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Biomechanical Risk Assessment of Non-Contact Anterior Cruciate Ligament Injury in Taekwondo Athletes

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ABSTRACT

Non-contact anterior cruciate ligament (ACL) injury can occur in many sports. It is interrelated with gender, anatomy, biomechanics, and neuromuscular control. Taekwondo athletes have a higher incidence of ACL injury than athletes from other sports. **Objective:** This study aimed to determine the biomechanical gender differences and mechanism of taekwondo athletes with ACL injury. **Methods:** A total of 28 taekwondo athletes (aged 14–19 years) were randomly selected and grouped by gender. Feet high floor, one foot high floor, and single leg squat were analyzed by a Vicon motion analysis system and Kistler 3D force platform for action. The knee joint angle and ground force were evaluated. **Results:** Results demonstrated biomechanical differences in knee joint between male and female athletes. **Conclusion:** ACL injury in taekwondo female athletes indicated the biomechanical mechanism of the knee joint, and it can be prevented by neuromuscular control training.

1. Introduction

Non-contact anterior cruciate ligament (ACL) injury is usually caused by abnormal stress of the ACL due to its own action without an external force. Approximately 80% of ACL injuries are caused by non-contact events[1,2]. Epidemiological studies have shown that female athletes have 2~8 times the incidence of injuries than male athletes[3–5]. No gender difference in ACL injury before puberty has been reported, and the incidence is small. Many differences in anatomy, endocrine control, and neuromuscular control exist between males and females during puberty (14~19 years old), which may be the factors leading to gender differences in injury[6–9]. Among many factors, anatomy, endocrine, joint relaxation, and genetic factors are inherent in the human body, whereas biomechanical factors and neuromuscular control can be changed through intervention.

ACL injuries happen occasionally in various sports, so strengthening the risk factor assessment study of ACL injuries is important to prevent injuries[10,11]. In our work, we found that ACL injury is a common injury in taekwondo. Among the 26 members of the provincial taekwondo team, 7 athletes, 6 females, and 1 male reported ACL injuries in the past 2 years, among which 6 cases were non-contact ACL injuries. Taekwondo mainly involves attacking and defending the lower limbs. A single leg is required for scoring moves, such as a cross kick or a

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downward split. In taekwondo, the striking leg moves into rapid knee extension while supporting the leg with rotation and forward and backward movement. For example, the uncoordinated contraction of the quadriceps and hamstrings can cause a sudden increase in ACL stress, leading to injury. This study assessed the risk of ACL injury by analyzing the biomechanical risk factors of lower limbs and neuromuscular control factors of taekwondo athletes.

2. Research Methods

2.1 Research Objects

This study involved 13 male and 15 female taekwondo team members, aged between 14 and 19 years. The differences in age, height, weight, and sports years between men and women were determined.

Table 1. Comparison of height, weight, age, and sports years of male and female athletes

	Age	Height (cm)	Weight (kg)	Sports year
Male (n=13)	16.2±2.7	178±6.8	68.6±9.5	6.3±3.1
Female (n=15)	16.5±2.9	175±5.6	65.7±7.3	5.9±2.9

No significant difference in height and weight was found between males and females. All athletes had no history of ACL injury or serious knee injury (e.g., meniscus injury, collateral ligament injury, and traumatic synovitis).

2.2 Experimental Methods

2.2.1 Landing Biomechanics Test Method

Given that most of the ACL injuries of taekwondo athletes occur when the supporting leg jumps to the ground or moves forward and backward, the kinematics changes in the arrangement of the hip, knee, and ankle joints of the lower limbs when landing at a high place should be tested to monitor the risk of knee ACL injuries. Foreign studies have confirmed that internal rotation of the hip joint and valgus and rotation of the knee joint are risk factors of ACL injury when landing at a height. The high peak of ground reaction force and the lack of effective buffer are also known risk factors. Through the biomechanical test of landing on high ground, we explored whether any difference exists between male and female taekwondo athletes. The landing on high ground movements we designed included landing on two feet, landing on one foot, and squatting on one leg. We hypothesized that there is a clear difference in the biomechanical performance of the lower limbs when male and female athletes land on high ground; there is a difference in ground cushioning between male and female athletes when they land; and the biomechanical indexes of lower limbs of male and female athletes in special movements differ.

2.3 Data Processing

A pelvic coordinate system, thigh coordinate system, and leg coordinate system were established based on the coordinates of marker points. The pelvic coordinate system is determined by the right anterior superior iliac spine point, the left anterior superior iliac spine point and the midpoint of the posterior superior iliac spine. On the basis of the research data of Bell et al. and the pelvic coordinate system, the center coordinate of hip joint rotation was calculated. The thigh coordinate system is determined by the medial femoral condyle point, the lateral femoral condyle point, and the hip joint center point. The center of rotation of the knee was the midpoint of the medial and lateral condyles of the femur. The leg coordinate system was determined by the outside malleolus point, the inside malleolus point, and the knee joint center point. Knee joint angle was defined as the Euler angle between the thigh coordinate system and the calf. The first rotation around the x axis was used to obtain the flexion angle (negative angle of flexion); the second rotation around the y axis was used to obtain the adduction and abduction angle (positive angle for adduction and negative angle for abduction); and the third rotation around the z axis was used to obtain the internal and external rotation (positive angle of internal rotation and negative angle for external rotation).

2.4 Statistical Analysis

Mixed ANOVA was conducted to determine the influence of gender, movement, and before and after training on biomechanical indexes of lower limbs. The dependent variables of ANOVA included the impact peaks of the front, back, up, and down directions of the ground reaction force at the first peak moment of the ground reaction force after the feet touched the ground, as well as the knee valgus angle and knee flexion angle. The significance of statistical analysis was defined as a type of error probability not greater than 0.05, and all statistical analysis were performed in SPSS16.0 software.

2.5 Results

As reported by domestic and foreign research, in the process of landing foot touchdown within 30~100 ms, buckle valgus knee joint, and stretching angle is too large, a lack of buffer is an ACL injury main biomechanical factors, studies the ground directly to the eversion of the knee joint angle as an ACL injury risk factors predicted. Thus, this research adopted the vertical ground reaction

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force, ground level backward reaction force, angle of knee flexion, and knee valgus angle as a measure of athletes' ground movement. The single first step was squatting on the ground, so only the knee joint angle was measured. The measurement index was the value when the ground reaction force was the maximum during landing. The average angle of the knee joint of the left and right lower extremities upon landing of both feet was determined. The ratio of ground force to body weight was standardized.

As shown in Table 2, there is a significant difference between men and women in the vertical reaction force of the ground and the knee flexion angle when landing on both feet. The knee flexion angle has obvious gender difference, and women are smaller than men. There is no significant difference in horizontal backward force and knee valgus angle.

In the one-foot landing movement, the vertical reaction force of the female athlete on the ground is greater than that of the male, and there are obvious differences. There was no significant difference in knee flexion angle and ground level backward force. There is no significant difference between men and women in knee valgus angle.

When squatting on one leg, no significant difference was observed between the flexion angle and eversion angle of the knee.

3. Discussion

In foreign studies, the main research is on the mechanism of ACL injury in football, basketball, handball, rugby, skiing, etc. The applied movements include landing, lateral cutting, sudden stop, and takeoff [12–15]. The present study mainly analyzed the biomechanics of the knee joint during the landing process, including landing on both feet, landing on one foot, and squatting on one leg. These movements were related to the technical characteristics of taekwondo.

We adopted several indicators that have been proven in foreign countries to predict non-contact ACL injury with high sensitivity, including ground vertical reaction force, ground horizontal backward reaction force, knee flexion angle, and knee eversion angle. Among these indicators, the vertical ground reaction force represents the body's buffering ability during landing, and landing without buffering will Increase knee stress and risk of injury. The valgus angle of the knee joint is considered the most sensitive predictor of non-contact ACL injury. The simultaneous action of forward and rotating violence of the knee joint when the knee joint is in the internal buckle of the semi-flexion position can lead to an instant increase in ACL stress, which will lead to ligament fracture.

In the landing process, the intercept time of the test index is adopted from the time when the foot touches the ground to the time when the maximum reaction force reaches the ground. Foreign studies reported that non-contact ACL injury usually occurs in 30-100 ms when the foot initially touches the ground after landing [16].

The ground reaction force and landing knee flexion angle significantly differed between male and female athletes before the intervention. In women, ground vertical reaction after the intervention was significantly lower than that before training, and the knee flexion angle increased before training. After training, the knee flexion angle between male and female athletes showed no obvious difference. Our research shows that male and female athletes have no significant difference in knee valgus angle during landing. By contrast, most foreign studies believe that the knee valgus angle of female athletes increases, and there are significant differences between male and female athletes. This difference may be related to our research objects and sample size. Most foreign studies tested non-professional college or high school athletes and involved thousands of test samples [17–19]. Our test samples were young elite athletes, whose training years were 4–6 years. After systematic strength training, our test samples were only 30. However, the increased valgus angle of the landing knee joint was mostly due to the weak strength of the hip joint, the obvious development of height and bone

Table 2. Biomechanical index treatment of landing limbs before and after training for male and female athletes

	Landing on both feet		Landing with one foot		Squatting on one leg			
	Male	Female	Male	Female	Male		Female	
Vertical ground reaction force	4.35±0.64	6.48±0.87*	5.06±0.96	6.81±1.24 a				
Ground level backward reaction force	1.18±0.56	1.45±0.63	1.34±0.75	1.67±0.53				
Angle of knee flexion	43.4±5.4	35.6±5.1*	14.2±3.1	13.8±4.7	89.4±10.4		81.4±8.1	
Knee valgus angle	7.5±1.5	8.4±2.4	9.7±2.1	8.6±1.6	13.7±3.7		13.2±4.7	

* indicates a significant difference between male and female athletes ($p<0.05$).

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in adolescent females, and lack of muscle strength and neural control. The vertical ground reaction force reflects the cushioning ability of landing, which varies greatly from individual to individual. When the knee flexes at a small angle, the vertical ground reaction force is large but decreases when the reaction force is strong. In this respect, male and female athletes show some differences, which may be related to the strength of the leg muscles.

No relevant study on landing on one foot has been conducted abroad, but we chose this index because taekwondo athletes move and jump on one leg in most cases. The research results were similar to those of landing on two feet, and significant differences were noted between male and female athletes in the ground vertical response and knee flexion angle.

Single-leg squats have been used in several studies to clinically measure knee control of hip muscle function. Athletes stand on one leg, place their hand on the hip, squat as hard as they can, and stand up again without losing their balance. Researchers stood in front of the athletes and observed the position of the lower limbs and knee joints during the squats. Three levels were suggested: 0 to 2.0 for good action, 1 for average completion, and 2 for poor performance. Level 0 exhibits no significant pelvic tilt, no significant knee eversion, and no significant outward or inward movement of the knee. Level 1 demonstrates a tilt of the pelvis, a slight valgus of the knee, and a slight medial or lateral movement. Level 2 indicates significant lateral tilt of the pelvis, significant eversion of the knee, and medial and lateral movement [20,21,23].

In non-contact ACL injuries, such as cutting step, rotation, acceleration, deceleration, or high landing, fatigue can increase the incidence of injury [24–26]. Decreased knee flexion angle, greater hip flexion angle, knee eversion, increased internal rotation of hip joint, internal and external rotation of patella, and flat foot have been reported as the mechanisms of ACL injury. Which effect occurs at the time of injury or immediately after has long been under debate in the field. The video analysis of ACL injuries revealed that most ACL injuries occur within 30–100 ms after landing [27]. Non-contact ACL injury occurs after the foot touches the ground, with internal rotation and adduction of hip joint, strong contraction of quadriceps, and knee flexion angle is less than 30 degrees. The eversion of the knee is compensated for rotational displacement after ACL injury.

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Research Progress of Yupingfeng Powder in Clinical Application

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ABSTRACT

Yupingfeng Powder is widely used in the treatment of respiratory, digestive, urinary, dermatological and ENT diseases. The author reviewed the animal pharmacology experiments and clinical cases in recent years, and summarized and analyzed the diseases he treated, providing ideas and methods for clinical users.

1. Introduction

Yupingfeng,is a well-known Chinese medicine prescription, was put forward by Wei Yilin, a doctor of the Yuan Dynasty(1277-1347AD), in the book "The World Health Efficacy" . The prescription includes 30g of *Astragalus*, 60g of *Atractylodes Rhizome* (Fried) and 60g of *Atractylodes macrocephala Koidz*.In theQing Dynasty(1662-1735AD), the typhoid scientist Ke Yunbo said: *Astragalus* is good at driving wind, *Atractylodes Rhizome* is good at solidifying the surface, so it can prevent external evils, *Atractylodes* is good at solidifying, so it can be solid inside. "If you are good at driving away the wind with wind prevention, you can get astragalus root to fix the surface, then there is a guard outside, and if you get Atractylodes root to fix the inside, then there is evidence inside. Wind evil goes away and never comes again. Those who want to disperse wind evil should lean like a screen and be as precious as jade.(" 夫以防风之善驱风，得黄芪以固表，则外有所卫，得白术以固里，则内有所据。风邪去而不复来，此欲散风邪者，当倚如屏，珍如玉也。故名玉屏风 ").Decoctions were subsequently modified into granules. This article mainly summarized the pharmacological effects of Yupingfeng Powder and its application in clinical departments. Regularity provides a basis for clinical application.

2. Pharmacological Action

Modern clinical pharmacology studies have shown that Yupingfeng Powder has the functions of enhancing immune function, promoting immune cell activation and anti-inflammatory and anti-aging effects. Chen Xiangtao [1] used Yupingfeng polysaccharide to evaluate the effects on

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the immune function of cyclophosphamide-induced immunocompromised mice. At the same time, the spleen lymphocytes of mice with delayed immune allergic reaction were used as target cells, and the effects were observed. The results showed that the polysaccharides of Yupingfeng had different effects on non-specific immunity, humoral immunity and cellular immune function caused by cyclophosphamide（COX）. Wu Xuefang applied the traditional Chinese medicine serum pharmacological method [2] to observe the effect of Yupingfeng Powder on the activation of mouse peritoneal macrophages. The results showed that the Yupingfeng Powder serum could activate mouse macrophages after 30 min~90min treatment, which indicated that some components in Yupingfeng can be absorbed activate immune cells at a faster rate. Bao Yingcun et al [3] found that after Yupingfeng Powder's drug-containing serum acted on spleen lymphocytes of aged mice, decreased senescent cells, increased total superoxide dismutase (T-SOD) activity, reduced malondialdehyde (MDA) and cellular active oxygen (ROS) content. SOD is an antioxidant enzyme that protects cells from oxygen free radical damage. MDA content can reflect the degree of lipid peroxidation. Both are important indicators of antioxidant damage. The results showed that Yupingfeng Powder can inhibit cell senescence by increasing T-SOD, decreasing MDA activity and intracellular ROS levels in spleen lymphocytes of aged mice. Yan Hongwei et al [4] reported the histological changes of ovary and testis in Jiayufengping aging mice, and discussed them from the perspective of anti-inflammatory and anti-aging. In addition, astragaloside, atractylodone and cimicin, the main active components of Yupingfeng powder, have been proved to have the functions of anticancer, promoting the apoptosis of inflammatory cytokines and enhancing the immune mechanism[5-8],This provides a basis for the wide use of Yupingfeng Powder in clinical practice.

3. Clinical Application

Based on the pharmacological effects of Yupingfeng Powder on anti-inflammatory, immune enhancement and anti-cancer, Yupingfeng powder is widely used in respiratory, digestive, urinary, blood and other sstem diseases.

3.1 Respiratory Ssystem

Yupingfeng Powder is widely used in respiratory diseases and is commonly used in acute upper respiratory tract infections, allergic rhinitis, chronic obstructive pulmonary disease, and variant asthma. Acute upper respiratory tract infection belongs to the category of traditional medical exogenous diseases Yupingfeng Powder can supplement the lungs, regulate the righteousness, and help the evil out, so it is better in treating respiratory diseases. Wang Yusheng et al [9] observed the effect of Yupingfeng Powder on improving the efficacy of qi-deficiency cold patients through clinical experiments; Niuyang [10] professor used Yupingfeng powder plus pueraria and gypsum as the basic prescription in clinical practice, under the guidance of dialectical theory of lung spleen deficiency to treat allergic rhinitis. The mechanism may be related to lung-spleen deficiency, lung heat, and spleen and stomach imbalance. Yan Youcang et al [11] have shown that Yupingfeng Powder can effectively treat chronic obstructive pulmonary disease. 128 patients with chronic obstructive pulmonary disease remission were randomly divided into observation group (64 cases) and control group (64 cases). The control group was treated with conventional western medicine inhalation therapy, and in the observation group, based on conventional western medicine, patients were treated with Guizhi Thickening Puxingzi Decoction and Yuping Pingfeng Powder Both groups were treated for 1 month, and the changes in pulmonary function indexes of the two groups were observed.The functional indicators changed, and after treatment, the Yupingfeng group achieved significant curative effect in treating diseases. Cough Variant Asthma (CVA) can develop into typical asthma if not treated in time [12-13]. Traditional Chinese medicine classifies CVA as "cough, asthma" and other areas. The pathogenesis is complicated, and there are many certificates of virtual standard, false and real. Li Hua Li [14]celected 88 children with CVA and randomly divided them into treatment group and control group with 44 cases in each group. The control group was treated with montest sodium chewable tablets, and the treatment group was treated with Yupingfeng powder and acupoint sticking. Observe the clinical effect of the two groups. It turns out that the therapeutic effect of Yupingfeng powder combined with Acupoint Application on CVA in children total effective rate is 93.18%,control group is 84.09%. Compared with the montelukast sodium chewable tablets by YupingfengPowder combined with acupoint sticking, the results showed that the effects of Yupingfeng were better than the control group.

3.2 Digestive System

Yupingfeng Powder can supplement the function of lungs and spleen, so the application of the digestive system is also very effective. Li Xuemei [15] and others successfully treated diarrhea with Yupingfeng Powder. 102 patients with spleen and stomach diarrhea admitted to our hospital were divided into study group and control group, 51 cases in each group. The control group was treated with mont-

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morillonite powder + trimebutine maleate tablets. The research group was treated with Yupingfeng Powder and Xiangsha Liujunzi Decoction. The results showed that the total effective rate of the study group was higher than that of the control group; the time of recurrence of stool and the time of recurrence of stool were shorter in the study group than in the control group; the level of inflammatory factors in the study group was lower than that in the control group; Control group. The advantages of Yupingfeng Powder scattered Xiangsha Liujunzi Decoction in treating spleen and stomach diarrhea are more obvious, which can shorten the recovery time of stool and reduce the severity of inflammation, thus further improving the quality of life. Ulcerative colitis "Traditional Chinese Medicine Treatment Program" belongs to the category of "Jiuyu" [16]. Professor Ye Bai [17]treated 1 ulcerative colitis in the remission period based on the principle of strengthening the body, using Yupingfeng Powder as the main prescription to achieve the goal of maintaining remission and reducing the recurrence rate.

3.3 Urinary System

Nephrotic syndrome edema is closely related to lung, spleen and kidney. Yupingfeng Powder can be used to treat nephrotic syndrome. Du Ruige [18] selected 60 patients in hospital and randomly divided into 30 groups in each group. The two groups were treated with hormones. The experimental group was treated with Yupingfeng Powder and Zhibai Dihuang Decoction. The renal function of the two groups was observed. Indicators, TCM symptom scores and adverse reaction rates.The conclusion is: After treatment, the 24h urine protein quantitation, BUN, Scr, TCM syndrome scores and adverse reaction rates were lower than those before treatment, and the experimental group was lower than the control group. Conclusion: Yupingfeng Powder group is effective in treating adult nephrotic syndrome and can improve renal function.

3.4 Gynecological Diseases

According to the common pathogenesis of imaginary deficiency, trauma and evil, and the treatment principle of "different disease treatment", Yupingfeng Powder and its compound preparations have achieved satisfactory results in the prevention and treatment of various diseases in gynecology. The results of modern pharmacological experimental studies showed that Yupingfeng Powder can enhance the phagocytic index of macrophages, increase the proliferation of T lymphocytes, and regulate cellular immune function [19]. Professor Wei Shaobin [20] used "salt liver and spleen, help righteousness" as the treatment of patients with postoperative surgery, with Sini Sijun Yupingfeng plus blood circulation and phlegm, combined with rectal administration, ear acupuncture, acupoint application, etc. The characteristic therapy of traditional Chinese medicine, combined with internal and external, has achieved satisfactory results in postoperative menstruation, assisted pregnancy, pain relief and anti-recovery. In addition, Wei Shaobin used TCM comprehensive prevention and treatment program to treat patients with recurrent pelvic inflammatory disease remission, the prevention group was treated mainly by Yupingfeng Powder, and the control group was mainly based on health education. After 8 weeks of treatment, the comprehensive prevention group total effective rate was 97.14 % and control group total effective rate was59.18%,the effect treatment group was better than contorl group. Professor Wang Qi [21] believes that kidney yang deficiency type ovulation disorder, if lost treatment and mistreatment, Jinshui Xiangsheng, son stealing maternal qi, causing lung and kidney deficiency, lung qi deficiency is not outside the yang qi venting kidney is also very. The main body was given the addition and subtraction of "two immortal soup and Yupingfeng powder". After three cycles of treatment, the incidence of side effects such as follicular diameter, intima thickness, and spontaneous ovarian hyperstimulation syndrome (OHSS) decreased. Xie Sizhen [22] used Jiawei Yupingfeng Powder to treat 62 cases of qi deficiency type postpartum sweating, 62 cases of oral administration of oryzanol plus Vitamin B1, 5 days for 1 course of treatment, 2 courses of treatment after Yupingfeng group recovery rate and total The efficiency (50%, 95.17%) was significantly higher than the control group (22.58%, 38.71%).

3.5 Blood System

Yupingfeng Powder is also widely used in the treatment of allergic purpura. Allergic purpura (HSP) is an allergic disease involving multiple organ tissues caused by pathological changes of microangiitis[23]. Chinese medicine believes that the incidence of HSP mainly lies in the child's body of juvenile yin and yin and yang, lack of qi and blood, The condition is easy to turn into a deficiency, and the deficiency of the lung and spleen is caused by the infirmity of the health， In addition, the heat is suddenly conducted into the blood, forming purpura. Therefore, the treatment should be based on the principle of benefiting the qi and strengthening the body [24]. Bian Hongen [25] and others observed the clinical effects of Yupingfeng Powder combined with Western medicine in the treatment of children with allergic purpura (HSP). 98 children with HSP who met the inclusion criteria were randomly divided into 2 groups and 49 cases according to the random number table

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method. The group was treated with conventional western medicine, and the research group was treated with Yupingfeng Powder on the basis of the treatment plan of the control group. Results after 1 month of treatment: 95.92% of the total effective rate of clinical efficacy, 79.59% higher than the control group. Conclusion: Yupingfeng Powder combined with Western medicine treatment of children with HSP can alleviate clinical symptoms, inhibit inflammatory response, improve complement level and cellular immune function, and improve therapeutic effect.

3.6 Skin Disease

Yuping Feng Powder's function of external defense and evil spirits makes it show unique advantages in the treatment of skin diseases. Sun Xiaochen [26] used western medicine and western medicine plus Yupingfeng scattered for the treatment of allergic dermatitis. The result was better than that of the western medicine group, which highlighted the effect of Yupingfeng Powder. Kong Danyi [28] randomly divided 128 patients with urticaria into Jiawei Yupingfeng Powder treatment group (64 cases) and levocetirizine hydrochloride tablets control group (64 cases) for 4 weeks， After 4 weeks of treatment, the results showed that the effective rate in the treatment group was 98.43%, and the effective rate in the control group was 93.75%.Therefore, it is considered that Jiawei Yupingfeng Powder has a significant effect on the treatment of urticaria. Wu Shuang [29] and others have confirmed that Yupingfeng Powder has a good therapeutic effect on facial recurrent dermatitis. They received 58 patients with facial allergic dermatitis and were randomly divided into two groups, 29 in each group. The control group (conventional western medicine treatment) and the experimental group (conventional western medicine combined with Yupingfeng powder treatment). The results showed that the symptoms of facial itching, flushing, swelling, papules or erythema were significantly lower in the experimental group than in the control group after 2 weeks. The effective rate and effective rate of the experimental group were 55.2% and 41.4% after 3 courses of treatment. Both were higher than the control group, indicating that the combination of Yupingfeng Powder on the basis of conventional western medicine treatment for patients with facial allergic dermatitis can effectively improve the symptoms of patients, and the long-term treatment effect is good. Zhao Wenxue [30] and other treatments for chronic eczema showed that this side also has a good therapeutic effect on chronic eczema. 120 patients with chronic eczema were randomly divided into treatment group and control group with 60 cases each. The treatment group received oral Chinese medicine decoction (Xiefeng Sanyu Yupingfeng Powder addition and subtraction) combined with external dehumidification and itching ointment treatment. The control group was treated with topical external application of dehumidification and itching ointment. The two groups were treated for 4 weeks. EASI scores were used as indicators of observation and their efficacy was evaluated. Results: The total effective rate and cure rate of the treatment group were 91.67% and 46.67%, respectively. The control group was 66.67% and 18.33%, respectively. Conclusion: Yupingfeng Powder combined with western medicine can effectively treat chronic eczema.

3.7 ENT

Because of Yupingfeng's replenishing lung, dispelling heat and Strengthen the body, it has a good therapeutic effect on conjunctivitis and keratitis. Peng Ju [31] and other 78 patients with spring conjunctivitis (both eyes) were randomly divided into two groups. The treatment group was treated with Shengsiwu Decoction and Yupingfeng Powder for internal and external washing. The control group was given azelastine hydrochloride. Eye drops were treated and the clinical efficacy and recurrence rate of the two groups were compared. Results: The total effective rate was 93.88% in the treatment group ， and 62.07% in the control group. After 1 year of follow-up, the results showed that the recurrence rate was 17.39% in the treatment group and 66.67% in the control group.This explained Yupingfeng powder had a good therapeutic effect on spring conjunctivitis.

3.8 Other Effects

This prescription can also be used to treat spontaneous sweating [32], and has a certain inhibitory effect on primary liver cancer and cirrhosis [33-34]. And have a certain clinical effect on stomach pain, edema, rheumatoid arthritis, psoriasis, gastroptosis, viral myocarditis, and hypertension.

4. Conclusion

Yupingfeng Powder and its compound have a wide range of pharmacological effects and clinical applications. If we can study its mechanism of action in depth, further explore its clinical therapeutic effects and make important guarantees for human health, it will be the direction that needs further research in the future.

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Myocardial Protective Effect of Gas Signal Molecule Hydrogen Sulfide on Cardiovascular Disease

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ABSTRACT

Cardiovascular diseases increase continually in the worldwide scale, and its specific pathogenesis has not been completely clear. The gas signal molecule hydrogen sulfide (H_2S) is a new type of neuroactive substance, which plays many biological roles in many systems such as cardiovascular system. In recent years, a lot of research has confirmed H_2S has myocardial protective effect on cardiovascular diseases such as atherosclerosis, ischemia-reperfusion injury, hypertension and heart failure. This paper reviews the research status of myocardial protective effect of H_2S on cardiovascular diseases.

1. The Research Background

With the continuous progress of social development level and the aging process of population structure in China, the continuous increase of cardiovascular patients received in clinic, which has seriously affected people's health[1].In the past decade, scholars at home and abroad have done a lot of researches on the prevention and treatment of cardiovascular disease, but still have not found an effective cure[2].In 2014 Xu et al [3] studies indicate that the behavior of hydrogen sulfide (H_2S) is similar to nitric oxide (NO) and carbon monoxide (CO), and may exert myocardial protective effects by inhibiting mitochondrial pathways ,resisting Ca^{2+}overload and antioxidant stress. This paper will summarize and analyze the latest research progress of H_2S in myocardial protection and therapeutic potentialn in cardiovascular system diseases such as ischemia-reperfusion injury, atherosclerosis, hypertension and heart failure of recent years, the aim is to provide a new idea for the clinical prevention and treatment of cardiovascular diseases such as ischemia-reperfusion injury.

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2. Generation and Metabolism of H_2S

The production of H_2S in mammals has two pathways: non-enzyme catalysis and enzyme catalysis. H_2S in the non-enzyme pathway is mainly produced by elemental sulfur and sulfur-containing compounds, only a small part of H_2S is produced by the non-enzyme catalytic pathway, and most of H_2S is produced by the enzyme catalytic pathway. It has been found that the production of endogenous H_2S is regulated by the following five enzymes: D-amino acid oxidase (DAO), cysteine-lyase (CSE), cysteine -synthase (CBS)[4], cysteine transaminase (CAT), and 3-mercaptopyruvate sulftransferase (3-MST)[5]. For example, DAO is mainly distributed in the kidney and cerebrum, CBS is mainly distributed in the central nervous system, CAT and 3-MST can synthesize H_2S in the brain and vascular endothelium, and CSE is the most critical enzyme in the sulfur transfer pathway of the human cardiovascular system[6]. L-cysteine is the main catalytic substrate for CSE, CBS and CAT, while D-cysteine is the substrate for DAO and 3-MST[7]. H_2S generated in the body is mainly characterized in two forms:1/3 is in the form of H_2S, and 2/3 is in the form of Sodium hydrosulfide (NaHS), H_2S and NaHS can be transformed into each other and form a dynamic balance in vivo[8] (H_2S: NaHS=1:2).The endogenous H_2S is rapidly oxidized to thiosulphates and sulfates in the mitochondria of cells catalyzed by a variety of enzymes and detoxified, and finally discharged through the kidneys, intestines and lungs[9].

3. Effects of H_2S on Cardiovascular Disease

Endogenous H_2S level is mainly regulated by H_2S generating enzyme. When the expression or activity of the generating enzyme is down-regulated, H_2S level will be significantly reduced, leading to cardiovascular disease. Gao et al.[10] found in their study that compared with normal subjects, Plasma H_2S level was significantly reduced in patients with coronary atherosclerosis.Hong Kong et al. conducted a study on 110 patients with coronary heart disease using sensitive sulfur electrode method to determine the plasma H_2S content and found that the plasma H_2S level in patients with acute myocardial infarction and unstable angina was lower than that in patients with stable angina[11].Salloum et al[12]. Found that endogenous H_2S can not only reduce myocardial ischemia-reperfusion injury, but also regulate blood pressure, fight atherosclerosis, promote vasodilation and regulate negative myocardial strength. The myocardial protective effect of endogenous H_2S on cardiovascular diseases has been confirmed, and the myocardial protective effect of exogenous H_2S on cardiovascular diseases has been gradually confirmed. Supplementation of exogenous H_2S can also reduce myocardial injury, improve heart failure and improve cardiac function.

3.1 H_2S and Ischemia-Reperfusion Injury

Myocardial ischemia is mainly refers to the blood perfusion of heart is reduced caused by Atherosclerosis (AS), leading to reduced oxygen supply to the heart, circulatory failure, or even sudden death , reperfusion is necessary to improve myocardial ischemia , but the injurious changes caused in the ischemic period are more serious after recanalization, irreversible myocardial damage, serious arrhythmia and even lead to sudden death.Through comparative analysis of 100 patients with acute myocardial infarction and 100 patients with normal coronary angiography, He Bosheng et al[13]. found that H_2S content could determine the scope and clinical efficacy of myocardial infarction, and confirmed that H_2S has a certain correlation with myocardial ischemia reperfusion injury. When myocardial ischemia occurs, H_2S mediated chemical modification of cardiac protein is significantly increased, thereby rapidly activating protective pathways, increasing coronary microvascular reactivity, improving cardiac function, and ultimately reducing the damage caused by myocardial ischemia to the body[15].In addition, some scholars have pointed out that pretreatment with H_2S donor (NaHS) before ischemia also has a certain myocardial protection effect.Studies on rat myocardial ischemia model indicate that animals with reduced CSE activity and significantly reduced endogenous H_2S could increase myocardial perfusion, improve arrhythmia, and thus reduce myocardial injury after artificial NaHS pretreatment[16].The following is a summary of several major mechanisms by which H_2S exerts myocardial protection.

3.1.1 Mechanism 1: Anti-apoptosis

Numerous studies have shown that H_2S plays a crucial role in its resistance to apoptosis by inhibiting mitochondrial pathways and endoplasmic reticulum pathways.Mitochondrial pathway is the endogenous apoptosis pathway, in which the anti-apoptotic protein Bcl-2 gene and the pro-apoptotic protein Bax gene can change the mitochondrial membrane integrity, and their relative levels determine the fate of cells and are key factors affecting the survival of myocardial cells[6]. The expression of Bcl-2 gene in mitochondrial outer membrane can inhibit the transport of cytochrome C to cytoplasm and thus resist apoptosis. After activation , Bax gene is inserted the mitochondrial outer membrane through allosteric translocation, thus destroying the integrity of the membrane ,and resisting

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anti-apoptotic proteins, thus promoting cell apoptosis. H_2S up-regulated the expression of anti-apoptotic protein Bcl-2 and decreased the expression of pro-apoptotic protein Bax, finally achieving the purpose of anti-apoptosis and protecting cardiomyocytes[17].Citi et al. found that H_2S inhibited apoptosis by down-regulating mRNA and protein expression levels of transcription factor homologous protein, an important molecule of unfolded protein, and glucose-regulating protein 78 during myocardial ischemia and reperfusion[18].

3.1.2 Mechanism 2: Antioxidant Stress

During ischemia-reperfusion, the increase of free radicals,reactive oxygen species (ROS) and Reactive nitrogen species (RNS) in the body leads to lipid peroxidation of biofilms, imbalance of oxidation system and antioxidant system, DNA damage, and finally myocardial cell damage[19]. Al-Magableh et Al have shown that H_2S can reduce ROS and protect vascular endothelium under acute stress by decomposing single electron chemicals such as HS^-[20]. Zhang et al[21]. treated the rats with hydrogen peroxide (H_2O_2), an activated oxygen donor, to simulate acute ischemia-reperfusion injury, the pretreatment of H_2S donor before H_2O_2 treatment revealed that H_2S donor could reduce oxidative stress, thereby protecting myocardial cells.

3.1.3 Mechanism 3: Anti-Ca^{2+} Overload

During ischemia-reperfusion, a large amount of Ca^{2+} aggregation can change the permeability of mitochondrial membrane by activating the phospholipase on the mitochondrial membrane, and finally cause myocardial damage.Numerous studies have demonstrated that H_2S protects cardiomyocytes against Ca^{2+} overload, thereby reducing the incidence of cardiovascular disease. Studies have found that H_2S can promote the opening of ATP-sensitive potassium channels and accelerate the uptake of Ca^{2+} in the sarcoplasmic reticulum. H_2S can also inhibit Ca^{2+} overload and avoid excessive contraction of cardiomyocytes by inhibiting the opening of L-type Ca^{2+} channels[22].In addition, H_2S can enhance the activity of Ca^{2+}-ATPase in the sarcoplasmic reticulum by activating protein kinase C(PKC) in myocardial tissue, accelerate Ca^{2+} exchanger-mediated ion exchange, inhibit Ca^{2+} overload, and thus reduce ischemia-reperfusion induced cardiac infarction.After slow injection of H_2S donor into myocardial ischemia rat models, Ca^{2+} overload can be inhibited, thus reducing myocardial ischemia range and promoting cardiac function recovery, resulting in significant myocardial protective effects[23].

3.2 H_2S and Atherosclerosis

The role of H_2S in AS pathological changes cannot be ignored, such As Wang treatment with NaHS apolipoprotein E knockout (apoE - / -) mice, the study found that H_2S can inhibit expression of the aortic intercellular adhesion molecule - 1 (ICAM 1) , ICAM - 1 plays an important role in the formation and developmentn of thrombosis and As , the direct relationship between H_2S and AS lesions was demonstrated for the first time [24].A large number of studies have shown that H_2S has various vascular protective effects against As diseases, including regulating blood lipid content, promoting endothelial cell proliferation and migration, reducing foam cell formation, inhibiting platelet aggregation, and inhibiting the expression of aortic chemokine receptor 1 antibody (CX3CR1) and chemokine CX3CL1. Zhao et al. demonstrated that H_2S can inhibit the production of foam cells through the CATP/ERK1/2 pathway of human monocyte derived macrophages[25]; After NaHS treatment, intracellular lipid accumulation was reduced, indicating that H_2S had a certain effect on inhibiting the As lesions.Du et al[26]. found that H_2S reduces macrophage inflammation induced by ox-LDL by inhibiting the phosphorylation of nuclear factor Bp65, thereby reducing the harmful effects of lipoprotein in the development of atherosclerosis.

3.3 H_2S and High Blood Pressure

Collagen fibers have strong toughness and low elasticity.If the amount of collagen in the heart's blood vessels increases,Narrow blood vessels, high blood pressure,Long-term hypertension is often accompanied by target organ function or organic damage, which seriously affects people's health and quality of life.H_2S, on the other hand, relaxes myocardium and vascular smooth muscle in a variety of ways, thereby lowering blood pressure.First, H_2S induces phosphorylation of FOXO1 and FOXO3a by inhibiting endothelin-1 (ET-1), thereby promoting their nuclear translocation and binding to the target gene promoter.Furthermore, ATP sensitive potassium channel (KATP) was activated to significantly improve endothelium-dependent systolic function in hypertensive rats,promote vascular smooth muscle relaxation and relieve hypertension[27].Polhemus et al. found that some non-specific KATP blockers and mitochondrial MEMBRANE KATP channel blockers can reduce myocardial contractile force,This leads to increased cardiovascular load, which leads it is to increased blood pressure, while activation of the KATP channel reduces vascular load, which leads is in turn lowers blood pressure[28].In addition, Song Zhiqiang et al. stimulated Cl-/ HCO3- channel with NaHS to reduce intracellular pH value and increase H+ concentration, thus activating

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KATP channel, reducing vascular tension and alleviating hypertension[29].Third, regulate the balance of myocardial collagen fibers:Always there is a dynamic balance between the generation and degradation of myocardial collagen fibers to maintain the stability of collagen content. Once the collagen content in myocardium increases and the collagen configuration changes, myocardial fibrosis occurs.Homocysteine (Hcy) level is high in hypertensive patients, and high Hcy level can affect the balance of myocardial collagen regulation, leading to fibrosis of extracellular matrix of cardiomyocytes[30].Peng chao et al. pointed out that endogenous H_2S level can be used as a signal molecule of essential hypertension to reduce blood pressure and slow down heart rate[31].

3.4 H_2S and Heart Remodeling

Cardiac remodeling is characterized by ventricular dilatation, myocardial fibrosis, and heart failure.In recent years, there has been a significant increase in patients with heart failure in China. The myocardial protective effect of H_2S is a new research direction in the field of cardiovascular disease, providing a new idea for the treatment of heart failure.Liu et al[32]. confirmed that H_2S can up-regulate endothelial NO level, thereby reducing stress load and preventing myocardial injury.Low levels of endogenous H_2S can lead to death in patients with heart failure[33].H_2S can inhibit of myocardial hypertrophy and fibrosis by reducing the activity of angiotensin Ⅱ and raised link 43 (Cx43) protein expression .Givvimani et al[34]. found that H_2S can activate matrix metallopro-teinases-2 (MMP-2) and inhibit matrix metallopro-teinases-9 (MMP-9), thereby enhancing vascular endothelial growth factor (VEGF) synthesis and angiogenesis , reducing the level of anti-angiogenic factors, and reducing intracocardial fibrosis and heart remodeling in mice with pressure overload. In 2017, Wu et al[35]. found that NaHS treatment could reduce myocardial cell apoptosis, interstitial fibrosis and cardiac hypertrophy in mice, and the overall survival rate of mice was relatively high, so it was speculated that exogenous H_2S had a good therapeutic effect on ischemic heart failure.

4. Summary and Prospect

A large number of studies have shown that H_2S, a gas signal molecule, has a myocardial protective effect on cardiovascular system diseases by inhibiting apoptosis, resisting Ca^{2+} overload, anti-oxidative stress and so on. However, due to the narrow physiological range of H_2S and its extremely toxic effect, relevant research data are mainly from mouse and other animal model experiments, while human experiments are seldom carried out, so there is still a lack of strong clinical evidence.In addition, H_2S is also affected by statins, aspirin, metformin and other clinical drugs, making its clinical use more difficult[36].The mechanism of H_2S in protecting cardiomyocytes needs to be further explored, and how to regulate the concentration of exogenous H_2S for the treatment and prevention of cardiovascular diseases also needs to be further studied.

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Influence of Personality Characteristics and Psychological Intervention on Treatment Satisfaction of Juvenile Orthodontic Patients

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ABSTRACT

Orthodontics is the correction and treatment of malocclusion deformity caused by a variety of reasons. Malocclusion malformation has a direct impact on people's facial features, while likely to cause some diseases involving the mouth in the long-term life. For adolescents, malocclusion has a great physical and mental impact. This article first have a simple overview of malocclusion deformity and orthodontic treatment, analysis of youth physical and mental development characteristics and adolescent personality traits. Through the way of completely random sampling, eighty teenage orthodontic patients can be divided into two groups, respectively as the control group and psychological intervention group. Though survey assessment after several stages treatment, explore impact on the psychological intervention in patients with juvenile orthodontic treatment satisfaction degree.

1. Introduction

The research and treatment of malocclusion deformity is an important branch of the current oral medicine. In foreign country orthodontic treatment of malocclusion deformity is known as dental orthodontics and maxillofacial correction, in domestic commonly referred to as orthodontic treatment. With the development of medical technology equipment progress, orthodontics treatment not only limited to the correction of teeth, also of alveolar bone in areas such as the jaw facial deformity were studied, to analysis pathogenesis and to explore the treatment measures. If the patients without any treatment, not only influence the facial features correct and beautiful, at the same time for each part of the oral cavity has serious influences on the development and the teeth chewing function, easy to cause systemic disease[1]. This age is the rapid changes in the physical and mental development of adolescents, is the key of the orthodontic treatment period. Influenced by the teenagers as the main body of the orthodontic patients, many teenagers in the face of orthodontic treatment showed anxious mood, on the one hand, is worried about micromaxillary deformity affect their appearance, on the other hand is a process for treating a variety of means of discomfort, cause psychological conflict, at the same time, it has teeth sensitivity high low tolerance of objective factors, causing them to worry about poor treatment effect[2].

2. Overview of the Development of Malocclusion and Orthodontics

Orthodontics has gone through several stages of development and is now hundreds of years old. One of the

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first doctors in Rome began to guide patients through the hand and basic tools to correct the misalignment of teeth. It was the oldest documented technique, but it had little effect. Dentistry evolved in the Middle Ages, but there were no professional dentists, and many people started trying to correct dental parts through the profession of hairdressers. Until the modern times, with the development of industrial technology, is known as the "father of modern dentistry" French dentist Pierre Fucha published his latest book, describes in detail a precise straightening device, but even so, still orthodontics science development is very slow, it is not very effective means of micromaxillary deformity correction. In 1819, the invention of bow-wire control therapy greatly promoted the development of orthodontics, and it is also the evolution of the orthodontic techniques we use today. And with the development of technology, and new materials are being developed, production materials used in orthodontics is also enriched, steel, copper, gold, rubber, etc., in the 1960 s, a variety of technology maturity, prompted orthodontics and rapid development, has begun to use silk bow to control the tooth jaw state, achieve the goal of straight teeth. In micromaxillary deformity treatment process, modern medicine found that patients often appear psychological problems, this is due to the current living standards improve, people pay more attention to their appearance, some people looks poor growth in the learning process prone to mental insecurity, inferiority, autistic, gradually in orthodontics treatment, so the necessary psychological intervention, can better help patients regain confidence. Modern medicine actively advocates the model of bio-psycho-social medicine, and more and more people pay attention to the psychological problems caused by malocclusion. In the actual treatment process, some patients are particularly severe malocclusion, but the heart of the patient is positive and optimistic, there are also slight malocclusion, but the patient is extremely anxious, serious psychological problems. Therefore, special psychological counseling, intervention and treatment should be carried out according to the actual situation in the treatment of malocclusion [3].

3. Personality Analysis of Juvenile Orthodontic Patients

3.1 The Basic Features of Personality

Characteristic mentions in the definition of personality is the individual and the environment interaction, so personality in essence is also a person's social attributes, due to the concept of personal values, behavior in the process of physical and mental development, such as demand, motivation factors, each individual has a different personality traits, though in the same growth environment, characteristics of similar, but not identical, visible personality that is affected by environmental factors, also have the effect of individual subjective initiative, through the outer and inner jointly promote, make the individual foreign show different response and handling the same thing. The formation of personality is affected by a variety of factors, so after the formation of the basic personality characteristics, generally will not be easily changed, personality can profoundly reflect the individual's mental state, in the aspect of psychology, the in-depth and comprehensive study of personality is the necessary premise of personal psychological counseling therapy. Modern psychology were studied, the basic features of the personality of the mainstream school of thought says that personality traits is generalized, individuals with neural psychological structure, each person has a different personality traits, the characteristics of wide variety, complete personality characteristics, the leading experts in the field of Eysenck personality traits as, summarized the different characteristics of collection, and categorizing the personality, can effective personality traits for factor analysis, has the very high research value [4].

3.2 Personality Analysis of Juvenile Orthodontic Patients

Through psychology studies have shown that personality traits are the influence of psychological factors, is a heart external performance, the key to the development of adolescent physical and mental integrity stage, its attention to the outside world and view is very sensitive, if oral micromaxillary deformity is relatively serious, has negative effect on the facial features, such as facial image, so easy to cause adolescent anxiety, panic mentality, inner stress yourself in life long learning process, produce psychological barriers, seriously affect the normal development of personal physical and mental health. Many experts and scholars on the related research, patients with moderate and severe micromaxillary deformity, afraid to face the eyes of others in our daily life, worry about discrimination and make fun of, at the same time due to tooth jaw bone deformity teeth arrangement is not whole, not in communication with people consciously to carry on the output resistance, isolated gradually, in the past for a long time to produce inferiority mentality, the results showed that micromaxillary deformity cowardice and decisive, adaptation and anxiety in patients with personal characteristics and the classification of the deformity and significantly associated with severity [5].

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4. To Explore the Influence of Psychological Intervention on Treatment Satisfaction

4.1 Research Object

In order to study the effect of psychological intervention in patients with juvenile orthodontic treatment, especially recently in our dental treatment process by experiment or interested in 80 governance orthodontics patients, the main concentration between 12 to 20 years old age, the age is in micromaxillary deformity correction of the golden age, the sex ratio is close to 1:1, and ruled out the intelligence factor and the patients with other mental illnesses, ensure fair and objective of experimental results, and patients in the trials will experiment content in advance, to be agreed and signed written informed consent began to group. A total of 80 subjects were randomly classified by computer, including 40 in the experimental control group and 40 in the psychological intervention group.

4.2 Research Methods

The control group was treated with sliding straight wire arch correction and observed with normal medical procedures without psychological intervention. While the psychological intervention group on the basis of the sliding straight wire bow orthodontic treatment, psychological cognitive intervention, the first is before the treatment of psychological intervention, by psychological counseling, reduce patients to treatment process of nervousness and resistance point of view, and make the wrong jaw correct knowledge, make the patient know that the more correct knowledge and need to pay attention to in the process of place, reduce the fear of treatment, regularly under medical observation at the same time, closely observe changes in the process of psychological treatment, to guide their healthy psychology and good living habits, to overcome the anxiety and concern, cause patients to understand treatment is necessary and harmless. It is of great significance to the future life[6].

4.3 Results Analysis

At each stage of the experiment, the two experimental groups were investigated with questionnaires on whether they were anxious, satisfied with the treatment process, felt good about themselves and satisfied with the treatment results.

The two groups were analyzed and evaluated during the operation, one week after the operation, one month after the operation and half a year after the operation. The main evaluation indexes were VAS pain degree, anxiety/depression index SAS/SDS and self-efficacy index. The data were analyzed by questionnaire.

Table 1. Comparison of VAS scores between the experimental control group and the psychological intervention group

Group	VAS score		
	Intraoperative	One week after surgery	One month after surgery
Experimental control group	6.8±2.62	4.7±1.47	2.6±1.02
Psychological intervention group	4.2±1.37	2.8±0.62	1.2±0.44

Table 2. SAS/SDS scores of anxiety and depression

Group	Anxiety and depression SAS/SDS				
	Preoperative	Intraoperative	One week after surgery	One month after surgery	Half a year after surgery
Experimental control group	53.5±10.6	64.8±9.62	64.7±8.47	62.6±8.02	61.7±7.47
Psychological intervention group	52.6±8.2	54.2±8.37	42.8±7.62	38.2±7.44	32.8±6.62

Table 3. Comparison of self-efficacy scores

Group	Self-efficacy score			
	Preoperative	One week after surgery	One month after surgery	Half a year after surgery
Experimental control group	2.21±0.37	2.28±0.21	2.47±0.4	2.52±0.42
Psychological intervention group	2.24±0.36	2.43±0.32	2.66±0.27	2.86±0.51

The results showed that: (1) There was no significant difference in emotional anxiety between the two groups at the initial stage of treatment; in the middle stage of treatment, there were significant emotional fluctuations in the experimental control group; anxiety and depression showed a cumulative state with the treatment time; and the rise curve of emotional anxiety in the psychological intervention group was significantly slower. (2) In terms of post-treatment quality of life, compared with the experimental control group, the psychological intervention group was significantly better than the experimental control group in terms of positive emotional expression, happiness, satisfaction and self-value improvement after treatment.

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5. Conclusion

Modern medicine actively advocates the model of bio-psycho-social medicine, which lays a foundation for the development of modern stomatology. In recent years, more and more attention has been paid to the psychological problems caused by malocclusion. Malocclusion can cause some mental health problems, which is not conducive to the healthy and happy growth of teenagers. Psychological intervention in the process of juvenile orthodontic treatment can effectively improve the patient's self-efficacy, greatly ease the treatment process of the negative factors, such as pain, discomfort, risk reducing psychological problems, keep positive and optimistic attitude, increase the degree of recognition of treatment process and result, improve the quality of life, improve the effect of correction, is worth for popularization and application in the process of oral orthodontic treatment.

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A Meta-analysis of Therapeutic Effect of Thalidomide on Ankylosing Spondylitis

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ABSTRACT

Objective: To study the therapeutic effect of thalidomide on ankylosing spondylitis (AS) by meta-analysis. **Methods:** Personal digital library, Cochrane library, and China Biology Medicine disc (CMBdisc), as well as relevant pharmaceutical and medical journals, were collected and reviewed. After the analysis of characteristics of the selected document and the evaluation of the risk of bias, the therapeutic effect of thalidomide on ankylosing spondylitis (AS) and its influence on related indexes were analyzed by literature data. **Results:** The meta-analysis results of 8 pieces of literature showed that the total effective rate of thalidomide in the treatment of ankylosing spondylitis (AS) was significantly improved, compared with conventional treatment or sulfasalazine (SASP) treatment ($P<0.05$). Furthermore, the time of morning stiffness, BASDAI score, C-reactive protein (CRP) level, and other related symptoms and indexes were significantly optimized ($P<0.05$). **Conclusion:** By rational utilization of thalidomide in the treatment of ankylosing spondylitis (AS), related symptoms and indexes of patients can be effectively improved, the total effective rate of the treatment was significantly improved and the safety of the treatment can be guaranteed.

1. Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease, spinal apophysis, sacroiliac joint, paraspinal soft-tissue and peripheral joint of patients will be invaded after onset. Moreover, extra-articular manifestations may also occur. The patients with more severe ankylosing spondylitis (AS) have the spinal deformity and ankylosis. At present, there is no radical cure for ankylosing spondylitis (AS) in clinical practice. Drug treatment, surgical treatment, and proper exercises are usually used to relieve and control the disease. With the development and progress of drug research in recent years, the application of tumor necrosis factor-α (TNF-α) antagonist in clinical treatment is more and more extensive. This kind of medicine can not only quickly relieve the stiffness, pain, and other symptoms of patients but also inhibit bone destruction and improve body function and quality of life of the patients. However, due to the higher economic cost and the exclusion from urban medical insurance, such biological agents cannot be widely used in the clinical treatment of anky-

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losing spondylitis (AS). Related research and experiment of thalidomide (Thalomid) found that thalidomide can not only inhibit the production of TNF-α selectively by normal monocytes but also reduce the level of serum TNF-α of the patients with erythema nodosum leprosy (ENL) and tuberculosis (TB). Moreover, the application of thalidomide in the treatment of ankylosing spondylitis (AS) can obtain a relatively remarkable effect, and the related research is gradually enriched.

2. Materials and Methods

2.1 Inclusion Criteria

(1) Test type: contrast test.

(2) Type of patients into groups: diagnosed as ankylosing spondylitis (AS) without joint deformity.

(3) Test method: the control group was treated with conventional non-steroidal anti-inflammatory drugs (NSAIDs) or sulfasalazine (SASP), while the observation group was treated with thalidomide based on conventional treatment.

(4) Observation index: the total effective rate, morning stiffness time, finger to floor distance, occipital wall distance, Schober test, degree of chest expanding, BASDAI score, C-reactive protein (CRP) level, erythrocyte sedimentation rate (ESR), number of peripheral joints with swelling and adverse reactions.

2.2 Retrieval Methods

Electronic retrieval was mainly used for data retrieval. Ankylosing spondylitis (AS) and thalidomide were input as keywords in the personal digital library, Cochrane library, and China Biology Medicine disc (CMBdisc) for literature search.

2.3 Data Filtering and Extraction

The first was to screen preliminarily the title and abstract of articles, and the second was to read the content of the articles to finally select the included literature.

2.4 Assessment of Risk of Bias

The Cochrane evaluation system was used to evaluate the risk of bias of the selected literature. The risk of bias of the selected literature was set as a, B and C, and the corresponding literature risk coefficient was low, medium, and high.

3. Results

3.1 Analysis Results of Literature Search

74 pieces of literature were initially collected through the database search, and there were 38 left after screening. The literature with incomplete data and insufficient follow-up time were removed after full-text reading. Finally, 8 pieces of literature were selected as reference documents for the study, involving 610 patients with ankylosing spondylitis (AS). The reference documents are in Chinese or English.

3.2 Characteristics of Inclusion Documents and Analysis of the Risk of Bias

The eight reference documents included were all used for the study of the contrast test. The observation group was treated with thalidomide and the control group was treated with conventional treatment or sulfasalazine (SASP). The risk of bias of six reference documents was moderate, and that of two of them were low.

Table 1. Characteristics and Risk of Bias of Inclusion Documents ($n = 8, \overline{x} \pm s$)

Researcher (Year)	Study design	Number of patients		Assessment of risk of bias						
		T	NT	1	2	3	4	5	6	Grade
XIE Denghua (2020)	CT	40	40	Y	U	U	Y	Y	Y	B
WANG Zhe, ZHAO Xiaoying, QUAN Bingtao, et al. (2019)	CT	40	40	Y	U	U	Y	Y	Y	B
RAN Jian (2019)	CT	38	38	Y	U	U	Y	Y	Y	A
HOU Tao (2018)	CT	44	44	Y	U	U	Y	Y	Y	B
ZENG Xianlin (2017)	CT	32	32	Y	U	U	Y	Y	Y	B
GUI Yinli, SHI Lipu, XUN Wen, et al. (2017)	CT	41	41	Y	U	U	Y	Y	Y	B
LI Guangke & YUAN Yao (2016)	CT	30	30	Y	U	U	Y	Y	Y	A
LI Yonghong, TAO Lihong & QIAN Kewei (2016)	CT	40	40	Y	U	U	Y	Y	Y	B

CT: contrast test; T: thalidomide; NT: non-thalidomide treatment; 1: random method; 2: randomly hidden; 3: blind method; 4: loss to follow-up; 5: selective reporting; 6: confounding bias; Y: appropriate; U: unclear; N: inappropriate

3.3 Statistical Analysis

Through a comprehensive analysis of relevant research results, thalidomide in the treatment of ankylosing spondylitis (AS) has a very significant therapeutic effect, improving the total effective rate of clinical treatment, and related indicators of patients.

3.3.1 The Total Effective Rate of Treatment

Six pieces of literature have studied the total effective rate of treatment. It was found by contrast test that the total clinical effective rate of thalidomide in the treatment of

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ankylosing spondylitis (AS) is significantly higher than that of the conventional treatment or sulfasalazine (SASP) treatment.

3.3.2 Morning Stiffness Time

Four pieces of literature have studied the morning stiffness time. It was found by contrast test that the morning stiffness time of the patients in the observation group after treatment was significantly less than that of the patients in the control group and thalidomide could improve morning stiffness of the patients significantly.

3.3.3 Finger to Floor Distance and Occipital Wall Distance

One piece of literature has studied finger to floor distance and six pieces of literature have studied the analysis of occipital wall distance index. It was found by contrastive analysis that finger to floor distance and occipital wall distance of the patients after treatment all significantly declined but the two indexes of the patients after the treatment with thalidomide were lower than that of the patients in the control group.

3.3.4 The Number of Peripheral Joints with Swelling

Six pieces of literature have studied the number of peripheral joints with swelling. It was found by the study and tests that the number of peripheral joints with swelling of the patients after the targeted treatment significantly declined and the index of the observation group was significantly lower than that of the control group.

3.3.5 Schober Test

Two pieces of literature have studied the Schober test. It was found by contrast test that the Schober test result of the patients in the observation group after treatment was significantly higher than that of the patients in the control group and the difference between the two groups was statistically significant.

3.3.6 Degree of Chest Expanding

Eight pieces of literature have studied the degree of chest expansion. It was found by contrastive analysis that the degree of chest expansion of the patients in the observation group was significantly higher than that of the patients in the control group.

3.3.7 BASDAI Score

Three pieces of literature have studied the BASDAI score. The score of the observation group after treatment was lower than that of the control group.

3.3.8 C-Reactive Protein (CRP) Level

Six pieces of literature have studied the C-reactive protein (CRP) level. The study found that the CRP level of the patients in the two groups after treatment significantly declined and the CRP level of the patients in the observation group was significantly lower than that of the control group.

3.3.9 Erythrocyte Sedimentation Rate (ESR)

Five pieces of literature have studied the erythrocyte sedimentation rate (ESR). Through comparison, we found that the ESR of the patients in the two groups after treatment significantly declined, and the ESR of the patients in the observation group was significantly lower than that of the patients in the control group.

3.3.10 Adverse Reactions

Three pieces of literature have studied adverse reactions. Some studies found that the incidence of adverse reactions of the patients treated with thalidomide was significantly lower than that of the patients treated with sulfasalazine (SASP), and sulfasalazine was more likely to cause skin dryness, drowsiness, and gastrointestinal reactions. Furthermore, other studies found that there was no difference in the incidence of dizziness, nausea, and vomiting between patients.

4. Discussions

Ankylosing spondylitis (AS) as a chronic inflammatory disease, may seriously affect the joint function and daily life of patients, causing damage to the physical and mental health, leading to lower quality of life of patients, and also causing greater pressure on patients' families and society. The traditional treatment of ankylosing spondylitis (AS) includes proper exercises and taking NSAIDs and SASP. In clinical treatment, the local glucocorticoid treatment is used. Tumor necrosis factor-α (TNF-α) antagonist has obvious effects in the treatment of ankylosing spondylitis (AS) but cannot be popularized and applied due to the high price. Thalidomide is a synthetic glutamic acid derivative, initially used in the treatment of pregnant women with pregnancy reaction, but limited due to neurotoxicity and teratogenesis. With the development and improvement of drug research, thalidomide has been gradually found and confirmed in inhibiting the production of TNF-α by monocytes, costimulation of human T lymphocytes, and assisting T-cell response, and

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its clinical application is gradually extensive. In recent years, some studies have pointed out that thalidomide has more significant effects in the treatment of ankylosing spondylitis (AS), and has significant anti-inflammatory and anti-immune effects through its inhibition of angiogenesis and adhesion molecule activity. Animal experiments have confirmed the effect of thalidomide on the improvement of arthritis in rats.

In this study, The meta-analysis results of 8 pieces of literature showed that the total effective rate of thalidomide in the treatment of ankylosing spondylitis (AS) was significantly improved, compared with conventional treatment or sulfasalazine (SASP) treatment ($P<0.05$). Furthermore, the time of morning stiffness, BASDAI score, C-reactive protein (CRP) level, and other related symptoms and indexes were significantly optimized ($P<0.05$). Besides, thalidomide in the treatment of ankylosing spondylitis (AS) significantly improved the clinical symptoms of patients, promoted the recovery of joint function, and improved the quality of life of the patients. Meanwhile, thalidomide in the treatment of ankylosing spondylitis (AS) can play a significant role in immunosuppression and regulation, to form a good anti-inflammatory effect by targeting inhibition of neutrophil chemotaxis. In clinical treatment, a large number of studies and tests have confirmed the therapeutic effect of thalidomide in the treatment of ankylosing spondylitis (AS) and its significant effects on the improvement of disease-related indexes. Thoracic mobility of patients can reflect the severity of thoracic spine involvement. When thalidomide was applied in the treatment of ankylosing spondylitis (AS), the index of thoracic spine involvement of patients was significantly improved, and the severity of thoracic spine involvement was significantly reduced compared with the conventional treatment. Meanwhile, the results of the Schober test reflected the degree of lumbar spine involvement, and this index was significantly improved, indicating that the degree of lumbar spine involvement was significantly declined. Occipital wall distance reflected the degree of cervical spine involvement, and this index value declined, indicating the degree of cervical spine involvement declined. The time of morning stiffness shortened, indicating that the degree of peripheral joint involvement was significantly declined. All in all, thalidomide can significantly improve the symptoms of patients with ankylosing spondylitis (AS).

In conclusion, relevant symptoms and indexes of patients can be effectively improved by the rational application of thalidomide in the treatment of ankylosing spondylitis (AS), the total effective rate of treatment significantly improved, and the safety of treatment can be guaranteed. Eight pieces of literature selected in the study for meta-analysis, the study is more dependent on the original data and has some limitations on the integrity and effectiveness of data information. Therefore, the conclusion of the study should be analyzed reasonably and used cautiously.

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Advances in Single Nucleotide Polymorphisms of Vitamin D Metabolic Pathway Genes and Respiratory Diseases

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ABSTRACT

Vitamin D is a fat-soluble vitamin. It is an essential vitamin for human body. It has a classical effect on regulating calcium and phosphorus metabolism. Participate in cellular and humoral immune processes by regulating the growth, differentiation and metabolism of immune cells. A large number of studies in recent years have shown that vitamin D deficiency increases the incidence of respiratory diseases. Respiratory diseases mainly include bronchial asthma, chronic obstructive pulmonary disease, tuberculosis, acute upper respiratory tract infection and pneumonia. Vitamin D metabolic pathway genes play a very important regulatory role in the transformation of vitamin D into active vitamin D, including *CYP2R1, CYP27B1, CYP24A1, VDBP, VDR* five genes. Genetic polymorphism of genes is the molecular basis of individual differences and disease development. Therefore, this paper summarizes the research on single nucleotide polymorphism of vitamin D metabolic pathway gene and respiratory diseases. In order to provide a new idea for future treatment.

1. Overview

1.1 Sources D Vitamins and Physiological Effects

Vitamin D (VD) is a necessary fat-soluble vitamin, mainly derived from the skin, a small amount from food[1]. In addition to the classical function of regulating calcium and phosphorus metabolism, the role of cell proliferation, anti-infection, and immun-modulation has attracted more and more attention[2].

1.2 VD Genes of Existing Forms and Metabolic Pathways

Various forms of VD are present in the body, including 25-hydroxyvitamin D (25-(OH) D),1,25-dihydroxyvitaminD (1,25-$(OH)_2$D)[3]VD first forms 25-(OH)D in the liver under the hydroxylation of 25- hydroxylase encoded by CYP2R1 gene, and 25-(OH)D is considered to be Biomarkers that can best represent the overall level of VD in human body[4].Then in the kidney through the *CYP27B1* gene encoding 1-αhydroxylase hydroxylated to form 1,25-$(OH)_2$D[5].1,25-$(OH)_2$D is the active form of VD, forming 1,24,25-$(OH)_2$D under the action of 24 hydroxylase encoded by the *CYP24A1* gene)$_3$,24 Hydroxylase can also add 25(OH) D and 1,25-$(OH)_2$D degradation, negative feedback regulation[6]Vitamin D binding protein (VitaminD Binding Protein,*VDBP*), edited by

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VDBP genes, binds to vitamin D and promotes vitamin D transport in the liver and kidney. Vitamin D receptor (VitaminD Receptor,*VDR*) edited by *VDR* gene, with 1,25-$(OH)_2$D combination promotes its biological effect. Vitamin D metabolic pathway gene refers to VD conversion to 1,25-$(OH)_2$DThe genes that play a regulatory role in the D process mainly include *CYP2R1*、*CYP27B1*、*CYP24A1*、*VDBP*、*VDR* five genes. The abnormal expression of VD metabolic pathway genes may affect the level of serum VD and thus affect the exertion of biological efficacy[7].

1.3 Single Nucleotide Polymorphisms

Genetic variation is the molecular basis of individual differences and disease development[8].Single nucleotide polymorphisms (SNPs), as the third generation genetic markers, are the most common genetic variants, which are dynamic and relatively stable in diagnosing the relationship between genes and diseases[9].

1.4 VD Effects on Respiratory Health

Respiratory diseases include bronchial asthma, chronic obstructive pulmonary disease, tuberculosis, acute upper respiratory tract infection and pneumonia[10]A study by Song Hang has shown that VD can reduce wheezing diseases in children[11];Huang Tao studies have shown that VD may affect the prognosis of pulmonary tuberculosis[12];Wang Qingqing and other studies have shown that vitamin D supplementation can improve lung function and quality of life of male COPD patients with severe smoking with vitamin D deficiency and reduce the number of acute exacerbation[13]VD can improve respiratory diseases to some extent and ensure respiratory health.

2. Genetic Polymorphism Related to Vitamin D Metabolic Pathway Associated with Respiratory Diseases

2.1 Genetic Polymorphisms Related to Vitamin D Metabolic Pathway and Bronchial Asthma

Bronchial asthma is a chronic respiratory heterogeneity disease controlled by environmental and genetic factors, which is mainly characterized by dyspnea, bronchospasm, airway remodeling and so on. Bu FX and other studies in the Caucasian population found that *CYP2R1* gene rs12794714 locus was associated with serum 25-(OH) D rise, but no association was found with bronchial asthma susceptibility[14]Li Fei and others conducted similar studies in the Han population of northern China and found no correlation with bronchial asthma[15]The possible reason for this speculation is that rs12794714 site (C>T) has undergone synonymous mutations but has not altered its encoded amino acid sequence and has not undergone structural and functional changes. Zhou Xiaoting and others also carried out the same type of research, but obtained the opposite results, the results showed that *CYP2R1* gene polymorphism and bronchial asthma have a certain correlation, vitamin D metabolic dysfunction may affect the occurrence of bronchial asthma[16]Zhang Y et al. study showed that rs4646536 in the *CYP27B1* gene was significantly associated with the development of bronchial asthma in Han children, and that expression of this locus was positively associated with increased risk of bronchial asthma[17]Studies by Oussama L et al on the same type of population in Tunisian adult bronchial asthma show that the rs10877012 genotype of this gene is higher than that of male bronchial asthma population TT and the expression of this locus plays an important role in the development of bronchial asthma[18]Studies such as Yu Mei have shown that rs10877012 in *CYP27B1* genes may not be significantly associated with bronchial asthma in children due to G/T mutations[19]From the above studies, we can see that the expression of different loci of *CYP27B1* gene plays a different role in bronchial asthma.Two common SNP sites in the *VDBP* (*GC*) gene rs4588、rs7041 located in exon XI. Studies have shown that the *GC1* and *GC2* genes encoded by these genes are associated with susceptibility to bronchial asthma, among which *GC1* genes may be protective factors for bronchial asthma[20]Zella LA et al. found that *GC* knockdown could reduce the 25-(OH) D content in human serum[21]At the same time, studies have found a positive correlation between lung function and serum 25-(OH) D levels in patients with bronchial asthma[22]Moria et al. showed that there was no statistical difference in the expression of rs1544410 in *VDR* genes in children in Hunan Province between the bronchial asthma population and the normal population, but the genotype expression analysis of rs7975232 showed that this locus played an important role in the occurrence and development of the bronchial asthma population, but its mechanism needs to be studied[23]Rasoul N K and other studies of the Kurdish population in different countries showed no significant association between *VDR* gene rs1544410 and bronchial asthma, but a case-control meta-analysis by Tizaoui et al found a significant association between homozygous wild-type rs1544410 and bronchial asthma. According to the above studies *VDR* the degree of homozygosity of individual gene loci also affects the development of bronchial asthma in human body[24-25]. To sum up, the single nucleotide polymorphism of vitamin D metabolic pathway gene is associated with the development of

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bronchial asthma.

2.2 Genetic Polymorphisms Associated with Vitamin D Metabolic Pathways and Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is a common chronic disease characterized by airflow obstruction. Chronic obstructive pulmonary disease, like asthma, may have been associated with vitamin D at an early stage[26]. Studies have shown that chronic obstructive pulmonary disease can be improved by *VD* supplementation[27-29]David AJ et al. conducted a blood sample survey in the London COPD population in the UK and found that *CYP2R1* genes were not associated with COPD and that genetic variation in vitamin D pathways was not associated with vitamin D status or COPD severity[30]. Mathyssen C et al. detected the expression and localization of key enzymes and vitamin D channel receptors in lung tissue of COPD explants. *CYP27B1* was not expressed in vascular endothelial cells, but in bronchial epithelium. *CYP27B1* expression is high in lung endothelial cells, suggesting that vitamin D may be inactivated before reaching epithelial cells and tissue immune cells[31]The polymorphism of *VDBP* gene and the related report of COPD were not found by consulting a lot of literature.1,25-$(OH)_2$Studies such as D regulate gene expression by binding to vitamin D receptors (*VDR*) suggest that VD deficiency is associated with COPD susceptibility[32]The level of serum 25(OH) D in COPD patients was significantly lower than that in the control group[33]These studies suggest that vitamin D deficiency may be associated with the occurrence and development of COPD.

2.3 Genetic Polymorphisms Related to Vitamin D Metabolic Pathway and Tuberculosis

Tuberculosis is one of the most common chronic respiratory diseases in tuberculosis. In recent years, due to the abuse of antibiotics, the drug resistance of Mycobacterium tuberculosis has increased, the prevalence of tuberculosis has increased, and the cure rate of the disease has not increased. The main manifestations are weak body, night sweat, breathing and so on. To explore the occurrence and development of tuberculosis from the genetic aspect has become a research hotspot in recent years. Junaid K studies on Pakistan positive pulmonary tuberculosis showed that the absence of vitamin D increased the prevalence of pulmonary tuberculosis, but there was no significant difference in the genotype distribution of the *CYP2R1* gene in the metabolic pathway between the case group and the control group, and there was no significant correlation with the susceptibility of the population to pulmonary tuberculosis[34]Asadollah M and other studies on the population of tuberculosis in Iran show that there is no significant correlation between the genotype distribution of rs7975232、rs1544410 locus in the *VDR* gene and the risk of tuberculosis, but the polymorphism of its rs7975232、rs1544410 may have some protective significance for tuberculosis in the European population[35] ShihWei L and other studies on the rs7041 and susceptibility to tuberculosis in the *VDBP* genes of the Han population in Taiwan indicate a certain correlation between Gc1F carriers and tuberculosis[36]Wang Xi and other research centers on tuberculosis susceptibility genes in Xinjiang Kazakh population show that most of the T alleles in *VDR* genes are common genes in tuberculosis patients and most of the t alleles are protective genes to protect the population from Mycobacterium tuberculosis[37]The rs731236 study of TB patients in Iran and Yunnan showed that the frequency of "tt" genotypes" in TB patients was low, and that the polymorphism of vitamin D related gene loci might be associated with resistance to TB[35,38].

2.4 Genetic Polymorphisms Related to Vitamin D Metabolic Pathway and Acute Upper Respiratory Infection and Pneumonia

The upper sense is the general term of acute upper respiratory tract (nasal cavity, pharynx or larynx) infection. The immune function is easy to infect the upper sense, but the general prognosis is good. Unlike the upper sense, pneumonia mainly occurs in the lungs, in addition to causing fever, cough and other cold symptoms, severe cases will also appear dyspnea. The David A and others confirmatory experiments in children in Manchester, England, found that the rs10500804、rs2060793、rs10766197 of the three polymorphic loci of the *CYP2R1* gene had no significant correlation with the upper sense, but the frequency of the locus rs12060793 the median gene was increased to a certain extent compared with that of the normal population, suggesting that it may be related to the upper sense, but further research is needed to prove it[39]Tian Huiqin and others analyzed the unrelated Han population in Jiangsu and Anhui regions and found no statistically significant difference in the SNP locus of *CYP27B1* gene rs10877012 susceptibility to nasal infection[40]There was no significant correlation between the SNP locus rs464537 rs4646536 and acute upper respiratory tract infection[41]The SNP locus rs1260 of *CYP27B1* genes is also associated with peripheral blood concentrations, which may influence the development of

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nasal inflammation[42]. Through retrieval, There are no reports α- hydroxylase or its corresponding *CYP27B1* gene polymorphism and pneumonia. Validation experiments in children such as David A in Manchester, England, six SNP sites in the *GC* rs7041,rs4588, rs12512631, rs2070741, rs2298849,rs16846876 Correlation analysis of with acute upper respiratory tract infection[43]. It was found that there was no significant correlation between the above 6 sites and the upper sense, The P rs7041 the site was 0.06, There may be no statistical difference between the two due to insufficient sample size. Jolliffe DA and other studies of American children show that, *VDR*, of 8 SNP sites rs9409929 rs10783219, rs4516035, rs2238136, rs1544410, rs2228570, rs2853559, rs7975232 had no significant correlation with upper sense, The other three *VDR* sites rs4334089, rs11568820, rs7970314 analysis revealed statistical differences, It shows that it has a certain correlation with the upper sense[39]Ren Jing et al. showed that *VDR* gene Fok I loci were associated with RSV susceptibility to pneumonia, and the Taq I loci were less correlated with susceptibility to pneumonia due to synonymous mutations[44]. These studies suggest that single nucleotide polymorphisms in genes associated with vitamin D metabolic pathways may regulate the progression of upper sense and pneumonia.

3. Summary and Prospect

The influence of genetic factors on disease is a hot topic. As the third generation genetic marker, single nucleotide polymorphism can more accurately explore the relationship between genes and diseases. Therefore, this paper summarizes the correlation between single nucleotide polymorphism of vitamin D metabolic pathway gene and respiratory diseases. So far, there have been more studies on this area, but the results are not consistent. The differences in the population and the size of the sample size may affect the results. The prevalence of these problems requires the use of larger samples and the summary analysis of multiple research results in future studies. At the same time, the analysis of single nucleotide polymorphisms of single genes should also consider the comprehensive analysis of multiple gene polymorphisms of different chromosomes. The ultimate goal of this improvement is to explore the relationship between vitamin D metabolic pathway related genes and respiratory diseases more comprehensively. To explore a new diagnosis and treatment plan for clinical treatment.

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Research Progress of Vitamin D and Pathogenesis of Bronchial Asthma

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ABSTRACT

At present the incidence of bronchial asthma on the rise, its pathogenesis and the genetic immune and the relationship between social environment and other aspects are inseparable the activity of vitamin D (Vit D) in the body in the form of 1, 25 - (OH) 2 d3, mainly involved in bone metabolism and calcium absorption in addition to this, a growing number of studies show that in Vit D plays an important role in the pathogenesis of bronchial asthma, play a role in the immune function of bronchial asthma growth hormone sensitivity adjustment and airway remodeling in this paper, the development of a variety of mechanisms, such as Vit D. Review the possible mechanisms affecting bronchial asthma, hoping to provide adjuvant treatment for patients with bronchial asthma, discover new treatment approaches, and improve the quality of life for patients.

1. Function and Metabolism of Vitamin D (VitD)

Vit D is a fat-soluble steroid derivative, mainly related to the function of nutritive bones, and is often used to promote and regulate the metabolism of calcium and phosphorus in bones [1]. It has been found that a large amount of 7-dehydrocholesterol exists in human skin, and studies have shown that it is the main source of VitD[2]. The formation of cutaneous 7-dehydrocholesterol (Vit D3) by ultraviolet radiation is followed by the production of 25 (OH) D3 by liver 25 hydroxylase and 1, 25 (OH) 2D3 by kidney 1 hydroxylase. Active VitD ACTS on VitD receptors in cells through blood circulation and other pathways, and then plays a series of biological roles. In addition to the above bone functions, VitD, as an immunomodulatory molecule, also has important bone functions such as immunomodulatory, defense and repair [3]. In addition, studies have shown that patients with vitamin

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D deficiency are more likely to cause bronchiectasis, asthma and other lung diseases [4]. In addition, Esfandiar et al. found through a large number of clinical investigations that the risk of asthma in children with vitamin D deficiency was 3~16 times that of children with normal vitamin D[5],indicating that vitamin D deficiency increased the risk of asthma in children. VitD plays an important role in the occurrence and development of asthma.

2. Bronchial Asthma

Bronchial asthma is a chronic inflammation in which the respiratory tract cells are damaged, granulocytes are damaged, cells proliferate, lymphocytes and tissue cells are damaged. This chronic inflammation leads to hyperresponsiveness of the airways,often with extensive reversible airflow limitations, and leads to repeated wheezing, shortness of breath, or coughing. The main pathophysiological manifestations are chronic airway inflammation andairway remodeling, and it is now believed that the change of Th1/Th2 cell ratio is the basic mechanism of bronchial asthma, especially the most important basis of Th2 cell hyperfunction[6]. Bronchial asthma can be divided into three levels according to the severity of the disease: light, medium and severe. The most common risk groups are children or teenagers, people with allergic constitution and people with family history of bronchial asthma. In recent years, the role of Vit D as an important treatment for bronchial asthma has been gradually recognized, .but the specific mechanism of its involvement in asthma has not been clarified.

3. VitD ACTS on the Related Mechanism of Bronchial Asthma

3.1 VitD ACTS on Th2-mediated Asthma

An important immunological mechanism of asthma is the Thl/Th2 imbalance caused by the preponderance of regulatory lymphocyte responses to Th2 cytokines involved in asthma formation[7].Studies have shown that VitD plays a certain regulatory role in maintaining Th1 and Th2 balance and reducing airway inflammation[8]. In addition,studies have shown that 1,25(OH)2D3,can promote the attraction of eosinophils in non-inflammatory sites by up-regulating the expression of CXC chemotaxis cytokine receptor 4 (CXCR4) on eosinophils[9]. Therefore, when VitD is insufficient in human body, the balance of immune Thl/Th2 will shift towards Th2, leading to increased synthesis of Th2 cytokines represented by IL-4 and IL-5. Because Th2 stimulates B cells to produce specific IgE and inflammatory cytokines, which in turn stimulates the production of inflammatory mediators, such as eosinophil, leading to allergic. reactions in vivo, VitD deficiency may lead to airway hyperreactivity (AHR) and asthma[10].

3.2 Vit D Acted on Treg Cells

Treg cells can inhibit excessive immune response, and a study has found that Treg cell population is damaged in asthma patients, which is directly related to low vitamin D level[11]. Forkhead box P3(FoxP3) is a transcription factor that plays an important role in T cell development and function, and is also involved in the maintenance of human autoimmune tolerance. The effect of 1,25-(0H) 2D3 is to up-regulate the expression of FoxP3 in Treg cells, increase the production of il-10, and exert an anti-inflammatory effect by affecting the balance of Th1/ Th2 cells[12],suggesting that vitamin D can promote the secretion of il-10. On the contrary, inadequate differentiation and functional defects of Treg cells are the key causes of hyperfunction of Th2 cells and asthma[13]. A mouse experiment showed that CD4+CD25+Treg cells were significantly increased in mice given topical 1,25-(OH) 2D3 treatment or ultraviolet B(UVB) radiation, and the immunosuppressive effect of CD4+CD25+Treg cells in vivo was also significantly enhanced compared with the control mice[14]. In addition, vitamin can promote the production of Treg cell chemokine CCL22 by myeloid dendritic cells and up-regulate the activation of Treg cells[15]. On the contrary, inadequate differentiation and functional defects of Treg cells are the key causes of hyperfunction of Th2 cells and asthma[13]. A mouse experiment showed that CD4+CD25+Treg cells were significantly increased in mice given topical 1,25-(OH) 2D3 treatment or ultraviolet B(UVB) radiation, and the immunosuppressive effect of

CD4+CD25+Treg cells in vivo was also significantly enhanced compared with the control mice[14]. In addition, vitamin can promote the production of Treg cell chemokine CCL22 by myeloid dendritic cells and up-regulate the activation of Treg cells[15].

3.3 VitD ACTS on Th17 Cell Mediated Asthma

In recent years, more and more studies have found that Th17/Treg imbalance plays an important role in asthma[16]. Pfeffer et al. found that VitD can play an anti-inflammatory role by regulating the response of epithelial cells to stimulation[17]. Among them, IL-35 secreted only by regulatory T cells has important inhibitory properties on cells, especially Th17 cells. Th17 cells secrete IL-6 and IL-17, which are involved in the inflammatory response of asthma by promoting prostaglandin and acute phase protein synthesis. 1I1-17 is a proinflammatory cytokine that

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can act on airway epithelial cells, etc., and can promote the recruitment of neutrophils and macrophages by stimulating chemokines and other cytokines to trigger inflammatory responses[18]. In addition, Zhong Jie et al. found that SOCS-1 and SOCS-3 were related to Th17/Treg imbalance and were associated with allergic asthma. This further elucidates the mechanism by which VitD ACTS on Th17 cells to mediate asthma[19]. This further elucidates the mechanism by which VitD ACTS on Th17 cells to mediate asthma.

3.4 Vit D Affects the Sensitivity of Glucocorticoids

The preferred long-term treatment for asthma is inhaled corticosteroids (ICS), but long-term use of ICS can contain many side-effects, including inhibiting growth, causing osteoporosis and lowering the immune system. The study of Kelly et al [20] showed that the average height of children receiving ICS treatment was 1.2cm lower than that of the control group in adult follow-up. To alleviate the symptoms of bronchial asthma, ICS activates effective anti-inflammatory genes by encoding related cytokines, chemokines, and enzymes and receptors involved in inflammation[21]. However, it is difficult to control asthma symptoms of some patients after long-term use of ICS, namely, corticosteroid resistant Asthma (SRA)[22]. On the one hand, studies have shown that SRA is related to the functional expression of Th17 cells, while Vit D can reduce the production of Th17 cells[23]. Vit D can have a synergistic effect with ICS in the treatment of bronchial asthma, and the mechanism is that Vit D can up-regulate the production of ICS-induced IL-10, so as to affect the balance of Th1/Th2 cells and thus exert an anti-inflammatory effect[24]. On the other hand, the occurrence of SRA may include a decrease in the affinity of ICS to its receptor[25]. A large number of studies have found that Vit D plays an anti-inflammatory role of ICS by down-regulating the expression of NF- B in lymphocytes to enhance binding affinity between ICS and hormone receptors[26]. In addition, Xiong's study showed that Vit D can increase the expression of MAPK phosphatase 1 activated by mitogen and reduce the expression of chemokines, thus reducing the phosphorylation of ICS receptors and enhancing the anti-inflammatory effect of ICS[27].

3.5 VitD and Respiratory Tract Infection

Respiratory tract infection is an important factor that induces asthma. Vit D is closely related to upper respiratory tract infection and can play a role in resisting the invasion of respiratory tract pathogens by enhancing the innate immunity of human body[28]. The research results of BERRY et al. also proved the same conclusion, that when the level of 25(OH)D was increased by 4ng/mL, the risk of respiratory infection was correspondingly reduced by 7%[29]. In addition, VitD can also affect the pathogenesis of asthma by influencing; the cell cycle of airway smooth muscle (ASM) cells and regulating ASM cells to participate in the genetic transcription of airway remodeling.

3.6 Vit D ACTS on Airway Remodeling

Airway remodeling is an experience of a series of pathophysiological changes from airway epithelial injury, increase of airway smooth muscle cells (ASMCs), and angiogenesis during the progression of asthma. No effective control method is available[30]. Many studies have confirmed that in patients with asthma, the expression of the nf-kappa B increases significantly and participate in the process of airway remodeling, in asthma model in mice, Vit D treatment reduced the airway remodeling, reduced the airway of a series of physiological and pathological changes, inhibit the nf-kappa B p65 nuclear transfer, at the same time by inducing increased I kappa alpha B predominate mRNA level and reduce I kappa alpha phosphorylation B predominate in order to increase the I kappa alpha B protein levels predominate[31]. Cupta et al[32] found that the low level of Vit D in children with asthma was significantly correlated with the increase of ASMCs, which alleviated a series of pathophysiological changes in the airway, inhibited the nuclear translocation of NF- B P65, and increased the level of I B protein by inducing increased I B mRNA levels and reduced I B phosphorylation[31]. Cupta[34] et al. found that the low level of Vit D in asthmatic children was significantly correlated with the increase of ASMCs, which alleviated a series of pathophysiological changes in the airway, inhibited the nuclear translocation of NF- B P65,and increased the level of I B protein by inducing increased I B mRNA levels and reduced I B phosphorylation[31]. Cupta[32] et al. found that the low level of Vit D in children with asthma was significantly correlated with the increase of ASMCs, which alleviated a series of pathophysiological changes in the airway, inhibited the nuclear translocation of NF- B P65, and increased the level of I B protein by inducing increased I B mRNA levels and reduced I B phosphorylation[31].Cupta et al.[32] found that the low level of Vit D in children with asthma was significantly correlated with the increase of ASMCs, which alleviated a series of pathophysiological changes in the airway, inhibited the nuclear translocation of NF- B P65,and increased the level of I B protein by inducing increased I B mRNA levels and reduced I B phosphorylation[31]. Cupta et al. [32] found that the low level of Vit D in children with asthma was significantly correlated

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with the increase of ASMCs. 1,25-(OH) 2D3 can reduce the proliferation of ASMCs by inhibiting the phosphorylation of retinoblastoma protein (Rb) and cell cycle monitoring point kinase 1(Chk1)[33]. Vit D can down-regulate the expression and mRNA levels of the two proteases in ASMCs sensitized by Adistintegrin and metalloproteinase 33, ADAM33 and matrix metalloproteinase9, MMP9,and effectively inhibit ASMAS proliferation[34].

4. Conclusion

As an immunomodulator, Vit D may inhibit the pathways involved in the occurrence and development of asthma, thus playing a certain role in the occurrence and development of bronchial asthma. Qu Jumei et al. showed that the level of Vit D in children with bronchial asthma was significantly lower. After supplementing with Vit D, asthma symptoms were significantly relieved[35],which further verified the close relationship between vitamin D and bronchial asthma. Therefore, the revelation of the mechanism of Vit D's influence on asthma opens up a new horizon for the treatment of asthma.

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Research Progress of Vitamin D and Autoimmune Diseases

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ABSTRACT

As a fat-soluble vitamin, Vitamin D is a necessary hormone to maintain normal physiological activities of the body. In recent years, vitamin D has been considered as a new neuroendocrine-immunomodulatory hormone, and researchers have paid more attention to the study of immune regulatory mechanism. It is not only related to calcium and phosphorus metabolism, bone metabolism and other important metabolic mechanisms of the body, but also closely related to the immune regulation mechanism of the body. Vitamin D deficiency caused by many factors can play a certain role in the development of autoimmune diseases. In this paper, the related mechanisms of vitamin D affecting autoimmune diseases were reviewed, with a view to expound the close correlation between vitamin D and autoimmune diseases, so as to find new diagnosis and treatment approaches for clinical autoimmune diseases and improve the quality of life of patients with autoimmune diseases.

1. Introduction

Vitamin D (VitD) is a fat-soluble vitamin necessary for human growth and development, Which cannot be synthesized by itself, but can be obtained through food or through the skin absorption of ultraviolet isomerism. The main regulatory activity in the human body is 1, 25dihydroxyvitamin D3 [1, 25(OH)2D3] [1] ,not only plays an important role in calcium and phosphorus metabolism, bone metabolism, cell growth and differentiation, also play an inhibitory effect in a variety of autoimmune diseases [2] . A large number of studies have shown that vitamin D deficiency is closely related to the occurrence and development of autoimmune diseases, tumors, cardiovascular and cerebrovascular diseases, diabetes and other diseases [3-8]. At the same time Vit D also play an important role in anti-inflammatory and immune regulation, reduction of vitamin D levels in many autoimmune

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disease patients is widely reported [9-10]. Based on this, a review on the research progress of vitamin D and autoimmune diseases is presented.

2. Immunomodulatory Effects of Vitamin D

Vitamin D plays an indispensable role in the immune system. Because immune cells express vitamin D receptor (Vitamin D Receptor, VDR), vitamin D can be combined with VDR in immune cells to affect the biological activity of vitamin D metabolic pathway to regulate innate and non-adaptive immunity. The main factor of its vitamin D metabolism pathway to regulate the body is its active form [125-(OH)2-Vit D 3], its effect on immune regulation is bidirectional, through the degree of expression can not only improve the body's own immunity, but also inhibit abnormal strong immune response [11].Active vitamins D reduce the production of autoimmune systemic diseases by regulating innate and adaptive immunity, autoimmune diseases such as systemic lupus erythematosus and rheumatoid arthritis have been validated in mouse models [12-13]. In innate immunity 1,25-(OH)2-VitD3 mediates further monocyte differentiation into macrophages, Causes macrophages to produce immunosuppressive prostaglandin E2, Inhibition of macrophage secretion of inflammatory factors and chemokines; At the other hand, it can directly regulate the expression of anti-microbial peptide gene and enhance the of anti-infection ability. In adaptive immunity1, 25-(OH) 2-VitD3 can affect the differentiation of activated T cells and inhibit Th1 cell response, may also indirectly inhibit the proliferation of activated B cells by regulating Th cells [14] .

3. Vitamin D and Autoimmune Diseases

3.1 Vitamin D and Autoimmune Thyroid Disease

Autoimmune thyroid disease (Autoimmune Thyroid Diseases, AITD) is an organ-specific autoimmune disease. Its main pathological types are Graves disease (Basedow Disease, GD) and Hashimoto's thyroiditis (Hashimoto Thyroiditis, HT).

Clinical studies have shown that autoimmune thyroid disease is associated with vitamin D deficiency in recent years [15-17], KE and other studies of GD patients show that normal people have higher levels of vitamin D than GD patients. Tamer studies show that, The deficiency of vitamin D in HT patients makes its incidence much higher than that of healthy control population [16]; Studies by He Jing et al on patients diagnosed with AIDT and vitamin D deficiency show that, Vitamin D supplements can reduce antibody levels in AIDT patients, Has been relieved and even significantly improved [17], All these studies have one thing in common: people with low levels of vitamin D, Higher incidence of autoimmune diseases and timely vitamin supplementation D help patients improve autoimmune diseases. The pathogenesis of AITDs is also regulated by genetic factors. Abnormal expression of genes related to vitamin D metabolic pathway leads to uncontrolled autoimmune monitoring and abnormal proliferation of autoantibodies, which leads to the production of autoimmune thyroid diseases [17-18]. This shows that vitamin D plays a certain role in the occurrence and development of AITD.

3.2 Vitamin D and Rheumatoid Arthritis

RA (Rheumatoid Arthritis, RA) is a chronic autoimmune inflammatory disease, characterized by autoantibody production, chronic synovial inflammation, progressive joint destruction and deformity [19-20]. RA is a devastating and common autoimmune disease, A lifetime prevalence rate of 1% worldwide, Female, smoking and family history of the disease are more likely to suffer from [21] disease. Although the main cause of RA is unclear, But there have been reports that, The development of rheumatoid arthritis is caused by genetic and environmental factors, Vitamin D metabolic pathway gene VDR is one of the important genes of RA susceptibility [22-23].In recent years, Single nucleotide polymorphism (Single Nucleotide Polymorphism,) by VDR gene SNP) the search for RA risk related genes has become a research hotspot and VDR gene polymorphisms may affect the occurrence and development of vitamin D by affecting the function and serum level. Tizaoui K et al. Meta-analysis of 1,703 cases and 2,635 healthy controls in 12 case-controls yielded results in homozygotes, In the dominant and allele comparison model, There was a significant correlation between VDR polymorphism TaqI and RA diseases, suggesting that our vitamin D related gene polymorphisms play a role in the occurrence and development of RA. Vitamin D receptor (Vitamin D Receptor,) simultaneously VDR) it is also closely related to the occurrence and development of RA. And VDR, are widely expressed in immune cells such as dendritic cells, macrophages, activated T lymphocytes and B lymphocytes, The results suggest that the immunomodulatory effect of vitamin D can be by regulating factors acting on immune cells [24] . By combining with VDR, Vitamin D inhibits the increased activity of immune cells involved in adaptive autoimmune responses, by inhibiting inflammatory response to regulate immune homeostasis [25]. And then abnormal levels of vitamin D can disrupt that balance, By inhibiting proliferation of Th1 cells, So that bone loss, eventually leading to osteopenia and osteoporosis [26]. To sum up, Vitamin D down to the molecular level,

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Up to the receptor protein has obvious correlation with rheumatoid arthritis.

4. Vitamin D and Systemic Lupus Erythematosus

SLE (Systemic Lupus Erythematosus, SLE) is mediated by autoimmunity, of autoimmune diseases involving multiple organs and systems[27] . The pathogenesis of the disease involves immune, environmental, hormonal and genetic factors, Lack of specificity, it's usually chronic or occult, at present, the pathogenesis is complex and there is no effective treatment [28]. SLE is common among women of childbearing age, and the disease has the characteristics of repeated delay, easy recurrence, multi-system involvement, at the same time, the clinical treatment of hormones and immunosuppressants will cause a serious burden on the physical and mental health of patients [29-30]. Although the pathogenesis of SLE remains unclear, some studies have shown that vitamin D plays an important role the occurrence and development of SLE [30]. A number of clinical meta-analyses show that, the decrease in vitamin D in SLE patients is widespread, the metabolic rate of vitamin D decomposition in patients was faster than that in healthy people [31]. Islam MA et al .34 case-control studies (2265 SLE patients and 1846 healthy controls) showed that regular vitamin supplementation D help SLE the treatment of patients. And compared to healthy people, the serum vitamin D level of SLE patients was obviously low [32]. Through the above research, we know that there is a certain correlation between vitamin D and SLE disease activity, Provide data support for the prevalence of vitamin D deficiency in SLE, Hint that we can regularly supplement vitamin D as part of the health management plan.

5. Conclusion

To sum up, vitamin D, as an immunomodulatory hormone, plays an important immunomodulatory role in immune diseases. As the relationship between vitamin D and autoimmune diseases is deeply studied, it is a research direction to understand the pathogenesis of autoimmune diseases from the gene level, and it can provide a new way for the treatment and prevention of autoimmune diseases. For a better understanding of the role of vitamin D in autoimmune diseases, we need high-quality evidence-based medical evidence and broader prospective studies to provide a new diagnosis and treatment for autoimmune diseases.

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Expression of miR-21 in Colorectal Cancer and Its Relationship with Clinicopathological Characteristics of Colorectal Cancer

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ABSTRACT

Objective: To investigate the expression of miR-21 in colorectal cancer cells, and to analyze the relationship between the level of miR-21 and the clinicopathological characteristics of colorectal cancer patients. **Methods:** 210 patients with colorectal cancer treated in our hospital from January 2016 to June 2019 were selected. Cancer tissue specimens (study group) and adjacent normal tissue specimens (control group) were surgically collected, and the quantitative quantitative PCR was used to detect and compare the miR-21 expression of the two groups. **Results:** The expression of miR-21 in the study group was higher than that in the control group, and the difference was statistically significant (P <0.05). There were significant differences among patients with early and intermediate TNM, patients with low differentiation and patients with moderate to high differentiation, patients with lymph node metastasis and patients without lymph node metastasis, patients with high infiltration and patients with low infiltration, patients with high CEA levels, and patients with low CEA, and the difference was statistically significant (P <0.05). **Conclusion:** In colorectal cancer, miR-21 is highly expressed, which is closely related to stage and differentiation, and can be used to reflect the patient's condition.

1. Introduction

Colorectal cancer is very common in gastrointestinal tumors, and its incidence has always been high. The main causes are: family genetic factors; benign adenomas of the intestine; malignant changes in the intestinal tract; lack of sperm fibers in the diet; too much fat and carbohydrates. It is not conducive to defecation, causing a large amount of carcinogens to stay in the intestine, causing irritation to the intestinal mucosa and causing it to become cancerous; rectal polyps or ulcerative colon cancer are induced[1]. Although patients can perform colorectal cancer through a healthy diet and regular inspection, colorectal cancer has the characteristics of early symptoms concealment of most cancers, so it is difficult to detect cancerous changes in the clinic. Imaging is also

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a common method for the diagnosis of colorectal cancer, such as MRI, CT, ultrasound, etc. are widely used in the diagnosis of colorectal cancer, and its diagnostic accuracy is relatively high, however, after all, these methods obtain images indirectly, and do not directly observe pathological results, so there may be missed or misdiagnosed results. With the development of science and technology and medical technology, clinical studies have found that dysregulated microRNA expression is the most common feature of colorectal cancer. Clinically, it is possible to understand the occurrence and development of tumors by detecting the level of tumor specimens. The miR-21 is one of the most common oncogenes, and its residues are responsible for the occurrence, development, and metastasis of colorectal cancer. The clinical test results are often used as a reference basis for screening colorectal cancer and evaluating the treatment effect of colorectal cancer.

2. Materials and Methods

2.1 General Information

A total of 210 patients with colorectal cancer treated in our hospital from January 2016 to June 2019 were selected. The clinical data are as follows: ① Gender composition: 116 males and 94 females; ② Age distribution: the youngest is 30 years old and the largest The patients were 84 years old, with an average age of (57.29 ± 12.34) years. ③ TNM staging: 6 cases of stage I, 108 cases of stage II, 70 cases of stage III, 26 cases of stage IV; ④ lymph node metastasis: 92 cases with metastasis, 118 cases without metastasis; Level: 124 cases above 3.4ng / mL, 86 cases below 3.4ng / mL; ⑥ degree of local infiltration: 110 cases in T4, 68 cases in T3, 30 cases in T2, 2 cases in T1; ⑦ poor differentiation 60 cases, 150 cases of moderate and high differentiation.

2.2 Methods

Cancer tissue specimens (study group) and adjacent normal tissue specimens (control group) were surgically collected. After the specimens were removed from the patient, they were stored in RNA sample preservation solution and quickly frozen with liquid nitrogen, and was then stored at -80 ° C for future use.

Take about 1g of tissue from the frozen specimen, grind it into a powder by liquid nitrogen grinding method, drip 1mL of Trizol reagent, and use TRIzol reagent to extract total RNA from cancer tissue and normal tissue adjacent to the cancer. For extraction method and operation steps, please refer to the instruction manual. After extraction, the purity and concentration of RNA were measured by a UV spectrophotometer, and the integrity of RNA was detected by agarose gel electrophoresis.

CDNA was synthesized according to the relevant requirements of the kit. The RT primers with specific stem and loop in the structure were derived from the quantitative PCR kit. The primer sequences were:

5'-GTCGTATCCAGTGCTGGGTCCGAGTGATTCG-CACTGGATACGACTCAACATC-3 '

&

5'-GTCGTATCCAGTGCTGGGTCCGAGTGATTCG-CACTGGATACGACTCACAAGT-3'.

Ribonuclease, reverse transcription primer is 50nmol / L, RNA template is 2.5μL, heated to 70 °C, heat denatured, given 5 minutes after ice bath, after cooling for 2 minutes, add 1μL of 10mmol / L dNTP mixture / 0.5 Reverse transcription reaction was performed under the reaction conditions of 16 °C for 30 minutes, 42 °C for 20 minutes, and 85 °C for 5 minutes.

Real-time PCR quantitative detection using a fluorescent PCR instrument and related kits, the reaction system is 0.03mL, 3μL of 10x buffer, 1μL of cDNA, 3μL of 25mmol / L magnesium chloride solution, upstream primer 0.33μmol / L and downstream primer 0.33μmol / L, 3.6 μL of 2.5 mmol / L dNTP, 1.5 U of rYaq polymerase. The reaction conditions were: 40 cycles, predenaturation at 94 °C for 3 minutes, 94 °C for 20 seconds, and 60 °C for 40 seconds. U6 was selected as the internal reference, and the relative expression of miR-21 in colon cancer cells was determined by the 2- △△ Ct method. - △△ Ct is (miR-21 • Ct-U6 • Ct) cancer tissue- (miR-21 • Ct-U6 • Ct) normal tissue adjacent to the cancer[2].

2.3 Observation Indicators

(1) Compare the PCR results of miR-21 in two groups of specimens;

(2) Compare the results of miR-21 detection in patients with different clinicopathological characteristics.

2.4 Statistical Methods

The clinical data of all subjects in this study were included in the SPSS version 19.0 statistical software. Count data were expressed as n (%), $\chi 2$ test was performed, measurement data was expressed as ($\bar{x} \pm s$), and t test was used for statistical analysis. If the latter result is $P < 0.05$, it means that the difference is statistically significant.

3. Results

3.1 Expressions of miR-21

The expression of miR-21 in the study group was (5.16 ± 1.07), which was higher than that in the control group (0.68

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± 0.13), and the difference was statistically significant (t = 60.231, P = 0.000 <0.05).

3.2 Relationship between mir-21 Expression and Clinicopathological Characteristics

Among patients with early and intermediate TNM, patients with low differentiation and patients with moderate to high differentiation, patients with lymph node metastasis and patients without lymph node metastasis, patients with high infiltration and patients with low infiltration, patients with high CEA levels, and patients with low CEA, their miR-21 expressions were significantly different, and the difference was statistically significant (P <0.05). See Table 1.

Table 1. Relationship between miR-21 expression and clinicopathological characteristics (n, %)

Clinicopathological features	**Cases**	miR-21 Expressions	P
Early TNM (I, II)	114	1.69	0.000
TNM mid-late stage (III, IV)	96	7.22	
Poorly differentiated	60	7.54	0.005
Medium to high differentiation	150	2.88	
Lymph node metastasis	92	7.22	0.000
No lymph node metastasis	118	1.75	
Infiltration T1 ~ T3	100	1.72	0.006
Infiltrated T4	110	5.46	
CEA above 3.4ng / mL	124	0.39	0.000
CEA below 3.4ng / mL	86	6.32	

4. Discussion

Colorectal cancer is a malignant tumor with a very high incidence both at home and abroad. The pathological process is more complicated, involving multiple factors, going through multiple stages, and related to multiple genetic changes. Many studies have shown that the occurrence and development of colorectal cancer are related to inactivation of tumor suppressor genes and activation of oncogenes in genetics, and that the abnormal regulation of MiRNA is the main reason for inactivation of tumor suppressor genes and activation of oncogenes. As a type of non-coding small molecule RNA that can regulate gene function, MicroRNA has specific recognition effect on the 3′-terminal untranslated region in mRNA, wihch can be combined with it in a targeted manner to degrade mRNA or inhibit translation. After transcription, it will effectively regulate the expression of target genes. Clinically found that MicroRNA has a regulatory effect on a variety of human diseases, and has abnormal expression in a variety of tumor tissues. It is either the presence of tumor suppressor genes or the presence of oncogenes, with high or low expression, and is involved in the generation, proliferation, and differentiation of tumor cells. The research object miR-21 in this paper is a kind of miRNA with carcinogenic properties. It is the only miRNA that is found to be highly expressed in non-solid tumors and solid tumors at this stage, miR-21 plays a role very similar to oncogenes, and the high expression of miR-21 means the occurrence, development, proliferation, invasion, and metastasis of tumors, and even it has a very important impact on angiogenesis and drug resistance, which promotes a series of biological behaviors of tumors.

As a kind of MicroRNA, miR-21 has very distinct active properties, and has high expression in breast cancer, pancreatic cancer, lung cancer, and colorectal cancer, and its expression level is closely related to tumor development and patient prognosis. In this paper, miR-21 expression was detected for colorectal cancer tissues and adjacent normal tissues. The results showed that the expression of miR-21 in colorectal cancer tissues was higher than that of normal adjacent tissues (P <0.05), which undoubtedly proves that miR-21 high expression is closely related to canceration. At the same time, existing studies have pointed out that the level of miR-21 is closely related to pathological features such as lymph node metastasis, clinical stage, and differentiation. This paper also compared the expression of miR-21 in patients with different pathological characteristics, and the results showed that, patients with early TNM are lower than patients with advanced stage, patients with lower differentiation are lower than patients with moderate to high differentiation, patients with lymph node metastasis are higher than patients without lymph node metastasis, patients with high degree of infiltration are higher than patients with low degree of infiltration, and patients with high CEA level are lower than CEA Patients (P <0.05), which undoubtedly proves the close relationship between the high expression of miR-21 and the occurrence and development of colorectal cancer.

It is worth noting that, in view of the regulatory effect of miR-21 expression on colorectal cancer, clinical treatment can be adopted for patients to improve the prognosis of patients.

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