrhythmia induced by anaphylactic shock, along with the diagnosis and treatment methods employed in the case. The article provides a detailed explanation of the causes and mechanisms of allergic reactions caused by neuromuscular blocking agents and the subsequent cardiac arrhythmias. It also discusses treatment methods such as precordial thump. This article can serve as a reference for clinicians dealing with similar cases.

Keywords: Allergic Shock; Arrhythmias; Case Analysis

1. Background Introduction

The frequency of systemic allergic reactions during anesthesia varies according to studies, ranging from 1/1250 to 1/18600[1-7]. Among them, neuromuscular blocking agents (NMBAs) have been reported as the main cause of most perioperative allergic reactions[8, 9]. Approximately 50% of systemic allergic reactions in adults during the perioperative period are detected through early symptoms such as hypotension, circulatory failure, and cardiac arrest[10]. A study in France reported that 72.9% of severe drug-induced systemic allergic reactions can be confirmed through skin testing [11].

2. Clinical Case

A 20-year-old male patient with a weight of 100kg was admitted to the hospital due to “right ear pain with decreased hearing for more than 3 years.” He has a history of sinusitis and seafood allergy (symptoms include skin rash on the hands and mild itching), but no other significant medical history. Preoperative examination revealed abnormal blood glucose and creatine kinase levels (glucose: 6.31mmol/L, creatine kinase: 354IU/L). The electrocardiogram showed sinus rhythm. No other specific abnormalities were found in the examination. The patient was classified as ASA Grade II. Microscopic surgery was performed on the right ear after admission. Prior to anesthesia induction, the patient was conscious and provided coherent responses. The drugs used for induction included Penehyclidine Hydrochloride Injection 0.5mg, Midazolam Injection 2mg, Sufentanil Citrate 25ug, Cisatracurium Besilate 14mg, and Propofol 100mg. During anesthesia induction, the patient experienced severe shock and subsequently developed ventricular arrhythmia (initially premature ventricular contractions, rapidly transitioning to ventricular tachycardia). Non-invasive blood pressure measurement was unsuccessful. Based on the temporal relationship between symptom onset and injection, it was diagnosed as anaphylactic shock caused by anesthesia induction drugs, as well as arrhythmia triggered by anaphylactic shock. The medical staff immediately administered precordial thumps to the patient, and the patient recovered sinus rhythm. Subsequently, Adrenaline Hydrochloride Injection 200ug, Methylprednisolone 40mg, and Calcium Gluconate Injection 1g were administered, and fluid infusion was expedited to treat anaphylactic shock. Simultaneously, rapid endotracheal intubation and mechanical ventilation were performed. A new venous access was established to administer Norepinephrine at a rate of 5ug/kg/min to maintain blood pressure. With timely rescue measures, the patient’s vital signs gradually improved. Following the goal of maintaining systolic blood pressure above 90mmHg, vasoactive drugs were dynamically adjusted. After communicating the condition with the patient’s family, they requested to proceed with the surgery. The surgical procedure proceeded smoothly, and with close monitoring and appropriate medication adjustments, the patient’s vital signs remained relatively stable. Postoperatively, the patient still required a significant amount of vasoactive drugs to maintain vital signs. After thorough discussions and communication with the patient and their family, the decision was made to transfer the patient to the ICU for further treatment. The following day, the patient’s condition improved. Cardiac echocardiography showed normal lower limits of left ventricular systolic function. Electrocardiogram revealed sinus bradycardia with arrhythmia, and “J” point elevation was observed in

leads V3-V6. The patient was discharged upon recovery. During the follow-up period, the patient did not experience any significant discomfort. After discharge, an allergy test conducted outside the hospital revealed a possible allergy to neuromuscular blocking agents (Table 1, Table 2, Table 3).

Table 1

Skin Prick Test,SPT				
Drug Name	Concentration of Stock Solution	Concentration for Skin Prick Test	Wheal Size	Result
NMBAs				
Rocuronium Bromide	10mg/ml	5mg/ml(1:2)		(−)
vecuronium bromide	4mg/ml	0.4mg/ml(1:10)		(−)
Cisatracurium Besilate	2mg/ml	2mg/ml(stock solution)		(−)
sedative-hypnotic				
Midazolam	5mg/ml	5mg/ml(stock solution)		(−)
Propofol	10mg/ml	1mg/ml(1:10)		(−)
opioid drug				
Fentanyl	50ug/ml	50ug/ml(stock solution)		(−)
Remifentanil	50ug/ml	50ug/ml(stock solution)		(−)
Sufentanil	5ug/ml	5ug/ml(stock solution)		(−)
Others				
Chlorhexidine	5mg/ml	5mg/ml(stock solution)		(−)
Cefazolin	20mg/ml	20mg/ml		(−)

Table 2

Intradermal Test,IDT			
Drug Name	Result recorded		
NMBAs	1:10000	1:1000	1:100
Rocuronium Bromide	/	(−)	
vecuronium bromide	(−)	(±)	
Cisatracurium Besilate	(−)	(−)	(±)
sedative-hypnotic	1:1000	1:100	1:10
Midazolam	(−)	(−)	(−)
Propofol	(−)	(−)	(−)
opioid drug	1:1000	1:100	1:10
Fentanyl	/	(−)	(−)
Remifentanil	(−)	(−)	(−)
Sufentanil	(−)	(−)	(−)
Others	1:1000	1:100	1:10
Chlorhexidine	/	/	(−)
Cefazolin	(−)	/	/
conclusion	Based on the patient's previous anesthesia records, intradermal tests were conducted using vecuronium bromide, cisatracurium besilate, midazolam, propofol, sufentanil, and remifentanil. Among them, intradermal tests with cisatracurium besilate and vecuronium bromide showed suspicious positive reactions. Further cross-reactivity testing was performed, and the intradermal test with rocuronium bromide was negative. Based on previous experience, the primary allergen causing severe perioperative allergic reactions is neuromuscular blocking agents. It is recommended to avoid the use of cisatracurium besilate and vecuronium bromide in the future and consider using rocuronium bromide as an alternative. Enhanced monitoring during the surgery is still necessary.		

Table 3

provocation test			
Test drug: cefazolin		Route of administration: Intravenous (IV)	
Dosage:	50mg	200mg	250mg
Administration time	09:40	10:25	11:00
confirmation time	10:15	10:55	11:55
rash	none	none	none
peak flow rate	650	650	650
Heart rate	80	76	72
Blood oxygen saturation	98%	98%	97%
Blood pressure	110/70	109/67	116/77
Respiratory rate	20	19	19
Result	The result of the skin test and provocation test for cefazolin was negative, indicating that the patient is not allergic to cefazolin.		

3. Diagnosis and treatment

Based on the patient's medical history, clinical presentation, and relevant test results, it was initially suspected that the patient may have an allergic reaction to certain anesthetic drugs. The allergic reaction occurred rapidly and developed rapidly, with severe symptoms (rash/shock/arrhythmia), requiring continuous epinephrine infusion during the anesthetic surgery. The clinical presentation met the diagnostic criteria for allergic reactions and refractory allergic reactions [12, 13]. In order to further confirm the diagnosis, the patient underwent intradermal tests with cis-atricurium and vecuronium according to our recommendation, and the results showed that the patient had a suspected positive reaction. In response to the patient's ventricular tachycardia, we immediately performed precordial thump therapy, effectively restoring the patient's sinus rhythm.

4. Discussion

4.1 Causes of anaphylactic shock

During anesthesia surgery, the drugs that the patient has been exposed to are: Penehyclidine Hydrochloride Injection, Midazolam, Propofol, Sufentanil Citrate, Cisatracurium Besylate, and Cefozolin. The relevant drug stimulation test and skin prick test (SPT) conducted by the patient after surgery did not report positive results, while the intradermal test (IDT) indicated suspicious positivity of vecuronium and cisatracurium. Among them, no relevant experiments have been conducted on Penehyclidine Hydrochloride Injection, and there have been almost no reports of allergies related to it. Therefore, we can temporarily assume that the possibility of allergies to Penehyclidine Hydrochloride is extremely low, while there is a higher possibility of allergy to neuromuscular blocking agents.

4.2 Allergic reactions and anaphylactic shock caused by neuromuscular blocking agents

In recent years, the frequency of allergic reactions during anesthesia has been reported to be increasing in most developed countries [9, 14], and neuromuscular blocking agents (NMBAs) have been identified as the main cause of most perioperative allergic reactions [8, 9]. Furthermore, they are responsible for 80% of cases of anaphylactic shock occurring in patients after anesthesia [9, 15]. Allergic reactions caused by NMBAs can be classified into type I hypersensitivity reactions and non-specific hypersensitivity reactions [9, 16-18].

The main mechanism of hypersensitivity reactions caused by NMBAs is acute type I allergic reactions, accounting for 50-70% of such reactions during anesthesia [16-18]. NMBAs can also induce degranulation of mast cells and release of allergic mediators by activating MRGPRX2, a receptor that can activate mast cells and cause non-specific hypersensitivity reactions. Approximately half of the non-specific hypersensitivity reactions during the perioperative period are attributed to NMBAs [9].

As specific IgE level testing was not performed, the specific type of NMBA allergy in this patient was not clearly identified.

4.3 Causes of arrhythmia

We believe that the patient's arrhythmia was triggered by an allergic reaction. Allergic reactions can cause any type of arrhythmia [19], but possible mechanisms include arrhythmias caused by decreased cardiac perfusion due to anaphylactic shock and abnormal contraction function, rhythm, and coronary artery tension caused by chemical mediators released during the allergic reaction period [20].

4.4 Precordial thump,PT

PT is undoubtedly a simple and feasible treatment method when it is necessary to restore organized cardiac electrical activity and transform patients from ventricular tachycardia to a more stable and organized rhythm. It uses appropriate force to hammer the surface precordial area of the body, causing the resulting shock to oscillate in the arrhythmic heart. Under the mechanical electrical feedback, the myocardium undergoes depolarization, which may be the reason why PT can effectively terminate the patient's ventricular arrhythmia. For patients with cardiac instability who cannot be immediately defibrillated, PT can be the first choice [21]. Sometimes in patients with ventricular tachycardia, a single chest blow can lead to a transition to sinus tachycardia [22]. This method is relatively safe [23], and in specific hospitalization and monitoring environments, hammering stimulation can be attempted for patients at the onset of potentially fatal arrhythmias. In this case, PT was successfully used to rapidly convert ventricular tachycardia into sinus tachycardia, which saved the patient the shortest possible time to recover effective circulation. But there are also opinions that in the process of cardiopulmonary resuscitation such as cardiac arrest and ventricular fibrillation, these alternative techniques cannot delay standard CPR measures [22, 24, 25].

5. Conclusion

In this case, the patient may have experienced an allergic reaction and arrhythmia due to an allergy to neuromuscular blocking agents. During treatment, continuous infusion of epinephrine through a pump and precordial thump (PT) were both effective. It is important to note that allergic reactions can cause various types of arrhythmias, and prompt measures should be taken. Additionally, precordial thump can be the first choice when defibrillation is not immediately available for unstable cardiac patients. Although this method is simple and feasible, clinicians should possess basic skills in ECG analysis and identifying different types of arrhythmias. Furthermore, during the treatment, attention should be given to the force and the precise location of the precordial thump to avoid causing secondary harm to the patient. Precordial thump is a safe and effective treatment method, but it should be used with caution and under the guidance of medical professionals.

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Contributions of Integration of Traditional Chinese and Western Medicine to the Prevention and Treatment of Respiratory Diseases

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Abstract: Respiratory disease is a relatively common disease currently recognized in society, which brings a burden to individuals and society that beyond measure. The Integration of traditional Chinese medicine (TCM) and Western medicine(WM) to prevent and treat respiratory diseases is a new method of comprehensive application of TCM and WM for prevention and treatment. Its advantage point in the treatment of respiratory diseases have become increasingly prominent, becoming one of the important measures in the field of disease control Nowadays. Integration of TCM and WM(ITCWM) brings a more effective and sustainable approach to the prevention and treatment of respiratory diseases and alleviates the pain and suffering of patients during treatment. The contribution of ITCWM to the prevention and treatment of respiratory diseases is not only reflected in treatment, but also in prevention, health-care and health education. This article will explore the particular contribution of ITCWM in the prevention and treatment of respiratory diseases in the disease control and human well-being.

Keywords: Integration of Traditional Chinese and Western Medicine; Prevention and Treatment Of Respiratory Diseases; Contribution on Disease Control

Introduction

With the improvement of people's living standards, respiratory diseases have gradually become one of the main diseases affecting human health. These diseases cause a lot of health problems physically and mentally. The ITCWM to control diseases is a new method of chronic treatment to respiratory disease, which organically combines the advantages of both TCM and WM, comprehensively employing their practices of regimen, conditioning, medical treatment and rehabilitation, to bring new viable methods to the treatment of respiratory diseases. This method appear superior that it can get the disease under control , relieve symptoms, and reduce the side effects of drugs swiftly, which has played a positive role in promoting the particularity of life. This article will discuss the remarkable contribution made by the ITCWM in the prevention and treatment of respiratory diseases.

1. Brief Intro of the Prevalence of Respiratory Diseases and the Exploration of the Medical Community

Respiratory diseases refer to diseases that affect the function of the respiratory system, including lung diseases, bronchial diseases, tracheal diseases, pleural diseases, pulmonary hypertension and the likes. Due to the influence of environmental and social factors such as pollution, tobacco, dust, allergens and so forth, the incidence and mortality of respiratory diseases have continued rising in recent years, becoming one of the health problems of global concern.

According to the World Health Organization Statistic, up to millions of lives died of respiratory diseases worldwide every year, of which chronic obstructive pulmonary disease and lung cancer account for the highest proportion on cause of death, especially obvious in developed countries. The incidence and mortality of respiratory diseases in China are, without exception, rising year by year to boot, especially respiratory diseases such as pneumonia, tuberculosis and lung cancer, severely threaten people's health.

To this end, the medical community is constantly exploring a variety of effective methods of prevention and treatment as well. TCM has tradition and experience of a long history, while modern WM yet possesses high-tech and sophisticated medical methods. Therefore, numerous experts in the medical field have gradually being aware of the significance and necessity of ITCWM to prevent and treat respiratory diseases, advance nonstop the research and practice of ITCWM, and are actively digging for better treatment options.

The experience of traditional Chinese medicine are devoted into “balance and harmony”, emphasizing the coordination of yin and yang, and unclogging the movement mechanism of qi and blood veins. From the perspective of TCM,the symptom of respiratory diseases are mainly manifested as “qi stagnation, phlegm coagulation”, such as qi deficiency of lung , pulmonary hemorrhoids and other diseases, and the treatment methods are mostly warmly-dredging method and invigorating method. In practical applications, Both of TCM and ITCWM adopt traditional Chinese herbal and decoction medicine, meridian massage, acupuncture and other means, which can effectively relieve symptoms such as inflammation and swelling of the trachea, bronchi and other body parts, and are conducive to the recovery and health of the respiratory system.

WM, meanwhile, has outstanding advantages in modern advanced medical technology, Application of technologies such as thoracoscopy, stent and others can more precisely locate and act on the lesions of respiratory diseases. When patients suffer from respiratory diseases, WM would adopts a series of treatments such as through inhaling various drugs to exert locally stimulative effects to accelerate the diffusion and absorption of drugs in the local area.

ITCWM to prevent and treat respiratory diseases, in essence, requires comprehensive consideration of the specific etiology, pathology and other factors in any aspect of the disease, as well as numerous detailed factors such as different groups of different ages and various environments, combined with miscellaneous professional skills such as acupuncture, Tuina(manipulation), cooling, and expectoration, to offer well-rounded treatment services to patients.

TCM is, in contrast, widely proficient in application of herbal medicine, and whose relatively mild medicinal properties can decline the internal side effects caused by Western medicine, and somewhat lives up to “balance and harmony” of producing a positive therapeutic effect [1]. In summary, the ITCWM in the prevention and treatment of respiratory diseases has a wide range of application prospects in the exploration and practice of the medical community, take full advantages of the experience and medicine of TCM and WM of two, making no mean feat to the prevention and treatment of respiratory diseases.

2. Discussion on the Application of Integrated Traditional Chinese and Western Medicine in the Prevention and Treatment of Respiratory Diseases

The prevention and treatment of respiratory diseases by ITCWM has always been a hot issue in the medical community. Considering the complexity and diversity of respiratory diseases, it is tough for a single treatment method to achieve the desired therapeutic effect, and ITCWM thus plays a significant role in the prevention and treatment of respiratory diseases.

2.1 Advantages of TCM in the Prevention and Treatment of Respiratory Diseases

As an excellent traditional medicine in China, TCM possesses tradition and experience of a long history. In the diagnosis and treatment of respiratory diseases, TCM often takes them from the whole condition, not only considering the disease itself, but also paying attention to the physiological and psychological causes of the onset of the disease. TCM has a particular way with the treatment.

(1) Meridian massage. Meridian massage is one of the techniques of common use in TCM. As per different etiologies and pathologies, through kneading, patting, pinching, manipulation and other techniques to stimulate acupuncture points, adjust meridians, and thus achieve the effects of expectorant and cough-relieving, qi-reorganizing and pain-dispelling .

(2) Acupuncture therapy. Acupuncture is one of the unique treatment methods of traditional Chinese medicine. By stimulating acupuncture points, it can achieve the purpose of regulating the body’s own recovery function, enhancing resistance and immunity, and do wonders for the treatment of respiratory diseases.

(3) Decoction of Chinese medicine. Decoction is one of the most common treatments in Chinese medicine. Commonly used Chinese herbal medicines can exert clearing heat and dissipating phlegm, releasing heat and cough, etc., which are of profound application value. Compared with Western medicine, Chinese medicine has relatively fewer side effects and cause overdue burdens to the body [2].

2.2 Status Quo and Problems of Western Medicine in the Prevention and Treatment of Respiratory Diseases

With the continuous development of medical technology, many respiratory diseases can be treated in a better manner. However, the following problems still remain. (1) Drug treatment. At present, WM mainly adopts drug treatment for respiratory diseases. Although the efficacy of Western medicine synthetic drugs is remarkable, its side effects are significant. Once the patient takes it improperly, it is very likely to cause severely negative effects on the body. (2) Surgical treatment. Surgical treatment of respiratory disease usually involves surgery to remove the lesion. Surgical treatment, however, may bring secondary injury and adverse sequelae for some special occasions, and once the treatment is done, it is quite likely to cause more serious irreparable consequences to the patient.

2.3 Application of the ITCWM in Prevention and Treatment of Respiratory Diseases

2.3.1 The ITCWM

Given the distinctive directions and thought process of traditional Chinese and western medicine, the ITCWM thus combine the advantages of TCM and WM, which can considerably improves the treatment effect. TCM often takes diseases from the root and may not prove obviously efficacious in the short term, but it can establish a solid foundation of the patient's body and make it possible to heal itself spontaneously. Western medicine, otherwise, can act on and work out something quickly in emergency situations to avoid adverse consequences to occur.

2.3.2 Application of Acupuncture, Massage and Other Traditional Chinese Medicine Techniques

The unique treatment techniques of TCM, such as acupuncture, manipulation, massage and others, play an increasingly important role in the treatment of respiratory diseases, which can not only alleviate the their symptoms, but also work wonders in promoting the recovery from the diseases and regeneration of body. Especially in the aspects of pain relief, blood circulation promoting, therapy targeting, and immunity regulation, TCM is incomparably of expertise.

2.3.3 Appropriate Cooperation of Chinese and Western Medicines

The ITCWM can maximize the efficacy of medicines and drugs, in the treatment of respiratory diseases. TCM mainly focus on warm-dredging and qi-activaing, while Western medicine antibiotic, inflammation-reducing, allergic resistance and the likes. The drug effects of them complement each other, which can help patients alleviate symptoms better and speed up the treatment process.

2.3.4 Improvement of Treatment Effect to Prevent the Recurrence of the Disease

There is still a long haul for ITCWM in the treatment of respiratory diseases to press forward. Its treatment methods should adjusted timely, improving the treatment effect to prevent the recurrence of the disease. TCM reckons that the root of diseases stems from the disorder of balance in body, and different treatments must be exercised to adjust the balance of the well-being. In light of this standpoint, the ITCWM in the treatment of respiratory diseases should not only pay attention to external manifestations of the disease like the symptoms, but also emphasize adjusting the patient's body functions, regulating the body's qi, blood, internal organs, and so forth and thus stifling the possibility of disease recurrence from the source. The ITCWM possesses remarkable advantages in the prevention and treatment of respiratory diseases. In addition to the characteristic methods of TCM and WM, it also includes health-care treatments such as exercise and diet. Being able to solve the cases of drug tolerance, medical side effects, and relapse of disease wonderfully in the process of treatment, the ITCWM is a kind of efficient approach to improve the treatment effect, refine, personalize and scientize the prevention and treatment of respiratory diseases. Down the line, the application of the ITCWM in the prevention and treatment of respiratory diseases will definitely be more extensive. Medical institutions and teams of various scales should, however, also strengthen exchange and cooperation to jointly advance the further development and innovation of ITCWM in the prevention and treatment of respiratory diseases.

3. Summary on the Role and Value of ITCWM in the Prevention and Treatment of Respiratory Diseases

As a modern medical method, the ITCWM has been praised both from medical community and by many patients and their families for its more systematic and outstanding overall performance. The role and value of ITCWM in the prevention and treatment of respiratory

diseases have been verified in practice. the superiority of ITCWM in the prevention and treatment of respiratory diseases have been proved in terms of the prevention and treatment, conditioning of patients with different conditions and the sequalae of diverse phases.

3.1 Role

(1) Overall Treatment.

The treatment method of ITCWM for the prevention and treatment of respiratory diseases emphasize the integrity, and treatments start from all aspects of the front and side of the body, which enhances the therapeutic effect under its own specificity and overall effect, puts the disease under control and meanwhile prevents the disease from recurring.

(2) Scientific Selection of Drugs

The ITCWM to prevent and treat respiratory diseases employs both the decoction treatment method of TCM and the chemical synthetic drug treatment method of WM. It is able to coordinate two different treatment methods better, scientifically select drugs in accordance with the development of the disease, and avoid the defect of drug tolerance enhancement inside body out of long-term heterogeneous treatment.

(3) Maximum of the Drug Efficacy

Traditional Chinese medicine generally takes longer time to prove efficacious yet causes relatively minor harm, Western medicine is, otherwise, to get effects instantly but prove so potent and even formidable for organs to absorb so as to Incur a lot more side effects according to the diversity of drug ingredients. The ITCWM can, in contrast, maximize the efficacy of the drug while cutting down the negative effects caused by drugs abuse and inappropriate as much as possible.

(4) Dietetic Therapy

Dietetic therapy can be adopted in the ITCWM in the prevention and treatment of respiratory Diseases as well. Different dietary regulation or Dietetic regimen must be prescribed ad per the patient's condition, so as to strengthen the body constitution. For instances, clearing heat and dissipating phlegm, moisturizing the lungs, regulating the stomach and the other, recover and enhance function of body's natural defense mechanism through die, and thus to enhance immunity, improve the treatment effect, and prevent the recurrence of the disease to the utmost [4].

3.2 Value

(1) Physical Constitution Improvement

The elementary regulation of the patient's body is the kernel of prevention and treatment of respiratory diseases through the ITCWM, of which aim at multiple aspects such as exercise, diet, and psychology to treat. This method can, based on holistic harmony, increase the patient's body's overall coordination, immunity and body element balance, consequently improve the patient's body's resistance and resiliency, thereby ultimately achieving the goal of recovery.

(2) Restoration from Condition and Recurrence Prevention

ITCWM to prevent and treat respiratory diseases can formulate a series of selected optimal treatment plans oriented to different diseases, to achieve the goal of promptly managing the disease. It can not only control the disease, but also effectively prevent the reappearance of the disease, enhancing the therapeutic result by leaps and bounds. As for chronic respiratory diseases, TCM techniques such as acupuncture and massage can be exercised to minimize the recurrence of the disease, increase the cure rate, and reduce the disability rate of the disease.

(3) Reduction and Even Elimination of the Side Effects of Drugs

The ITCWM to prevent and treat respiratory diseases can maximize the therapeutic effect of drugs while minimizing the side effects of drugs, allowing patients to recover earlier with little negative impacts on the body. For long-term medication or chronic diseases requiring long-term treatment, the ITCWM's methods can minimize drug dose and avoid patients from adverse reactions to drugs [5].

With the ITCWM to prevent and treat respiratory diseases as a medical method, its practical value and role are of great significance, which has unique advantages that it can make full use of the functions of two different medical methods, alleviate the pain and side effects of patients, and at the same time prevent from developing drug tolerance through abuse of a drug or a treatment, and even from emerging mul-

tiple side effects. In a nutshell, the method of preventing and treating respiratory diseases by ITCWM is more humane, systematic, personalized, and green. The development of this method is bound to be a typical representative in the field of rehabilitation medicine.

Conclusion

The ITCWM for the prevention and treatment of respiratory diseases has been widely recognized by more and more of the medical community, patients and society. It not only shortens the treatment course, but also improves the treatment effect, reduces the recurrence rate of the disease, the development of drug tolerance and the appearance of drug side effects. The contribution of ITCWM in the treatment of respiratory diseases is notable, which effectively secures people's health and quality of medical service, alleviate some suffering from patients caused by treatment, and effectively prevents the recurrence of diseases. The active exploration should be encouraged in the field of medicine, combining traditional Chinese and Western medicine, continuously strengthen cooperation and exchange, to make greater contributions to the prevention and treatment of respiratory diseases. At the same time, the method of ITCWM should be promoted on end, expanding the field and depth of ITCWM in the prevention and treatment of respiratory diseases, to serve the people's welfare dedicated as always.

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Study On The Mechanism Of Jiedu Sanjie Recipe In The Treatment Of Liver Cancer Based On Network Pharmacology

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Abstract: Objective: to study the mechanism of action of Jiedu Sanjie Recipe in the treatment of Liver Cancer through network pharmacology. Method: Collect and screen the active ingredients of Jiedu Sanjie Recipe through the Traditional Chinese Medicine System Pharmacology Database and Analysis Platform (TCMSP), and search for the human target protein corresponding to the active ingredients in the database; screen out the target set of liver cancer-related diseases through GeneCards and OMIM database; construct a Venn diagram to obtain the key target of Jiedu Sanjie Recipe for treating liver cancer; use Cytoscape 3.8.0 software to construct drug-component-target-pathway network; use Cytoscape software and BisoGenet plug-in to construct protein interaction network, use CytoNCA plug-in and R language to perform network topology analysis, gene ontology functional annotation (GO) and KEGG rich Collect pathway analysis to understand the possible biological processes and pathways of Jiedu Sanjie Decoction in treating liver cancer. Results: A total of 89 active ingredients of Jiedu Sanjie Prescription, 170 targets and 1885 liver cancer targets were obtained; After mapping, 114 potential targets of Jiedu Sanjie Recipe for liver cancer are obtained, and the core active ingredients are quercetin, luteolin, kaempferol, wogonin, baicalein, etc.The core targets NTRK1, TP53, CUL3, ESR1, MCM2, etc., involving lipids and atherosclerosis, chemical carcinogenesis-receptor activation signaling pathways, Kaposi's sarcoma-associated herpes virus infection, fluid shear stress and atherosclerosis Cirrhosis, hepatitis C, AGE-RAGE signaling pathway, hepatitis B, human cytomegalovirus infection, cancer proteoglycan, TNF signaling pathway, IL-17 signaling pathway, etc.Conclusion: This study reveals the mechanism of the multi-component, multi-target, and multi-channel treatment of liver cancer by "Knowing Du Sanjie Decoction", and provides a basis for the clinical application of Chinese medicine prescriptions for liver cancer.

Keywords: Jiedu Sanjie Recipe; Liver Cancer; Internet Pharmacology; Mechanism of Action

Introduction

Liver cancer is a common malignant tumor in China, and in recent years, the incidence rate of liver cancer ranks the 4th and the fatality rate ranks the 2nd in China, which is a serious threat to the life and health of our people [1]. At present, the treatment of hepatocellular carcinoma by western medicine is mainly based on drug, immunization and surgery, which is not very effective for the long-term prognosis of patients. Traditional Chinese medicine has reliable efficacy and unique advantages in the clinical practice of treating hepatocellular carcinoma. With years of clinical experience, Professor. Hu Zhenbin created an empirical formula "Jiedu Sanjie Recipe" for hepatocellular carcinoma, which has been applied for many years in the Department of Liver Diseases of the First Affiliated Hospital of Guangxi University of Traditional Chinese Medicine. In this study, we investigated the mechanism of detoxification and knot-dissolving formula in hepatocellular carcinoma by using network pharmacology to provide further evidence to support the clinical application of detoxification and knot-dissolving formula.

1. Material And Methods

1.1 Screening Of Active Ingredients And Collection Of Target Data Of Jiedu Sanjie Recipe

The TCM Systematic Pharmacology Database and Analysis Platform (TCMSP) was searched to obtain Radix Bupleuri, Hedysarum Multijugum Maxim, Chuanxiong Rhizoma, Angelicae Sinensis Radix,Pseudobulbus Cremastrae Seu Pleiones, Agrimonia Eupatoria, Polyporus Umbellatus (Pers) Fr, Coicis Semen, Hedyotis Diffusae Herba, and Scutellariae Barbatae Herba in Jiedu Sanjie Recipe for their chemical composition and their associated ADME parameters. Based on the oral bioavailability (OB) OB ≥ 30% and drug-likeness (DL) DL ≥ 0.18,

the target proteins of the active ingredients of each traditional Chinese medicine were retrieved from TCMSP, de-emphasized and then integrated, and the data of the active ingredients and targets of the traditional Chinese medicines in Jiedu Sanjie Recipe were finally obtained.

1.2 Acquisition Of Information On Liver Cancer Targets

Based on GeneCards (https://www.genecards.org) and OMIM (https://www.omim.org) databases, we searched for liver cancer-related targets using “Liver cancer” as the keyword, de-emphasized them and integrated them to obtain a set of liver cancer targets.

1.3 Construction Of A Visualization Network For Jiedu Sanjie Recipe And Hepatocellular Carcinoma

Using R software, the above obtained targets of Jiedu Sanjie Recipe were mapped with liver cancer related targets to obtain the potential action targets of Jiedu Sanjie Recipe for the treatment of liver cancer, and the Wayne diagram was plotted. The dataset of active ingredients of traditional Chinese medicines and their target proteins were imported into Cytoscape 3.8.0 software, and the traditional Chinese medicine-active ingredient-target network was constructed using Cytoscape 3.8.0 software.

1.4 Target Network Analysis

Cytocsape 3.8.0 software and its BisoGenet plug-in were used to import common target genes to construct a drug-disease related PPI network, and CytoNCA plug-in was used to analyze the network topology as follows:1）Extraction of key network: The Degree Centrality (DC) values of the network targets were statistically analyzed, and the DC values were ranked according to the DC values from the largest to the smallest, and the target proteins with higher number of connecting nodes and tighter interactions were screened to construct the target interactions network, and the core network was constructed according to the distribution of the Betweenness Centrality (BC) values.Then, according to the distribution of the Betweenness Centrality (BC) value of each target, statistical analysis was performed again to obtain the core target, and network topology analysis was performed to construct the core network (see Figure 4);2）In order to investigate the physiological functional process of Jiedu Sanjie Recipe, the constructed core network was subjected to more GO enrichment analysis and KEGG pathway enrichment analysis by utilizing the R language and Bioconductor platform (http://bioconductor.org/biocLite.R), so as to explore the physiological functional process. R package installation in R language includes

#install.packages(“colorspace”),#install.packages(“stringi”),#install.packages(“ggplot2”),#install.

packages(“BiocManager”),#BiocManagerinstall(“DOSE”，#BiocManager install(“clusterProfiler”)， #BiocManager install(“enrichplot”) Get GO enrichment analysis table, KEGG enrichment analysis pathway plot, and get GO, KEGG enrichment analysis bubble and barplot were performed to investigate the biological process and signaling pathway of Jiedu Sanjie Recipe in the treatment of hepatocellular carcinoma.

2. Result

2.1 Bioinformatic Data Of Jiedu Sanjie Recipe

Through screening, the results of the chemical constituents of the herbs in the formula for detoxification and dispersal of knots were as follows: 349 from Radix Bupleuri, 89 from Hedysarum Multijugum Maxim, 189 from Chuanxiong Rhizoma, 125 from Angelicae Sinensis Radix,18 from Pseudobulbus Cremastrae Seu Pleiones,41 from Agrimonia Eupatoria,31 from Polyporus Umbellatus(Pers)Fr,38 from Coicis Semen,37 from Hedyotis Diffusae Herba,94 from Scutellariae Barbatae Herba. A total of 89 active ingredients were obtained after de-weighting, and 170 targets of action were obtained by excluding duplicate targets of action in the active ingredient targets and excluding non-human targets of action through standardization in the UniProt database (https://www.uniprot.org/).

2.2 Hepatocellular Carcinoma Target Data

Based on the international bioinformatics databases, a total of 16804 GeneCard and 450 OMIM targets were retrieved for allergic rhi-

nitis, and 1885 targets were screened and de-emphasized. The names of the retrieved targets were standardized to facilitate further research.

2.3 Wayne's Diagram Of Common Target Genes

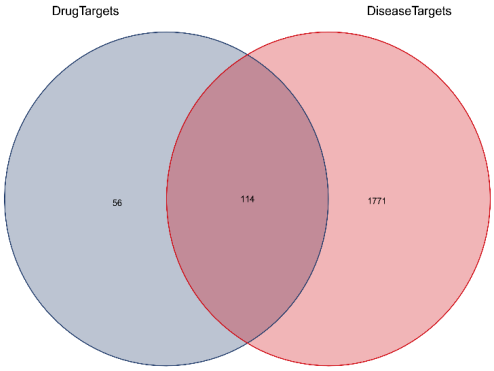

Figure 1 Wayne's diagram of the active ingredient targets of Jiedu Sanjie Recipe and liver cancer targets

Note: 170 active ingredient target genes and 1885 hepatocellular carcinoma target genes take the intersection to get 114 common target genes

2.3.1 Traditional Chinese Medicine-active Ingredient-target Network

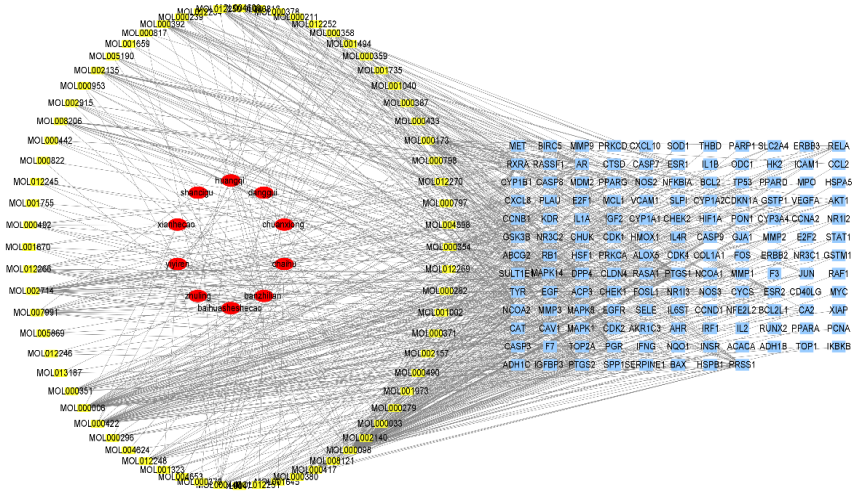

Figure 2 Chinese medicine-active ingredient-target network diagram

Note: The red circle in the figure indicates the traditional Chinese medicine, the square octagon indicates the active ingredient of the traditional Chinese medicine, and the blue rhombus indicates the target of the active ingredient.

Table 1 Ranking of degree values of active ingredients of Jiedu Sanjie Recipe

Ingredient ID	Ingredient Name	Source	Degree Value
MOL000098	Quercetin	Radix Bupleuri、Hedysarum Multijugum Maxim、Scutellariae Barbatae Herba、Agrimonia Eupatoria、Hedyotis Diffusae Herba	107
MOL000006	Luteolin	Scutellariae Barbatae Herba、Agrimonia Eupatoria	47
MOL000422	Kaempferol	Radix Bupleuri、Hedysarum Multijugum Maxim、Agrimonia Eupatoria	39
MOL000173	Wogonin	Scutellariae Barbatae Herba	30

MOL002714	Baicalein	Scutellariae Barbatae Herba	24
MOL000354	Isorhamnetin	Radix Bupleuri、Hedysarum Multijugum Maxim	19
MOL002135	Myricanone	Chuanxiong Rhizoma	17
MOL000392	Formononetin	Hedysarum Multijugum Maxim	17
MOL012250	7-hydroxy-5,8-dimethoxy-2-phenyl-chromone	Scutellariae Barbatae Herba	16
MOL000351	Rhamnazin	Scutellariae Barbatae Herba	16
MOL000378	7-O-methylisomucronulatol	Hedysarum Multijugum Maxim	16
MOL000417	Calycosin	Hedysarum Multijugum Maxim	16

As analyzed by Cytoscape software, the active ingredient Quercetin (107) possessed the most targets, followed by Luteolin (47), Kaempferol (39), Wogonin (30), Baicalein (24).From the perspective of the target of action, the top 5 targets of the linkage were Prostaglandin G/H Synthase 2 (PTGS2), Prostaglandin G/H Synthase 1 (PTGS1), Nuclear Receptor Coactivator 2 (NCOA2),Recombinant Protease, Serine 1 (PRSS1), Progesterone Receptor (PGR).

2.4 Network Topology Analysis, GO Enrichment Analysis And KEGG Enrichment Analysis

2.4.1 Network Topology Analysis

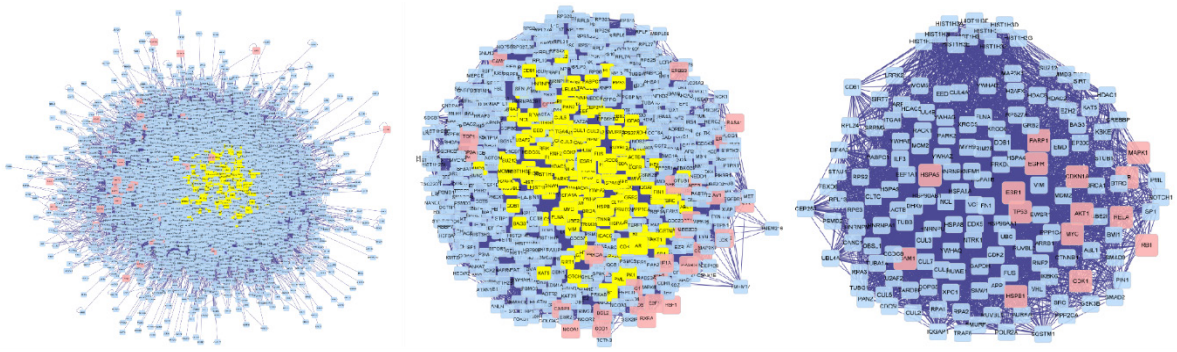

Figure 3 Network topology diagram

As shown in Figure 3, 114 common targets were uploaded to BisoGenet to construct a protein interaction network, where nodes denote proteins and edges denote correlations, involving a total of 5411 nodes and 134106 edges. Degree≥100 was selected as the key target by the number of gene interconnections, at this time, there were 663 nodes, and then the core target was screened by BC≥600 to construct the core network, and the top 5 targets were ranked by BC≥600.The core network was constructed, and the top 5 were: neurotrophic receptor tyrosine kinase 1 (NTRK1), tumor protein 53 (TP53), Cullin-3 (CUL3), estrogen receptor 1 (ESR1), and microchromosome maintenance complex component 2 (MCM2).

2.4.2 GO Enrichment Analysis

GO includes biological processes, molecular functions and cellular composition [2]. The GO analysis was performed on the core network, and the bar charts and barplot plots of the GO functional enrichment analysis of the top 10 molecular functions, cellular components, and bioprocesses were obtained after running the core network in R language, see Fig. 4. The results show that the therapeutic effects of detoxification and dispersal formula for liver cancer treatment in biological processes mainly involve cellular response to chemical stress, response to oxidative stress, response to drugs, response to nutrient levels, response to metal ions, response to lipopolysaccharides, response to molecules of bacterial origin, response to steroid hormones, cellular response to oxidative stress, response to reactive oxygen species, and so on; Cellular components are mainly involved in membrane rafts, membrane microregions, membrane zones, transcriptional regulatory com-

plexes, RNA polymerase II transcriptional regulatory complexes, organelle outer membranes, plasma membrane caveolae-like invaginations, protein kinase complexes, plasma membrane rafts, and cell cycle protein-dependent protein kinase holoenzyme complexes; The molecular functions mainly involve DNA-binding transcription factor binding, RNA polymerase II-specific DNA-binding transcription factor binding, ubiquitin-like protein ligase binding, cytokine receptor binding, nuclear receptor activity, ligand-activated transcription factor activity, transcriptional cofactor binding, repressor of transcription factor binding, steroid hormone receptor, and transcriptional coactivator binding.

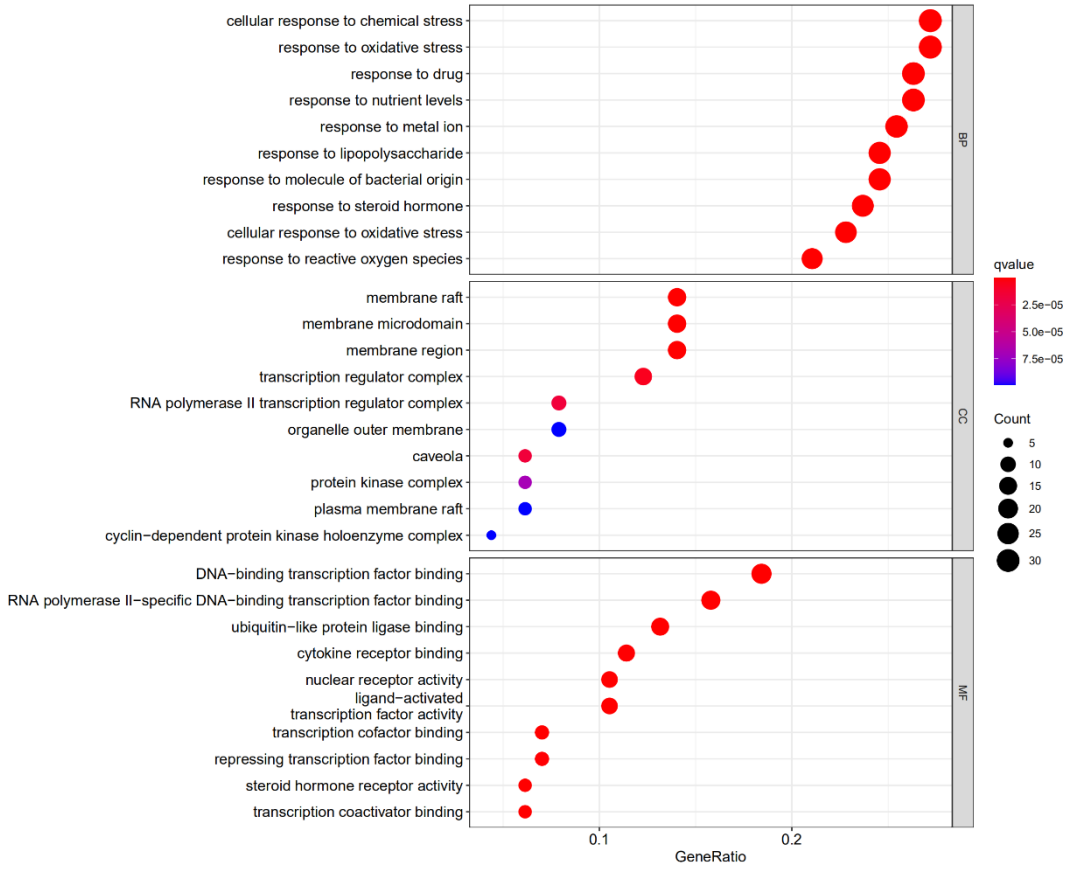

Figure 4 Functional enrichment of GO gene, a core target of Jiedu Sanjie Recipe for hepatocellular carcinoma treatment

Note: The size of the bubble area represents the number of genes enriched, and the color of the bubble represents the degree of significance, with the color ranging from blue to red, and the redder the color, the more significant the degree of significance. The redder the color, the more significant the degree.

2.4.3 KEGG Enrichment Analysis

The 114 intersecting targets were subjected to KEGG pathway enrichment analysis using the R language program, and 158 pathways were obtained after the run, and the results of the top 30 in terms of significance were obtained as bubble diagrams, see Fig. 5, with the vertical coordinates denoting the names of the pathways, the horizontal coordinates denoting the number of enriched genes, and the colors denoting the p-values, with the smaller p-values the redder the color and the higher the significance, and the bigger p-values the bluer the color, and the higher-significance network maps of the KEGG pathways and the associated target genes were obtained at the same time, see Fig. 6.

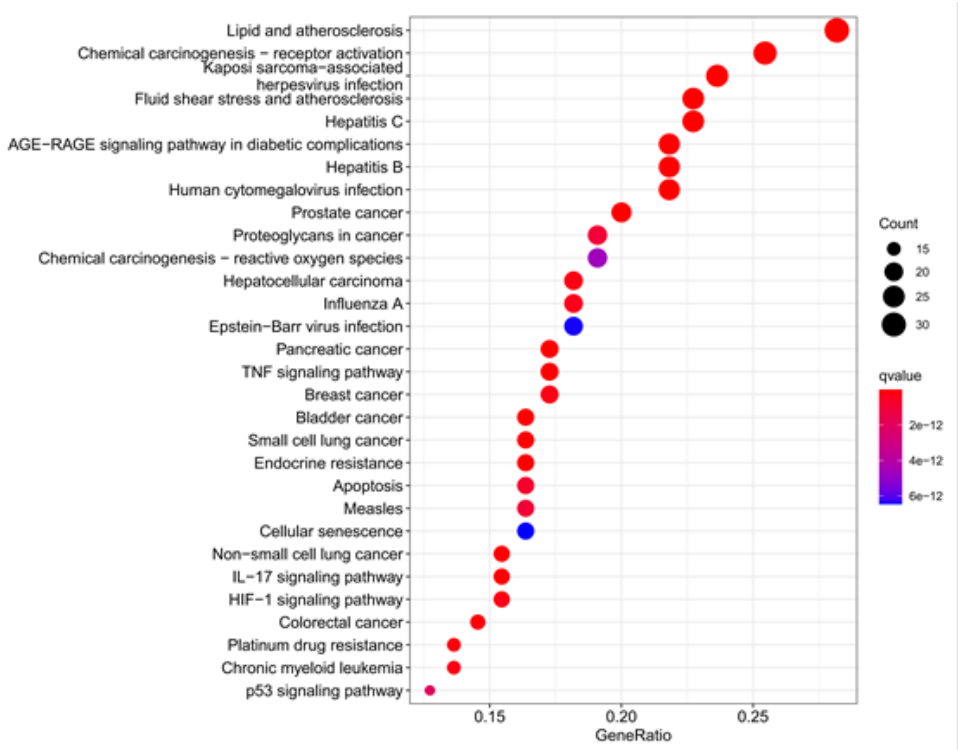

Figure 5 KEGG Enrichment Bubble Plot

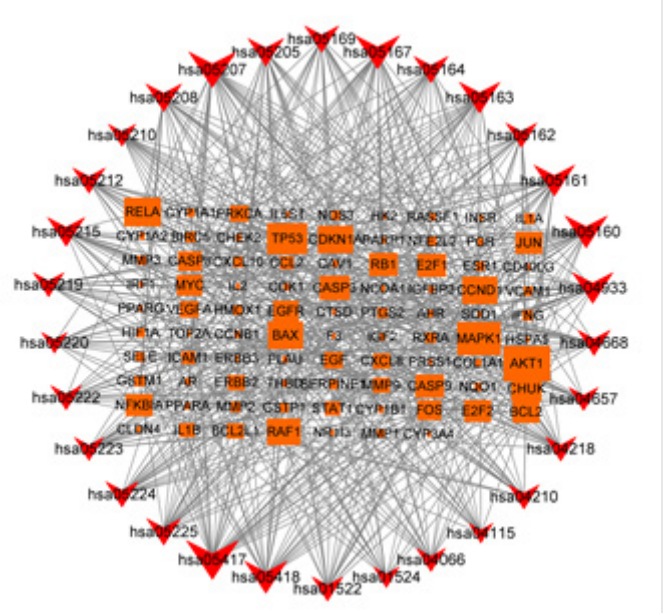

Figure 6 Relevant target gene-KEGG pathway map

The results showed that the key gene target pathways of Jiedu Sanjie Recipe for hepatocellular carcinoma mainly involved lipids and atherosclerosis, chemical carcinogenesis-receptor activation signaling pathway, Kaposi's sarcoma-associated herpesvirus infection, fluid shear stress and atherosclerosis, hepatitis C, AGE-RAGE signaling pathway, hepatitis B, human cytomegalovirus infection, proteoglycans in cancer, TNF signaling pathway, and IL-17 signaling pathway.

3. Conclusion

Currently, the pathogenesis of liver cancer is complicated. The vast majority of liver cancer patients have a history of chronic liver

disease, and the liver tissues of these patients are affected by various factors for a long period of time causing inflammation, which gradually develops into hepatic fibrosis, cirrhosis, and then develops into liver cancer. This paper analyzes the mechanism of Jiedu Sanjie Recipe for the treatment of hepatocellular carcinoma based on the method of network pharmacology, and provides a scientific basis for the subsequent in-depth study of Jiedu Sanjie Recipe.

The active ingredients Quercetin, Lignans, Kaempferol, Wogonin and Baicalein have the most abundant targets. Among the potential compounds, Quercetin is a common component of Radix Bupleuri, Hedysarum Multijugum Maxim, Scutellariae Barbatae Herba, Hedyotis Diffusae Herba and Hedyotis Diffusae Herba, which can exert anti-inflammatory effects by balancing Th1/Th2 and inhibiting the formation of antigen-specific antibodies [3], and also inhibit the proliferation of human hepatocellular carcinoma cells by inducing a TP53-non-dependent G2/M cell-cycle block as well as by promoting apoptotic cell death [4];

The Lignans enriched in Scutellariae Barbatae Herba and Agrimonia Eupatoria can inhibit the growth of hepatocellular carcinoma cells and exert antitumor effects by inhibiting the proliferation of hepatocellular carcinoma cells, blocking the growth cycle of hepatocellular carcinoma cells, inhibiting their angiogenesis, and inducing apoptosis of the cells [5]; Kaempferol is present in Radix Bupleuri, Hedysarum Multijugum Maxim, and Agrimonia Eupatoria, and can induce apoptosis in human hepatocellular carcinoma HepG2 cells via the mitochondrial pathway and the endoplasmic reticulum stress pathway [6]; Wogonin can exert antitumor effects by inhibiting the proliferation of human hepatocellular carcinoma cells [7]; Flavopiridol can inhibit the migration of human hepatocellular carcinoma cells and can cause them to undergo autophagy thus achieving anti-tumor effects [8].

NTRK1, TP53, CUL3, ESR1, and MCM2 were the target proteins with the highest number of connected nodes and the strongest interactions in the network topology analysis, in which the signaling pathways mainly involved in high-affinity nerve growth factor (NTRK1) were related to cell proliferation, inflammatory response, and inhibition of apoptosis; Tumor protein 53 (TP53), also known as P53, is an oncogene that is mainly involved in mitochondrial autophagy apoptosis in quercetin-regulated hepatic steatosis process [9]; Cullin 3(CUL3)plays an important role in a variety of cellular physiological processes, including cell cycle,cell proliferation and differentiation, and signal transduction; Microchromosome maintenance complex component 2 (MCM2) plays an important role in DNA replication and is mainly involved in suppressing tumor cell proliferation [10].

GO analysis shows that the cellular sites where the effect of detoxification and dispersal formula is exerted are structurally and functionally coherent, and that it exerts its therapeutic effect on hepatocellular carcinoma by participating in complex biological processes such as protein metabolism regulation process, enzyme-receptor binding process, and cellular response to chemical stresses.

The treatment of hepatocellular carcinoma by Jiedu Sanjie Recipe contains multiple pathways, which are related to lipid and atherosclerosis, chemical oncogenic-receptor activation signaling pathway, Kaposi's sarcoma-associated herpesvirus infection, hepatitis C, AGE-RAGE signaling pathway, TNF signaling pathway, and IL-17 signaling pathway according to KEGG enrichment analysis. Among other things, AGE is associated with a variety of diseases including diabetes, vascular disease, aging, kidney disease and tumors. Numerous studies have shown that AGE can induce a series of inflammatory responses by activating NF-κB, causing it to rapidly phosphorylate, and by regulating gene transcription. In addition, signaling pathways related to cell proliferation and apoptosis are activated through the binding of AGE and RAGE to participate in tumor cell proliferation, apoptosis, autophagy, invasion and distant metastasis [11]. Jiedu Sanjie Recipe can also play a therapeutic role by regulating TNF signaling pathway, IL-17 signaling pathway, HIF-1 signaling pathway, p53 signaling pathway and so on. The TNF signaling pathway regulates important biological activities such as immune response, inflammatory response, apoptosis and tumorigenesis. It has been found that the interaction of TNF-α with its ligand TNFR is involved in the development of cancer disease. IL-17 is an inflammatory factor secreted by Th17, which can activate a variety of immune cells to secrete inflammatory regulatory factors and play an important role in the body's immune response, which can lead to sustained inflammation and liver damage, so elevated IL-17 is positively correlated with the occurrence and development of hepatocellular carcinoma [12]. Hypoxia-inducible factor (HIF-1) consists of two subunits, α and β, and is a transcriptional regulator expressed in the cell nucleus. HIF-1α is highly expressed in a variety of tumors, and positively correlates with the hypoxic level of tumors, which promotes the regulation of the homeostasis of the intra-tumor environment by VEGF in the hypoxic microenvironment of tumors, stimulates the growth of tumor blood vessels, and promotes the massive growth and proliferation of

tumor cells [13]. Inhibition of the activity of the P53 signaling pathway can maintain the activation of various tumor cytological behaviors such as malignant proliferation, apoptosis inhibition, and invasion and metastasis in hepatocellular carcinoma cells, which in turn provide opportunities for hepatocellular carcinoma development [14]. It can be concluded that Jiedu Sanjie Recipe can play an anti-tumor role by inhibiting the expression of multiple pathways and blocking their signaling pathways.

In summary, relevant basic research in modern medicine has shown that Radix Bupleuri, Hedysarum Multijugum Maxim, Angelicae Sinensis Radix, Coicis Semen, Hedyotis Diffusae Herba and Pseudobulbus Cremastrae Seu Pleiones have powerful anti-tumor effects. Based on network pharmacodynamics, this study explored the potential mechanism of Jiedu Sanjie Recipe for the treatment of hepatocellular carcinoma, which, to a certain extent, illustrated that Jiedu Sanjie Recipe can treat hepatocellular carcinoma with multi-targets and multi-pathways, and provided the basis for in-depth elucidation of the material basis and mechanism of action of Jiedu Sanjie Recipe in the treatment of hepatocellular carcinoma, which provides more possibilities for the treatment of hepatocellular carcinoma in clinic.

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Universe
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Pulmonary Artery CTA and CT Abdominal Plain Enhancement One-Stop Scanning Methods and Application Value

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Abstract: Objective: To investigate the feasibility and application value of one-stop scanning method of CTA angiography of pulmonary artery and plain abdominal enhancement. Methods: In the following study, a total of two patients were selected from our hospital to undergo CTPA and plain abdominal enhancement scanning, and the feasibility of one-stop scanning was investigated by analyzing the examination parameters of the two patients. Results: The one-stop scanning method of pulmonary artery CTA and CT abdominal plain enhancement can provide accurate clinical information, shorten the examination time and reduce the use of contrast agents after parametric and clinical evaluation.

Keywords: Pulmonary Artery CTA; One-Stop Scanning Imaging; Pulmonary Embolism

1. Introduction

With the development and progress of science and technology, “one-stop” scanning and imaging has become the mainstream scanning method, how to ensure the image quality and diagnostic requirements, as well as to ensure the safety of the patient under the premise of saving the scanning time, reduce the dose of contrast medium, reduce the patient’s examination cycle has become the need to consider the matter of each technician teacher. The present study focuses on the feasibility and application value of CTPA and CT abdominal plain enhancement one-stop scanning method.

2. Information

In this study, the data of one patient with pulmonary artery CTA and one patient with CT abdominal plain enhancement were extracted from the patients examined in our hospital for comparative analysis.

The patient with pulmonary artery CTA (hereinafter referred to as patient A) is a 68-year-old man who came to our hospital for treatment of a right lung space-occupying lesion, with the following clinical diagnosis: right lung space-occupying lesion; right lung patchy shadow: tumor? Other? Lung infection: CT abdomen plain enhancement Patient (hereinafter referred to as Patient B) Male, 81 years old, came to our hospital for treatment of esophageal malignant tumor, clinical diagnosis history: esophageal malignant tumor.

3. Methods

3.1 Before performing the enhanced examination, first of all, the enhanced scanning conditions should be available: contrast infusion facilities are: high-pressure syringes, syringes, infusion devices. High-pressure syringe can be used single or double barrel, no high-pressure syringe hospitals can use ordinary syringe hand-push method or air-pressurized intravenous drip method for CT enhancement scanning. Rescue care facilities: (1) staffing: CT room personnel in addition to physicians and technicians (need to have a license), must be equipped with nurses (need to have a license), with a certain degree of first aid and cardiopulmonary resuscitation ability of nurses is particularly suitable for work in the CT room. (2) First aid cart: first aid medicines, syringes, infusion sets, wheels, oxygen tubes and blood pressure monitors should be placed in order in the first aid cart. (3) Oxygen cylinder, oxygen bag, if there is a central oxygen supply CT room should be equipped with connecting tube. (4) Emergency green channel: Due to the limited resuscitation facilities and resuscitation ability of CT room, when allergic reaction occurs, while actively resuscitating the patient, we should simultaneously ask the emergency room of the hospital or the related clinical departments for assistance, and escort the patient to the emergency center as soon as possible if necessary. Therefore, a green channel for allergy rescue between CT center, emergency center, cardiology, respiratory medicine, anesthesiology and other related departments should be established. [1]

The CT model selected for patient A was the UCT860 256-slice spiral CT of UNION, and the [Pulmonary CTA] examination sequence was chosen, with a collimation width of 80 mm, a pitch of 0.8938, a rotation time of 0.5 S, a minimum layer thickness of 0.5 mm, a dose of 120 KV, and a contrast agent of [iodophorol] (100 ml/74.1 g). During scanning, the monitoring layer was placed at the pulmonary artery, with a detection threshold of 80 HU, the first phase of the pulmonary artery phase, with a trigger time of 5-6 seconds (see below for the monitoring map), and the scanning time was about 10-15 seconds after the injection of the contrast agent, the second phase was the late arterial phase, and the scanning was performed immediately after the end of the scanning of the pulmonary artery phase, which showed a partially strengthened portal vein; all the structures of arterial supply were shown optimally. The scan time is approximately 20-25 seconds after contrast injection.

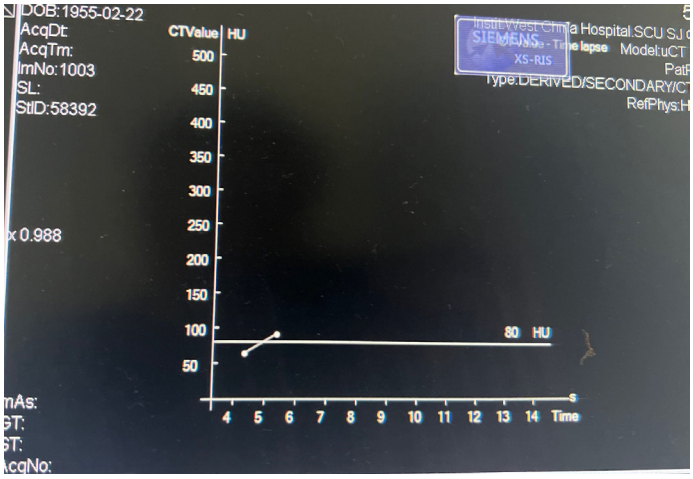

Figure 1:The patient A's Monitoring charts

The CT model selected for patient B was the UCT860 256-slice spiral CT with [Abdomen C] examination sequence, collimation width of 80 mm, pitch of 0.9937, rotation time of 0.5 S, minimum layer thickness of 0.5 mm, dose of 120 KV, and contrast agent of [iophorol] (100 ml/74.1 g). During scanning, the monitoring layer was placed at the descending aorta with a monitoring threshold of 210 HU, and the detection started after 10-12 seconds, with a trigger time of about 15 seconds (see below for the monitoring map), plus the breathing preparation and scanning time, which was approximately 18-25 seconds after contrast injection.

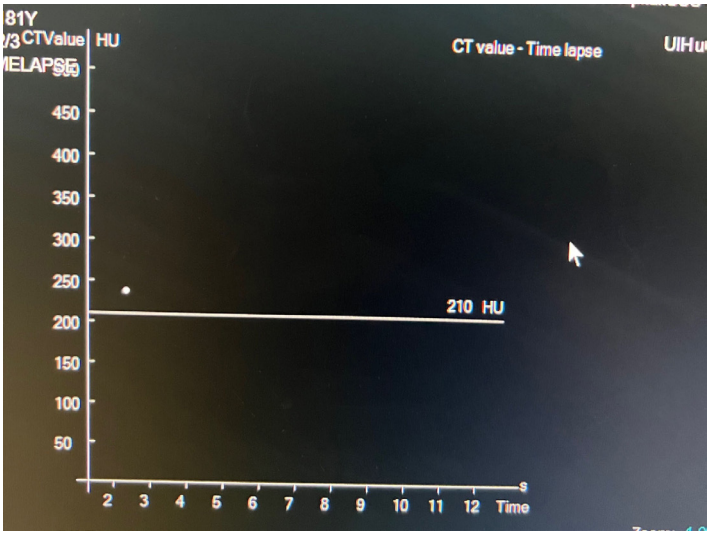

Figure 2:The patient B's Monitoring charts

3.2 "One-stop" scanning: Assuming that patient C wishes to undergo both "CTPA" and CT abdominal plain enhancement, the sequence can be changed to a first pulmonary phase, with the monitoring layer placed at the pulmonary artery, and the scanning of the chest, resulting in the pulmonary artery being visualized by the contrast and the aorta not being visualized. The aorta is not visualized. The second phase is

the aortic phase, which is scanned immediately after the completion of the first phase and covers the chest plus the abdomen, with an approximate scan time of about 20 seconds after contrast injection, resulting in visualization of both the aorta and the pulmonary arteries. The third phase is the venous phase, which takes about 1 minute and 10 seconds and covers the entire abdomen. The result is visualization of the veins.

4. Discussions

Pulmonary CTA has good clinical diagnostic significance for patients with pulmonary artery embolism. Among 31 patients with pulmonary artery embolism taken from the relevant literature, the presence of lobar and segmental pulmonary artery embolism accounted for 64.52%, the presence of segmental and subsegmental pulmonary artery vascular embolism accounted for 32.26%, the presence of embolism of both sides of the lower pulmonary arterial trunks accounted for 35.48%, and the presence of embolism of the left pulmonary arterial trunks and the right The percentage of embolization in the main trunk of left and right pulmonary arteries was 29.03%, and the percentage of embolization in segmental and subsegmental pulmonary arteries only was 19.35%. In 17 cases, the improvement rate of pulmonary embolism was 58.82%, and the thrombus clearance rate was 41.18% when the pulmonary artery CTA was performed again after 1 month to 6 months of treatment. Therefore, in the clinical diagnosis and outcome assessment of patients with pulmonary artery embolism, adopting the method of pulmonary artery CTA examination can get better results. [2] And the accuracy rate of enhanced CT in diagnosing abdominal tumors in patients (90.74%) was significantly higher than that of conventional CT diagnosis (72.22%), and the difference between the two groups was statistically significant ($P<0.05$). The accuracy of enhanced CT in diagnosing abdominal metastasis of the patient's tumor was significantly higher (94.44%) than that of CT (72.22%), and the difference between the two groups was statistically significant ($P<0.05$). The length of implant foci, width of implant foci and minimum area of implant foci in patients detected by enhanced CT were smaller than those detected by CT, and the difference between the two groups was statistically significant ($P<0.05$). Therefore, enhanced CT has good effect in diagnosing intra-abdominal metastasis of tumors in patients with abdominal tumors, which can well determine the tumor foci and metastasis status of patients, and can detect smaller tumor tissues, which has high clinical application value. [3] Since the two patients use the same concentration of contrast agent and the scanning time is approximately the same, after diagnosis and clinical assessment of the effect of the diagnostic criteria, at the same time, it can greatly reduce the amount of contrast agent, shorten the examination cycle, saving time and economic costs for patients, if there is a need for the two kinds of examination to be carried out at the same time, it can be popularized and used.

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Severe Myelosuppression Induced by Piperacillin/Tazobactam: A Case Report

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Abstract: This case report presents an elderly patient who developed severe bone marrow suppression following the administration of Piperacillin/Tazobactam. The patient exhibited a declining trend in platelet and white blood cell counts during Piperacillin/Tazobactam treatment. Subsequently, upon discontinuation of Piperacillin/Tazobactam, platelet and white blood cell counts gradually increased. Negative drug allergy test results and the absence of evidence for bone marrow suppression caused by platelet antibodies or other drugs led to the consideration of the possibility of immune-mediated bone marrow suppression induced by Piperacillin/Tazobactam. This report emphasizes the importance of close monitoring of hematological parameters to mitigate the risk of bone marrow suppression during the clinical use of Piperacillin/Tazobactam.

Keywords: Piperacillin/Tazobactam; Myelosuppression; Adverse Drug Reaction

Introduction

Piperacillin is a semi synthetic penicillin antibiotic, while tazobactam serve as a β- Lactam enzyme inhibitor. The combined use of Piperacillin/Tazobactam can cover most gram-positive and gram-negative bacteria (especially Pseudomonas aeruginosa), and Piperacillin/Tazobactam has high safety, which is the most commonly used antibacterial drug for hospital infection [1,2,3]. The most common adverse reaction of piperacillin is diarrhea [4]. Hematological abnormalities are serious adverse reactions of piperacillin and tazobactam, and symptoms such as leukopenia and thrombocytopenia have been reported in relevant case reports after the use of piperacillin [4,5,6]. Here, we report a case of severe thrombocytopenia caused by the use of piperacillin tazobactam. After the application of anti allergic therapy and discontinuation of piperacillin tazobactam, platelets and white blood cells rapidly rebounded. This report reminds us that for patients who use Piperacillin/Tazobactam, regardless of whether the skin test results are negative, hematological parameters should be closely monitored.

Case report

On December 28, 2022, a 78-year-old male patient was admitted to the Tumor Treatment Center of Traditional Chinese Medicine at our hospital. He presented with a persistent cough lasting for 14 days and worsening asthma and fatigue over the past 7 days. The patient had a medical history of hypertension and a previous appendectomy. He denied any prior history of drug allergies. Upon admission, the patient's vital signs were as follows: body temperature of 36.3 ℃, pulse rate of 76 beats per minute, blood pressure measuring 118/73 mmHg. The patient was alert and oriented, and physical examination revealed prominent breath sounds in both lung fields, with a few crackles in the lower lung regions. No other positive findings were noted during the remaining physical examination.

Additional investigations yielded the following results: A chest computed tomography (CT) scan revealed multiple inflammatory changes in both lung fields. The complete blood count indicated a white blood cell count of 5.92 × 10^9/L, with a differential count showing 82.5% neutrophils and a platelet count of 222 × 10^9/L. C-reactive protein (CRP) was elevated at 21.33 mg/L, and the partial pressure of oxygen measured 79 mmHg. Furthermore, the novel coronavirus antibody test returned a positive result.

In response to the patient's condition, a treatment regimen was initiated. Piperacillin/Tazobactam (Zhuhai United Laboratories, batch number: 28083201) was administered at a dosage of 4.5g every 8 hours to address the infection. Moreover, the patient received dexamethasone sodium phosphate (6mg) to manage inflammation and asthma symptoms. Esomeprazole was prescribed for acid suppression and gastric protection. The patient also underwent low-flow oxygen inhalation (3-5 L/min) to enhance oxygenation. In addition, the patient was administered an oral traditional Chinese medicine decoction known as Maxing Shigan Decoction. On January 5, 2023, the patient's cough and asthma symptoms improved compared to before. The blood routine examination showed that white blood cells were 7.94 * 10 ^ 9/L, neutrophil

percentage was 77.8%, platelet count was 171 * 10 ^ 9/L, and CRP results showed no abnormalities. The blood gas analysis showed oxygen partial pressure was 77mmHg, and the coagulation test showed no abnormalities. Therefore, dexamethasone and esomeprazole were discontinued, and piperacillin tazobactam was continued to be used according to the course of treatment.

On January 10, 2023, a blood routine examination revealed that the patient's white blood cell count was 3.69×10^9/L, with a neutrophil percentage of 65.9%, and a platelet count of 46×10^9/L.

The patient was suspected to be allergic to piperacillin and tazobactam, prompting an immediate cessation of the medication. Subsequently, the patient received a 25mg intramuscular injection of promethazine hydrochloride, and cetirizine hydrochloride was administered orally as an antiallergic agent. A consultation with the hematology department was sought, which strongly suspected drug-induced thrombocytopenia. However, other hematological conditions could not be definitively ruled out. Therefore, a comprehensive workup was recommended, including an enhanced evaluation of antinuclear antibodies, antiplatelet membrane glycoprotein autoantibodies, and consideration of a bone marrow puncture. The patient was prescribed 0.3g of caffeic acid tablets three times a day for oral platelet elevation treatment, following the consultation's guidance. The patient adhered to the recommendations and exhibited no abnormalities in subsequent evaluations of antinuclear antibodies and antiplatelet membrane glycoprotein autoantibodies. However, the patient declined to undergo a bone marrow puncture procedure. Throughout this period, the patient continued to take the traditional Chinese medicine decoction orally. Daily blood routine examinations showed a progressive increase in platelet counts, coinciding with the gradual resolution of the skin rash.

On January 16, 2023, a blood routine examination revealed that the patient's white blood cell count had risen to 5.08×10^9/L, and the platelet count was measured at 108×10^9/L. A chest CT examination indicated a reduction in the extent of inflammation in both lungs, with certain lesions exhibiting decreased density compared to previous scans. As a result of these positive developments, the patient's treatment with caffeic acid tablets was discontinued, and he was subsequently discharged from the hospital.

On January 25, 2023, during a follow-up appointment, the patient's blood routine revealed a platelet count of 156×10^9/L, indicating a further improvement in platelet levels after discharge.

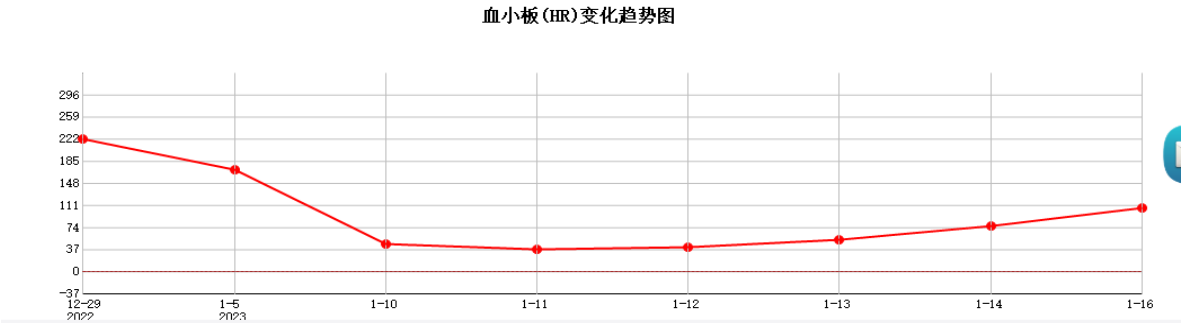

Figure 1: Platelet changes

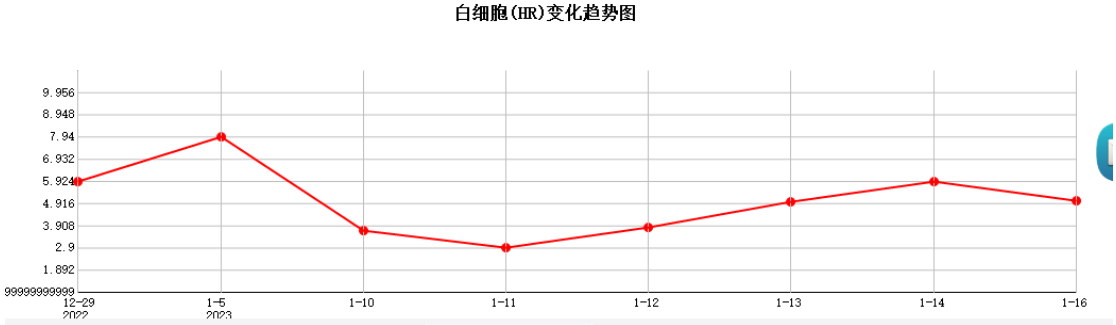

Figure 2: Changes in white blood cells

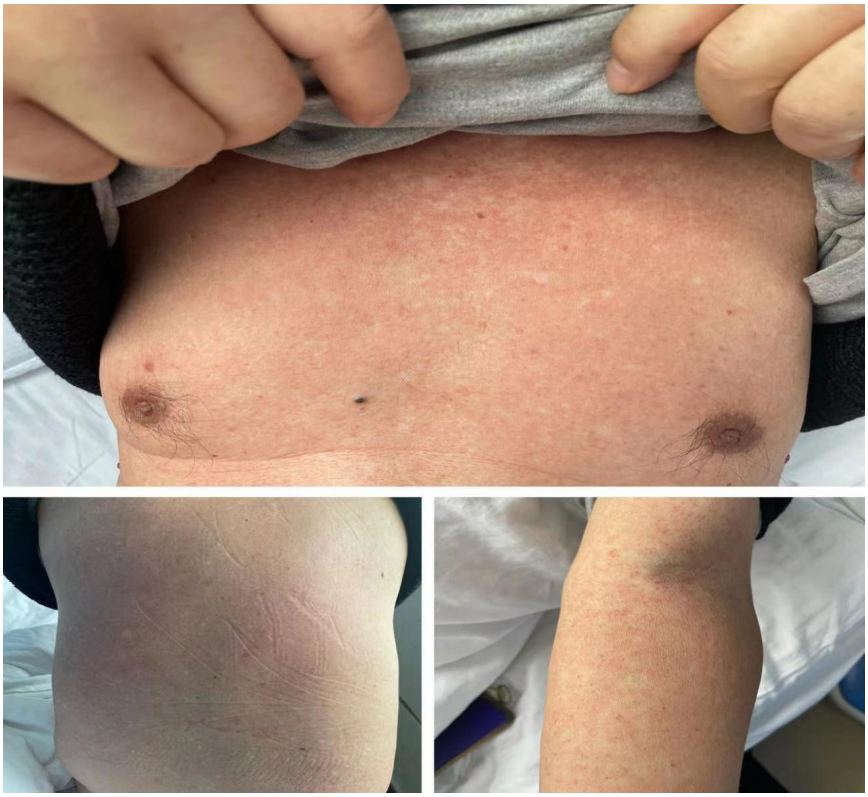

Figure 3 Rash situation of the patient

Discussion

This case report presents an elderly man who developed severe bone marrow suppression following the administration of Piperacillin/Tazobactam. The predominant manifestations included thrombocytopenia, accompanied by leukopenia and allergic skin reactions. Notably, the patient experienced severe thrombocytopenia on the 14th day of Piperacillin/Tazobactam treatment, followed by the onset of allergic skin reactions on the 15th day. Discontinuation of Piperacillin/Tazobactam and the introduction of anti-allergic medications led to significant improvements in both bone marrow suppression and skin reactions.

Throughout the treatment course, both dexamethasone and esomeprazole were administered, and it's noteworthy that neither of these medications showed any indications of adverse reactions related to bone marrow suppression in their respective instructions or within existing literature reports. Simultaneously, due to the patient's positive novel coronavirus antibody status, we advised oral intake of Maxing Shigan Decoction, a traditional and well-established Chinese herbal prescription containing ephedra, almond, gypsum, and licorice. Notably, our review of research reports on the application of Maxing Shigan Decoction did not reveal any hematological-related adverse reactions [7,8].

It's important to highlight that bone marrow suppression resulting from the use of Piperacillin/Tazobactam is a rare and severe adverse reaction, with reports indicating that such adverse events typically manifest between days 11 and 17 of treatment [4]. The most commonly observed hematological abnormality in these cases is a reduction in both neutrophils and platelets [9]. As of now, there is a paucity of research investigating the precise mechanisms underlying bone marrow suppression triggered by Piperacillin/Tazobactam. Nonetheless, some studies have proposed a positive correlation between the cumulative dose of Piperacillin/Tazobactam and bone marrow toxicity [10], with higher dosages and longer durations of treatment increasing the likelihood of hematological adverse reactions. It is pertinent to note that thrombocytopenia may arise from either bone marrow suppression or immune-mediated platelet destruction [6]. The patient received dexamethasone intervention during the early stages of treatment, resulting in a gradual decrease in platelet counts and an upward trend in white blood cell counts. Following the discontinuation of dexamethasone, platelet and white blood cell counts experienced a sudden decrease, accompanied by the onset of allergic skin reactions. These observations indirectly hint at the possibility of immune-mediated bone marrow suppression.

Therefore, in clinical application of Piperacillin/Tazobactam, especially in patients with high-dose and long-term use, it is necessary to closely monitor hematological related indicators and be vigilant for the occurrence of bone marrow suppression.

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