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Pathogenesis and Current Status of Treatment of Severe Pneumonia in Chinese and Western Medicine

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Abstract: *Pneumonia is one of the common diseases in pediatrics. It is a respiratory infectious diseases with cough, expectoration and fever as the main symptoms caused by the pathogen invading the bronchus. With the continuous development of the disease, it can gradually evolve into severe pneumonia, which involves the circulatory, digestive, and neurological systems of the organisms, and seriously threatens the lives of the children. At present, modern Western medicine mainly focuses on antibiotic treatment, but the problems of antibiotic abuse and pathogen resistance are becoming increasingly serious. Traditional Chinese medicine therapy has good efficacy and unique advantages in treating severe cases of bronchopneumonia. This article reviews the pathogenesis and clinical treatment progress of this disease, aiming to provide reference for its clinical treatment.*

Keywords: *Severe pneumonia; Chinese and Western medicine; Review*

1. Introduction

Pneumonia is one of the infectious diseases of the lower respiratory tract caused by bacteria, viruses, mycobacteria, Mycoplasma pneumoniae, Chlamydia and other pathogens. The main clinical manifestations of this disease are fever, cough, shortness of breath, dyspnea and fixed moist rales of the lungs. The onset of the disease can occur throughout the year, the growth of the children's development caused by the severe impact [1]. Severe Pneumonia (SP) is diagnosed after the diagnosis of infectious pneumonia with any of the above critical signs such as persistent vomiting, refusal to eat, convulsions, lethargy or coma, transcutaneous oxygen saturation <0. 92 (at sea level) or central cyanosis, severe respiratory distress (moaning, severe inspiratory depression of the chest wall) or hypoxemia, etc. The diagnosis of severe bronchopneumonia is based on the clinical symptoms of severe bronchopneumonia. Severe bronchopneumonia(SP) is highly prevalent and has a rapid onset of severe disease, with involvement of all systems of the body, and is the leading infectious disease causing death in children under five years of age globally. Studies show that 30 to 50 percent of people with severe pneumonia will eventually die [2]. In recent years, the number of SP patients has increased significantly due to the COVID-19 epidemic. In 2019 alone, about 700, 000 children under the age of 5 died of pneumonia globally, which is staggering [3]. The treatment of this disease in modern medicine is mainly based on empirical medicine, and appropriate antibiotics are selected based on pathological results. If necessary, glucocorticoids are used in combination [4], or ventilators and symptomatic treatment are used to treat related complications. However, due to the misuse of antibiotics caused by clinical non-standardization of the use of medication, the frequent occurrence of drug resistance, the difficulty of treatment and the rate of therapeutic failure steeply increased [5]. As a treasure of Chinese medicine, Chinese medicine has a unique role and healing advantages. Still, due to the lack of evidence-based systematic evaluation of its efficacy, safety, etc., it is not valued. By searching the relevant literature in the past five years, this paper summarizes the pathogenesis and diagnosis and treatment plan of severe diseases in children from two perspectives of traditional Chinese and Western medicine, so as to provide reference for the clinical practice of the disease.

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2. Pathogenesis

2.1. Modern medical research

The pathogenesis of severe pneumonia is still unclear, some foreign scholars [6]. Some foreign scholars believe that the pathogenesis of SP is related to the abnormal immune mechanism, bacteria or endotoxin, etc. Pathogenic bacteria and toxins invade and damage the airway mucosa or lung parenchyma, causing inflammation, edema and exudation of the mucosa, which leads to complete or incomplete obstruction, resulting in emphysema, pulmonary atelectasis, necrotizing pneumonia, lung abscess or pus thorax, which then induces acute and critical complications such as hypoxemia and hypercapnia. In addition, pathogens trigger the immune response, leading to systemic inflammatory response, multiple organ failure, diffuse intravascular coagulation (DIC), septicemia, and other acute and severe complications, and seriously jeopardizes life and health.

2.1.1. Vitamin Deficiency

Children's digestive system lacks development, and their intake of micronutrients is limited. Related literature suggests that vitamin deficiencies can lead to the occurrence and development of severe pneumonia, which mainly include vitamin A, vitamin D and vitamin E. Vitamin D, known as calcitriol, can promote intestinal absorption of calcium and phosphorus, enhance its deposition in bones, maintain average growth and development of bones, increase bone density to help resist rickets, osteomalacia, etc. [7]. In recent years, foreign research has found that VD participates in various processes of human life-regulating activities, which is inseparable from infectious diseases [8]. Yang Shenglin [9] reached his conclusion by comparing 150 children with pneumonia:it was concluded that the severity of bronchopneumonia in children was positively correlated with low vitamin D levels, which means that children with low vitamin D levels are more likely to develop severe pneumonia, and the risk of post-disease re-infection is correspondingly higher. Another study of infant and young child pneumonia patients [10] showed that serum vitamin A levels were significantly lower in patients with pneumonia compared to healthy control group. It is suggested that low vitamin A level can lead to immune system dysfunction and aggravate pneumonia. Admittedly no strong clinical evidence [11] has been found to suggest that fat-soluble vitamin E is associated with the onset of pneumonia. However, it is undeniable that supplementation of vitamin E is an effective method to enhance the immunity of children and reduce the difficulty of treating SP, and it is worthwhile to promote this method in the clinic.

2.1.2. Pulmonary fibrosis

Some in the medical community believe that pneumonia and pulmonary fibrosis are two separate diseases, but there are few scholars who believe that "pneumonia is a pathological outcome, pulmonary fibrosis is only its relative clinical or imaging manifestation" [12]. The akt pathway is an important signalling pathway that regulates cell growth and metabolism, and studies have shown that the Akt/HIF-1α pathway is related to the formation of pulmonary fibrosis. Bacteria or viruses can stimulate Akt phosphorylation, activating the expression of the downstream effector gene HIF-1α, while HIF-1α can induce abnormal proliferation and apoptosis of lung cells, affecting the synthesis of alveolar surface-active substances, creating a chronic hypoxic internal environment that causes damage to the cells, which leads to abnormal proliferation, resulting in an increase in the synthesis of the collagen matrix Collagen III, which ultimately promotes fibrosis and aggravates the symptoms of pneumonia. Flastin can improve lung tissue injury and fibrosis in rats with severe pneumonia, but the mechanism of action remains unclear. Wei fei [13] et al. found through research that compared with the observation group, The pulmonary fibrosis score, p-Akt/Akt, HIF-1α and Collagen III protein levels in lung tissue of rats with severe pneumonia after treatment with azinosin were decreased, which confirmed that collagen deposition could be inhibited by inhibiting the activation of Akt/ HIF-1α pathway and promoting lung tissue repair in rats with severe pneumonia.

2.1.3. Genetic phenotype

Lv Beili [14] et al. found that the gene polymorphism and expression level of HSP70-2+1267A/G locus were closely related to the inflammatory state and clinical prognosis of patients with severe pneumonia. HSP, known as Heatshockportein, is a widely distributed stress protein in the human body, of which HSP70 has anti-inflammatory and antioxidant effects, and plays an essential role in the process of the onset and progression of severe infections and sepsis. Peroxisome proliferator-activated receptor γ (PPAR-γ) prevents the binding of the promoter site of the transcription factor pro-inflammatory factor, and serves to inhibit the function of inflammation. PPAR-γgene polymorphism is associated with pneumonia, sepsis and other diseases by regulating the expression of

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PPAR-γ. Lulu Zhang [15] et al. drew a conclusion by comparing the children in the severe pneumonia group and the healthy control group, that the polymorphism of rs10865710 in the PPAR-γ gene is closely related to the susceptibility and regression of severe pneumonia, in which children with CG/GG type are more susceptible to the disease, more challenging to treat, and slower regression. The mechanism of action may be related to the regulation of the expression of inflammatory factors such as COX-2, which needs to be further explored.

2.2. Ancient Medical Research

2.2.1. Etiology and pathogenesis

There is no record of the specific name of "severe pneumonia" in Chinese medicine. According to the pattern of onset and clinical characteristics, it can be categorized under the categories of "pneumonia, wheezing and coughing", "wind temperature" and "lung fever" in Chinese medicine, in which "lung fever" and "wind and temperature" are described in ancient texts with the same symptoms as in modern medicine. Contemporary medical practitioners often use the theories of Wei Qi, Ying Blood and San Jiao to guide the diagnosis and treatment of severe pneumonia. As the so-called "warm evil up received, the first offence lung, reverse pericardium", the lung for the five organs and six bowels of the Huagai, but also belongs to the delicate organs, the opening of the orifices in the nose, outside the skin and hair, the main body of the table. Therefore, when the foreign evil attacks, from the mouth and nose to enter, the first offense of the upper jiao lung. The early stage of pneumonia is mostly weifen syndrome, symptomatic coughing and coughing up phlegm, nasal congestion and runny nose, body heat and cold and other mild symptoms of exogenous sensations, most of them are empirical. Severe pneumonia has a rapid onset, rapid change, and dangerous disease, it is basically qi, ying, blood syndrome, which can be caused by untreated minor illnesses of the weifen syndrome, and also can be caused by a new sensation that triggers the lung meridian and the onset of ambient heat. External evil easily damages the positive qi of the body, weak positive qi is easily suppressed by evil qi. The heat and poison blazing, the lack of positive qi, will attract the evil into the body, resulting in the progression of the disease.

Wu Jutong in the "Differentiation of Syndromes in Epidemic Febrile Diseases" put forward the wind temperature and fever disease Sanjiao changes in the law: At the beginning, the wind is warm and hot, and the toxin attacks the surface, passing in the qi in a clockwise manner [16]. The lungs lose their ability to clear and regulate, and the waterways are imbalanced. It accumulates dampness and generates phlegm, and the stagnation and heat are transformed into heat. This creates a phenomenon of phlegm and heat blocking the lungs. Evil affects the middle energizer, inhibits the qi mechanism, loses the healthy circulation of the spleen, and dampness is endogenous. Common manifestations of dampness and heat in the middle energizer. If the heat and toxin are abundant and remain unsolved, it is easy to penetrate into the lower energizer in the later stage, burn the true yin of the liver and kidney, and the blood becomes stagnant due to insufficient blood, then the syndrome will change and rise. As if the evil toxin is invaginated, phlegm is obstructing the mind, and it can also reversibly transmit to the pericardium. Even if the heat and poison are deeply trapped, the righteous qi will collapse, leading to the danger of yin and yang separation, internal closure and external detachment. To sum up, severe pneumonia is located in the lung, which is closely related to the heart, spleen, liver, kidney and pericardium. The etiology and pathogenesis of severe pneumonia in children are basically the same as above. Moreover, due to the delicate organs of children, the five and six organs are incomplete and not yet strong, mainly manifested in the deficiency of the lungs, spleen, and kidneys, making them more prone to lung diseases; The lack of positive qi in the body can easily lead to the entry of pathogenic factors, leading to critical and severe cases.

2.2.2. Traditional Chinese Medicine (TCM) dialectic and typing

In the "Traditional Chinese Medicine Clinical Diagnosis and Treatment Terminology-Symptoms Section", the disease is divided into the following five types: Syndrome of phlegm heat blocking the lung, Syndrome of Phlegm turbidity obstructing the lung, Syndrome of wind cold closing the lung, Syndrome of wind heat blocking the lung, syndrome of qi deficiency of lung and kidney. Zhang Ye et al. suggested that [17] the pathogenesis of severe pneumonia in children is the deficiency of body and phlegm toxin damaging the lungs. Lan Jiaxin [18] believes that the core pathogenesis of severe pneumonia in children is the deficiency of vital energy and the damage to the lungs caused by heat toxicity. A retrospective analysis by Lin Yanlin [19], showed that the five most common types of severe pneumonia in chindren, are wind heat invading the lung syndrome, phlegm heat obstructing the lung syndrome, lung stomach heat excess syndrome, heat closed pericardium syndrome, and qi yin

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deficiency syndrome;From this, it can be seen that different doctors have different understandings of this disease, and there are also differences in dialectics. The prescription and medication used in the future are also not completely the same. The essence of this is due to the dialectical emphasis on three factors and appropriate measures in traditional Chinese medicine. On the one hand, it is beneficial for precise treatment, but on the other hand, it is not conducive to clinical promotion. This is also one of the key directions for future research.

3. Treatment

3.1. Western medical treatment

Modern medical treatment of severe pneumonia is based on symptomatic treatment such as anti-infection, mechanical ventilation, etc. However, with the increased use of immunosuppressants and broad-spectrum antibiotics, the drug resistance of the patients increases year by year, and the symptoms are not significantly relieved under the conventional treatment with poor therapeutic efficacy, so it is urgently needed to explore the novel therapeutic ideas in order to improve therapeutic efficacy.

3.1.1. Combined dopamine treatment

Dopamine has the effect of dilating pulmonary blood vessels and reducing obstruction of pulmonary circulation, while dobutamine is a selective β1 agonist, with the effect of promoting myocardial contraction, improving cardiac output and reducing the risk of pulmonary obstruction and promoting fecal excretion [20]. Therefore, the application of dopamine in children with severe pneumonia can alleviate the ischemic and hypoxic state of the tissues and organs of children and the symptoms of heart failure. Zhao Qingkun [21] observed 130 children with severe pneumonia and found that the combination of low-dose dopamine and dobutamine with conventional treatment can effectively reduce the levels of inflammatory factors in the serum, alleviate clinical symptoms of pneumonia, and improve lung function.

3.1.2. Fibrobronchoscopic lavage treatment

There is a large amount of pus and phlegm in the airway of the SP children, which is prone to airway obstruction, affecting the capillary barrier and blood-bronchial barrier, causing breathing difficulties and respiratory failure, posing a severe threat to life safety. The biggest drawback of conventional treatment is that it cannot effectively remove thick secretions deep in the airway, and the fibrobronchoscopic lavage treatment can effectively solve this thorny problem. Fiberoptic bronchoscopy can aspirate pus sputum, sputum tether and other secretions under direct vision, which improves the accuracy of treatment. The irrigation treatment can reduce the viscosity of sputum and stimulate the local mucous membrane, which promotes the cough reflex, reduces the airway resistance, improves the patient's pulmonary ventilation capacity, and alleviates the symptoms related to hypoxemia. On the other hand, the conventional method of collecting pharyngeal swabs to obtain specimens is prone to contamination, while collecting sputum under fiberoptic bronchoscopy can effectively reduce contamination, which is beneficial for the accuracy of detection results, and thus provides the possibility for clinical selection of more sensitive and effective antibiotics. A clinical observation trail [22] targeting 41 patients with severe pneumonia, in which bronchoscopy alveolar lavage was used in addition to conventional treatment, showed that 40 cases had symptom relief and 1 case had no effect, with significant therapeutic effects. However, it cannot be ignored that bronchoalveolar lavage surgery is an invasive procedure. If not performed properly, adverse reactions such as vomiting and increased heart rate may occur during treatment, which can even damage the airway, increase the risk of infection, and reduce treatment effectiveness. So it requires clinicians to be skilled in the operation of the operation. Therefore, it is necessary for clinicians to be skillful in the operation and to accurately assess the situation before bronchoscopy and related treatments are feasible.

3.1.3. Sivelestat sodium

Sivelestat sodium (SE), a specific neutrophil elastase inhibitor, was used as a targeted drug for the treatment of acute respiratory distress syndrome during the novel coronavirus pneumonia epidemic [23]. SE has a strong and specific anti-inflammatory effect. Several basic studies at home and abroad have shown that SE can reduce lung tissue injury in a mouse model of severe pneumonia. A retrospective study in Japan suggested that PaO2/FiO2, body temperature, heart rate and respiratory rate improved in patients with severe pneumonia in the group that used SE at an early stage, which affirmed the effectiveness of SE in the treatment of severe pneumonia. However, this drug has not yet been widely

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used in clinical practice, and the successful experience in treating severe pneumonia in children is insufficient. There is a lack of evidence-based evidence and safety evaluation, which requires further improvement in clinical practice.

3.1.4. Probiotics

SP children may have multi-system involvement, and the digestive system is most likely to be involved in clinical disorders of the bacterial flora. At the same time, because antibiotics are the first choice of treatment for this disease, the use of antibiotics can not only kill pathogenic bacteria in the body, but also eliminate some of the body's probiotics, which will also lead to disorders of the intestinal flora and increase the risk of intestinal infections. Related studies have shown that reducing the incidence of enterogenous infections in severe pneumonia is one of the key factors for successful treatment of this disease. Through the use of probiotics, it is conducive to the reconstruction of intestinal flora in patients with severe pneumonia, reduces the invasion of pathogenic bacteria on the intestinal tract, improves the digestive function of the body, and reduces the probability of intestinal infections. The fluctuation of blood glucose in children with severe infectious diseases has always been the focus of domestic and foreign scholars' research. Clinical research has found that the combined use of probiotics can not only effectively regulate and stabilize the blood sugar levels of children with SP, but also prevent the further development and deterioration of severe pneumonia. Therefore, the combined use of probiotics in the treatment of severe pneumonia is worth promoting.

3.1.5. Immunotherapy

SP patients often have immune dysfunction and inflammatory factor disorders in their bodies, which can further cause inflammatory mediator cascade reactions and promote the occurrence and development of severe pneumonia. Therefore, combining immunotherapy with conventional treatment can help improve the clinical efficacy of severe pneumonia. Chao Yiqun [24] et al. randomly divided 86 cases of severe pneumonia patients into observation group and control group, the observation group in the control group on the basis of conventional treatment combined with the use of thymopeptide α1 immunotherapy, the conclusion shows that the observation group's clinical total effective rate of 76.7%, the morbidity and mortality rate of 11.6%, while the control group effective rate of 48.8%, the morbidity and mortality rate of 27.9%, the observation group is significantly higher than the control group.

3.2. Traditional Chinese Medicine

3.2.1. TCM dialectic treatment

Although different doctors have not reached a unified consensus on the dialectics of this disease, the main pathogenesis of severe pneumonia is phlegm heat obstructing the lungs, and the phlegm heat obstructing the lungs syndrome is also the most common in clinical practice;As stated in the ancient scriptures, "the spleen is the source of phlegm generation, and the lung is the organ for storing phlegm. " Therefore, the overall treatment plan should add the concept of promoting stomach and spleen health, regulating qi and resolving phlegm on the basis of conventional methods of clearing the lungs and resolving phlegm, relieving cough and asthma. Hu Ziran [25] et al. used 12 herbs such as Ephedra, Sangbaipi, Poria, Scutellaria, Fritillaria, Perilla and other herbs to form Qing Jin Hua Phlegm Benefit Lung Soup and combined with Bao He Pills to alleviate the symptoms of heat, cough, phlegm and wheezing, and achieved satisfactory results. Lift and Shift San has the effects of lifting and clearing turbidity, soothing qi, dispersing wind and clearing heat, and promoting lung and qi stagnation [26]. Qiang Weiping [27] et al. randomly divided 80 cases of phlegm-heat congested lung-type severe pneumonia patients into observation group and control group, the control group patients took conventional western medical treatment, the observation group patients in the control group on the basis of the combination of elevation and dispersal of the addition and subtraction of the treatment group. After two weeks of treatment, the treatment group's effective rate is higher than that of the control group, and it can improve the patient's level of inflammatory factors and the level of peripheral T-lymphocyte group, which has a better clinical value.

3.2.2. Proprietary medicine injection

Proprietary medicine injection is a sterilized solution or suspension made by extracting the active ingredients of Chinese herbs, which acts on the human body through intravenous injection, intramuscular injection, acupoint injection and other ways, and is more widely used in the field of pediatrics. Phlegm Fever Clear Injection is composed of Scutellaria baicalensis, honeysuckle, laurel,

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bear bile powder and cornelian cherry [28]. It has the efficacy of clearing heat, detoxifying, resolving phlegm, and resisting infection, used for the treatment of severe pneumonia, with significant therapeutic effects [29]. Ma Jianping [30] divided patients with severe pneumonia into two groups, azithromycin was administered to the control group, and the treatment group was combined with Xingnaojing injection. The results suggest that the treatment group can significantly reduce the inflammatory response of the body and effectively improve lung function, and the clinical effective rate is higher than that of the control group. Hou Yuwei randomly divided 84 patients with severe pneumonia into control group and study group. The control group was given linezolid injection treatment, while the study group was given linezolid and Xuebijing injection combined treatment. The results of the study found that the therapeutic efficiency of the treatment group was higher, and the difference was obvious in comparison. The combination of the two drugs could better relieve clinical symptoms and improve lung function, and the results were statistically significant and worthy of clinical promotion. On the basis of alveolar lavage therapy, Deng Ming combined Shenfu Injection intravenous drip therapy with 50 SP patients, and found that the treatment group had great advantages in shortening symptom relief time, inhibiting inflammatory reactions, improving lung function, and enhancing immune levels.

3.2.3. Combination of Chinese and Western medicine

There are numerous successful cases of combining Chinese and Western medicine in the treatment of severe pneumonia. Zhang Ruhan et al. [31] found that Jinshui Liujun Decoction combined with the conventional program to treat severe pneumonia with phlegm-heat congestion of the lungs, had a higher overall effective rate than the control group, improved lung function more effectively, and the rate of adverse reactions was lower than that of the control group, which was a better safety profile. Ge Yanping et al. [32] added Qingfei Huatan Tang to the treatment group on the basis of the control group, and finally concluded that the treatment group has advantages in improving traditional Chinese medicine syndrome scores, restoring blood gas indicators, decreasing levels of inflammatory factors, and improving immune function. A systematic evaluation and meta-analysis of the combined treatment of SP patients with Chinese and Western medicines showed that compared with pure Western medicine, the combination of Chinese and Western medicines in the treatment of pediatric severe pneumonia can shorten the time of symptom disappearance, alleviate the clinical symptoms, and improve the lung function.

4. Conclusion

Chinese medicine and modern medicine have their own achievements and advantages in the pathogenesis of severe pneumonia, and the research progress of this disease will have a bigger breakthrough if we choose to use both Chinese and Western medicine to treat this disease and consult and learn from each other. Therefore, developing a unified treatment plan for integrated traditional Chinese and Western medicine as soon as possible can be the focus of the next research step.

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