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ORIGINAL ARTICLE

Current Situation of TCM Treatment of Schizophrenia

Chen Lin*

Wenzhou Medical University, Wenzhou 325035, China. E-mail: 937391056@qq.com

Abstract: Schizophrenia is a common clinical disease in the department of psychiatry. Traditional Chinese medicine treatment of schizophrenia has a long history, rich experience, small side effects, to a certain extent can alleviate the condition of patients with schizophrenia. This article reviews the current situation of TCM treatment of schizophrenia in recent years from three aspects: TCM treatment, acupuncture treatment and catgut embedding treatment.

Keywords: Schizophrenia; TCM Treatment

Schizophrenia is a common cause of unknown serious mental illness, with greater social harm. There is no "schizophrenia" in the ancient Chinese medicine literature, according to its clinical manifestations, it is classified as "epilepsy" category. With the rapid development of society and the continuous increase of people's mental pressure, the incidence of schizophrenia is on the rise[1]. Due to the high safety of TCM treatment, the majority of patients will accept and choose this method to treat schizophrenia.

1. Understanding of schizophrenia in Chinese medicine

Both epilepsy and mania are clinical manifestations of mental disorders. The textbook of the tenth edition of Internal Medicine of Traditional Chinese Medicine (edited by Boli Zhang and Mianhua Wu) has a clear definition: epilepsy is characterized by mental depression, indifferent expression, silence, incoherent speech, quietness and inactivity. Crazy syndrome is characterized by mental excitement, manic rigid violence, disturbance and restlessness, destruction, beating and swearing, and more anger. The two clinical symptoms coexisting cannot be completely separated, so they are called madness. The earliest written records of diseases related to madness can be found in the Book of History, Weizi, written in the late Yin Dynasty (about the 11th century BC). The first name of madness is found in the Huangdi Neijing, which has a systematic description of its symptoms, etiology, pathogenesis and treatment. For example, in "Su Wen • Pulse to Subtle", clothes are not collected, words good and evil, do not avoid friends and relatives, this god's chaos. Describes the symptoms of the patient at the time of onset; in terms of the pathogenesis of madness, "all manias belong to fire" in the book "Su Wen • On the Importance of Truth" describes that the evil fire and the heart can cause the disease. "Yang Qi is on the top, Yin Qi is on the bottom, the bottom is empty and the top is solid, so it is called crazy disease" in Su Wen·Mai Jie, which describes that the imbalance of Yin and Yang can cause disease. "Su Wen·Tiao Jing Lun" in "more blood, then anger, lack of laughter", describes the disorder of qi and blood can cause disease. In "The Madness of

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Lingshu", "The of Hunger", "The Great Fear of Gain", "The Great Joy of Gain", and in "Su Wen • Strange Disease", "People born with a disease, what is the name of the disease, and what is it ?" Qi Bo said, "The disease is called fetal disease. When the disease is acquired in the womb, the mother is somewhat shocked." In Su Wen·Xuanming's Five Qi Theory, "The five evils are disordered; when the evils enter the Yang, they are mad; when they beat the Yang, they are epileptic.", "Su Wen • On the Alternation of Qi", "The fire is too hot in the New Year, the heat is popular illness and delirium." and so on respectively from the sentiment, the innate heredity, the exogenous pathogenic factors, the seasonal and so on discussed the madness disease etiology. "Su Wen • Disease can discuss" in "How cure ? Qi Bo said: take actually already make it drink pig iron." and so on discussed the treatment of madness[2].

2. Traditional Chinese medicine treatment

Traditional Chinese medicine has certain effect in the treatment of schizophrenia. Chenxia Liu, *et al*.[3] selected 60 patients with chronic schizophrenia and randomly divided them into 2 groups with 30 patients in each group. Patients in the treatment group alone were treated with aripiprazole; the combined treatment group was given traditional Chinese medicine decoction on the basis of the single treatment group. Specific prescription of TCM decoction: Poria cocos 15g, Pachyrhizus 12g, Radix Bupleuri 10g, Rhizoma Chuanxiong 10g, Pinellia tuber 10g, rehmannia root 10g, jujube seed 10g, Yuanzhi 10g, Xiangfu 10g, peach kernel 10g, Dannanxing 10g, tangerine peel 10g, Paeonia lactiflora 10g, liquorice 10g. Decocted in water for oral dose, 1 dose/d, 2 times/d, 4 weeks for a course of treatment, a total of 3 courses of treatment. After 6 and 12 weeks of treatment, SQLS score of patients in the group of TCM decoction combined with aripiprazole was significantly lower than the group of aripiprazole alone, indicating that TCM decoction combined with aripiprazole could significantly improve patients' sense of self-efficacy and improve the quality of their life. Shuhua Wu[4] randomly divided 60 patients into the control group and the observation group with 30 patients each. Sulpiriol 200mg was taken orally twice a day in both groups. Eight weeks is a course of treatment. The observation group was treated with traditional Chinese medicine. Take 1 dose daily, decocted in water for 3 times, for a course of treatment for 15 days, take 2 courses continuously. The total effective rate of the observation group was 96.7%. The total effective rate of the control group was 80.0%. The difference of total effective rate between the two groups was statistically significant ($P < 0.05$). The results showed that the combined treatment of traditional Chinese and western medicine plays a role in mending depression, not only improves the clinical cure rate, but also reduces the adverse drug reactions. Jinming Huang[5] self-designed clam the nerves and control epilepsy soup (American ginseng, Fushen, fried jujube seed, white peony root, dens draconis, pig iron fall, etc.) has the effect of soothing the nerves and nourishing brain, dispersing liver and relieving depression, and dredging collaterals and relieving phlegm. He thinks the syndrome of asthenia in origin and asthenia in superficiality and the treatment of symptoms and causes should be taken into comprehensive consideration. After 3 courses of treatment, 12 of the 32 patients were cured, with a total effective rate of 93.75% and a cure rate of 37.5%, and no side effects, which were easily accepted by the patients.

3. Acupuncture treatment

3.1 Acupuncture treatment

Guimei Zhao[6] reported the clinical effect of acupuncture combined with low-dose antipsychotics in the treatment of schizophrenia. A total of 50 patients were compared before and after treatment. Acupuncture at these points: Baihui, Shenting, Shangxing, Fenglong, Taichong, Shenmen, Sanyinjiao, Shanzhong, GuanYuan, in addition, connected to the electroacupuncture instrument, 30 mins each treatment, 3 times a week, the treatment course is 4 months. During the treatment with conventional low-dose clozapine. After treatment, the total score of positive and negative symptom scale (PANSS), negative scale and general psychopathology scale and Hamilton anxiety scale (HAMA) were significantly reduced, and the differences were significant at different time points ($P < 0.05$). It shows that it can improve mental symptoms and relieve anxiety. Wei Liang[7] reported that acupuncture has a good effect on patients with chronic schizophrenia. A total of 58 patients were se-

lected and randomly divided into the control group and the observation group. The control group received oral olanzapine alone, while the observation group received combined acupuncture treatment (Taichong, Renzhong, Dazhui, Daling, Quchi, Fengfu, Neiguan and Fenglong). Acupuncture treatment was performed once a day for 30min each time and the course of treatment was 8 weeks. After treatment, two groups of patients of SOD (superoxide dismutase) and MDA (malondialdehyde) levels drop, GPX (glutathione peroxidase) activity decreased, alzheimer's disease pathological behavior evaluation form (BEHAVE-AD) scores are to a certain extent reduce the immune indexes such as CD3 +, CD4 +, CD8 +, IgG and so on which levels are rising to a certain extent. The indicators in the observation group of patients with optimal range are more obvious. There were significant differences between the two groups ($P < 0.05$). It shows that acupuncture can improve oxygen free radical metabolism, harsh immune resistance, and thus improve the symptoms of patients. Jihong Wu[8] believed that through dialectical application of needles and combined use of various points, the effect of strengthening the spleen, regulating qi and eliminating phlegm, and awakening the mind and preventing insanity could be achieved. Take the main acupoints: Renzhong, Yamen, and Dazhui; with auxiliary acupoints to take Baihui, Sishencong, Neiguan, Shenmen, Zhongyuan, Fenglong, Taichong, etc, once a day, 10 times for a course of treatment. The total effective rate was 95.45%. Wei Zheng, *et al*.[9] believed that acupuncture could improve the cognitive function of patients with chronic schizophrenia. Seventy patients were selected and divided into acupuncture group and control group. The control group took antipsychotic drugs before entering the group and maintained the effective dose unchanged. At the same time, the acupuncture group combined acupuncture on the basis of the control group and took four magic needles, Neiguan (double), Sanyinjiao (double), Yintang points and other points. Each treatment lasted for 30min, 5 times per week, 10 times for 1 course of treatment, a total of 6 weeks. There were statistically significant differences in WMS memory quotient, DST total net points, error rate and WCST persistent error between the two groups after treatment (all $P < 0.05$).

3.2 Acupoint catgut embedding therapy

Haifang Zhu, *et al*.[10] randomly divided 90 schizophrenic patients into 2 groups. Risperidone oral liquid was used to treat schizophrenia in the control group, and traditional Chinese medicine wire embedding method was used in the observation group. Buried line selected in the Shanzhong, Zhongwan, Zhongji, Guan Yuan, Baihui, Dazhui, Shenting, Yaoyangguan, Mingmen, Jizhong and so on acupoints. Once buried in 15 days and 3 times as a course of treatment. The control group patients with negative symptoms (SANS) score and brief psychiatric scale (BPRS) scores, Hamilton depression scale (HAMD) score and side effect scale (TESS) score were higher than the patients of the observation group, the difference was statistically significant, that the embedding thread therapy of traditional Chinese medicine in the treatment of negative symptoms of schizophrenia clinical curative effect is good. Yazhi Lv[11] used "embedding thread and adjusting mind" to treat schizophrenia at Jiaji points of Huatuo, which is located at the 1st to 7th thoracic vertebrae, and the 4th and 5th lumbar vertebrae to the 1st sacral vertebra. This method proved to be satisified. Shian Li, *et al*.[12] selected 52 schizophrenic patients and treated them every 30 days, including Fengchi (double), Dazhui, Jinsuo, Jiu Wei, Shenshu (double), Sanyinjiao (double) and Yongquan (double), once a month for four months as a course, which the total effective rate was 88.5%. It is an excellent method to treat schizophrenia, which cost less time and had no side effects, and the curative effect was definite. Wei Zhang, *et al*.[13] believed that embedding wires was effective in the treatment of intractable auditory hallucinosis. 70 patients were selected and randomly divided into the embedding group and the control group. The embedding group was treated by embedding wires at Tinggong point and combined with chlorpromazine. The embedding wires at Tinggong point was performed once a month and chlorpromazine hydrochloride tablets were taken twice a day. The control group was treated with chlorpromazine hydrochloride alone. The results showed that the score of brief psychiatric symptom evaluation was lower than the control group ($P < 0.05$), and with significant effect, the dopamine inhibition ability was greatly improved. In concussion, the treatment effect of the embedding group was better than the control group ($P < 0.05$).

4. Conclusion

To sum up, a large number of clinical practice results show that TCM has achieved satisfactory results in the treatment of schizophrenia, and TCM treatment combined with low-dose antipsychotic medication can achieve satisfactory efficacy, which is superior to western medicine alone, and can reduce the amount of antipsychotic medication and side effects to a certain extent. Moreover, TCM treatment is perfect at starting from the whole, focusing on the main contradictions of the onset, and strictly observing the pathogenesis. Both in compatibility of traditional Chinese medicine and acupuncture point should be treated based on syndrome differentiation to make the treatment more focused, so that the key points of the disease can be grasped without neglecting the overall situation. I believed that the position of TCM in the treatment of schizophrenia will be paid more and more attention.

References

1. Zhao J. The event-related potential study of abnormal cognition function in schizophrenia [master's thesis]. Xi'an: Air Force Medical University; 2013.
2. Xu T, Su J. Textual research on theories of Dian and Kuang in Chinese Medicine. Chinese Journal of Basic Medicine in Traditional Chinese Medicine 2011; 17(1): 29–32.
3. Liu C, Zhu L. Efficacy observation of traditional Chinese medicine decoction combined with aripiprazole in the treatment of chronic schizophrenia. Journal of Clinical Medicine in Practice 2019; 23(17): 119–122.
4. Wu S. Clinical observation on first-episode schizophrenia treated with integrated traditional Chinese and western medicine (in Chinese). Journal of Practical Traditional Chinese Medicine 2014; (9): 840.
5. Huang J. Self-made Ningshen Zhendian decoction for 32 cases of schizophrenia (in Chinese). Fujian Journal of Traditional Chinese Medicine 2001; 32(6): 50.
6. Zhao G. A clinical controlled study of acupuncture and moxibustion combined with low-dose antipsychotics in the treatment of schizophrenia (in Chinese). China Health Care & Nutrition 2013; (8): 174.
7. Liang W. Observation on therapeutic effect of acupuncture on 29 cases of chronic schizophrenia (in Chinese). China Health Industry 2014; (25): 192–193.
8. Wu J. Acupuncture treatment of 44 cases of mania (in Chinese). Chinese Acupuncture & Moxibustion 1994; (5).
9. Zheng W, Zhang L, Huang H, *et al*. Effect of acupuncture therapy on cognitive function of patients with chronic schizophrenia (in Chinese). Modern Practical Medicine 2020; 32(1): 75–77.
10. Zhu H, Sheng Y, Luo J, *et al*. Clinical analysis of the effect of Chinese medicine embedding on negative symptoms of schizophrenia. Contemporary Medicine 2019; (22): 132–133.
11. Lv Y. Clinical preaentation on 100 schizophrenic cases with treatment of catgut-embedding method in Back-Shu and Jiaji points. Chinese Acupuncture & Moxibustion 1988; (5): 12–14.
12. Li S, Peng H, Zhang X, *et al*. Acupoint catgut implantation for 52 cases of schizophrenia (in Chinese). Shanghai Journal of Acupuncture and Moxibustion 2015; (5): 452–453.
13. Zhang W, Sheng L, Du H, *et al*. A controlled study of catgut embedding at Tinggong point in treating obstinate auditory hallucinations (in Chinese). Journal of Clinical Psychosomatic Diseases 2015; 21(z2): 107.

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ORIGINAL ARTICLE

Research on the Training Method of Clinical Thinking in Human Anatomy Teaching

Gaigai Su*

Xuchang University, Xuchang 461000, China. E-mail: 754396749@qq.com

Abstract: Human anatomy is a science to study the normal human body shape and structure. It is an important basic medical course, and closely related to various medical disciplines, especially to clinical medicine. Under the concept of comprehensive quality education, anatomy teachers should not only impart theoretical knowledge and professional skills, but also pay attention to the cultivation of students' clinical thinking ability, so as to lay a solid foundation for students' subsequent professional study and clinical practice. This paper focuses on the training of clinical thinking in human anatomy teaching.

Keywords: Anatomy Teaching; Clinical Thinking; Training Methods; Research

Clinical thinking ability refers to the use of basic medical theory knowledge in clinical practice to make reasonable analysis, accurate research and judgment of clinical cases, and put forward targeted clinical solutions. Clinical thinking ability is one of the clinical abilities that medical students must possess, and can help students learn how to deal with various clinical problems. Under the traditional medical teaching mode, it focuses on the cultivation of students' clinical thinking ability during clinical observation and practice, but the effect is not so good. The main reason is that under the traditional examination oriented education system, the basic medical curriculum is seriously divorced from the clinical practice, and the students passively accept knowledge, losing the initiative and enthusiasm of learning, and limiting the development of logical thinking and creative thinking ability. At present, in order to cultivate more medical talents, it is necessary to train students' clinical thinking ability throughout the whole basic course teaching. Starting from human anatomy, students should be guided to play their subjective initiative, actively think and cooperate in exploration, so as to cultivate students' good clinical thinking ability while mastering professional knowledge and skills.

1. Optimizing the teaching content of anatomy and infiltrating clinical thinking concept

With the continuous progress of medical technology in our country and the rapid development of medicine, the content of traditional anatomy knowledge must keep pace with the times and introduce new technology and new ideas, so that students can fully master the real-time updated anatomy knowledge. Based on this, medical teachers in colleges and universities should pay attention to the latest anatomy research in real time, master new technology, knowledge and concept, and abandon the backward and wrong teaching content and concept at the first time so as to draw lessons from the latest clinical

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research results, strengthen the connection between anatomy teaching content and clinical medicine, and pay attention to the cultivation of science step by step in teaching clinical thinking ability, creative thinking ability. For example, when explaining the knowledge points of the "digestive system" chapter, teachers can use classic cases such as clinical duodenal ulcer and gastric ulcer to focus students' attention in class with specific and vivid clinical manifestations, promote students' deep thinking through close combination with clinical cases, and compare the similarities and differences of gastric and duodenal mucosa in anatomical structure, which is beneficial for students to understand and master the anatomical structure of duodenum and stomach, and fully grasp its clinical application scope; in addition, we can also expand the extension link to introduce the relationship between helicobacter pylori and gastropathy to students, so as to not only explain the theoretical knowledge of anatomy, but also enable students to understand clinical medical knowledge, broaden their horizons and cultivate students' comprehensive medical science ability and quality.

2. Innovating teaching methods and stimulating students' clinical thinking consciousness

In the process of anatomy teaching, teachers should give full play to the main role of students in teaching, build a harmonious, democratic and equal relationship between teachers and students, and adopt group cooperation, problem-oriented and task-driven teaching methods. As the organizer and director of teaching, teachers should pay attention to active classroom atmosphere, create a relaxed and pleasant teaching atmosphere, and make use of scientific and efficient teaching methods to cultivate the clinical thinking ability of the students step by step. For example, when learning the knowledge points of the chapter "appendicitis", the teacher can arrange the preview task first, so that the students can understand the position and shape of the appendix in the human body through the human body specimen in the preview process; in the classroom teaching, teacher can make full use of the video, animation, pictures and other carriers in the multimedia teaching technology, so that students can intuitively and vividly feel the human body structure of the appendix. For the organization of practical teaching, in the form of group cooperation, students can carry out appendectomy through human specimens, and in the process of their hands-on operation, teachers track the whole process and ask questions in real time. For example, what harm does acute appendicitis have? Where is the best operation position of acute appendicitis? If surgery is performed, what incision should be made? How to find appendix during operation? etc. It is important to pay attention to guide students to correctly understand the anatomical basis of appendicitis. In this way, students can learn, think and operate, effectively stimulate students' interest and enthusiasm in learning anatomy, so as to guide students to divergent thinking, cultivate their clinical thinking ability and creative thinking ability, achieving comprehensive development.

3. Attaching importance to experimental teaching and building a perfect clinical practice platform

Medical specialty is practical and skilled. Experimental teaching is an important part of human anatomy course, which plays an irreplaceable role in training students' clinical practice ability and clinical thinking ability. Human anatomy belongs to the category of morphology in biology. Therefore, we must attach importance to experimental teaching and increase the proportion of experimental teaching in the teaching process. Teachers should pay attention to the construction of a perfect experimental and practical platform, so that students can have a comprehensive and profound understanding of human anatomy knowledge, understand the human body structure, accumulate rich clinical experience, and lay a solid foundation for the follow-up career. At present, the anatomy laboratory of our college provides a variety of specimens to meet the needs of students' anatomy learning, including (box, model, plasticization, section, etc.) specimens and general specimens, which are placed in the display cabinet of each laboratory. In the specific experimental teaching process, students can find the corresponding specimens according to the learning requirements of each chapter, under the guidance of teachers, and carry out targeted learning with a careful observation[1]. The anatomy laboratory of our college is open all day (except winter and summer vacation), and students

can enter and leave freely, which provides great convenience for students' experimental study. In addition, in the experimental teaching, teachers should not leave the students alone, should increase the interaction with students, and point out the problems encountered in the process of observing specimens, so as to correct students' wrong cognition in time. When learning the key anatomical structure, teachers should timely put forward targeted problems related to clinical diseases[2], guide students to think deeply and cooperate in exploration, in order to better help students master the anatomical structure, and cultivate their clinical thinking ability and comprehensive ability and literacy.

4. Carrying out clinical advanced study and enhancing the comprehensive quality of anatomy teachers

As we all know, the learning quality of anatomy course of medical students largely depends on the teaching philosophy and teaching methods of professional teachers. In order to train the clinical thinking ability of medical students and improve their comprehensive quality, we must pay attention to optimizing the structure of anatomy teachers and strengthening the professional teachers. First of all, the purpose of introducing new and professional medical teachers is to improve the quality of young teachers[3]. Secondly, strengthen the training of on-the-job teachers. We should pay attention to guide anatomy teachers to establish the concept of lifelong learning, enrich their knowledge reserves and enhance their professional ability by participating in various continuing education training classes and all-round and multi angle learning; schools should also organize or encourage teachers to participate in various teaching and scientific research activities to grasp the latest research trends and progress of anatomy at home and abroad in real time; we should organize anatomy teachers and clinical teaching teachers to regularly cooperate to prepare lessons, discuss teaching plan and schedule, teaching content and mode, etc., so as to realize the mutual penetration and integration of the two courses, enhance the clinical thinking ability and level of anatomy teachers imperceptibly. At present, medical specialty in colleges and universities should strengthen cooperation with local hospitals, organize anatomy teachers to major hospitals, especially affiliated hospitals, for clinical observation and practice in winter and summer vacation[4], national day and other holidays, and enrich their own clinical case material reserve through practice, so as to find the close relationship between anatomy and clinical medical knowledge in specific participation, summarizing and reflecting, to apply it to the follow-up teaching.

5. Conclusion

To sum up, the learning of anatomy knowledge aims to serve the follow-up clinical medical treatment, so it is very important to apply clinical thinking in anatomy teaching. Based on this, in the teaching of anatomy, teachers should actively change their concepts, correctly realize the importance of clinical thinking in anatomy teaching, and optimize the teaching mode from all aspects and angles, so as to cultivate students' clinical thinking ability.

References

1. Liao Y. Application of clinical thinking ability training in human anatomy teaching (in Chinese). Modern Vocational Education 2019; (24): 138–139.
2. He Y. The training of clinical thinking ability should be appropriately expanded in the teaching of human anatomy (in Chinese). Journal of Seeking Knowledge Guide 2019; (1): 70.
3. Liu J, Zhang X, Huang H. Training of clinical thinking in anatomy teaching (in Chinese). Basic Medical Education 2018; (2): 79–81.
4. Zhao Q, Zhang H, Zhang Z. Preliminary study on the combination of human anatomy teaching and clinical practice (in Chinese). Special Health 2018; (17): 179.

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ORIGINAL ARTICLE

Development Predicament and Countermeasures of Anti-tumor Biosimilar Industry in China

Yingjie Xie*

Hangzhou Medical College, Hangzhou 310053, China. E-mail: 2287129407@qq.com

Abstract: Biosimilar has the advantages of precise efficacy, high safety and stable quality, and occupy an important position in the field of anti-tumor therapy. In order to reduce the expenditure of drugs, the research and development of biosimilar drugs has attracted much attention. Compared with European and American countries in the development of the anti-tumor biosimilar industry, there are still some shortcomings and parts that need improvement in China. According to the current development status of China, analyzed the reasons for the development dilemma of my country's anti-tumor biosimilar industry, and put forward suggestions for the development of this industry.

Keywords: Biosimilar; Anti-tumor; Industry; Development; Countermeasure

1. Development overview

With the gradual expiration of patent protection of biosimilar drugs, the expansion of domestic market demand and the development of research and evolution technology, the improvement of biosimilar drugs has become a hot spot for medical institutions, companies and cancer patients. In recent years, due to the accurate efficacy of biosimilar, it has played an important role in the field of tumor treatment. In the field of tumor treatment, the research and development of monoclonal antibody biosimilar drugs is in full swing, which is expected to optimize clinical decision-making and patient treatment options in the future[1]. Currently, biopharmaceuticals are still doing follow-up and imitation research in China, and will occupy a leading position in the market for a long time in the future[2]. Especially in low- and middle-income countries, biosimilars have gradually become the main method of anti-malignant drug over-priced[3].

2. Existing difficulties

2.1 Technical problems of production equipment

For biosimilars to be "highly similar" to proved biotech drugs, developers must not only use the most advanced technology to demonstrate that their products are produced with consistent quality standards, but they must also be sufficiently similar to reference drugs. This not only places higher requirements on the professional competence of researchers, but also has corresponding requirements on the advanced nature of production equipment and the ability to operate equipment. Although many biosimilar companies in my country have introduced a large number of production lines

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with advanced technology in order to improve the efficiency and quality of biosimilars, some companies have not established modern operation and management models, and only position biopharmaceuticals as machinery for products. Processing, resulting in increased equipment failure problems. Therefore, technical personnel who understand and use advanced production equipment are needed to assist.

2.2 Brand awareness issues

Because according to the Pharmaceutical Advertising Management Law some drugs cannot be advertised in mass media other than professional journals. Except for professionals and those who often pay attention to this aspect, they know a little more lar brands, and others don't know much about biosimilar brands. Due to the limited channels for obtaining relevant news, some people do not know how to get the latest news. There are also patients who pay less attention to the brand. For example, one of the anti-tumor biosimilar drugs approved for marketing in China is bevacizumab. There are three types of bevacizumab, which are under the three manufacturers of Betta Pharmaceuticals, Bio-Thera and Innovent Biologics. The patient may know that I want to use bevacizumab, but it is not clear which manufacturer it is.

2.3 Reference listed drug selection problem

We lack a comprehensive database. At present, there are 3 kinds of orange books that are most widely used in the world. They are the orange books promulgated by the WHO, the US (FDA) and the JPN (PMDA). The Orange Book of various countries has clear regulations on reference listed drug and has established a detailed catalog of reference listed drug. In order to better promote the research and development of biosimilars in my country, the former China Food and Drug Administration (CFDA) issued the Guiding Principles for the Development and Evaluation of Biosimilar Drugs (Trial) in March 2015[4]. In order to standardize the reference listed drug and other indicators of generic drugs, my country will officially release the China Listed Drug Catalogue similar to the Orange Book database on December 29, 2017. Compared with the establishment of databases in other countries, the consistency evaluation system is still in the process of development and growth.

2.4 The problem of industrial clusters

As a typical high-tech industry, biopharmaceuticals have their own distinctive industrial characteristics. Biopharmaceutical industry has a long industrial chain, each node requires professional technology to be realized. The closeness of each link of this industry is higher than that of other traditional industries and even some high-tech industries[5]. In 2016–2020 China's biomedical industry cluster development model in-depth analysis and development strategy research report, it issued that my country has initially formed a fast-growing industrial cluster with the Yangtze River Delta and Bohai Rim as the core, and the Pearl River Delta, northeast and other eastern regions. However, the problem of regional unbalanced development has also been further revealed. For research and development, there is a trend of further gathering in Shanghai and Beijing, and accelerating the gathering of manufacturing links in Jiangsu and Shandong. Although the overall growth of my country's biopharmaceutical companies is relatively fast, these companies have problems such as small scale, weak anti-risk ability, weak research and development capabilities, and single varieties. Most of the same varieties have multiple manufacturers, leading to serious homogeneity competition. For example, some new biomedical companies such as Da An Gene and Ke Hua Biology focus on the fields of gene kits and blood products, which makes the degree of diversification low. Due to the short history of my country's industrial cluster construction, there are still shortcomings such as imperfect industrial chain layout and blind construction.

2.5 Talent construction issues

China has fewer high-level talents in the field of biotechnology drugs. The backwardness of talents will lead to backward research and development and products, backward marketing management, etc., which will make the domestic pharmaceutical industry completely backward. This is because the cultivation of biopharmaceutical talents in my country ranges from junior college to doctor, with a huge vertical span. Although it seems that there are a large number of people studying biopharmaceuticals, due to various reasons such as employment situation, job demand and so on, and when they arrive at a master's degree or doctor degree, their majors are more refined, which will make the few num-

ber of people who will eventually study anti-tumor biosimilar. Compared with European and American countries, China's education level still has some differences, such as the backwardness of teaching data and the scarcity of professional equipment. There is also a lack of relevant talents engaged in basic research and development talents.

3. Counterplan

3.1 Establish a talent introduction system

The development of the industry is inseparable from the training and introduction of professional talents. Senior professionals are the driving force for the development of the anti-tumor biosimilar industry. Under the situation of industrial development, focus on the construction of professional teams and strengthen the standardization and institutionalization of talent introduction. Second, build a carrier that is conducive to the growth of talents, such as the establishment of new technology training bases, and the construction of related scientific research workstations to provide a strong growth environment for the development of professional talents. Furthermore, China's talent development environment is weaker than European and American countries. Therefore, the country and the governments must implement the talent introduction policy and improve the legal system that respects knowledge achievements and knowledge technology. Attract more high-quality, highly sophisticated talents to stay in China.

3.2 Technological innovation

A complete and advanced technology in anti-tumor biosimilars is inseparable from academic research and accumulation. China's research results in this area are still relatively lacking. The country can arrange for professional and senior talents to go to technologically powerful countries to exchange and study, broaden our knowledge reserves, and improve my country's technological level and innovation capabilities. It also needs to strengthen technologies such as large-scale and high-throughput gene cloning and protein expression, antibody humanization and human antibody preparation, new vaccine adjuvants, large-scale cell culture and protein purification. Innovate in key paths such as biological activity, impurity control, stability, toxic and side effects control, evaluation methods, and clinical research to develop high-precision biosimilar.

3.3 Enhance cognitive level

At present, all anti-tumor biosimilars that have been marketed in China are monoclonal antibody biosimilars. However, the clinical data of biosimilars before the market is limited, and some potential rare or serious safety problems have not been fully exposed. The differences in immunogenic responses of populations with different indications may bring potential safety hazards to patients with biosimilar indications[6]. Therefore, for companies, keep abreast of the latest developments and get cutting-edge news in time to improve their core competitiveness. For personnel in the medical industry, participate in more relevant training to improve their awareness. As far as patients and their families are concerned, they usually pay more attention to anti-tumor biosimilar-related news in case of unexpected needs.

3.4 Improve quality standards

With the introduction of standards for biosimilar, the current domestic production standards for anti-tumor biosimilar are mainly based on the Chinese Pharmacopoeia (2015 Edition). Most companies aim to meet the pharmacopoeial quality requirements, and rarely can in-depth quality analysis. For instance, the purity of the product, the immunogenicity of recombinant human growth hormone and insulin, plenty of creatures believe that it has a great relationship with the impurities in the drug. Recombinant human interferon is easier to polymerize under certain conditions, and the polymerized polymers can produce a more powerful immune response, which can directly illustrate the important connection between active products and impurities[7]. Therefore, my country needs to make further improvements under the current quality standards, which is very necessary.

3.5 Strengthen inter-regional communication

The technical strength, equipment production conditions, and information channels possessed by an enterprise are limited. If there is more communication and cooperation between enterprises and between regions and regions, the effective sharing of resources can be realized, and joint efforts will be made to promote the

progress of China anti-tumor biosimilar and technology, and accelerate the improvement of product quality in this industry. Furthermore, the government can strengthen the relationship between the government and introduce relevant development plans based on economic and policy factors in various regions to jointly guide the development of the industry.

4. Conclusion

Anti-tumor biosimilars have the advantages of definite curative effect, high safety and stable quality, and its wide clinical application is an inevitable trend. Due to the impact of the patent protection of biosimilars, there are not many companies that develop biosimilars, and technical exchanges in this area are relatively lacking, and it is difficult to form specific mature technical standards. This article analyzes some of the problems of anti-tumor biosimilars in China, and finally puts forward some countermeasures from the five perspectives of establishing a talent introduction system, technological innovation, enhancing cognition, improving quality standards, and enhancing inter-regional communication. Provide assistance in the development and implementation of biosimilars. I hope that one day in the future, anti-tumor biosimilars can benefit cancer patients and improve their quality of life.

References

1. Guo R. Development and clinical application of anti-tumor biosimilar drugs (in Chinese). Journal of Practical Oncology 2020; (4): 310–313.
2. Li Y, Tian L. Research on biosimilar pharmacovigilance (in Chinese). 2013 Annual Meeting of the Pharmaceutical Affairs Management Professional Committee of the Chinese Pharmaceutical Association and the "Medicine Safety and Scientific Development" Academic Forum (in Chinese); 2013.
3. Blanco-Garcá E, Ledón N, Lage-Dávila A. Rising cancer drug prices: What can low- and middle-income countries do?. MEDICC Review 2018; 20(4): 35–39.
4. Huo Y, Yang J. Discussion on the reasons for the cluster development of biopharmaceutical industry (in Chinese). Science & Technology Progress and Policy 2005; (1): 84–86.
5. Xie X, Wu J. Study on status and countermeasures about biosimilars in China. China Biotechnology 2012; (3): 136–142.
6. Meng X, Gao S, Shu C. Analysis of biopharmaceutical development and countermeasure research of China. China Soft Science 2014; (4): 14–24.
7. Yang Y, Yang B. Thoughts on the pharmaceutical research of biosimilars (in Chinese). World Latest Medicine Information 2017; (A1): 85.

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ORIGINAL ARTICLE

Application Value of Coagulation Function Test in Prognosis of Patients with Cardiovascular and Cerebrovascular Diseases

Jing Luo*

Ruikang Hospital Affiliated to Guangxi University of Chinese Medicine, Nanning 530011, China. E-mail: luojingfish@163.com

Abstract: Objective: to explore the application value of coagulation function test in the prognosis of patients with cardiovascular and cerebrovascular diseases. Methods: from December 2018 to December 2019, 100 patients with cardiovascular and cerebrovascular diseases were randomly selected as the study group. According to the follow-up results of patients, they were divided into study group A (good prognosis, n = 64) and study group B (disability or death, n = 36) 100 subjects served as the control group. The test results of coagulation function of the two groups were analyzed retrospectively. The test results of the study group before and after treatment were compared with those of the control group, and the test results of the study group A and study group B after treatment were compared. Results: the coagulation function of the study group after treatment was significantly improved compared with that before treatment ($P < 0.05$), and there was a significant difference between the two groups before treatment ($P < 0.05$), and there was no difference after treatment ($P > 0.05$); after treatment, the coagulation function of study group A and study B was significantly different ($P < 0.05$). Conclusion: coagulation function test has a certain application value for the prognosis of patients with cardiovascular and cerebrovascular diseases, and can be used as an index to judge the patient's condition and treatment effect, which has good application value in clinical practice.

Keywords: Coagulation Function; Cardiovascular and Cerebrovascular Diseases; Prognosis; Application Value

In recent years, the incidence of cardiovascular and cerebrovascular diseases in clinical increased significantly, and showed an obvious upward trend. The elderly population is the main disease population of the disease. Most patients with cardiovascular and cerebrovascular diseases have poor prognosis and have high death rate. Therefore, it is necessary to pay attention to it and carry out intervention treatment as soon as possible Clinical studies have pointed out that[1], cerebral hemorrhage is a symptom of most patients with cardiovascular and cerebrovascular diseases, so hemostasis is an important means to treat this type of patients. With the deepening of research, some studies have pointed out[2] that coagulation factor is the key factor affecting the hemostatic effect and prognosis of patients with cardiovascular and cerebrovascular diseases. Therefore, the detection of coagulation function in patients with cardiovascular and cerebrovascular diseases can provide valuable scientific reference for the prognosis judgment of patients. Based on this, 100 healthy subjects and 100 patients with cardiovascular and cerebrovascular diseases were included in this study.

1. Data and methods

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1.1 General information

From December 2018 to December 2019, 100 patients with cardiovascular and cerebrovascular diseases were randomly selected as the study group. According to the follow-up results, they were divided into study group A (good prognosis, n = 64) and study group B (disability or death, n = 36). Then 100 healthy subjects who received physical examination in our hospital at the same time period were selected cases were used as control group. In the control group, there were 56 male subjects and 44 female subjects in the control group, all aged from 51 to 75 years old, with an average of (63.62 ±5.49) years old. There were 57 male patients and 43 female patients in the 100 patients group in the study group, all aged from 51 to 75 years, with an average of (64.02 ± 5.32) years. The study met the requirements of the ethics committee, and was carried out with the knowledge of the patients and their families and the permission of the ethics committee. The baseline data of the control and study groups were compared by SPSS20.0 system, and there was no difference (P > 0.05).

1.2 Method

The blood coagulation function of the two groups were analyzed retrospectively. Test method: the fasting venous blood was collected and placed in the test tube with sodium citrate anticoagulant. The force line was performed for 10 minutes at the speed of 3000rad / min. The upper plasma was tested by automatic blood coagulation instrument.

1.3 Observation index

The results of coagulation function test were compared. It includes PT (prothrombin time), TT (thrombin time), APTT (activated partial thromboplastin time), FIB (fibrinogen), AT Ⅲ (antithrombin III), D-D (D-dimer), ET-1 (endothelin-1), a total of 7 indexes.

1.4 Statistical treatment

Statistical data are divided into counting data (%) and measurement data ($\bar{x} \pm s$) according to the way of expression. Chi square value (X^2) and T are used for detection, P value is used for evaluation, and SPSS20.0 is used for data processing. If and only if P < 0.05, there is statistical significance.

2. Results

2.1 Comparison between the study group and the control group before and after treatment

The coagulation function of the study group after treatment was significantly improved compared with that before treatment (P < 0.05), and there was significant difference between the two groups before treatment (P < 0.05), but there was no difference after treatment (P > 0.05). See **Table 1** for details.

Table 1. Comparison between the study group and the control group before and after treatment.

Index	Study group		Control group
	Before treatment	After treatment	
PT/s	10.52±3.12 (2)	12.44±0.86 (1) (3)	12.36±2.20
TT/s	13.75±1.84 (2)	19.33±2.56 (1) (3)	19.21±3.63
APTT/s	24.55±3.13 (2)	30.05±2.35 (1) (3)	29.57±2.42
FIB/g/L	4.04±1.22 (2)	3.43±1.02 (1) (3)	3.10±1.12
AT Ⅲ/mg/L	397.66±29.75 (2)	318.53±30.60 (1) (3)	312.53±23.47
D-D/mg/L	0.84±0.25 (2)	0.10±0.03 (1) (3)	0.13±0.02
ET-1/pg/ml	1.34±0.13 (2)	0.86±0.08 (1) (3)	0.84±0.07

Note: (1) Compared with the study group before treatment, there was significant difference (P < 0.05); (2) Compared with the control group, there was significant difference (P < 0.05); (3) Compared with the control group, there was no difference (P > 0.05).

2.2 Comparison of study group A and study group B after treatment

After treatment, there was significant difference in coagulation function between study group A and study group B (P < 0.05). See **Table 2** for details.

Table 2. Comparison of study group A and study group B after treatment.

Index	Study group A	Study group B	t	P
PT/s	13.05±0.82	10.64±1.73	9.4416	0
TT/s	20.88±2.61	13.48±3.10	12.7433	0
APTT/s	32.16±3.04	27.29±3.18	7.5633	0
FIB/g/L	3.12±0.99	3.66±0.95	2.6560	0.0092
AT Ⅲ/mg/L	265.31±28.97	327.66±30.14	10.1819	0
D-D/mg/L	0.10±0.10	0.50±0.21	9.6693	0
ET-1/pg/ml	0.79±0.18	1.02±0.29	4.8951	0

3. Discussion

The study pointed out that the coagulation function test for patients with cardio cerebrovascular disease, especially for patients with thrombosis and need hemostasis treatment, can effectively evaluate the treatment effect of patients and judge the prognosis of patients[3]. In this study, PT, TT, APTT, FIB, AT Ⅲ, D-D and ET-1 were selected to test the coagulation function. The basis was that after the onset of the disease, exogenous coagulation factors would pour into the blood and participate in the blood circulation process, stimulating the external coagulation system and causing hypercoagulability. In addition, the damaged vascular endothelium can accelerate the diffusion of endogenous coagulation factors and stimulate the endogenous coagulation system. When exogenous and endogenous sources are activated at the same time, it will increase the consumption of fibrinogen, produce a large amount of fibrin, and cause thrombosis and coagulation dysfunction[4].

The results showed that the coagulation function of patients in the study group was significantly different from that in the control group before treatment, which indicated that compared with healthy people, the coagulation function of patients with cardiovascular and cerebrovascular diseases had obvious obstacles; in addition, after treatment, the coagulation function of the study group was significantly improved compared with that before treatment, and there was no difference between the two groups, suggesting that the effective treatment can promote the improvement of coagulation function in patients with cardiovascular and cerebrovascular diseases; the difference of coagulation function among patients with different prognosis of cardiovascular and cerebrovascular diseases is obvious, which indicates that the coagulation function of patients with good prognosis is better than that of patients with poor prognosis, and the prognosis of patients with cardiovascular and cerebrovascular diseases has a certain correlation with coagulation function.

In conclusion, coagulation function test has a certain application value for the prognosis of patients with cardiovascular and cerebrovascular diseases. It can be used as an index to judge the patient's condition and treatment effect, and has good application value in clinic.

References

1. Ruan J. The value of coagulation function test in prognosis of patients with cardiovascular and cerebrovascular diseases (in Chinese). Clinical Laboratory Journal (Electronic Edition) 2020; 9(3): 39–40.
2. Zhou L, Yang P. Analysis of the prognostic value of blood coagulation function in patients with cardiovascular diseases (in Chinese). Cardiovascular Disease Journal of Integrated Traditional Chinese and Western Medicine 2018; 15: 34.
3. Lai H, Li Y, Jiang F, *et al*. The value of coagulation function test in the prognosis of patients with cardiovascular and cerebrovascular diseases (in Chinese). Prevention and Treatment of Cardiovascular Disease 2017; (8): 78–80.
4. Wang M, Gong G, Liu Y. The value of coagulation function test in the prognosis of patients with cardiovascular and cerebrovascular diseases (in Chinese). Psychological Doctor 2018; 24(23): 33–34.

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ORIGINAL ARTICLE

Application and Prospect of Robotic Technology in Medical Clinic

Haowei Ma*

University of Malaya, Kuala Lumpur 50603, Malaysia. E-mail: mhwfangzhang@mail.com

Abstract: In the process of gradually improving the level of clinical medical treatment and continuously developing industrial technology, the application of less invasive and non-invasive surgical methods in medical clinic is increasingly widespread. In the face of this situation, the inevitable trend of the development of surgery has been inclined to minimally invasive surgery. Under the background of a large number of new technologies in the clinical application of medicine, the application space of surgical minimally invasive surgery technology has become more and more extensive. The first successful laparoscopic cholecystectomy in 1987 is an important sign of the arrival of the era of minimally invasive surgery. The research and development of surgical robots based on this is a predictor of the gradual beginning of the era of surgical information processing. At this time, it will inevitably promote the qualitative improvement of surgical accuracy, and a new era of minimally invasive surgery will gradually open. At present, the latest "Da Vinci" surgical robot developed by ISRG company has been widely used in medical clinic.

Keywords: Robotic Technology; Medical Clinic; Application; Prospect

1. Introduction

As an important part of people's livelihood and well-being, people pay more attention to it. Medical robots, which represent the coming of the era of artificial intelligence, have gradually entered the public's attention with their deepening application in the medical field. Surgical robotics technology was developed and applied earlier in European and American countries, followed by Europe and finally Asia. It is worth noting that although China has a large-scale medical device market, from the actual situation of huge market size, about 95% of high-end devices are often imported. Therefore, the development of medical equipment in China is particularly urgent, and one of the important directions of the development of the whole industry has begun to focus more and more on the intelligent equipment, with the application of more and more new technologies on the equipment. It can be predicted that more and more systematic and intelligent medical equipment will inevitably be formed in the future, and the era of more precise medical diagnosis will gradually come, while robotic technology will become an important component of intelligent medical care.

2. Application of surgical robot in clinic

The first generation of Da Vinci surgical robot was born mainly in 1999, and with the completion of the first vascular surgery in the same year, Da Vinci surgical robot began to be widely used in the medical field.

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Today, Da Vinci surgical robotic system has gradually been popularized in many disciplines worldwide. And the clinical application has gradually expanded to all levels and branches of surgery, through the application of surgical robots can carry out a wide range of complex surgical procedures, such as colon and hemicolectomy and other eight types of gastrointestinal surgery (gastrointestinal surgery); the first generation of Da Vinci surgical robot was born mainly in 1999, and with the completion of the first vascular surgery in the same year, Da Vinci surgical robot began to be widely used in the medical field. Today, Da Vinci surgical robotic system has gradually been popularized in many disciplines worldwide. And the clinical application has gradually expanded to all levels and branches of surgery, through the application of surgical robots can carry out a wide range of complex surgical procedures, such as colon and hemicolectomy and other eight types of gastrointestinal surgery (gastrointestinal surgery); the first operation carried out by urology with the aid of surgical robots was prostatectomy, followed by pyeloplasty and kidney transplantation. The earliest surgical field of Da Vinci surgical robots was coronary artery bypass grafting cardiac surgery, and with the success of this surgical case in 1999, the history of surgical robots opened. It has promoted the wide application of surgical robots in various types of open-vision cardiac surgery, and Da Vinci surgical robots have also gradually been involved in a large number of thoracic and gynecological operations[1]. The wide variety of surgical procedures, the improvement of surgical accuracy, and the emergence of a large number of successful surgical cases have made surgeons increasingly recognized and respected Da Vinci surgical robots. Since the introduction of the first generation of Da Vinci surgical robots in China in 2006, surgical robots have been gradually popularized in a large number of surgical fields in the mainland of China.

Surgical robots relying on broadband technology can be docked to devices with digital interfaces, thus achieving the purpose of remote transmission and control, providing sufficient guarantee for the development of remote surgery. The successful completion of laparoscopic cholecystectomy by a long-distance manipulated surgical robot in the United States in 2001 marked a leap forward in the era of surgery. At the same time, this operation is also an effective extension of the surgical robot to the field difficult to reach by conventional laparoscopic surgery. Compared with ordinary minimally invasive surgery, the advantages of surgical robots are very significant[2].

3. Other applications of robotics in medicine

Robotic technology is not only applied in surgical operations, but also widely used in the field of rehabilitation, such as the advantages of rehabilitation medical robots in the fields of disability assistance and elderly care are also very significant. At this time, rehabilitation robots (patients with arm disability), intelligent wheelchairs (patients with lower limb disability), mobile rehabilitation robots (patients with binocular blindness) are the main areas of robot technology research. Hospital service robots mainly provide assistant functions for the completion of some work of nurses, such as food and drug delivery; while robot walking design based on sensor and motion planning algorithm is more applicable in structured environment[3]. Under the background of the gradual development of micro-electromechanical system technology, the micro-medical robotic endoscopy technology has been further studied and developed, and this technology has also begun to gradually spread to the clinic. With the increasing maturity and development of robotic technology, robotic medical assistant technology has begun to be more widely used, such as the use of medical robots in liver and kidney puncture to assist, can effectively avoid rib vessels and abdominal cavity and other important organs, thereby achieving a safer abdominal puncture.

Relevant reports show that China's micro medical robots have been successfully developed by the relevant specialties of the School of Engineering, the Chinese University of Hong Kong, and the research and development of this medical robot provides great convenience for the precise delivery of drugs to specific parts of the human body, thus implying that this technology can be applied in the future in the targeted treatment of cancer, cerebral infarction and stroke and other diseases. The micro-robot controlled by an external magnetic field can precisely deliver drugs to tiny parts of the human body. At the same time, it can shuttle in blood vessel, eye and brain, and then directly deliver drugs to places that

are difficult to reach by traditional methods, making full breakthroughs in the limitations of traditional treatment methods that can only be passively administered by means of blood vessel in the past, so as to ensure the real realization of active targeted drug delivery.

The research of ultrasonic diagnosis robot technology is also very extensive. The related exhibition of Waseda University was held in 2013, which enabled the ultrasonic remote diagnosis robot to be operated at portable terminals such as smartphones to be displayed. In the application of this device, the main portable terminal control device is the smartphone. Later, based on the application of proprietary operating probes, the rotation control objectives of 360 and 45 degrees tilt can be well achieved. At the same time, the control of translation within 10 cm can also be realized to ensure that the doctor can achieve the goal of remote operation of the ultrasonic diagnostic device, which is very helpful for the doctor to understand the bleeding and other conditions in the patients during the emergency transportation process, and also can provide great help for the rapid adoption of coping strategies after the patients arrive at the hospital[4].

4. Analysis of technical defects of medical robot

Robot technology applied in the medical field has obvious advantages such as operation precision and stability. Affected by this factor, it provides a great impetus for the development of modern medical technology. However, it is worth noting that surgical robot technology is gradually developing, so it is difficult to fully drive the traditional surgical methods, but also in medical behavior can not completely replace the role played by human beings. From the technical aspects of analysis, although robotic technology has advanced, but it still has shortcomings, specifically reflected in the following aspects.

Surgical risk. In the process of using surgical robot technology, it not only has the risk of conventional surgery, but also has a greater probability of mechanical failure such as machine crash during the operation compared with the endoscopic surgery system. It also increases the risk of intraoperative accidents while prolonging the operation time. The most important concern of patients and doctors is the risk of surgery. Once the probability of surgical risk is increased, the widespread popularity of surgical robots will be greatly restricted[5].

Tactile feedback system. In the absence of force tactile feedback system, the surgeon's "hand feeling" will be lost, which will lead to the increasing uncertainty and risk of surgery, and the further development of surgical robots will be limited.

Operative time. From the practical application of surgical robots, although it has a high accuracy, it is worth noting that the preoperative preparation and intraoperative device replacement operations using the surgical robotic process often take a long time, and the existence of this factor will also restrict the wide application of surgical robots in clinical practice[6].

High costs. When purchasing surgical robots, it has a higher purchase cost, while in clinical application, it will also produce a higher operation cost. In addition, affected by higher maintenance costs, it will not only make the operation of surgical robots more difficult gradually. At the same time, it is difficult to ensure that patients report for acceptance and other attitudes towards this surgical approach, which will also restrict the popularity of surgical robots.

5. Prospects

Surgical accuracy and reliability are significant advantages of robotic technology, so the development trend in the medical field is ideal, and good clinical effects are becoming more prominent[7]. In the future, it is still necessary to continuously improve the surgical robot technology, which can be mainly from the following aspects: strengthen the stability of the surgical system, so that the probability of mechanical failure can be effectively reduced, to provide help for the reduction of surgical risk, so that the psychological disorders of patients and operators gradually disappear; the tactile feedback system has been actively developed, which gradually reduces the uncertainty and risk of surgery. The technical research has been strengthened to ensure the flexible application of robotic technology and provide favorable conditions for the reduction of operation time. Strengthen efforts on new surgical robots to ensure that their use costs are gradually reduced while achieving more practical research and development goals of surgical robots;

develop medical robots with a wide range of roles to ensure that robotic technology can be widely used in all aspects of the medical field[8].

6. Conclusion

From the practical application of robotic technology, robotic technology has been widely promoted in the conventional application and clinical medicine of developed countries, and from the analysis of our current application situation, it is still dominated by high-end medical attributes. Under the background of further development of robotic technology, with the increasing progress and maturity of technology, it is bound to deeply and extensively study and apply various medical robotic technologies, medical robot assistant technologies, etc. At the same time, the public and patients will also recognize and accept robotic technology, and it can be seen that future robotic technology has a very broad development prospects.

References

1. Liu L, Wang D. Application and existing problems of artificial intelligence in medical field. Soft Science of Health 2020; 34(10): 23–27.
2. Tian B, Lu H, Zhang J, *et al*. Application of telemedicine robot in follow-up after liver transplantation from donation after cardiac death. Organ Transplantation 2019; 10(1): 79–83.
3. Hai H. Overview of research status and future development trend of dental medical robot. The Department of Oral Medicine Electronic Magazine (Electronic Edition) 2018; 5(34): 18–19.
4. Cai S, Song Y, Cao X, *et al*. Application status and research progress of orthopedic robots (in Chinese). Shandong Medical Journal 2018; 58(44): 90–93.
5. Guo C. Development and application of robots in craniomaxillofacial surgery remains a long and arduous task. Chinese Journal of Stomatology 2018; 53(8): 505–507.
6. Chen Z. AI for medical enabling smart medical market will reach 20 billion (in Chinese). Health Care Today 2018; (2): 4–6.
7. Zheng H. Medical robot: The curtain of the 100 billion-dollar market is opening (in Chinese). Romantic Generation 2017; (24): 18–19.
8. Zhang J, Gu H, Sun J, *et al*. Application and prospect of robot technology in medical clinic. Machine Tool & Hydraulics 2016; 44(3): 52–55.

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ORIGINAL ARTICLE

Advances in the Relationship between Tau Protein and Morphine Dependence in Cognitive Dysfunction

Qing Ji, Xin Li*

The First Affiliated Hospital of Jiamusi University, Jiamusi 154003, China. E-mail: Arashijq@163.com

Abstract: Morphine is an opioid drug. Long-term use can cause morphine dependence or addiction, and there are cognitive dysfunction such as abnormal mental behavior, decline in learning and memory, and decline in executive ability. The occurrence of this disease is related to many factors, such as oxidative stress, hippocampal neuronal injury, mitochondrial function injury, etc. Tau protein is a microtubule-associated protein involved in nervous system development. Studies have found that hyperphosphorylation of tau proteins can cause apoptosis of hippocampal neurons[1], and tau proteins can cause oxidative stress[2]. Therefore, tau proteins play an important role in the pathogenesis of cognitive disorders. The relationship between morphine dependence and cognitive dysfunction is now reviewed.

Keywords: Tau Protein; Morphine Dependence; Cognitive Impairment; Correlation

Morphine has a strong analgesic effect and is often used in anaesthesia and severe pain caused by terminal tumors. Long-term use of morphine can produce a strong dependence, leading to cognitive dysfunction, mental disorders, behavioral disorders and so on, and eventually cause psychological and physical damage to patients, and can lead to family rupture, which poses a threat to social stability. Cognitive impairment in patients with cognitive dysfunction caused by morphine dependence is mainly manifested in cognitive flexibility and working memory; cognitive flexibility is mainly reflected in selective attention, executive function, and working memory load ability. Reduced working memory load can cause a decline in decision-making ability[3–4]. The mechanism of cognitive dysfunction caused by morphine dependence is generally considered to be associated with mechanisms such as oxidative stress, hippocampal neuronal damage[3–4], apoptosis, abnormal secretion of monoamine neurotransmitters, altered synaptic plasticity, and mitochondrial dysfunction. However, the specific pathogenesis remains unclear. Tau protein is a tubulin involved in the regulation of tubulin stability[3].

Accumulation of neuronal fiber tangles caused by hyperphosphorylation of tau proteins is closely related to the characteristic manifestations of cognitive dysfunction in Alzheimer's disease. Morphine is an opioid, long-term use can cause morphine dependence or addiction, and there are mental and behavioral disorders, learning and memory decline, executive ability decline and other cognitive dysfunction[4]. Recent studies have confirmed that acute and chronic morphine treatment can cause abnormal hyperphosphorylation of tau proteins and nerve microfilaments in the cerebral cortex[5–6]. As a result tau proteins may be associated with cognitive impairment following morphine dependence. This article reviews the

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overview of tau proteins and their phosphorylation regulation, tau proteins and other cognitive disorders related diseases, tau proteins and morphine dependence, tau proteins may be involved in regulating the pathogenesis of cognitive dysfunction caused by morphine dependence, in order to provide new ideas for the treatment and prevention of cognitive dysfunction caused by morphine dependence.

1. Overview and phosphorylation regulation of tau proteins

1.1 Overview of tau proteins

Tau protein is a microtubule related protein, which can be involved in regulating the stability of tubulin. Human tau genes on chromosome 17(17 q21-q22). And there are six tau isomers in the brain, is caused by or without exon 2, 3/10 messenger mRNA composed of alternative splicing. Exon 10 contains a bule binding region, exon 10 insertion provides four repeat (4 R) tau isomers, and 3 repeat (3 R) tau isomers do not require the involvement of exon 10[5]. The adult brain mainly expresses 3 R and 4 R tau, under physiological conditions, they are mainly distributed in axons of neurons[6]. Neuronal fiber tangles composed of hyperphosphorylation of tau proteins are closely related to the main pathogenic causes of Alzheimer's disease[7]. Diseases occur around the terminal binding sites of tubulin C, which leads to the decrease of microtubule binding ability and the weakening of microtubule binding ability, indicating that microtubule regulation is impaired[8–9]. Tau with localized misdistribution can also lead to impaired microtubule regulatory function. Mislocalized tau can be hyperphosphorylated while forming fibrous seeds and deposits. Furthermore, the stability of hyperphosphorylated proteins and normal tau proteins increased. Abnormal action of filamentous actin with stable tau proteins can lead to prominent damage, mitochondrial integrity defects, and actin instability. As a result, pathological changes in tau proteins can damage cytoskeleton system, cell transport system, mitochondrial integrity and signal transduction system. As a result, tau proteins accumulate in a group of brain cells and transfer to other regions can lead to disease and neurodegeneration.

1.2 Phosphorylation regulation of tau proteins

Tau protein is a phosphoprotein whose phosphorylation state determines its function. The binding of phosphate group depends not only on the conformation of tau protein, but also on the balance between tau protein kinase and protein phosphatase activity. Normal tau proteins usually bind 2-3 phosphatases, and when the protein kinase and protein phosphatase are out of balance, tau protein-bound phosphatases become 5-9. Current research finds[8], there are 21 tau protein phosphorylation sites in Alzheimer's disease (AD) patients, protein kinase (PDPK) and non-proline guided protein kinase (non-PDPK) phosphorylation can be guided by proline. PDPK phosphorylation of serine and threonine containing Ser/Thr-pro sequences, including cell cycle dependent protein-5(CDK-5), glycogen synthesis kinase-3(GSK-3), mitogen-activated protein kinase (MAPK), the non-PDPK is mainly about Ser/Thr-X contained the serine of the sequence is phosphorylated with threonine, including calmodulin dependent protein kinase II (CaMKⅡ), microtubule binding regulatory kinase (MARK) and cAMP dependent protein kinase (PKA), etc. Moreover[9], protein phosphatase plays an important role PP2A regulating tau protein phosphorylation. The phosphorylation of Thr1620/1623 and Ser136 at the two sites of MAP-2 is mainly regulated by CaMK Ⅱ and GSK-3β, and PP2A plays an important role in dephosphorylation. Studies[10] have confirmed that the up-regulation of tau and MAP-2 phosphorylation levels in acute morphine mainly by inhibiting PP2A activity, while the activation of tau and MAP-2 phosphorylation in chronic morphine by enhancing GSK-3β and PKA activity sex. Patrick found that P25/CDK5 complexes can not only induce hyperphosphorylation of tau proteins, but also reduce the ability of tau proteins to bind to microtubules. Wang Xinbo[11] and others confirmed that Anshen Dingzhi can inhibit tau protein phosphorylation by activating BDNF/TrKB signal transduction pathway, thus improving the learning and memory ability of AD rats.

2. Tau proteins and other cognitive disorders

The biological activity of tau protein is the basis of maintaining its function. Moderate phosphorylation can maintain the biological activity of tau protein, but hy-

perphosphorylation can cause tau protein to accumulate and form neuronal fiber tangles (NFT), thus losing its biological activity. The study found that tau protein phosphorylation changes in Alzheimer's disease, Parkinson's disease, stroke with vascular cognitive dysfunction, post-operative cognitive impairment and other cognitive impairment-related diseases, while tau protein phosphorylation can cause a decline in microtubule assembly ability. It can also further damage microtubules through tubulin-related protein MAP1 and MAP2, affecting the synthesis, transport, release of neurotransmitters resulting in abnormal intercellular signal transduction. Hence, hyperphosphorylation of tau proteins is thought to be involved in regulating the pathogenesis of multiple cognitive impairment-related diseases.

2.1 Tau proteins and Alzheimer's disease

The characteristic lesion of Alzheimer's disease (AD)[12] neurofibrillary tangles (NFTs) is an important cause of neuronal lesions, which can be used as a marker of brain aging and is positively related to the degree of cognitive impairment in AD. Tau protein can produce a large number of abnormal post-translational modifications and aggregate to form paired helical filaments, NFTs is formed by further deposition of paired helical filaments. Phosphorylation and interception are the main forms of post-translational modification of tau proteins, and are closely related to the occurrence and development of AD. The degree of tau protein phosphorylation in the brain of AD patients is 3-4 times higher than that of ordinary people[13]. Tau protein phosphorylation is mainly regulated by phosphatase and phosphokinase to maintain the equilibrium state. When the equilibrium state is broken, it can cause abnormal hyperphosphorylation of tau protein, and hyperphosphorylation improves the aggregation ability of tau protein significantly. Loss of original function, accumulation in the form of spiral filaments NFTs, resulting in neuronal degeneration damage.

2.2 Tau protein and Parkinson's disease

Parkinson's disease (PD) is a common dyskinesia disease, the main pathological features of which are progressive neuronal degeneration in striatum and corpus callosum, and the widespread existence α- synaptic nucleoprotein aggregates-Louis corpuscles in cytoplasm. Where cognitive dysfunction is PD common nonmotor symptom, including Parkinson's disease dementia (PDD) and Parkinson's disease mild cognitive impairment (PD-MCI). The results showed[14] that the genotypes H1/H2 microtubule related tau protein (MAPT) genes and apolipoprotein Eε alleles were correlated with the dementia rate of Parkinson's disease. Cerebrospinal fluid β- amyloid42 decreased, phosphorylated tau protein and total tau protein levels[15] increased in PDD patients. Moreover, it was found that the tau level of serum phosphorylation in PD patients was significantly higher than that in the control group, and the level of serum phosphorylation tau in PD-MCI group was significantly lower than that in PDD group. The higher the serum tau protein phosphorylation level, the worse the prognosis.

2.3 Tau proteins and post-stroke cognitive impairment

Cognitive dysfunction after stroke belongs to vascular cognitive dysfunction (VCI), which refers to the impairment of one or more cognitive fields such as executive ability, language comprehension calculation, brain memory, structural ability and expression application. The study suggests that[16] β- abnormal proteins produced during stroke such as amyloid 1-42(Aβ-42) and tau protein may be associated with vascular cognitive dysfunction after stroke. Other studies have suggested that[17] tau proteins are related to the formation of microtubules in neuronal cells and are specific proteins in the nervous system. After stroke, tau are released from nerve cells into cerebrospinal fluid and leak to peripheral blood through damaged blood-brain barrier. Its level may be related to the degree of brain injury. The results showed that[18] the Aβ-42 of tau protein in the experimental group was lower than that in the control group, and the difference was statistically significant. The tau protein level was negatively correlated with the MoCA and MMSE score, suggesting that the Aβ-42 and tau protein level was associated with vascular cognitive impairment after stroke.

3. Tau protein and morphine dependence

Morphine is an opioid that can lead to cognitive decline such as learning and memory, but the specific reasons are unknown. Both acute and chronic morphine

treatment can increase the phosphorylation of tau protein and nerve microfilament in rat cerebral cortex. Recent studies have confirmed that acute morphine treatment can increase the expression of cycle-dependent protein kinase-5 (CDK5) in cerebral cortex cells, and CDK5 is one of the important kinases that catalyze the phosphorylation of tau protein and neurofilament protein. Increased CDK5 activity can cause abnormal hyperphosphorylation of tau protein and neurofilament protein. But other studies have different views. Narita[19] contet and other studies found that there was no significant change in the expression level of cerebral cortex CDK5 chronic morphine treatment, but the expression level of p-CDK5 (Ser159) increased and the activity of CDK5 increased. Suggesting that abnormal hyperphosphorylation of tau proteins and neurofilament proteins may be associated with increased p-CDK5 (ser159) expression levels and upregulation of CDK5 activity. Studies have also confirmed that[20] high dose exogenous CCK-8 can significantly reduce the damage of spatial reference memory in morphine dependent mice, and CCK-8 intervention can increase the PKA and GSK-3β activity caused by increasing the PP2A activity caused by acute morphine action and decreasing the chronic morphine action. It inhibited the increase of tau and MAP-2 phosphorylation induced by morphine.

4. Mechanisms of possible involvement of tau proteins in morphine-dependent cognitive impairment

Tau protein affects cognitive dysfunction caused by morphine dependence. A number of studies have found that tau proteins can not only affect apoptosis, but also affect nervous system and cognitive function through other ways. At present, the research includes the following aspects.

4.1 Tau proteins affect apoptosis

Apoptosis is an important regulatory mechanism to maintain the relative stability of physiological state. Its abnormal increase or decrease may lead to the change of function or structure of tissues and organs. The effects[21] of stilbene glycoside (TSG) on the phosphorylation of tau protein in NG108-15 cells induced by okadaic acid (OA) were studied. It was found that OA could lead to abnormal phosphorylation of tau protein in nerve cells and increase the aggregation of tau protein. Finally, apoptosis was caused. Acrylamide (AA)[22] induced apoptosis in vivo and in vitro, accompanied by oxidative stress. Oxidative stress can induce autophagy in neurons in the brain. But if the ROS level in the cell exceeds the clearance range of autophagy, it will cause excessive autophagy and eventually lead to autophagic death. The study found that[23] H_2O_2 acting on hippocampal neurons HT22 cells, autophagy bodies gradually increased and eventually died with the long action of free radicals, suggesting that oxidative stress can induce hippocampal neuronal death. The hippocampus is a related brain region of learning, memory and emotion in the brain. Studies have confirmed that local changes in the hippocampus, such as volume reduction, neuronal apoptosis or death, are important causes of cognitive function changes.

4.2 Tau proteins affect mitochondrial dysfunction

As a "power plant" in vivo, mitochondria play an important role in the formation of ATP through the process of oxidative phosphorylation. The damaged mitochondria can stimulate the production of a large number of reactive oxygen free radicals, which can cause oxidative damage to the central nervous system. The results showed that the expression of human tau protein could cause the dynamic imbalance of mitochondrial division and fusion between HEK293 cells and primary neurons, and the neuronal process was significantly shortened and the cell viability decreased[24]. Damage to mitochondrial function can affect mitochondrial endoplasmic reticulum (MAMs) structural coupling. Mitochondrial-endoplasmic reticulum structural coupling (MAMs) is a physical and biochemical connection between mitochondria and endoplasmic reticulum, and it is also a bridge between their structure and function. Studies have confirmed that changes in MAMs structure and function may be a key link in the pathogenesis of Parkinson's disease, Alzheimer's disease and other types of cognitive disorders, so MAMs injury is associated with cognitive dysfunction.

4.3 Tau proteins affect endoplasmic reticulum-related degradation pathways

The endoplasmic reticulum related degradation (ERAD) pathway refers to the process of degradation by the ubiquitin proteasome system (UPS) when the newly synthesized proteins or polypeptide molecules of the endoplasmic reticulum are non-folded proteins or misfolded proteins increase or cannot return to normal conformation. Abnormal tau protein accumulation can destroy endoplasmic reticulum related degradation pathway[25], hinder ubiquitin dependent proteasome degradation pathway, and then cause folding protein response. At the same time, endoplasmic reticulum stress is activated to induce neuronal apoptosis, which further affects cognitive function.

4.4 Effects of tau proteins on oxidative stress

Oxidative stress is a physiological process triggered by the breaking of the balance between reactive oxygen species and antioxidants, which can lead to lipid peroxidation, oxidative damage to proteins and DNA, and ultimately neuronal damage. Studies have shown that abnormal phosphorylation of tau proteins occurs AD the brain of patients and accumulates to form spiral filaments, that is, neuronal fiber tangles. However, hyperphosphorylated tau proteins lose the ability to bind to neuronal microtubules, resulting in the inability to regulate the structure and function of microtubules, thus causing neuronal axons to degenerate. The formation and growth of axons is the primary morphological change in neuronal differentiation, which makes cognitive functions such as information transmission, learning and memory more dependent on information transmission between neurons.

5. Summary

To sum up, tau protein is a microtubule-related protein of nerve cells, which has the function of synthesizing and stabilizing neurons and plays an important role in maintaining cell morphology, cell movement, signal transmission and other physiological processes. The NFT of hyperphosphorylation and aggregation of tau protein is one of the main pathological features in the brain of AD patients. Tau protein hyperphosphorylation is considered to be AD key pathogenic factor. The study found that the phosphorylation level of tau protein was increased in postoperative cognitive impairment, stroke with vascular cognitive impairment, diabetic encephalopathy and other cognitive dysfunction diseases, so a large number of studies believe that tau protein is involved in the regulation of cognitive impairment mechanism. The study found that the level of tau protein phosphorylation also increased during morphine dependence, so consider whether tau protein phosphorylation is involved in cognitive dysfunction caused by morphine dependence. This article reviews the overview of tau protein and its phosphorylation, its relationship with other cognitive disorders, tau protein and morphine dependence, and its possible effects on cognitive dysfunction caused by morphine dependence. In order to provide a new way of diagnosis and treatment for patients with cognitive dysfunction caused by morphine dependence and provide a new direction for the preparation of targeted drugs.

References

1. Zhang H, Wang H, Zhang M, *et al*. The influence of blood glucose fluctuation on hippocampal Tau protein phosphorylation of diabetic rats. Chinese Journal of Endocrinology and Metabolism 2017; 33(9): 776–780.
2. Puvenna V, Engeler M, Banjara M, *et al*. Is phosphorylated Tau unique to chronic traumatic encephalopathy? Phosphorylated Tau in epileptic brain and chronic traumatic encephalopathy. Brain Research 2016; 1630: 225–40.
3. Aribisala BS, Hernandez MCV, Royle NA, *et al*. Brain atrophy associations with white matter lesions in the ageing brain: The lothian birth cohort 1936. European Radiology 2013; 23(4): 1084–92.
4. Nikseresht S, Etebary S, Roodsari HRS, *et al*. The role of nitrergic system in antidepressant effects of acute administration of zinc, magnesium and thiamine on progesterone induced postpartum depression in mice. Tehran University Medical Journal 2010; 68(5): 261–267.
5. Miloi MM. The DsTau experiment: A study for Tau-neutrino production. Particles 2020; 3(1): 164–168.
6. Small GW, Siddarth P, Li Z, *et al*. Memory and brain amyloid and Tau effects of a bioavailable form of curcumin in non-demented adults: A double-blind, placebo-controlled 18-month trial. The American Journal of Geriatric Psychiatry 2018; 26(3): 266–277.
7. Ameri M, Shabaninejad Z, Movahedpour A, *et al*. Biosensors for detection of Tau protein as an Alzheimer's disease marker. International Journal of Biological Macromolecules 2020; 162: 1100–1108.
8. Horie K, Barthelemy NR, Mallipeddi N, *et al*. Regional correlation of biochemical measures of amyloid and tau phosphorylation in the brain. Acta Neuropathologica Communications 2020.

9. Ma D. P1-099: CIG suppresses tau pathology in a mouse model of tauopathy through regulating the activity of PP2A. The Journal of the Alzheimer's Association 2019; 15(7S): 272–273.
10. Cao M, Liu F, Ji F, *et al*. Effect of c-Jun N-terminal kinase (JNK)/p38 mitogen-activated protein kinase (p38 MAPK) in morphine-induced tau protein hyperphosphorylation. Behavioural Brain Research 2013; 237: 249–255.
11. Wang X, Zhao Y. The effect of AnshenDingzhi Fang on tau protein phosphorylation and BDNF/TrkB signaling pathway in Alzheimer's disease rats. Journal of Hainan Medical University 2019; 25(21): 1612–1616.
12. Frederiksen KS, Nielsen TR, Appollonio I, *et al*. Biomarker counselling, disclosure of diagnosis and follow-up in patients with mild cognitive impairment: A European Alzheimer' disease consortium survey. International Journal of Geriatric Psychiatry 2021; 36(2): 324–333.
13. Nicolia V, Ciraci V, Cavallaro RA, *et al*. GSK3 Fer-flanking DNA methylation and expression in Alzheimer's disease patients. Current Alzheimer Research 2017; 14(7): 753–759.
14. Huin V, Deramecourt V, Caparros-Lefebvre D, *et al*. The MAPT gene is differentially methylated in the progressive supranuclear palsy brain. Movement Disorders 2016; 31(12): 1883–1890.
15. Armentero MT, Sinforiani E, Ghezzi C, *et al*. Peripheral expression of key regulatory kinases in Alzheimer's disease and Parkinson's disease. Neurobiology of Aging 2011; 32(12): 2142–51.
16. Winston CN, Goetzl EJ, Schwartz JB, *et al*. Complement protein levels in plasma astrocyte-derived exosomes are abnormal in conversion from mild cognitive impairment to Alzheimer's disease dementia. Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring 2019; 11(1): 61–66.
17. Chen X, Jiang H. Tau as a potential therapeutic target for ischemic stroke. Aging 2019; 11(24): 12827–12843.
18. Tang SC, Yang KC, Chen CH, *et al*. Plasma h-Yueh,Chiu Ming-Japroteins in patients with vascular cognitive impairment. Neuromolecular Medicine 2018; 20(4): 498–503.
19. Viisanen H, Lilius TO, Sagalajev B, *et al*. Neurophysiological response properties of medullary pain-control neurons following chronic treatment with morphine or oxycodone: Modulation by acute ketamine. Journal of Neurophysiology 2020; 124(3): 790–801.
20. Yang S. Study on the role and mechanism of Tau and MAP-2 in CCK-8 mitigation of morphine-induced spatial memory damage (in Chinese) [PhD thesis]. Shijiazhuang: Hebei Medical University; 2013.
21. Ding K. Effect of the change of ghrelin and its receptor on accelerating diabetic thy by blood glucose fluctuation in GK rats. China Medical Abstracts (Internal Medicine) 2017; (1).
22. Xiao X, Sun J, Li S, *et al*. Acrylamide induced apoptosis in VSC4.1 cells through endoplasmic reticulum stress. Journal of Environmental & Occupational Medicine 2017; 34(12): 1087–1092.
23. Cao X, Qi X, Wang S. Protective effects of astaxanthin on hippocampal neurons damage induced by hydrogen peroxide. Chinese Journal of Marine Drugs 2012; 31(6): 45–49.
24. Szabo L, Eckert A, Grimm A. Insights into disease-associated tau impact on mitochondria. International Journal of Molecular Sciences 2020; 21(17): 6344.
25. Abisambra J, Jinwal U, Blair L, *et al*. O2lues, Mathew Cockman, Amirthaa Suntharalingham, Pengfei Li, Ying Jin, Christopher Atkins, Chad Dickeymemo-associated degradation. The Journal of the Alzheimer's Association 2013; 9(4S): 329–330.

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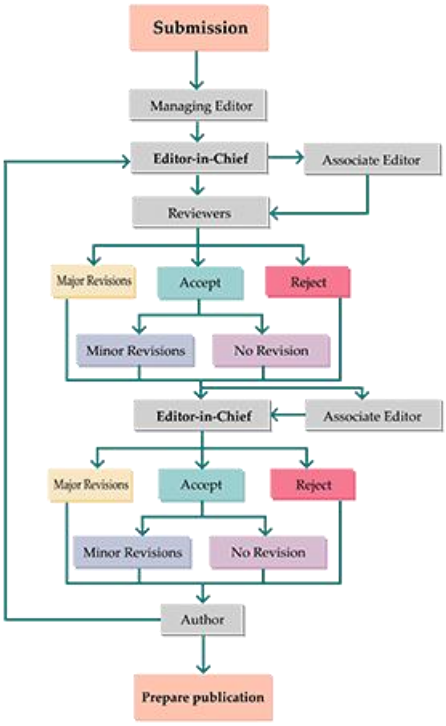

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Address: 73 Upper Paya Lebar Road #07-02B-03 Centro Bianco, Singapore

Phone: 0065-9863-3408

E-mail: contact@usp-pl.com

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