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Contents

original Articles

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Efficacy Analysis of Xiaoyao Pill Combined with Intense Pulsed Light in the Treatment of Chloasma

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Abstract: Objective To study the therapeutic effect of Xiaoyao Pill combined with intense pulsed light on stable chloasma. Methods 80 patients with stable chloasma in Shaanxi People's Hospital from September 2018 to September 2019 were enrolled in this prospective randomized controlled study. Randomly divided into control group and observation group, 40 cases in each group. The control group was treated with APT570; The observation group was treated with APT570 combined with oral Xiaoyao Pill Concentrated Pill. Follow-up for 8 months, the therapeutic effects of the two groups were compared. Chi-square test was performed on the data. Results The effective rate of the observation group was 95%, which was higher than that of the control group by 75% ($P < 0.05$). Conclusion During the treatment of chloasma, APT570 combined with Xiaoyao Pill, a traditional Chinese medicine, can significantly improve the effective rate, reduce the recurrence rate and significantly improve the facial skin quality, which has important clinical experience value.

Keywords: Intense Pulsed Light; Xiao-Yao Pill; Chloasma

Introduction

Chloasma, also known as liver spot and butterfly spot, is a common chronic acquired and symmetrical patchy pigmentation disease, which is more common in exposed parts such as face and neck, and is mostly irregular patches of light black, brown or light brown, with clear boundaries, which are mostly found in adolescent and childbearing women, and sometimes in menopausal women or men . The etiology and pathogenesis of chloasma in modern medicine are complicated, and there is no clear conclusion. It is related to factors such as sun exposure, heavy metal cosmetics, female pregnancy, endocrine disorder, race and family inheritance [1,2]. It is considered that this disease is marked by stagnation of qi and blood, which causes facial dullness. This is mainly due to the dysfunction of viscera, mostly due to deficiency of kidney qi, and the kidney water is not superior. Or due to stagnation of liver-qi, stagnation of liver-qi, heat from stagnation for a long time, and burn of yin-blood, facial qi-blood disharmony is caused; Or because of spleen deficiency, dampness accumulation, endogenous phlegm retention, blocking qi and blood, and not being able to be proud of the face, the color sink occurs [4]. The disease is easy to relapse and difficult to cure, so it is often treated by multiple means in clinic. According to the pathogenesis of chloasma in Chinese and Western medicine and personal clinical experience, the author studied the clinical efficacy and adverse reactions of patients who used intense pulsed light alone and oral Xiaoyao Pill Concentrated Pill by setting up a control experiment, which is reported as follows.

1. Data and experimental methods:

1.1 General information

80 cases in our department from September 2018 to September 2019 were selected. , randomly divided into control group and observation group. There were 40 cases in each group, and the control group was aged 25 ~ 48 years, with an average of 33 years. The course of disease is 8 months. The age of observation group was 27 ~ 46 years old, with an average of 37 years old. The course of disease is 8 months. There is no significant difference in general data between the two groups ($P > 0.05$), which is comparable.

Inclusion criteria: ① Young and middle-aged women; ② All of them have been treated with various injections, freckle removing cream and chemical stripping agent, but the effect is poor; ③ Facial lesions are covered with chloasma patches of cosmetics pigmentation or dark brown ecchymosis patches of dermis; ④ It is often symmetrically distributed in the zygomatic cheek of the face, showing butterfly shape, and in severe cases, it may involve the periorbital, forehead, upper lip and nose, with obvious edges; ⑤ No subjective symptoms and general discomfort; ⑥ The depth of stain is related to season, sun exposure and endocrine factors; ⑦ Mental stress, staying up late and fatigue can aggravate skin lesions; ⑧ It may be accompanied by menstrual disorder, irregular menstruation, poor sleep and dreaminess, listlessness and forgetfulness, etc.

Exclusion criteria: chloasma, freckles, Riel's melanosis, nevus OTA, nevus fuscocaerus zygomaticus; Women suffering from chronic diseases of liver, kidney, endocrine system and female reproductive system, pregnant and lactating women; Those who have been systematically treated or used for external depigmentation within 4 weeks

1.2 Method

Both groups were treated with the latest four-generation photon laser platform instrument produced by Feiton Company. Photonic handpiece is APT570, the treatment parameters are set at 18jm/cm, and the cooling rate is 50%. The pulse width is 12ms. Treatment once a month. Treatment for 8 consecutive times. The control group was given photon therapy alone, while the treatment group was given Lanzhou Foci Xiaoyao Pill-Concentrated Pill orally, 8 capsules (3g) at a time, three times a day. Take it orally in the morning and evening. Treatment continued for 10 months.

1.3 Observation index scoring standard.

① Scoring of lesion area: 0 is no lesion, 1 is less than 2cm2, 2 is 2 ~ 4cm2, and 3 is more than 4cm2. ② Skin lesion color score: 0 is normal skin color, 1 is light brown, 2 is brown and 3 is dark brown.

1.4 Curative effect standard

Basic recovery: the area of the plaque has shrunk by more than 90%, and the color has basically disappeared, and the index of decline of the score is greater than or equal to 0.8 ~ 0.9. Remarkable effect: the area of the plaque is reduced by more than 60%, the color is obviously lighter, and the index of decline of the score is 0.5 ~ 0.7. Effective: The area of the plaque is reduced by more than 30%, the color is improved, and the score decline index is 0.3 ~ 0.4. Invalid: degree of reduction of plaque area.Less than 30%, the color is basically not improved, and the score decline index is less than 0.3.

1.5 Treatment results: statistical treatment

SPSS20.0 software was used to process the data, and the counting data was represented by numbers or rates. Chi-square test showed that there was statistical significance ($P < 0.05$).

The total effective rate of the observation group was 95.00%, which was higher than that of the control group (75.00%), with significant difference ($P < 0.05$).

Table 1 Comparative analysis of therapeutic effects of the two groups [n(%)](n=40)

group	remarkable effective	effective	invalid	Total effective
observation group	20 （50.00）	18 （45.00）	2 （5.00）	38 （95.00）
control group	14 （35.00）	16 （40.00）	10 （25.00）	30 （75.00）
x^2	1.279	0.051	4.804	4.804
p	＞0.05	＞0.05	＜0.05	＜0.05

Compared with the control group, * $p < 0.05$.

There were no clear adverse reactions in all cases during the treatment.

Comparison of clinical efficacy between the two groups: the effective treatment rate of the treatment group was 95%, which was higher than that of the control group by 78%, with significant difference (P<0.05).

2 Typical cases:

a,b and c are before treatment; d, e and f were 8 months after treatment.

Fig. 1 Before and after treatment of chloasma (female patient, 38 years old, using intense pulsed light combined with oral Xiaoyao pill, chloasma spots were reduced, pigmentation was obviously improved, and skin quality was improved at the same time)

3. Discussion

Chloasma is a common chronic refractory skin disease characterized by pigment increase, which is mostly distributed in exposed parts such as cheeks, forehead and mandible, seriously affecting the beauty of patients. The causes of chloasma formation are complicated. At present, most people think that chloasma formation is related to sunlight, hormone level and heredity . Studies have shown that melanocyte activity in chloasma lesions is enhanced and melanogenesis is promoted. Therefore, how to inhibit melanocyte activity, reduce the formation of melanocytes and accelerate the degradation of melanocytes is the therapeutic direction of clinical treatment of chloasma [3]. With the widespread development and improvement of photoelectric technology, Q-switched laser, non-peeling dot-matrix laser, intense pulsed light, etc. have been widely used in the treatment of chloasma by using their selective photothermal principle [4]. In laser therapy, it is easy to damage skin, cause severe inflammatory reaction, activate tyrosinase activity, increase anabolism and produce more pigments. The new generation of photon therapy platform can accurately penetrate the skin and be selectively absorbed by the pigment mass (melanin) in the tissue. Without damaging the normal skin tissue, the pigment mass is destroyed and decomposed, so as to achieve the purpose of safe freckle removal. Studies have shown that angiogenesis and inflammatory reaction in chloasma lesions are involved in the generation of chloasma [5]. However, some scholars believe that the mechanism of intense pulsed light therapy for chloasma is not only the production of pigment, but also the mechanism of blood vessels [6].

However, the application of photoelectric technology has temporarily improved the treatment of chloasma, but the recurrence rate is different. How to reduce recurrence is a difficult problem that we need to solve. As a means of preventing recurrence, sun protection should carry out the whole treatment process of chloasma. Traditional Chinese medicine believes that the pathogenesis of chloasma is closely related to qi stagnation and blood stasis, yin deficiency of liver and kidney, spleen deficiency and dampness excess, and deficiency of qi and blood. The treatment principle should be soothing liver, strengthening spleen, nourishing blood, promoting blood circulation and removing blood stasis. Through clinical observation and investigation, it is found that all patients with chloasma have symptoms of liver depression and qi stagnation . Moreover, some scholar in traditional Chinese medicine believe that emotional disorder, such as stagnation of liver-qi, injury of spleen by worry, injury of kidney by panic, injury of liver by rage, etc., can all cause stagnation of qi, disharmony of veins, stagnation of qi and blood stasis, and blood can not be glorified on the surface and become the primary factor of chloasma. Therefore, Xiaoyao pill is the first choice in drug selection. Xiaoyao pill has the effects of soothing liver and nourishing blood, strengthening spleen and regulating stomach. It can regulate the emotion and endocrine of patients with chloasma, improve emotion, smooth qi and blood, and balance endocrine regulation, which can effectively reduce the recurrence rate of chloasma and assist in the treatment of photon macula. Therefore, this study adopted the method of combining traditional Chinese and western medicine, and achieved good curative effect by treating both symptoms and root causes. In this study, we found that: 1. The comprehensive treatment of chloasma is often better than a simple treatment, which may be related to the complicated factors of chloasma formation; 2. The intense pulsed light combined with Xiaoyao Pill has greatly improved the facial skin quality of patients with chloasma. We consider that there may be two reasons: first, the intense pulsed light is related to stimulating skin collagen metabolism after irradiating non-focus areas; Second, the influence of combined Xiaoyao Pill on patients' mental and psychological factors.

To sum up, choosing a photoelectric therapy that is harmless to the skin can reduce the secondary pigmentation of skin damage. Combined with concentrated pills of traditional Chinese medicine, complex decoction can be removed, which is convenient for patients to take orally, with good compliance and reduced pigment recurrence. The treatment of chloasma with integrated traditional Chinese and western medicine can significantly reduce pigmentation, and the curative effect is good. It is worthy of clinical promotion.

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Effects of Perioperative Psychological Intervention on Rehabilitation Process of Patients with Total Knee Arthroplasty

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Abstract: Background: This study focuses on evaluating the effects of perioperative psychological intervention on rehabilitation process of patients with total knee arthroplasty (TKA). Method: We selected 40 patients randomly which all need to receive total knee arthroplasty in Nanjing Drum Tower Hospital during the period from January 2022 to March 2022. The patients were randomly assigned to two Groups (20 in each group): an intervention group (Psychological intervention combined with routine nursing, drug and rehabilitation therapy) and a control group (routine nursing, drug rehabilitation therapy). During each patients' perioperative TKA surgeries, three scales (including VAS, ROM and ADL) are used to assess two groups. Result: After one week of psychological intervention, the pain score of the intervention group was lower than that of control group, the knee motion was greater than that of control group, and the ADL score was higher than that of control group. There was a significant difference in the treatment recovery between the two groups ($P<0.05$) Conclusions: Perioperative psychological intervention can promote the rehabilitation process of TKA patients, It can significantly improve pain, joint activity limitation, disuse muscle atrophy and other problems in a short period of time after surgery. Besides, it will effectively help patients to overcome the fear of movement, anxiety and improve patients' confidence, rehabilitation cooperation and prevention of complications, make patients adapt to the later rehabilitation life.

Keywords: Rehabilitation; Total Knee Arthroplasty; Perioperative Period; Psychological Intervention;

Introduction

With the continuous improvement of medical level, TKA has been widely used in degenerative osteoarthritis, rheumatoid arthritis, traumatic arthritis and so on[1].Surgical treatment that help patients rebuild knee function and avoid complications of various knee diseases (such as long-term bed-ridden pneumonia, venous thrombosis, pressure ulcers and so on) has been widely recognized and accepted by the society. However, a large number of studies have shown that the perioperative and postoperative rehabilitation effects of TKA are still unsatisfactory. At present, Fast-Track Surgery, (FTS) [2] has been deeply applied to the rehabilitation of perioperative TKA patients. The process of rehabilitation intervention is extremely rapid: On day 1 after the operation, appropriate passive activities of both lower limbs can be carried out by therapists; On day 2, the therapists can perform limb isometric, isotonic and joint rotation exercises; On day 3, the patients can carry on the walking training and ready to discharge.

However, since TKA is mainly aimed at elderly patients with inherent traditional concept of braking and surgical stress, most elderly patients generally have negative emotions such as fear of movement, anxiety and resistance. So this condition can be extremely detrimental to recovery. Many studies (such as PAN's research [3]) have proved that the patient's negative emotion is inversely proportional to the recovery degree of limb function. Therefore, this clinical study adopted the perioperative psychological intervention control study method. And the objective is to explore the influence and application value of systematic and targeted psychological intervention on the rehabilitation process of patients during the perioperative period of total knee replacement. The following report is made under this circumstances.

1. Data and Methods

1.1 General data

All 40 patients with perioperative TKA were from Nanjing Drum Tower Hospital during the period from January 2022 to March. All subjects met the audit standards of hospital ethics committee and obtained informed consent of patients and their families. Patients were randomly assigned to an intervention group and a control group with 20 cases each. There was no significant difference in basic data between the two groups. (P>0. 05), So this study possesses comparability. The author conducted the study design, and the implementation and evaluation were completed by the corresponding rehabilitation therapists.

1.2 Inclusion criteria:

(1) All patients underwent TKA after their first onset, and their vital signs are stable; (2)All patients without conscious and speech disorder have a certain ability to understand and express themselves ,they can cooperate in the evaluation of treatment；(3)They are all above primary school education; (4)They are all between 55 and 75 years old; (5)They all need to be assessed perioperatively (pre -, intra-, and postoperative)

1.3 Exclusion criteria:

（1）The patients had all kinds of psychological disorders, mental diseases and cognitive dysfunction before surgery；（2）The patients had coma, speech and hearing impairment, and was unable to cooperate with treatment and evaluation；（3）The patient has severe heart, lung, liver and kidney dysfunction.

1.4 Methods

The control group received routine perioperative TKA nursing, drug therapy, analgesia and rehabilitation treatment. In the intervention group, psychological intervention was added on the base of routine treatments of perioperative TKA

1.4.1 Routine treatments:

Routine treatments covers the following aspects：（1）Preoperative basic health education and rehabilitation exercise (including moderate passive and active)（2）Postoperative routine drug treatment（Inject 50mg flurbiprofen ester 0.5h before rehabilitation exercise to relieve pain during the training）, functional recovery training . The training consists of the following components: Ankle pump exercise (200 times a day, 20*10 groups); ② Knee stretching exercises (twice a day, 20-30min each time), knee bending exercises (10 times a day, bending to the maximum Angle for 1-2min); ③ Straight leg lifting exercise (lift 20cm from the bed); ④ Walking with the aid of walking AIDS.

1.4.2 Psychological intervention

Perioperative psychological intervention methods with easy operation and strong guidance were adopted to maximize the enthusiasm of patients within a reasonable range of indicators. The specific intervention methods are as follows:

(1) In preoperative TKA, therapists should establish friendly trust relationship with patients, attention to understand the needs of the patients, introduce the program of rehabilitation and Successful stories to patients and their families with straightaway language. therapists need to make patients clear about their actual situation and expectations in order to alleviate symptoms of patients' resistance and the fear of movement.

(2) Therapists pay attention to the use of facial expressions and body language during psychological intervention, They need to smile from beginning to end and be sincere in all kinds of investigations and evaluations to get closer to the patient.

(3) Brief psychodynamic psychotherapy[4]：①Therapists try to establish problems, complaints, goals, and solutions to guide patients to express their true feelings, thoughts and demands ,so in this way we can explore the key which causes anxiety and the fear of movement. At the same time, we also need to discuss with patients' families the space and methods for early improvement in a short period of time .②Rest period：This refers to that in the intermittent period of psychological intervention, patients need to recall and reflect on their psychological intervention and the conversation content at this stage .Meanwhile ,the therapists also have to sort out the treatment process during this period, summarize the existing

deficiencies and prepare content for feedback .③Positive feedback: During this period ,the patients 'cooperation, affirmation of the therapists' psychological intervention and efforts and wishes for rehabilitation need to be praised and praise. The therapists encourage the patients to continue to carry on and work hard, and at the same time assign some tasks to promote the patients' ability to solve and think about their own problems with the current plan.

(4) Relaxation training: Guide patients to perform abdominal breathing and learn to relax and relieve stress

(5) Eye movement desensitization and reprocessing (EDMR)[5]：therapists move the finger back and forth and asks the patients' eyes to follow the finger, while instructing the patients to open their eyes and visualize the situation during the onset of the disease. After repeated sessions, therapists guide the patient to re-experience the situation during the onset. So it can alleviate symptoms of persistent high alertness.

(6) Biofeedback therapy [6]：Using the equipment to train patients to consciously regulate the function of various metabolic organs in the body, to eliminate the pathological process, relieve postoperative pain, regulate emotions. The above treatment frequency remained during the whole perioperative period .

1.5 Observed indicator

The ROM, VAS, ADL score of patients in the intervention group and observation group was observed before operation and the 1st and 3rd day after operation

1.5.1 Range of Motion (ROM

This is the indicator to assess the range and degree of joint motor function impairment. Its main purpose is to determine whether the joint movement is limited and determine the degree of joint motion limitation;

1.5.2 Visual Analogue Scale（VAS）

It can effectively assess the pain of patients. On a scale of 10 points, 0 indicates no pain and 10 indicates the most unbearable pain.

1.5.3 Activity of Daily Living (ADL)

This scale includes 14 items respectively：Self-care (feeding, dressing, grooming, toileting, walking and bathing); Ability to use tools (making phone calls, shopping, housework, laundry, walking, using transportation, taking medicine and taking care of finances).

The scale has a total score of 100, the higher the score, the better the ability to live.'< 60' indicate moderate dysfunction and requiring help from others. When patients underwent treatment, '> 40'indicate the greatest benefit.

1.6 Statistical method

The data of the two groups were processed by SPSS software. The 't' was used to test ;The (t ±s） represent the measurement data; The 'X2' was used to test count data (%). P<0.05 was considered as statistically significant.

2. Results

Compared with the control group, the pain score of the intervention group was lower, the knee motion was greater, and the ADL score was higher. There was a significant difference in the treatment recovery between the two groups (P<0.05)

Table 1 Comparison of treatment recovery between the two groups

group	case	postoperative VAS score	postoperative ROM score	postoperative ADL score
intervention group	20	3.05±1.28	90.70±8.31	2.15 ±0.37
control group	20	3.8±1.32	76.20 ±7.66	2.40 ±0.50
't' value	-	-1.83	5.74	-1.8
'p' value	-	0.038	<0.001	0.040

The satisfaction of the intervention group was significantly higher than that of the control group, with statistical significance ($P<0.05$).

3. Discussion

Through the data analysis of the two groups before and after the intervention in this study, we can conclude that active and effective perioperative psychological intervention plays a great role in promoting the rehabilitation process of patients with TKA.

Psychological intervention therapy (perioperative psychological support, using short-range psychotherapy, relaxation training, biofeedback therapy and so on)can effectively overcome the early postoperative patients with fear psychology, mood stable patients, and to give patients the largest degree of confidence, enhance the patient's cooperation degree, greatly enhance the feasibility of the various rehabilitation program；

The pain score of the intervention group was lower than that of control group, so we can say that psychological intervention therapy has a very positive effect on relieving patients' pain problems after surgery and during rehabilitation and helps to improve pain tolerance. The knee motion was greater than that of control group, and the ADL score was higher than that of control group. This statistic data illustrate that timely psychological intervention can also contribute to the recovery of the overall body function of patients, and increase the stability, weight-bearing capacity, movement of patients' joints and core muscles. Patients' ability to survive and take care of themselves is improved as a result. These methods lay a solid foundation for a series of rehabilitation processes like walking training, and promote patients' self-care ability in daily life.

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Impact of Rhabdomyosarcoma (RMS) Characteristics on Prognosis of Pediatric RMS: A SEER Database Large Population Study

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Abstract: To provide a better insight into the epidemiology, characteristics, therapeutics, and outcomes of pediatric RMS. Data of 1,623 pediatric RMS were acquired from the Surveillance, Epidemiology and End Results (SEER) database. Detailed information on demographics, primary site, size, subtype, stage, surgery, and survival had been recorded during 1975-2016. The most common subtype was embryonal RMS (64.9%) followed by alveolar RMS (29.9%). Additionally, the majority of RMS size was larger than 5 cm. Multivariable analysis exhibited that the age over 10, unfavorable primary site, distant metastasis was respectively correlated with the poor OS, whereas surgery could improve the outcomes of pediatric RMS. In conclusion, our large population-based analysis described that age, subtype, primary tumor sites, stage and surgery are all independent prognosis factors for RMS.

Keywords: Rhabdomyosarcoma; Prognosis; Subtype; Survival; Surgery; SEER

Introduction

Rhabdomyosarcoma (RMS), mainly derived from certain mesenchymal cells that undergo an aberrant differentiation process in the embryonal development, is the most common malignant soft-tissue neoplasm of children. Identification the impact of biological characteristics and treatments on RMS survival is of significance for the patients, especially for the pediatric patients. To better optimize the RMS treatment procedures, it is critical to explore and identify sensitive prognosis factors, especially comparing the risk factors within tumor-related biological characteristics. In this study, we performed a comprehensive analysis of the RMS cases that were registered in the Surveillance, Epidemiology and End Results (SEER) database to investigate the clinical characteristics and outcomes of pediatric RMS.

1. Materials and methods

1.1 SEER database

SEER serves as a public database provided by the National Cancer Institute (NCI), which includes information from population-based cancer registries of 20 geographic areas, and covers approximately 34.6% of the United States population. Data of the pediatric patients with RMS from 1975 to 2016 in this study were extracted from the SEER database.

1.2 Identification of RMS cases

All of the pediatric RMS patients were diagnosed by the histological confirmation according to biopsy or surgical pathology. Total 1,103 in 2,726 cases were excluded because of unknowns in the pediatric age, gender, race, tumor size, vital status, survival months, primary site, subtype or stage.

1.3 Statistical analysis

For analysis, “age” was converted from a continuous variant to a categorical variant as “< 10” and “≥ 10”. The “race” was classified as white or non-white, and “stage” was used to define the RMS neoplasm development including “localized”, “regional”, and “distant”. “Localized” was identified as an invasive tumor confined entirely to the origin organ; “regional” was identified as an extended neoplasm, which invades 1) beyond the limitations of origin organs and directly to surrounding organs; 2) to the regional lymph nodes; 3) with extension and to regional lymph nodes; “distant” was identified as metastasis. The “subtype” was categorized into three sections: the “alveolar”, “embryonal” as well as “others” which contains pleomorphic, spindle cell, mixed type and ganglionic differentiation.

IBM SPSS Statistics (version 25.0) was used for analyzing the statistical significance. A nomogram and calibration plots were formed according to the results of multivariate analysis via the package rms26 in R program language (version i386 3.6.0). Results were considered statistically significant at $P < 0.05$.

2. Results

2.1 A prognosis nomogram for OS of pediatric RMS patients

A nomogram was used to analyze the potential prognosis factors in pediatric patients with RMS. Results showed a 0.742 index of concordance (C-index) for OS prediction (95% CI, 0.7234 - 0.7606), indicating that this nomogram is useful for the OS forecast of pediatric RMS patients (Fig. 1A). The calibration plot of survival probabilities at 3- and 5-year also presented a similar result in the RMS prediction via a nomogram and clinical observations (Fig. 1B and 1C).

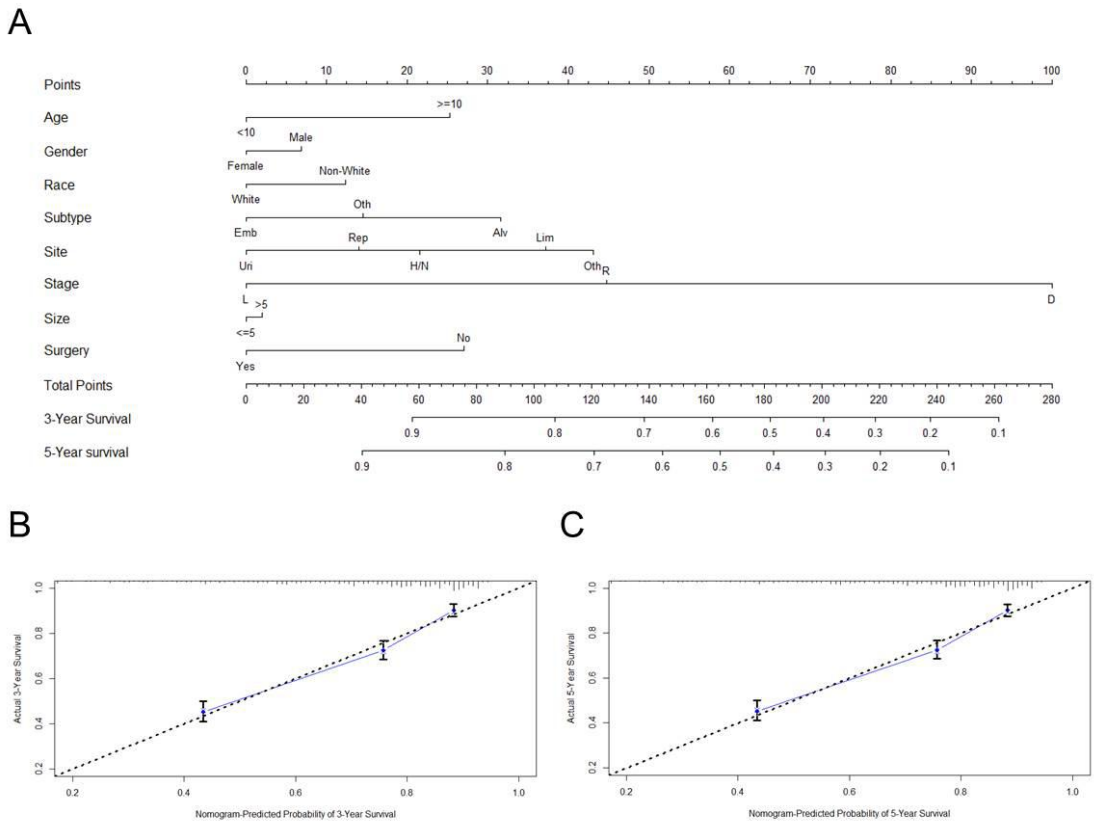

Fig 1. (A) A nomogram for pediatric RMS.

An individual child’s value was located on each variable axis, and a solid line was drawn upward to define the number of points received for each variable value. The sum of above numbers was located on the total point axis, and a solid line was drawn to the survival axes to define the likelihood of 3- or 5-year survival. (B-C) Two calibration curves were used for

predicting the 3-year OS (B) and 5-year OS (C) of pediatric RMS patients, respectively. X-axis refers to nomogram-predictied survival probability; y-axis refers to actual OS.

Abbreviations: Alv, Alveolar; Emb, Embryonal; Uri, urinary system; H/N, head/neck; Lim, limbs; Oth, other sites; L, localized; R, regional; D, distant.

2.2 Independent prognosis factors for pediatric RMS

As shown in Table 1, children older than 10 years old exhibited a higher risk of death (HR, 1.4673; 95% CI, 1.2218 - 1.7620; $P < 0.001$) compared with those of control. Then, the mortality was different according to each primary site. Compared with the reproductive system, HR for RMS in other sites rather than urinary system, head/neck and limbs was 1.5521 (95% CI, 1.1365 - 2.1199; $P < 0.001$). In addition, pediatric RMS patients in regional and distant stage presented a significantly higher mortality rate. HR was notably higher in patients with a regional stage (1.9683; 95% CI 1.5069 - 2.5710; $P < 0.001$) or a distant metastasis (4.5493; 95% CI, 3.4944 - 5.9225; $P < 0.001$). Taken together, these data show that age, primary site, and stage were all poor prognosis factors for outcomes of pediatric RMS.

We also found that the embryonal subtype and surgery could increase the OS of pediatric RMS. Embryonal RMS presented a higher survival rate (HR, 0.6196; 95% CI, 0.5019 - 0.7648; $P < 0.001$) compared with other subtypes. Surgery could also help to improve the survival rate of pediatric RMS (HR, 0.6638; 95% CI, 0.5467 - 0.8058; $P < 0.001$).

Table 1 Multivariable analysis of factors associated with overall survival in the pediatric RMS patients

Variables		HR[1]	95% CI[2]	*P*
Age (year)	< 10	1	Reference	
	≥ 10	1.4673	1.2218-1.7620	**0.00004 < 0.01**
Gender	Female	1	Reference	
	Male	1.1096	0.9254-1.3304	0.26173
Race	White	1	Reference	
	Non-white	1.2051	0.9892-1.4680	0.06399
Subtype	Alveolar	1	Reference	
	Embryonal	0.6196	0.5019-0.7648	**0.000008 < 0.01**
	Other	0.7716	0.4997-1.1915	0.24213
Primary site	Reproductive system	1	Reference	
	Urinary system	0.8084	0.4289-1.5235	0.51065
	Head/neck	1.1212	0.8053-1.5609	0.49810
	Limbs	1.4199	0.9966-2.0288	0.05221
	Other	1.5521	1.1365-2.1199	**0.00571 < 0.01**
Tumorsize (cm)	≤ 5	1	Reference	
	> 5	1.0308	0.8605-1.2351	0.74273
Stage	Localized	1	Reference	
	Regional	1.9683	1.5069-2.5710	**0.0000006 < 0.01**
	Distant	4.5493	3.4944-5.9225	**0.0000002 < 0.01**
Surgery	No	1	Reference	
	Yes	0.6638	0.5467-0.8058	**0.00003 < 0.01**

2.3 Independent prognosis factors for pediatric-alveolar/embryonal RMS

Table 2 displayed that in the pediatric alveolar RMS, the primary site was no longer a prognosis factor for OS. However, the death risk was increased to 1.89 times (HR, 1.8915; 95% CI, 1.0693 - 3.3459; $P < 0.05$) in the embryonal RMS located in limbs. This observation highlights that oncologists should thoroughly consider the impact of primary sites on outcomes of pediatric RMS according to different RMS subtypes.

Table 2 Multivariable analysis of factors associated with overall survival in the pediatric RMS patients according to the subtype

Variables	Alveolar (N = 485)			Embryonal (N = 1,053)		
Age (year)	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
< 10	1	Reference		1	Reference	
≥ 10	1.5803	1.21323-2.0584	**0.000691 < 0.01**	1.3490	1.0281-1.7701	**0.03080 < 0.05**
Gender						
Female	1	Reference		1	Reference	
Male	1.2792	0.98170-1.6669	0.068266	0.9797	0.7489-1.2818	0.88136
Race						
White	1	Reference		1	Reference	
Non-white	1.1932	0.90176-1.5789	0.216322	1.1354	0.8380-1.5382	0.41252
Primary site						
Reproductive system	1	Reference		1	Reference	
Urinary system	0.4880	0.06105-3.9012	0.498779	0.7898	0.3990-1.5635	0.49821
Head/neck	1.0087	0.49130-2.0711	0.981090	1.0472	0.6953-1.5772	0.82546
Limbs	1.1848	0.59281-2.3680	0.631220	1.8915	1.0693-3.3459	**0.02851 < 0.05**
Other	1.4826	0.73067-3.0084	0.275357	1.4117	0.9719-2.0506	0.07028
Stage						
Localized	1	Reference		1	Reference	
Regional	1.4768	0.97352-2.2403	0.066694	2.2201	1.5541-3.1715	**0.00001 < 0.01**
Distant	3.4562	2.29728-5.1998	**0.000002 < 0.01**	5.0804	3.5716-7.2266	**0.0000001 < 0.01**
Tumor size (cm)						
≤ 5	1	Reference		1	Reference	
> 5	0.8702	0.66835-1.1330	0.301729	1.2412	0.9532-1.6161	0.10865
Surgery						
No	1	Reference		1	Reference	
Yes	0.7343	0.55174-0.9772	**0.034187 < 0.05**	0.6347	0.4822-0.8356	**0.00119 < 0.01**

2.4 Independent prognosis factors for metastasis or non-metastasis RMS

Table 3 was shown that age, subtype, and surgery were independent factors related to the survival rate of pediatric RMS patients regardless of metastasis. To our surprise, primary site was a negative prognosis factor in non-metastasis RMS, while this phenomenon could not be observed in metastasis RMS. According to the observation in the non-metastasis group, pediatric RMS located in both head/neck and limbs displayed a significantly higher mortality with an estimated HR 1.6325 (95% CI, 1.0195 - 1.2.6141; $P < 0.05$) in head/neck group and 1.7147 (95% CI, 1.0067 - 2.9206; $P < 0.05$) in limbs group, respectively.

Table 3 Multivariable analysis of factors associated with overall survival in the pediatric RMS patients with or without metastasis

Variables	No metastasis (N = 1,175)			Metastasis (N = 448)		
Age (year)	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
< 10	1	Reference		1	Reference	
≥ 10	1.4870	1.1482-1.9257	**0.002637 < 0.01**	1.4492	1.1100-1.8919	**0.00638 < 0.01**
Gender						
Female	1	Reference		1	Reference	
Male	1.0661	0.8258-1.3763	0.623187	1.1337	0.8733-1.4719	0.34594
Race						
White	1	Reference		1	Reference	
Non-white	1.0942	0.8236-1.4535	0.534620	1.2412	0.9380-1.6425	0.13054
Subtype						
Alveolar	1	Reference		1	Reference	
Embryonal	0.4836	0.3608-0.6481	**0.000001 < 0.01**	0.7121	0.5279-0.9605	**0.02617 < 0.05**
Other	0.4863	0.2434-0.9716	**0.041208 < 0.05**	1.1441	0.6462-2.0258	0.64414
Primary site						
Reproductive system	1	Reference		1	Reference	
Urinary system	1.0841	0.3722-3.1579	0.882279	0.6602	0.2989-1.4582	0.30446
Head/neck	1.6325	1.0195-2.6141	**0.041300 < 0.05**	0.7771	0.4796-1.2592	0.30575
Limbs	1.7147	1.0067-2.9206	**0.047215 < 0.05**	1.0552	0.6540-1.7025	0.82586
Other	2.4004	1.5165-3.7994	**0.000186 < 0.05**	1.0320	0.6766-1.5742	0.88368
Tumorsize (cm)						
≤ 5	1	Reference		1	Reference	
> 5	1.0772	0.8273-1.4026	0.580707	0.9607	0.7455-1.2380	0.75669
Surgery						
No	1	Reference		1	Reference	
Yes	0.5691	0.4322-0.7495	**0.00005 < 0.01**	0.6818	0.5199-0.8940	**0.00560 < 0.01**

3. Discussion

In our study, the RMS embryonal and alveolar subtypes were both frequent in pediatric patients, and embryonal subtype accounted for 64.9% of all the subtypes. And embryonal subtype was a positive prognosis factor for the OS of pediatric RMS ($P = 0.000008 < 0.01$). We moved on to compare the risk factors in these two subtypes. Notably, compared with the alveolar subtype, the OS for embryonal RMS located in limbs was in a higher mortality rate (HR, 1.8915; 95% CI, 1.0693 - 3.3459; $P < 0.05$). In summary, these observations not only highlight that the embryonal subtype is the prognosis factor of RMS, but also indicates that the outcomes of embryonal RMS is strongly correlated with the tumor location.

Genitourinary and head/neck are the frequently original sites of pediatric RMS, even though RMS can be found in any anatomy area of human body. Bradley et al. showed that the most common primary site of RMS was reproductive system (40%), followed by para-meningeal (14%) and limbs (11%) [1]. However, the outcomes of RMS with different primary sites are controversial. Kirsch et al. confirmed that the survival rates were of no difference in multiple primary sites in female pediatric RMS patients in the period of 1973-2006 [3], while a lower 5-year survival rate of RMS was also reported with primary sites in extremities (25%), and other sites (28.9%) rather than orbit (57.2%), head/neck (51.3%), para-meningeal (41.2%), and genitourinary (79.8%) [2]. In fact, our study confirms this observation and suggests that the mortality was higher in the pediatric RMS located in other primary sites ($P = 0.00571 < 0.01$) rather than reproductive system, urinary system, head/neck, and limbs.

For the RMS stage, the majority is localized and less than 30% of the RMS neoplasms are with metastasis. In fact, distant metastasis is a poor prognosis factor for pediatric RMS. Kirsch et al. mentioned that 38.8% (N = 26) of, 16.2% (N = 11) of and 28.4% (N = 15) of RMSs were in the stage of localized, regional and distant, respectively [3]. Notably, tumor stage is a key biological characteristic in the diagnosis and treatment of pediatric RMS. Some prior studies on pediatric RMS had mentioned that a distant metastasis was correlated with a poor prognosis [4, 5]. Meanwhile, several studies also concluded that localized stage is the most favorable prognosis factor of RMS [6, 9]. Our multivariate analysis results identified the regional (HR, 1.9683; 95%, 1.5069 - 2.5710; $P < 0.001$) and distant (HR, 4.5493; 95%, 3.4944 - 5.9225; $P < 0.001$) stage as two independent predictors for mortality of pediatric RMS. In summary, these data display evidences that distant metastasis is a poor prognosis factor of pediatric RMS.

In conclusion, we studied a large population-based cohort of RMS and suggested that the biological characteristics, such as age, subtype, primary site, stage and no surgery are correlated with a poor outcome of pediatric RMS patients. Therefore, differences of the prognostic factors among populations with various characteristics should be thoroughly considered, and further investigations are needed to identify long-term poor prognosis impact from each RMS characteristics.

Disclosure of potential conflict of interest

No potential conflicts of interest were disclosed.

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Clinical Research Review of Acupuncture for Laryngopharyngeal Reflux Disease

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Abstract: In recent years, laryngopharyngeal reflux disease has attracted the attention of acupuncture clinicians. This article summarizes the acupuncture treatments (simple acupuncture, acupuncture combined with western medicine, acupoint application combined with Chinese medicine) and the corresponding treatment effects in the past 5 years. The current research has proved the effectiveness of acupuncture and moxibustion for laryngopharyngeal reflux disease, and provides methods and ideas for clinical treatment of laryngopharyngeal reflux disease.

Keywords: Laryngopharyngeal Reflux Disease; Acupuncture; Clinical Research Review

Introduction

Symptoms of laryngopharyngeal reflux disease (LPRD) include throat swelling, repeated throat clearing, hoarseness, dysphonia, and chronic cough[1]. Epidemiological reports in recent years show that the prevalence of LPRD in the United Kingdom, Greece, and Fuzhou, China is 34.4%, 18.8%, and 5.0%, respectively [2-4], and it has caused a relatively serious social medical and economic burden. In the past few years, laryngopharyngeal reflux disease has increasingly attracted the attention of clinicians. This review summarizes the clinical acupuncture and moxibustion treatment of LPRD in the past five years.

1. Pure acupuncture

Yang Xiaowei believes that LPRD patients often suffer from stagnation of liver qi due to the prolonged and repeated course of the disease.The treatment group was treated with pure acupuncture, while the control group was treated with esomeprazole for 4 weeks. The results showed that the RSI score of the observation group was significantly lower than that of the control group, $p<0.05$, and the difference was statistically significant,indicating that soothing liver and stomach acupuncture can improve the symptoms [5]. Zhang Tao administered acupuncture at a single point of Tiantu to 105 patients with LPRD, and evaluated the curative effect through a scoring scale combined with laryngoscopy. It was found that after acupuncture at this point, the RSI and RFS scores were both lower than those before treatment, and the difference was statistically significant ($P<0.05$), indicating that acupuncture at Tiantu acupoint is effective for reflux pharyngitis[6], and it is speculated that it may be related to the location of the occurrence of laryngopharyngeal reflux.

2. Acupuncture combined with Western medicine

Wang Yingying believed that the disorder of Qi movement was the main cause of reflux pharyngitis, and selected acupuncture points and oral western medicine accordingly, and the control group was only given western medicine. It was found that the evaluation indexes of the observation group were lower than those of the control group after treatment ($p<0.05$). The total effective rate in the observation group was 92.9%, which was better than 71.4% in the control group. It shows that acupuncture combined with western medicine can effectively control the symptoms of reflux based on the principle of Qi machine ascending and descending theory, and the curative effect is better than that of western medicine alone [7]. Zhang Tao et al. randomly divided 202 LPRD patients who met the inclusion and exclusion criteria into a treatment group

of 102 and a control group of 100. The treatment group was given PPI combined with acupuncture at Tiantu point, while the control group was given PPI only. The clinical symptom scores of the two groups were observed. As a result, there were statistically significant differences in the total effective rate and symptom and sign scores between the two groups, indicating that acupuncture at Tiantu point combined with PPI is effective in the treatment of LPRD[8]. The clinical efficacy of acupuncture and western medicine in the treatment of reflux pharyngitis is definite, which may be related to the improvement of esophageal motility and EGF level by acupuncture [9].

3. Acupoint sticking combined with traditional Chinese medicine

Liao Weiting used acupoint sticking combined with Shugan Jianpi Liyan Decoction to treat patients with reflux pharyngitis and observed the clinical efficacy. In the traditional Chinese medicine group, the observation results showed that there were statistically significant differences in the scores of symptoms and signs and adverse reaction rates between the two groups before and after treatment ($P<0.05$), indicating that acupoint sticking combined with Shugan Jianpi Liyan Decoction can not only effectively improve reflux pharyngitis Symptoms and signs of patients,but also with high safety [10]. Wu Yichao used acupoint sticking combined with traditional Chinese medicine to treat reflux pharyngitis with liver stagnation and spleen deficiency. The research group applied Chenshu Jianpi ointment on Ganshu, Neiguan, Zhongwan and other points, combined with oral Chinese medicine Chaihu Shugan Powder. The control group received omeprazole and mosapride. The results of the study showed that the RSI and RFS scores of the patients in the study group were significantly lower than those in the control group, and the difference was statistically significant ($P<0.05$) [11]. However, it is worth thinking about how the above research determines that acupoint sticking therapy is effective.

4. Outlook

In recent years, scholars at home and abroad have been hot on the pathogenesis of LPRD[12-15]. Wang Gang et al. found that patients with LPRD mainly have autonomic dysfunction characterized by relatively decreased vagal nerve activity and relatively increased sympathetic nerve activity, and vagal nerve activity in LPRD patients is negatively correlated with the severity of reflux symptoms and signs [16]. Numerous studies have shown that acupuncture can modulate vagal activity [17-18]. Modern medicine believes that acupuncture at corresponding acupoints (such as Zusanli, etc.) can enhance gastrointestinal function by regulating the excitability of the vagus nerve and inhibiting gastricacid secretion. However, Chinese traditional medicine believes that if the acquired essence is strong, the middle jiao will rise and fall spontaneously, and all reflux symptoms (acid reflux, belching, etc.) will be eliminated. Laryngeal reflux disease is inextricably linked with gastroesophageal reflux disease in a strict sense, and throat reflux disease is actually a special type of reflux disease. As far as this disease is concerned, whether further research can find specific acupoints or acupoint groups that have a certain neural pathway connection with the vagus nerve in this segment, and relatively increase the activity of the vagus nerve through acupuncture intervention, so as to reduce the symptoms of laryngopharyngeal reflux and reduce the symptoms of laryngopharyngeal reflux. Signs? The concept of neuronal hypersensitivity [19] suggests that targeting specific neuronal receptors in the peripheral and central nervous systems would be a very promising therapeutic direction. Similarly, can acupuncture stimulate certain receptors through the intervention of certain acupoints, thereby reducing the possibility of hypersensitivity? Relevant acupoint or meridian-specific studies are worthy of further exploration. Due to the lack of effective treatment measures for LPRD in Western medicine at present [20], the solution of the above problems may change the treatment pattern of LPRD.

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Universe Scientific Publishing

Research Progress of Improving MDD by Fecal Microbiota Transplantation Affecting Intestinal Microbiota-Gut- Brain Axis

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Abstract: It has been improved that fecal microbiota transplantation (FMT) can alleviate gastrointestinal disorders such as Clostridium difficile infection (CDI). Moreover, some studies have also concluded that FMT is available in alleviating Major Depressive Disorder (MDD), also known as depression widely, by regulating microbiota-gut-brain axis (MGBA), hence, this paper summarized the relationship between MGBA and MDD and mechanisms of MDD which is related with MGBA. And this review retrospected the animal experiments and clinical studies on the treatment of depression with FMT in recent years and discussed the future development of FMT, in order to assess whether FMT is potential and credible in the treatment of depression.

Keywords: FMT; Depression; Intestinal Flora

Background

Depression is the fourth largest disease in the world, but at present, the general public's cognition and prevention of depression is still in a vague stage, and the development of related drug research and development and treatment methods is also gradually stalled[1]. In recent years, with the development of science and technology, fecal microbiota transplantation (FMT), as a new treatment method, has been gradually applied in the diagnosis and treatment of various diseases, among which depression is one of the main indications. Fecal microbiota transplantation (FMT), which means transplanting the functional gut flora in the feces of healthy people into the gastrointestinal tract of the patient to rebuild new intestinal flora and realizing the treatment of intestinal and extraintestinal diseases, is currently used for the identification of Clostridium difficile Bacillus infection and other important methods for various flora-related diseases. Therefore, the disorder of intestinal will cause the occurrence of many diseases, one of these diseases is depression, that patients with depression will concomitant the symptom of increased levels of enterobacteriaceae or rijcidaceae, and decreasing levels of faecalis in the gastrointestinal tract during is also a significant sign of depressive appearance.

1. Relationships between MDD and intestinal microbiota-gut- brain axis

Gut microbes can interact with the brain in three particularly important ways: 1) Directly through the vagus nerve and the neural network that surrounds the gut and sends signals to the brain; 2) through immune cells that reside in the gut and travel to the brain;3) Metabolites produced by gut microbes first enter the blood, then the brain, and ultimately affect behaviori. Certain metabolites of gut bacteria can cause anxiety and autism-related abnormalities when injected into functioning mice. This further supports the possibility that microbial metabolic molecules link brain, gut, and neuro-emotional circuits in the neuroendocrine metabolic stress response system. The microbiota-gut-brain axis (MGBA) connects the central nervous system, gastrointestinal tract and gastrointestinal microbes through the above-mentioned approaches to regulate each other and jointly maintain body balance. Generally speaking, it can be roughly divided into five ways, namely, autonomic nervous system (ANS), hypothalamic-pituitary-adrenal (FPA), immune system, enteric nervous system (ENS) and circulatory system[2]. Any functional disorder of MGBA may induce the occurrence of depression. On top of that, the "leaky gut" hypothesis has also been linked to depression[3].

2. Technology of fecal microbiota transplantation

Fecal microbiota transplantation (FMT) is a highly efficacious and wide-used modality to treat recurrent or refractory infection (CDI), with overall curative radio of 90%. Therefore, FMT has been widely used for around 10 years[4]. The core technology is to extract beneficial bacteria from the feces of healthy people after centrifugation and filtration and transplant them into the gastrointestinal tract of patients, so that the gastrointestinal flora of patients can be remodeled and play a normal function, and then treat diseases related to intestinal flora disorder[5].

3. FMT animal models applied to MDD

Zheng[6] et al isolated and extracted feces from healthy control group (n = 5, male, 29-62 years) and MDD patients (n = 5, male, 27-61 years) and transplanted the flora into adult (6-8 weeks old) KM mice in order to determine whether intestinal flora can transmit depression and whether the mice were prone to depression. Two weeks after fecal microbiota transplantation, depression levels of mice in model group were assessed by a series of behavioral tests, including Open-field test (OFT), Y-maze test, Tail suspension test (TST) and Forced swimming test (FST), in both the model and control group. The final results showed that the lack of gut microbiota resulted in a reduction in immobility time in FST, and no difference was found in the total distance travelled between GF and SPF mice from the OFT. On the contrary, compared with SPF mice, the proportion of central movement distance in GF mice increased significantly ($P \geq 0.05$), indicating that the anxiety-like behavior of GF mice decreased, and GF mice showed better memory performance compared with SPF mice. In addition, by measuring the fecal flora content of the two groups of mice, it was found that the gastrointestinal bacterial phenotype of MDD mice was significantly different from that of healthy mice, and was consistent with the bacterial phenotype of their respective donors. This finding suggests that gut microbiota may influence the microbial-gut-brain axis by altering gastrointestinal metabolism, thereby "passing on" depression.

Schmidt[7] et al. gave intestinal flora of healthy SD rats that had suffered from spinal cord injury (SCI), and conducted behavioral experiments such as high plus maze (HPM). The results showed that transplantation of FMT from healthy rats to SCI induced depressed and anxious rats significantly reduced depressive and anxiety-like behaviors. These results suggest that fecal bacteria in healthy FMT rats can significantly improve SCI induced depressive behavior.

The use of FMT therapy in healthy and depressed mice demonstrated that FMT can cause depression in healthy mice, that means FMT can also be used as a new way to treat depression.

A series of animal experiments are listed above. Whether FMT is applied to healthy mice or depressed mice, it is used to induce depression or fight depression by interfering with the intestinal flora of experimental animals. While the exact mechanism by which FMT improves depression is unclear, it is undeniable that the microbial-gut-brain axis plays a large role.

4. Clinical application

Huang[8] et al. used FMT to treat 30 patients (18 males and 12 females, with an average age of 44 years) with refractory Irritable Bowel Syndrome (IBS), for 2 - 3 times of FMT stage treatment. Ibs-qol, IBS-SSS, GSRS, HAM-A and HAM-D scales were used to score the patients 1 and 3 months after FMT administration, and the results showed that gastrointestinal symptoms were significantly improved while depression and anxiety symptoms were alleviated.

Up to now, there is no clinical research data on the treatment of simple depression with FMT, most of which are similar to the above study. Although the mechanism of FMT improving depression is discussed and other disease factors interfere. Except for mental symptoms are significantly improved, there is no definite evidence that FMT can directly affect the depression of PATIENTS with IBS[9].shape

5. Discussion

At present, FMT is still in the stage of theoretical research, and it is still unknown when it can be really applied in clinical practice. Nevertheless, this kind of technology still shows great potential in the field of mental illness treatment, changing the inherent "stopgap treatment" of the traditional treatment thought, provides a new idea for the treatment of depression. It is hoped that more researchers will focus on this technology in the future, so as to overcome technical barriers and benefit patients as soon as possible.

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Estimation of the Incubation Period and the Serial Interval of COVID-19 in Chongqing, China

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Abstract: In December 2019, the initial case of COVID-19's disease appeared in Wuhan, Hubei Province, China. But it soon caused an outbreak in Chongqing as well. Reasonable estimates for the incubation period distribution and the serial interval distribution would provide timely information to guide intervention policy for the government of Chongqing. We collect individual information from Chongqing Center for Disease Control and Prevention(CQCDC). We use doubly interval-censored data to estimate the incubation period and the serial interval for confirmed cases exposed to COVID-19 during incubation period,the mean incubation period is estimated to be 7.5(6.6-8.6,95% CI) days and the mean serial interval is estimated to be 6.1 (5.0-7.5,95% CI) days. The analysis result show that COVID-19 could spread in the incubation period,which may complicate quarantine work. The implementation of control measures is indispensable in reducing the spread of asymptomatic incubation period in high-risk population.

Keywords: COVID-19; Incubation Period; Serial Interval; Chongqing; Coronavirus

Key Massages:

1.To estimate the incubation period and the serial interval for confirmed cases exposed to COVID-19 during both the incubation period and symptomatic period.

2.To verify that COVID-19 could spread in the incubation period.

3.To compare the differences of incubation period and serial interval among patients with different contact periods.

Introduction

In December,2019,an outbreak of novel coronavirus disease COVID-19 broke out in Wuhan, Hubei Province of China[1].The novel coronavirus SARS-CoV-2,dubbed COVID-19 (coronavirus disease 2019) by the World Health Organization (WHO) is characterized by fever,cough,fatigue, shortness of breath,pneumonia,and other respiratory tract symptoms[2–4],and in many cases will develop to death. Due to the migration of the annual Spring Festival,the epidemic spread rapidly.As a close neighbor of Wuhan,Chongqing has become one of the cities which was most affected by the coronavirus disease COVID-19 epidemic, during the early stage. As of January 21st, Chongqing has reported 5 cases of coronavirus COVID-19,including 2 cases in Wushan, 2 cases in Wanzhou and 1 case in Changshou[5]. All of the imported cases have lived experience of working in Wuhan. Fortunately, the officials have taken effective measures to control them.

As of February 24st,there were no newly confirmed cases in 13 districts and counties in Chongqing for 14 consecutive days,and there were no newly confirmed cases in 26 districts and counties for 7 consecutive days[6]. At the same time,the global epidemic is getting more and more serious.Key aspects of novel coronavirus disease (COVID-19) transmission dynamics in 2019 are still unclear [7].

Due to the lack of understanding of the key epidemiological and transmission characteristics of new pathogens,especially the limited understanding of their transmission ability and toxicity in the population.

Through the estimation of incubation period and serial interval and exposure type analysis, we provide the infection characteristics of COVID-19, that is, incubation period and serial interval, in order to provide clues to containment measures and reduce the spread of infection.

1. Method

1.1 Case definitions

According to standard clinical guidelines,COVID-19 suspected cases are defined as the combination of clinical characteristics and epidemiological histories. Clinical characteristics of suspected case must fit at least 2 of 3 following criteria: “fever and/or symptoms in respiratory system; radiographic evidence of pneumonia[8]; The white blood cell count is low or normal, or the lymphocyte count is low. ” Epidemiologic histories must fit at least 1 of 4 following criteria: “a history of traveling in Hubei Province or other districts that has confirmed cases reported within 14 days of symptom onset; Previous contact with a patient with fever or respiratory symptoms from Hubei Province or elsewhere who reported a confirmed case within 14 days of the onset of symptoms;Anyone who has close contact with confirmed case; cluster cases[8].” A confirmed case was defined as a case with respiratory specimens that tested positive for the COVID-19 by at least one of the following two methods:positive result by real-time Reverse-Transcription-Polymerase-Chain-Reaction (RT-PCR) assay for COVID-19 or a genetic sequence that matches COVID-19.

1.2 Data sources

The COVID-19 infectious disease report card and close contacts survey were obtained from the China Disease Control and Prevention Information System.The COVID-19 cases reported in Chongqing from January 21,2020 to March 31st were investigated and collected according to the notice of the "Notifications of the Sero-epidemiological Survey Plan for the Issuance of COVID-19 Asymptomatic Infectious Diseases" (National Office of inventions [2020] 14).We collect individual information including age, gender, source of infection, onset time of symptoms, diagnosis time, the left and right endpoints on the possible exposure interval.

We divide patients into three categories:

1. Incubation period exposure:When the patient comes into contact with infectious people,the infectious people are in the incubation period without any symptoms;
2. Symptomatic period exposure: When the patient contacts the infectious person,the infectious person has developed symptoms;
3. Unsure: the patient has contacted the infectious person who has not yet come into contact with the infectious person who has already developed the disease,but is not sure which kind of infectious person is infected.

The incubation period,that is,the time between infection to onset,is very important in the monitoring and control of infectious diseases,but it is usually only a rough observation[9].To estimate the incubation period,we delete the data of asymptomatic patients. We estimate the incubation period with doubly interval-censored data[10].

The serial interval of COVID-19 is defined as the time duration between a primary case-patient injector) having symptom onset and a secondary case-patient (infected) having symptom onset [11-12]. As for the serial interval,we use the time to diagnose the source of infection and the infected person instead of the onset time of symptoms.

1.3 Statistical Analysis

The incubation period is calculated with doubly interval-censored data by using Survival Analysis and the doubly interval-censored analyses[13].We use Survival Analysis for estimating the serial interval.In order to estimate the incubation period and the serial interval accurately,only confirmed cases are retained.

2. Result

Up to March 30th,2020,576 cases of COVID-19 have been reported in Chongqing,and we collect personal information on 552 confirmed cases.Among the 552 confirmed cases,the median age is 48 years (38-56) and 283 cases(51.2%) are female.In addition, we also analyzed the time interval from symptoms to diagnosis. The mean interval of 4.3 days.

2.1 Estimation of incubation period

For confirmed cases infected with COVID-19 during the incubation period,the Lognormal distribution provides the best

match with the data by using Survival Analysis (Tab. 1). We estimate that the mean incubation period in Chongqing is 7.5 (6.6-8.6,95% CI) days. The incubation period in Chongqing ranged from 1.1 to 23.4 days (2.5^{th} to 97.5^{th} percentile).Then we used the Lognormal distribution to fit the coarse data for estimating the incubation period. This time,the mean incubation period was estimated at 7.5 days (6.3-8.7 days, 95% CI).

For confirmed cases infected with COVID-19 during symptomatic period,the Gamma distribution provides the best fit to the data by using Survival Analysis(Tab. 2). The mean incubation period in Chongqing was estimated to be 6.0(4.9-7.2,95% 95% CI) days. The incubation period in Chongqing ranged from 0.9 to 19.3 days (2.5^{th} to 97.5^{th} percentile).Then we used the Gamma distribution to fit the coarse data for estimating the incubation period.The mean incubation period in Chongqing was estimated to be 6.0 (5.0-7.2,95% CI) days.

Tab. 1 Estimated incubation period for confirmed cases[a]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	7.5	(6.6,8.6)	356.9
Weibull	8.4	(3.5,17.9)	359.1
Gamma	8.1	(7.0.9.3)	357.0

AIC*:Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[a]:The confirmed cases exposed to COVID-19 during incubation period.

Tab. 2 Estimated incubation period for confirmed cases[b]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	5.4	(4.4,6.6)	244.3
Weibull	6.1	(4.7,8.1)	243.5
Gamma	6.0	(4.9,7.2)	241.7

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[b]:The confirmed cases exposed to COVID-19 during symptomatic period.

2.2 Estimation of serial interval

For confirmed cases infected with COVID-19 during the incubation period,the Lognormal distribution provides the best fit to the data by using Survival Analysis (Tab. 3). The mean serial interval in Chongqing was estimated to be 6.1 (5.0-7.5,95% CI) days. The incubation period in Chongqing ranged from 1.9 to 20.1 days (2.5^{th} to 97.5^{th} percentile).For confirmed cases infected with COVID-19 during symptomatic period,the Weibull distribution provides the best fit to the data by using Survival Analysis(Tab. 4). The mean serial interval in Chongqing was estimated to be 4.9(3.9-6.0,95% CI) days. The incubation period in Chongqing ranged from 0.4to 17.8 days (2.5^{th} to 97.5^{th} percentile).

Tab. 3 Estimated serial interval for confirmed cases[a]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	6.1	(5.0,7.5)	189.9
Weibull	6.7	(5.4,8.3)	194.8
Gamma	6.5	(5.3,8.0)	192.1

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[a]:The confirmed cases infected with COVID-19 during incubation period.

Tab. 4 Estimated serial interval for confirmed cases[b]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	4.1	(3.3,5.2)	382.4
Weibull	4.9	(3.9,6.0)	377.6
Gamma	4.7	(3.8,5.6)	378.3

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.

confirmed cases[b]:The confirmed cases infected with COVID-19 during symptomatic period.

2.3 Comparison of COVID-19 incubation period to other study

A comparison to the estimated incubation period distribution for COVID-19(Tab. 5) shows that there are difference between these values, but the differences are not significant.The estimated mean incubation periods for COVID-19 in Chongqing are slightly longer.

Tab. 5 Estimated incubation periods for coronaviruses from different studies

		Mean (Days)	
Study	Distribution	Estimate	(95% CI)
This study(Incubation period contact)	Lognormal	7.5	(6.6,8.6)
This study(Incubation period contact)	Weibull	8.4	(3.5,17.9)
This study(Incubation period contact)	Gamma	8.1	(7.0.9.3)
This study(Symptomatic period contact)	Lognormal	5.4	(4.4,6.6)
This study(Symptomatic period contact)	Weibull	6.1	(4.7,8.1)
This study(Symptomatic period contact)	Gamma	6.0	(4.9,7.2)
This study(Unsure)	Lognormal	5.7	(4.9,6.5)
This study(Unsure)	Weibull	6.4	(5.0,8.3)
This study(Unsure)	Gamma	6.2	(5.4,7.1)
Li Q[8]	Lognormal	5.2	(4.1,7.0)
Chun,J. Y. [14]	Lognormal	2.87	(2.33,3.50)
Ren,X. [15]	Lognormal	5.3	(4.6,6.0)
Du Z C [16]	Lognormal	4.958	(3.472,7.318)
Du Z C [16]	Gamma	5.083	(3.511,7.314)
Du Z C [16]	Weibull	5.695	(3.675,7.674)
Yang,L. [17]	Weibull	5.5	(4.8,6.0)

3. Discussion

This study provides an initial analysis among epidemiologic characteristics and two typical transmission phenomena of COVID-19 in Chongqing. The mean incubation period in Chongqing was estimated to be 7.5(6.6-8.6,95% CI)and 6.0(4.9-7.2,95% CI) days and the mean serial interval is estimated to be 6.1 (5.0-7.5,95% CI)and 4.9(3.9-6.0,95% CI) days.It can be seen from the results that both the estimation of incubation period and the estimation of serial interval,the cases exposed to infection in the incubation period were slightly longer than those in the symptomatic period. When collecting data,the exposure time range filled in by confirmed patients exposed to infected individual during the incubation period may be longer than the actual one,and it is difficult to recall the exact date. As for the serial interval,we replace the onset time of symptoms with the time of diagnosis of the source of infection and the infected person,because we found that the interval between the onset time and the diagnosis time of most patients is too long. Considering the imperfection of medical examination methods in the early stage of the epidemic and the patients' lack of active seeking medical treatment,we finally decided to use the diagnosis time to estimate the serial interval. In any case, there may be some unreasonable aspects in our way of

processing data in this way, but whether there is a more sensible way of data processing remains to be considered. The incubation period that we calculate is slightly longer according to other studies(Tab. 5).

It's not hard to find out that the estimated values of serial interval is shorter than the incubation period.This result can preliminarily prove the possibility of COVID-19 spreading in the incubation period.The infectivity of incubation period increases the difficulty of control and the risk of infection,which indicates that personal protective measures are necessary.

We estimate a mean serial interval for COVID-19 of 4.9 (3.9-6.0,95% CI) days and 6.1 (5.1-9.2,95% CI) days. Li et al. [8] estimated the serial interval distribution to have a mean of 7.5 days (5.5-19,95% CI) based on 6 observations,and the incubation period distribution has a mean of 5.2 days (4.1-7.0,95% CI) based on 10 observations. Other studies estimate the incubation period distribution to have a mean of 6.4 days (5.6-7.7 95% CI) [18],median of 5 days (4.0-5.8 95% CI)[19],mean of 5.2 days (range 1.8-12.4 days) [20],and a mean of 4.8 days (range 2-11 days) [21]. After comparison,our estimated results are close to those of other studies.It indicates that our estimation results have a certain reference value.

Although many scholars have found novel coronavirus pneumonia epidemiological characteristics,many countries have not effectively controlled the epidemic situation. Even after the successful control of the epidemic in China,some countries are still dissatisfied with such important measures as wearing masks and isolation,which is also the reason why it is difficult to effectively control the epidemic abroad.

In recent years,mankind has been faced with new crises,such as SARS,H1N1,Ebola COVID-19 pneumonia etc. The reason why we can control the epidemic so quickly is that we have studied SARS and gained experience before.Although the new epidemic in the future may be different from the COVID-19 pneumonia,it has left us with experience and knowledge on how to deal with sudden epidemic again.

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Application Effect of “3P” Nursing Management Mode in Emergency Patients with Acute Ischemic Stroke

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Abstract:**Objective:**To explore the application effects of the 3P(perfecting equipment,perfecting nursing ability, perfecting emergency pathway and application) nursing management mode of acute ischemic stroke nursing care. **Methods:** Clinical data of 80 cases of patients were selected as research group,and 80 acute ischemic stroke patients were selected as reference group. **Results:** Vein opening time, CT completion time and thrombolysis DNT in the research group were significantly lower than that of the reference group（$P < 0.05$）. **Conclusion:** The "3P" management mode can significantly shorten the patients' vein opening time, CT completion time and DNT time of thrombolysis, improve the first aid effect,improve the treatment effect of AIS, which can be widely used.
Keywords: “3P” Mode; Acute Ischemic Stroke; Emergency;

Introduction

Stroke is one of the major diseases leading to disability and death in humans. Acute ischaemic stroke (AIS) accounts for about 80% of all strokes. The timeliness and effectiveness of its treatment are essential to reduce the morbidity and mortality of patients and can greatly improve the quality of life of patients and improve the prognosis[1] .Nowadays,the prevention and treatment of cerebrovascular diseases have improved significantly in China. However, stroke is still the leading cause of the mortality and disability among Chinese residents.The incidence prevalence,recurrence rate and mortality of stroke in China remain high[2]. The burden of stroke disease in China is higher than the global average and is showing an increasing trend[3].The prevention and treatment of stroke still face huge challenges, and the system needs to be further improved and optimized[4].

Relevant research and work progress in China have proved that the use of the "3P" model (perfecting equipment, perfecting nursing ability,perfecting emergency pathway and application) to rescue critically ill pregnant and lying-in women has achieved good clinical effects[5].This research is aim to explore the application effect of “3P” mode in emergency patients with acute cerebral infarction.

1. Materials and Methods

1.1 Research object

80 patients with acute ischemic stroke who were treated before the implementation of the "3P" management model from January 2020 to December 2020 were selected as the reference group. 80 cases of acute ischemic stroke patients who had been nursing with the "3P" management model from January 2021 to December 2021 were selected as the research group. Both groups of patients were diagnosed with acute ischemic stroke by cranial CT examination and were included in the study on the basis of informed consent.There was no significant difference in gender, age ,and education level between the two groups ($P > 0.05$).

Inclusion criteria:Patients hospitalized in our department from 2020–2021 and met the following inclusion criteria were selected as study participants:(1) confirmed as ischemic stroke by cranial CT and MRI scans and met the diagnostic criteria in the Guidelines for the Diagnosis and Treatment of Acute Ischemic Stroke in China (2018)[6].; (2) stable vital signs; (3)

accepted a questionnaire survey and provided complete information.Exclusion criteria :(1)Malignant tumors; (2) Coagulation disorders; (3) Hematological diseases; (4) Combining brain tumors, cerebrovascular malformations, brain trauma, aneurysms and other diseases; (5) Persons with mental illness; (6) Persons with other acute and chronic critical illnesses.

1.2 Methods

The reference group received routine emergency nursing, given oxygen inhalation, monitoring of blood pressure, establishment of venous access, and close attention to changes in patients' vital signs according to their conditions. While the research group received “3P” nursing management mode, and the specific measures were as follows.

Specifically, perfecting equipment: the emergency room is now equipped with conventional equipment such as electrocardiograph, electrocardiograph, ventilator, defibrillator, and endotracheal intubation equipment. Timely inspection, timely maintenance, so that the instruments used are in the best standby state at any time.

Perfecting nursing ability:we set up a team of emergency stroke nurses , given theoretical and operational training of stroke treatment regularly.

Perfecting emergency pathway and application:The expert group discussed and formed the best rescue plan for different types of stroke patients and regularly organize nursing staff to carry out pre-plan drills, so that each nurse is familiar with the rescue plan, can skillfully apply first-aid skills in actual combat, and can be competent for each functional position in the rescue plan, so as to enhance the overall nursing ability of the emergency stroke team.

1.3 Statistical Methods

The experimental data were statistically analyzed and processed by SPSS20.0 software. The count data were tested by x^2, expressed by [n (%)], and the measurement data were measured by the t-test, expressed by (x±s). The difference was statistically significant when $P<0.05$.

2. Results

2.1 Comparison of Clinical Data between the Two Groups of Patients

There was no significant difference in gender, age ,education level,and disease type between the two groups ($P>0.05$), which were comparable, as shown in Table 1.

Table 1 Comparison of clinical data between the two groups of patients.

Category	Research group (n =80)	Reference group (n =80)	t/x^2	p
Gender（Male/Female）	47/33	45/35	0.435	＞0.05
Average age (years)	58.2±9.6	57.1±8.4	0.893	＞0.05
Education level				
College and above	24	26	0.202	＞0.05
High school	28	29	0.715	＞0.05
Middle school and below	32	35	0.362	＞0.05

2.2 Comparison of Treatment Time between the Two Groups of Patients

Vein opening time, CT completion time and thrombolysis DNT in the research group were significantly lower than that of the reference group （$P < 0.05$）, as shown in Table 2.

Table 2 Comparison of treatment time between the two groups of patients.

Category	Vein opening time(min)	CT completion(min)	thrombolysis DNT(min)
Research group (n =80)	2.5±3.1	10.36±3.76	41.9±10.5
Reference group (n =80)	5.8±6.2	18.91±4.56	62.4±15.7
t	9.267	7.395	5.136
P	＜0.05	＜0.05	＜0.05

3. Discussion

Acute ischemic stroke(AIS) is a medical emergency that requires intensive treatment and care in the early hours,because its fast diagnosis and proper interventions can lead to favorable results.Furthermore,delayed treatment can lead to considerable complications,higher mortality,and enormous costs for the person,families,and the healthcare system[7].According to the current medical research results, the gold treatment time of acute ischaemic stroke is 4.5 hr, which is commonly known as the "time window"of thrombolytic therapy.Therefore, shortening the treatment time as much as possible is the key to improve the treatment effect of AIS and improve the prognosis of patients[8].

This study showed that after the implementation of the "3P" management mode of , the treatment time of each link in the hospital was shortened, DNT was statistically significantly shortened, and the treatment efficiency of stroke was statistically significantly improved.Our hospital has clarified the division of responsibilities of emergency stroke nurses, quickly identified stroke, and opened green channels in time, which greatly improves the efficiency of rescue and improves the success rate of rescue.

In summary,the implementation of the "3P" management mode can improve the first aid effect,improve the treatment effect of AIS, which can be widely used.

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Tumor Vaccine Based on Targeted Neoantigen: A Powerful Immunotherapy Weapon in Acute Myeloid Leukemia

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Abstract： Acute myeloid leukemia (AML) is a common type of leukemia. The existing chemotherapy regimens and hematopoietic stem cell transplantation can not achieve the ideal treatment effect, and more efficient treatment methods are needed in the clinical treatment of AML patients. As a star method of immunotherapy, tumor vaccines have attracted much attention. Choosing neoantigen as the target antigen in vaccine is a new and exploreable design plan for AML. In this review, we will carefully summarize the current neoantigen-related vaccine research progress, reasonably speculate its application prospects in AML, and put forward the key challenges and risks in the research.

Keywords: Tumor Vaccine; Neoantigen; Immunotherapy; Acute Meyroid Leukemia

Introduction

1. Acute myeloid leukemia: the most common but intricate leukemia

As the most common diagnosed leukemia (1), acute myeloid leukemia (AML) is mainly characterized by the uncontrolled proliferation of primitive myeloid progenitor cells. These cells are not capable to further differentiate into normal mature leukocytes in vivo (2).

Chemotherapy is a common clinical treatment for AML. Moreover, according to the patient's physical fitness and chemotherapeutic drug sensitivity, adjuvant radiotherapy can be treated to enhance the therapeutic effect of the induction phase (3). In the consolidation period, the current clinical treatment is also to use high-dose cytarabine and other drugs combined with chemotherapy for consolidation therapy (4). In addition, hematopoietic cell transplantation (allo-HCT) is approved to treat patients with certain high-risk cytogenetic characteristics (such as FLT3-ITD without NPM1) and refractory patients or patients with relapsed AML achieving CR2 after re-induction therapy (5). In short, the traditional treatment of acute myeloid leukemia is often combined with sequential chemotherapy.

2. Tumor vaccine: a powerful weapon in immunotherapy

2.1 Tumor vaccine is an emerging active immunotherapy regime

In traditional concepts, vaccines refer to biological products made with various microorganisms for the prevention of infectious diseases. In tumor treatment programs, tumor vaccines are not only limited to preventive vaccines, but also include therapeutic vaccines, and most of them are used to reduce cancer recurrence after chemotherapy or surgery (6). In this review, we will only discuss therapeutic vaccines. This type of vaccine mainly refers to injecting specific cells or molecules into the patient's body, regulating the immune microenvironment in the peripheral blood, and inducing the body to actively amplify or produce a specific response (7). The goal of therapeutic cancer vaccines is to induce tumor regression, eradicate minimal residual disease, and ultimately establish a long-term anti-tumor memory to increase the patient's long-term disease-free survival rate (DFS) (8). There are two types of tumor vaccines: cellular vaccines and molecular vaccines. Cell vaccines include whole tumor cell vaccines and dendritic cells (DCs) vaccines. Peptide vaccines and granulocyte-macrophage-colony stimulating factor (GM-CSF) vaccines belong to molecular vaccines (9). So far, tumor vaccines have become a research hotspot in solid tumors. They have been used in ovarian cancer, lung cancer, melanoma, brain cancer, kidney cancerand other

cancers (10-16). Even in the development direction of cervical cancer, different from the preventive vaccines that have been on the market, cervical cancer therapeutic vaccines have been reported to be shown to induce a systemic immune response in patients, resulting in a reversion of immunosuppression in the tumor microenvironment (17).

3. Neoantigen tumor vaccine: Bringing dawn to the treatment of AML

For the current tumor vaccine target antigens for AML, most of the projects are based on TAAs， such as NY-ESO-1 vaccine and DCP-001 vaccine (18-19). Moreover, based on the high specificity and safety of neoantigen discussed above, the development of effective tumor vaccines based on various neoantigens in AML has become a new and valuable direction.

3.1 Two examples of neoantigen vaccines in AML

3.1.1 Vaccination with dendritic cell/tumor fusions

A research team has developed a multiple bone marrow vaccine in 2013. After injecting vaccine, the patient's auto-derived tumor cells and auto-dendritic cells can be fused to produce a variety of tumor genetic antigens, including neoantigens. It effectively captures tumor heterogeneity (20). In a phase I/II clinical trial, the median age of AML patients who received chemotherapy was vaccinated at 63 years. The result was that 71% of vaccinated patients were still in remission during the 5-year follow-up (21). With the research of this new personalized DC/AML fusion vaccine, after vaccination, checkpoint blockade leads to the enhancement of genes that regulate memory and effector T cell activation and proliferation, and enhances the diversity of T cell clones (22).

3.1.2 New OCV-501 peptide vaccine

The expression of WT1 gene (Wilms tumor gene1) in normal tissues in the body is extremely low and can be ignored, but it has extremely high expression in 96% of AML cells, producing a large amount of WT1 peptide. Moreover, WT1 is an oncogenic protein, and it does inhibit the growth of tumor cells, so WT1 is an ideal neoantigen for AML (23). OCV-501 is a synthetic peptide composed of natural sequences derived from the WT1 gene product protein without any modification or combination with other peptide sequences. It is an HLA II restricted WT1 adjuvant peptide therapeutic cancer vaccine (26).

Discussion

Based on the detailed discussions on neoantigens and vaccines for AML in our review, the analogy study of personalized neoantigen pulsed cancer vaccines in AML is reasonable. Compared with solid tumors that have been extensively studied, AML has a relatively low tumor burden. But neoantigen vaccine still has a prominent therapeotic potential.

In short, the personalized tumor vaccine based on neoantigen can be a potential treatment strategy for AML patients in the future, which can cure patients more accurately, efficiently, and with little harm. Especially， it may will reduce AML relapse rate after chemotherapy treatment or allo-HSC. Combination with this new type of vaccine with other immunotherapies is also a desirable idea (25-26).

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Universe Scientific Publishing

Multiple Linear Regression Model of Blood Oxygen Saturation

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Abstract: We used standardized regression analysis to analyze the influence of age and recent smoking status on blood oxygen saturation. We found that blood oxygen saturation was negatively correlated with age and recent smoking status, but whether smoking had a greater influence on blood oxygen saturation than age. In order to further explore whether age and recent smoking status could jointly affect oxygen saturation of blood, we used k-means clustering algorithm and took age as the control variable to conduct clustering analysis. Is obtained by polynomial fitting, and then the blood oxygen saturation under all ages about age, smoking status of recent expression of partial derivatives of recent smoking status, get the following conclusion: smoking is oxygen desaturation, and compared with the young, the elderly smoking more effect on the blood oxygen saturation degree, are more likely to suffer from cardiovascular disease.

When the regression results were tested for significance, the significance of all variables was investigated, and it was found that only age and current smoking status were significant for oxygen saturation, while BMI and gender showed no difference from zero in T test, indicating that oxygen saturation was not affected by BMI and gender. Then, taking oxygen saturation as the dependent variable and age and current smoking status as independent variables, the spline interpolation method with the best fitting effect was found, and its expression was given in the text.

Keywords: Standardized Regression; Neural Network

1. Introduction

Pulse oximetry is often used to test the patient's blood oxygen saturation level, during the period of continuous testing, through the model description of oxygen saturation model, for data of 36 people, each subject 1 Hz frequency, about an hour of continuous measurement of oxygen saturation, recorded the information about the participants, including age, gender, smoking status at present.

Question: In order to understand whether oxygen saturation is related to age, that is, what characteristics have changed in older people compared with younger people, the characteristics should have biological or medical significance.

2. Problem analysis

In view of the problem, we can know from the first ask conclusion blood oxygen saturation mainly related to age and smoking status, age, and smoking then using standardized regression analysis for the influence of oxygen saturation degree, and found that smoking status and age of blood oxygen saturation were negatively correlated, but carries on the data analysis and found smoking more influence on the blood oxygen saturation, that is to say, the influence degree of the age less than smoking status, in order to further analyze the association between age and blood oxygen saturation, we classified by using the method of cluster analysis, ages, and then use matlab for polynomial fitting, In the same way, the data of three age groups were substituted, and then the partial derivative of smoking was obtained to analyze the influence of smoking at different age groups on blood oxygen saturation. To find out the corresponding biological or medical significance of smoking in the elderly in relation to cardiovascular disease.

3. The problem is to establish and solve the model

3.1 Identification of the degree of influence of oxygen saturation based on standardized regression analysis

Based on the multiple linear regression model established by the first question, we have learned that oxygen saturation is only associated with age and recent smoking status, but not with BMI and sex. Therefore, in order to further study the influence of Age and recent Smoking status on human blood oxygen saturation, we conducted standardized regression with blood oxygen saturation as the dependent variable and Age and recent Smoking status as the independent variable.

Standard regression refers to the regression analysis carried out after eliminating the influence of units taken by dependent variables and independent variables. The size of standardized regression coefficient reflects the influence degree of each independent variable on dependent variables. The comparison results of normalized regression coefficients are only applicable to a specific environment, and they may vary from time to time and place to place.

DE dimensionality treatment:

For the samplex_1,x_2, x_3……x_n, And then after dimension $x_{stdi} = \frac{x_{i-\mu}}{\sigma}$

(where μ is the sample mean and σ is the sample standard deviation)

After treatment with {Oximetry} _I, Age and Smoking by stata , normalization regression was made. The results are shown as follows

oximetry	Coef.	Std. Err.	t	P>|t|	Beta
smoking1	0	(omitted)			0
smoking2	-.3972196	.5860163	-0.68	0.503	-.1343429
smoking3	-1.965321	.8380077	-2.35	0.025	-.4418871
Age	-.0380873	.0127138	-3.00	0.005	-.4918497
_cons	99.46954	.8152098	122.02	0.000	.

Figure1 Standardized regression analysis table for blood oxygen saturation

As shown in figure, standardized regression coefficient absolute value reflect the Age, the effects of Smoking on the blood oxygen saturation degree, the size of the absolute value expressed the influence degree of the independent variable on the dependent variable, such as can be seen table Smoking3 standardized regression coefficients was significantly greater than the Age, Smoking2, Smoking1, suggesting that the recent Smoking status of blood oxygen saturation for Smoking is greatest, Age for small affect blood oxygen saturation, quit Smoking relative to Smoking almost to won't affect the dependent variable.

3.2 Age-based K-means clustering model

In order to further explore whether age combined with recent smoking status could affect blood oxygen saturation, we used k-means clustering algorithm and took age as the control variable to conduct clustering analysis.

The K-means clustering algorithm is a clustering analysis algorithm solved through iteration. Its steps are as follows: first, specify the number of clustering centers as K, then randomly select K objects as the initial clustering center, calculate the distance between each object and each sub-clustering center, and assign each object to the nearest clustering center. The cluster center and the objects assigned to it represent a cluster. For each sample assigned, the cluster center of the cluster reiterates the calculation based on the existing objects in the cluster. This process is repeated until the termination condition is met.

Its principle mind map is as follows:

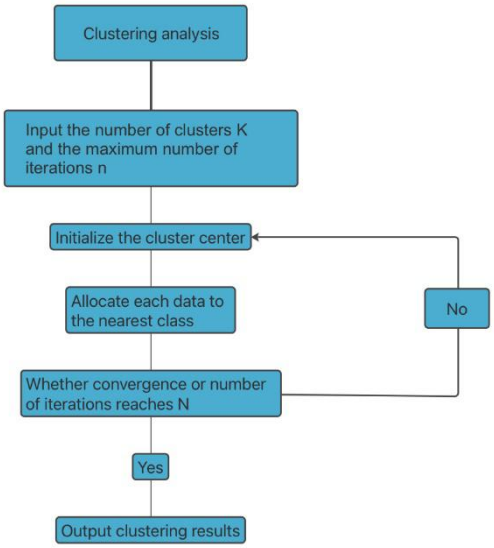

Figure2 Principle mind map

SPSS was used to conduct cluster analysis with age as classification variable and patient number as case labeling basis. The results are as follows:

Table1 Initial cluster center

Control variables	clustering		
	1	2	3
Age	19	49	70

Table2 Iteration history [a]

The iteration	Changes in clustering centers		
	1	2	3
1	2.050	3.917	5.500
2	.000	2.083	3.000
3	.000	.000	.000

The initial cluster centers were set as three, aged 19, 49, and 70 respectively. In each iteration, the samples were redistributed to the cluster centers according to the distance from each sample to each cluster center, and then the cluster center location was updated. After three iterations, the convergence is realized because there is no change or only slight change in the clustering center, and the minimum distance between the initial centers is 21.000.

3.3 Analysis model of the influence degree of blood oxygen saturation in different age groups based on polynomial fitting

Patients who are divided into three groups through k-means clustering algorithm adopt polynomial fitting method to fit the sample data of different age groups, and the equation obtained is shown in the following table:

Age	Fitting equation
[19,24]	$Oximetry_1(Age,Smoking) = 100.4 - 0.1034Age - 0.1257Smoking$
[35,49]	$Oximetry_2(Age,Smoking) = 101.7 - 0.0465Age - 1.738Smoking$
[55,70]	$Oximetry_3(Age,Smoking) = 112.6 - 0.1849Age - 2.426Smoking$

$Oximetry_i(Age,Smoking)$ Furthermore, to further discuss the effect of Oximetry on Smoking, the partial derivatives of Oximetry (Age, Smoking) are obtained from the three equations, and the partial derivatives of Oximetry (Age, Smoking) with respect to the variable Smoking are shown in the table below.

The age range	$\frac{\partial Oximetry}{\partial Smoking}$
[19,24]	-0.1257
[35,49]	-1.738
[55,70]	-2.426

As can be seen from the graph, the absolute value of Oximetry gradually increases with the increase of age, which indicates that the effect of Oximetry on blood oxygen saturation has increased with the increase of age. Therefore, the elderly should pay more attention to the effect of Smoking on cardiovascular disease.

Therefore, we note that although oxygen saturation decreases with age, increasing the risk of cardiovascular disease, smoking has a greater impact on oxygen saturation in older people, so older people should pay more attention to lifestyle to prevent cardiovascular disease.\

4. Model test

In question 1, we used a multiple linear regression model to analyze the independent variables that may influence oxygen saturation. The final conclusion was that oxygen saturation was only correlated with age and recent smoking status, but not with BMI and gender.

For problem 1, BP neural network is used to test the model.

BP neural network is chosen because it has the following advantages:

(1) Nonlinear mapping capability: BP neural network essentially realizes a mapping function from input to output. Mathematical theory proves that the three-layer neural network can approximate any nonlinear continuous function with arbitrary precision. This makes it especially suitable for solving complex internal mechanism problems, that is, BP neural network has strong nonlinear mapping capability.

(2) Self-learning and adaptive ability: DURING training, BP neural network can automatically extract the output and "legal rules" among output data through learning, and memorize the learned content in the network weight adaptably. It shows that BP neural network has highly self-learning and self-adapting ability.

(3) Fault-tolerant ability: BP neural network will not have a great impact on the global training results after local or partial neurons are damaged, that is to say, the system can still work normally even when local damage occurs. That is, BP neural network has a certain fault-tolerant ability.

We know from the analysis of problem number one. As one of the two important factors that mainly affect oxygen saturation, age and smoking status of 32 individuals (converted into dummy variables) were substituted into BP neural network, and 70% training volume and 15% validation15% Testing were set.

The neural network structure as shown in the figure below is used:

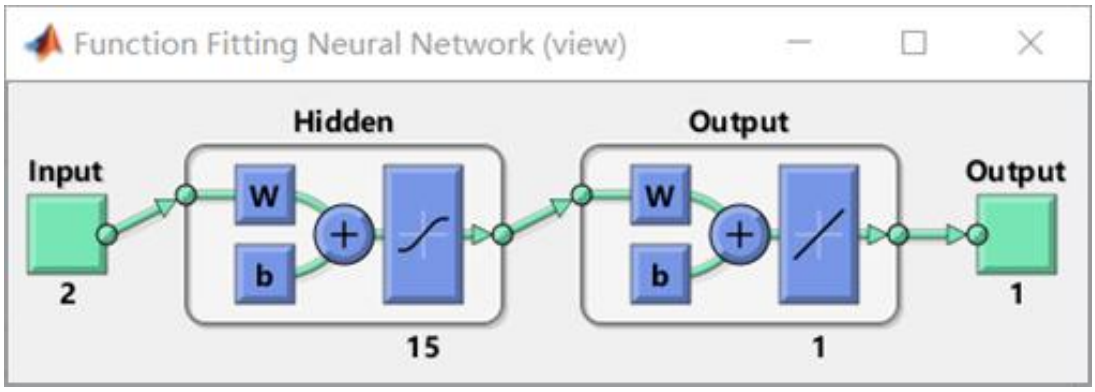

Figure3 Function Fitting Neural Network

After the Epoch after 1000 times, the Regression obtained is shown in the following figure

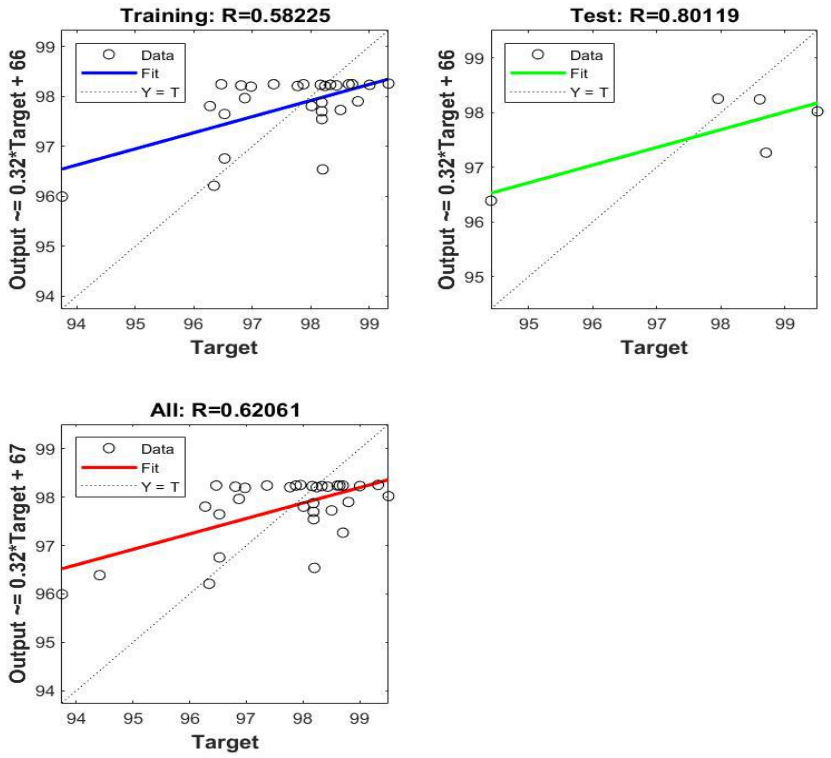

Figure4 The training data

We will use this neural network to predict the last four groups with SIM function, and obtain their relative errors as shown in the figure

It can be seen from the figure that the relative error is always below 2%, which indicates that the multiple regression model in question 1 is more reasonable. For this model test, we can see that under the same conditions, the difference between the results of multiple tests is small, which proves that the model establishment in question 1 in this paper is more in line with the actual situation.

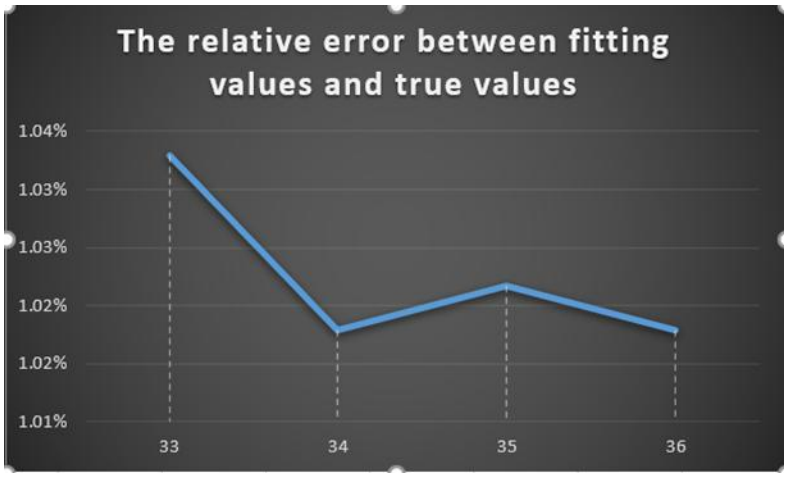

Figure5 The relative error between fitting value and true values

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