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Research Progress on Traditional Chinese Medicine Treatment for Refractory Mycoplasma Pneumonia in Children

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Abstract: ***Refractory mycoplasma pneumoniae pneumonia in children refers to pneumonia that has not been fully absorbed or has recurred after standard antibiotic treatment. The disease seriously affects the growth and development of children and quality of life, easy to lead to pulmonary fibrosis, lung function damage, and even systemic infection. Studies have found that traditional Chinese medicine has unique advantages for the treatment of this disease, such as significantly improving symptoms, reducing complications, and not easy to develop drug resistance. However, there are few literatures on TCM treatment of refractory pneumonia in children, and there is no unified treatment guideline. Therefore, in the future, we should focus on the dialectical classification direction of refractory mycoplasma pneumoniae pneumonia in children, and adopt internal administration and external use method according to the syndrome type, combined with western medicine treatment to improve the curative effect.***

Keywords: Chinese medicinal materials, Dialectical pattern, Refractory mycoplasma pneumoniae pneumonia, Children.

1. Introduction

Refractory Mycoplasma pneumoniae pneumonia (RMPP) in children refers to cases where pulmonary consolidation or infiltrates fail to fully resolve after standardized antibiotic therapy, or where pneumonia recurs following discontinuation of treatment. Clinical Characteristics and Management of Refractory Mycoplasma Pneumoniae Pneumonia in Children [1]. Recurrent Mycoplasma Pneumonia in Children (RMPP) is a common respiratory infectious disease that severely impacts children's growth, development, and quality of life, imposing significant psychological and economic burdens on both children and families. Mycoplasma pneumoniae is the primary pathogen causing RMPP in children. It exhibits drug resistance, readily induces abnormal immune responses, and may coexist with other bacteria, viruses, fungi, or parasites in mixed infections. Furthermore, RMPP's atypical clinical presentation — characterized primarily by persistent fever and cough in early stages with minimal pulmonary signs—often leads to misdiagnosis. This delays antibiotic administration, potentially triggering sudden onset of severe symptoms and complicating clinical management. Current treatment for Mycoplasma pneumoniae pneumonia primarily involves anti-infective therapy, expectoration, anti-inflammatory measures, and antipyretics. However, some pediatric patients still exhibit poor treatment outcomes.

Research indicates that traditional Chinese medicine (TCM) offers distinct advantages in preventing and treating mycoplasma pneumonia, including inhibiting Mycoplasma pneumoniae, alleviating cough and wheezing symptoms, reducing pulmonary inflammation, and minimizing complications, while demonstrating low susceptibility to drug resistance. Consequently, investigating the therapeutic efficacy of TCM for MPP and enhancing children's health outcomes represent both a priority and a challenge in current pediatric research. This paper provides a comprehensive review of the latest research progress on TCM treatment approaches for pediatric MPP.

2. Pattern Differentiation and Classification of RMPP in Traditional Chinese Medicine

In traditional Chinese medicine, RMPP falls under the categories of "pneumonia with wheezing and cough" and "exogenous febrile diseases." TCM attributes the pathogenesis of RMPP to both external and internal factors. External factors stem from exposure to wind-heat pathogens, while internal factors arise from the delicate nature of children's lungs and their compromised defensive functions. RMPP typically manifests in the lungs, often involving the heart, liver, spleen, and kidneys. The overarching pathogenesis involves stagnation and closure of lung qi. Pathological factors include heat, phlegm, toxins, and stasis. In Western medical progression, it is primarily divided into the initial stage, acute stage, and recovery stage. During the initial stage of MPP, the main symptoms include fever, cough, and redness of the throat, which in TCM manifests as wind-heat obstructing the lungs. The acute stage is characterized by persistent high fever, cough, copious phlegm, and yellow, sticky phlegm, corresponding to TCM manifestations of phlegm-heat obstructing the lungs, toxin-heat obstructing the lungs, and damp-heat obstructing the lungs. The convalescent stage is characterized by dry cough, scant sputum, night sweats, low-grade fever, and palmar-plantar heat. Corresponding TCM patterns include lung heat with yin deficiency and lung-spleen qi deficiency[2]. Compared to ordinary mycoplasma pneumonia, which primarily presents with common patterns like wind-cold obstruction of the lungs, wind-heat obstruction of the lungs, and phlegm-heat obstruction of the lungs, RMPP typically manifests with these common patterns alongside variant patterns including heart yang deficiency, pathogenic factors invading the Jueyin channel, and damp-toxin and blood stasis obstruction. In recent years, numerous scholars have conducted a series of studies on the aforementioned syndrome patterns of MPP.

Si Cai [3] retrospectively analyzed the distribution characteristics of TCM patterns in 889 pediatric cases of Mycoplasma pneumoniae pneumonia. They found that the distribution patterns of MPP in TCM were, in descending order: phlegm-heat obstructing the lungs, mixed cold-heat syndrome, wind-heat obstructing the lungs, wind-cold obstructing the lungs, and toxin-heat obstructing the lungs, with phlegm-heat obstructing the lungs being the most prevalent. Hui Yang [4] suggested that the TCM syndrome pattern for refractory pneumonia in children commonly presents as a combination of "lung + phlegm + heat." Both Jing Shu [5] and Yuejing Shi [6] identified wind-heat obstructing the lungs as the most prevalent syndrome pattern in pediatric pneumonia, followed by phlegm-heat obstructing the lungs, noting a potential association with the child's age and constitution. Based on current evidence-based research, the primary symptoms of pediatric MPP predominantly manifest as wind-heat obstructing the lungs or phlegm-heat obstructing the lungs. This may stem from the delicate nature of children's lungs and viscera. External pathogens invade, generating heat over time. Lung heat then steams and scorches body fluids, transforming them into phlegm. This phlegm obstructs the lung collaterals, leading to the disease. It is highly prone to shifting from an exterior syndrome pattern to other TCM syndrome patterns. Additionally, young children are naturally active, and pneumonia spreads rapidly. External wind pathogens readily invade the body, penetrate inward to generate heat, and manifest as wind-heat obstruction of the lungs—equivalent to mild pneumonia. If heat pathogens linger, they refine fluids into phlegm. The mutual entanglement of phlegm and heat, with phlegm-stasis obstructing the lungs, progresses to phlegm-heat obstructing the lungs syndrome, equivalent to severe pneumonia. If residual pathogens remain during recovery, the clinical presentation may be deficiency with lingering pathogens. If pathogenic heat has subsided but damaged qi and yin, the clinical presentation may be lung-spleen deficiency [7].

3. Primary Therapeutic Approaches of Traditional Chinese Medicine for Differentiating Syndromes in Pediatric RMPP

Based on the primary TCM patterns observed in pediatric RMPP, pattern-differentiated TCM therapies are widely applied in treating refractory pneumonia. Common patterns in pediatric RMPP primarily include wind-cold obstructing the lung, wind-heat obstructing the lung, and phlegm-heat obstructing the lung. As symptoms progress, other secondary patterns may emerge, such as heart yang deficiency and pathogenic factors invading the liver meridian. Treatment approaches for these patterns mainly include herbal decoctions and external therapies (e.g., acupuncture, massage).

3.1 Wind-Heat Obstructing the Lungs Pattern

Wind-Heat Obstructing the Lung Pattern manifests primarily with fever, slight aversion to wind and cold, cough with phlegm, thirst, reddened throat, red tongue body, thin white or yellow coating, and floating rapid pulse. Primary therapies include decoction therapy and external treatments.

3.1.1 Chinese Herbal Decoction Therapy

Research indicates that Ni Xuan [8], through observing 100 pediatric cases of pneumonia with wind-heat obstructing the lungs, found significant therapeutic efficacy when combining the Ma Xing Shi Gan Decoction (composed of ephedra, apricot kernel, licorice, and gypsum) with the Western medicine cefazolin for treating this condition. Wang Xiao et al. [9] applied a self-formulated cough-relieving and phlegm-resolving decoction to treat pediatric pneumonia with wind-heat obstructing the lungs. They found this decoction significantly improved treatment efficacy, enhanced therapeutic response rates, and improved inflammatory factor indicators and blood rheology parameters. This decoction primarily consists of fried ephedra, apricot kernel, raw gypsum, fish mint, Lonicera japonica, Glycyrrhiza uralensis, Trichosanthes kirilowii, and Forsythia suspensa. Similar to the Ma Xing Shi Gan Tang formula, it primarily functions to clear heat with pungent-cool herbs, clear and drain the lung and stomach, and relieve cough and asthma. It demonstrates significant efficacy for pediatric wind-heat lung obstruction syndrome. Xiaoxu Sun [10] found that the modified Qianjin Weijing Tang (with Winter Melon Seed, Coix Seed, Peach Kernel, Scutellaria baicalensis, Lugeng, Houttuynia cordata, Danshen, Fritillaria cirrhosa, Jiegeng, and Fried licorice) can improve immune function and peripheral blood inflammatory responses in children with mycoplasma pneumonia presenting wind-heat lung obstruction syndrome. This formula significantly alleviates clinical symptoms such as cough and fever. Qian Dong [11] found that modified Dimaiganjie Decoction effectively treats wind-heat lung obstruction pattern in pediatric pneumonia, alleviating clinical symptoms and suppressing inflammatory responses. The 2023 Integrated Chinese and Western Medicine Diagnosis and Treatment Protocol for Pediatric Pneumonia and Mycoplasma Pneumonia recommends that children with wind-heat obstruction of the lungs primarily receive Chinese herbal therapy based on the principles of dispersing wind-heat to open the lungs, promoting lung function, and relieving cough, using Yinqiao San combined with Ma Xing Shi Gan Tang with modifications. Comparing this with previous studies, it can be observed that adhering to the guideline's approach of dispersing wind-heat to open the lungs and promoting lung function for wind-heat obstruction of the lungs yields favorable outcomes for this pattern.

3.1.2 Traditional Chinese Medicine External Therapies

Additionally, pediatric MPP treatment may incorporate TCM external therapies such as cupping, moxibustion, herbal poultices, and pediatric massage as adjunctive approaches to alleviate symptoms and promote recovery. Qingdong Mao [12] treated 90 pediatric pneumonia cases with wind-heat lung obstruction syndrome using self-formulated herbal umbilical patches. They observed significant improvement in clinical symptoms. Chen Yun [13] found that pediatric massage can also effectively enhance treatment outcomes for community-acquired pneumonia in children, specifically manifested by reduced levels of inflammatory factors such as C-reactive protein, procalcitonin, and serum amyloid A following massage adjunctive therapy.

Hu Xiaowen [14] found that Qingfei Huazhuo Decoction

combined with acupoint plaster application as adjunctive therapy for pediatric pneumonia with wind-heat obstructing the lungs was effective. The acupoint plaster containing ephedra, which has lung-opening and asthma-relieving effects, may work by being absorbed through the skin, transported via the venous system to the affected area, promoting inflammation resolution, enhancing immunity, and thereby improving symptoms. Qiming Lu [15] observed that cupping therapy significantly alleviated fever symptoms in children with wind-heat lung obstruction syndrome. Additional studies indicate that four major head and face techniques (downward push on the occipital bone, liver-clearing and lung-regulating, clearing the celestial river, pressing and kneading the elbow crease, shoulder well grasping, and pinching and squeezing the throat and lung shu points), cupping, and acupuncture can also alleviate symptoms of wind-heat lung obstruction in pediatric patients. The above findings suggest that TCM external therapies, when used as adjunctive treatments, significantly alleviate symptoms of pediatric MPP. Their mechanisms of action resemble those of decoction therapy. Therefore, TCM external therapies can be effectively promoted and applied as supplementary measures in the clinical treatment of pediatric MPP.

3.2 Phlegm-Heat Obstructing the Lungs Pattern

The primary manifestations of phlegm-heat obstructing the lungs include high fever with restlessness, cough with copious sputum that is viscous and yellow, or wheezing in the throat, nasal flaring with shortness of breath, flushed face with thirst, cyanosis around the mouth, chest tightness and distension, scanty yellow urine, dry stools, red tongue with thick yellow coating, and slippery rapid pulse. Current primary TCM therapies for pediatric phlegm-heat obstructing the lungs include herbal decoction therapy and external TCM treatments (such as acupuncture, gua sha, and acupoint application).

3.2.1 Chinese Herbal Decoction Therapy

Lizhen Zhu [16] found that Ma Xing Shi Gan Tang with modifications combined with azithromycin demonstrated significant efficacy in 60 children with refractory pneumonia due to phlegm-heat obstructing the lungs. This suggests Ma Xing Shi Gan Tang is equally effective for both phlegm-heat and wind-heat obstruction of the lungs. Hongxia Zhao [17] applied modified Wuhu Decoction combined with Tingli Dazao Xiefei Decoction (Gypsum, Tinglizhi, Scutellaria, Earthworm, Zhebeimu, Perilla Seed, Mulberry Bark, Stiff Silkworm, Peucedanum, Licorice, Ephedra, Apricot Kernel) to treat children with refractory pneumonia due to phlegm-heat obstructing the lungs. The formula showed marked improvement in symptoms. This medication exerts effects of purging the lungs, relieving asthma, and resolving phlegm for pneumonia. add Bupleurum and Scutellaria for severe fever; add Pinellia for excessive phlegm). This formula demonstrates significant efficacy in alleviating symptoms of refractory pneumonia in children with phlegm-heat obstructing the lungs. It exerts effects including draining the lungs, relieving asthma, resolving phlegm, and stopping cough. Yu Xueming [18] demonstrated that Tongfa Xianzhuan Decoction (primarily composed of Ginkgo biloba, Tussilago farfara, Morus alba bark, Scutellaria baicalensis, Ephedra sinica, Perilla frutescens, Glycyrrhiza uralensis, and Prunus armeniaca) combined with azithromycin effectively treats children with refractory pneumonia due to phlegm-heat obstructing the lungs. This regimen rapidly controls the condition and improves traditional Chinese medicine syndromes. The above findings indicate that decoction treatments for children with phlegm-heat obstructing the lungs in MPP primarily focus on clearing heat, resolving phlegm, promoting lung function, and relieving asthma. This aligns with the “heat-clearing and phlegm-resolving” and “lung-opening and asthma-relieving” therapies outlined in the 2023 Integrated Chinese and Western Medicine Diagnosis and Treatment Protocol for Pediatric Mycoplasma Pneumonia. Therefore, adhering to the therapeutic principles and formulas outlined in the 2023 Integrated Chinese and Western Medicine Diagnosis and Treatment Protocol for Pediatric Mycoplasma Pneumonia effectively improves the phlegm-heat obstructing the lungs pattern in children with MPP, tailored to individual symptom presentations.

3.2.2 Traditional Chinese Medicine External Therapies

Similar to the wind-heat obstruction of the lungs pattern, numerous TCM external therapies demonstrate comparable efficacy for the phlegm-heat obstruction of the lungs pattern. Li Runhua [19] applied silicone gua sha as an adjunct therapy for children with refractory pneumonia due to phlegm-heat obstruction of the lungs, finding this supplementary approach significantly improved symptoms with excellent therapeutic outcomes. Xu Yang [20] found that combining Lung-Ning Plaster acupoint application with Western medication effectively improved the phlegm-heat obstructing the lungs pattern in pediatric bronchopneumonia, as evidenced by the disappearance of pulmonary wet rales and a significantly shortened disease course. Xiang Tianli [21] observed that combining Xuanfei Ditan Decoction with acupoint application effectively reduced inflammatory markers in children with phlegm-heat obstructing the lungs pneumonia presenting with wheezing and coughing. This approach also resulted in fewer adverse reactions and improved prognosis. Research indicates that external TCM therapies like gua sha and acupuncture stimulate meridians and acupoints to expel pathogenic factors, regulate internal yin-yang balance, and achieve effects such as cough suppression, phlegm resolution, and meridian unblocking [22]. Acupoint plaster therapy further enhances efficacy by incorporating herbal medicines absorbed through the skin. Additional research indicates that the “Three Lines” technique (involving the transverse lines of the palm and finger), combined with opening the Xuanji point and massaging the Fenglong point, forms an effective three-step phlegm-expelling method for treating lung obstruction due to phlegm-heat syndrome. The above findings suggest that TCM external therapies—including acupoint plaster application, gua sha, and acupuncture—can enhance the efficacy of decoction treatment for phlegm-heat obstructing the lungs syndrome when used as adjunctive measures.

3.3 Wind-Cold Obstructing the Lungs Syndrome

The primary manifestations of wind-cold obstruction of the lung syndrome include aversion to cold, fever, absence of sweating and thirst, coughing with shortness of breath, thin

white phlegm, pale red tongue with thin white coating, and floating tight pulse.

3.3.1 Chinese Herbal Decoction Therapy and External Treatments

Wang Yalie et al. administered rectal suppositories containing decoction of Huagai Powder (Ephedra 10 g, Perilla Seed 15 g, Apricot Kernel 15 g, Chenpi 15 g, Sangbaipi 15 g, Fuling 15 g, Gancao 10 g) to treat pediatric pneumonia with wheezing and cough (Wind-Cold Obstructing the Lungs pattern). They found this therapy effectively alleviated symptoms such as cough and fever in children, demonstrating potential for broader application. Liao Zehui [23] discovered that Shegan Mahuang Tang (Shegan 6 g, Mahuang 4 g, Ginger 6 g, Pinellia 8 g, Aster 6 g, Tussilago 6 g, Jujube 10 g, Asarum 2 g, Schisandra 5 g) de. monstrated significant clinical efficacy in treating wind-cold lung obstruction type bronchopneumonia in children, markedly reducing inflammatory responses and alleviating symptoms. Additional research suggests that Xiao Qinglong Decoction (Ephedra 5 g, Cinnamomum 5 g, Paeonia 5 g, Schisandra chinensis 5g, Pinellia ternata 5g, Prunus armeniaca seed 5g, Citrus reticulata peel 5g, Fritillaria thunbergii 5g, Gypsum fibrosum 15g) also demonstrates significant efficacy for wind-cold obstruction of the lungs in pediatric bronchopneumonia, demonstrating potential for broader application [24]. Current research indicates that traditional Chinese medical approaches primarily employ pungent-warm herbs to open the lungs, resolve phlegm, and relieve cough for treating wind-cold obstruction of the lungs syndrome. Particular attention should be paid to the degree of heat transformation during clinical application. Different formulas may be prescribed for varying symptoms. For cases with cold phlegm accumulation presenting wheezing, coughing, shortness of breath, chest tightness, phlegm rattling, and frothy white sputum, Xiao Qinglong Tang is the primary treatment. For cases where external cold pathogens constrict while internal heat develops, manifesting as aversion to cold, cold limbs, fever without sweating, restlessness, thirst, constipation, and thick, sticky phlegm, Da Qinglong Tang with modifications is used. For wind-cold obstructing the lungs syndrome, external TCM therapies follow similar principles to other patterns, using adjunctive treatments to enhance therapeutic efficacy. For instance, Wang Tingting [25] found that in pediatric wind-cold obstructing the lungs pneumonia with wheezing and cough, supplementing conventional Western drug therapy with a spleen-tonifying, distension-relieving poultice improved clinical symptoms and treatment outcomes.

3.4 Other Variant Patterns: Heart Yang Deficiency Syndrome, Pathogenic Factors Invading the Jueyin Pattern, Damp-Toxin and Stagnant Blood Obstruction.

Heart Yang Deficiency Syndrome, Pathogenic Factors Invading the Jueyin Liver Meridian Syndrome, and Damp-Toxin and Stagnant Blood Obstruction Syndrome are all manifestations of severe pediatric pneumonia. Among these, Heart Yang Deficiency manifests as sudden pallor, cyanosis of lips and fingertips, shallow and rapid breathing with difficulty, cold extremities, profuse sweating, mass in the hypochondrium, rapid and forceful heartbeat, restlessness, lethargy and apathy, decreased urine output, pale-purple tongue, rapid and fine pulse nearing cessation, and purple discoloration of fingerprints. The primary treatment principle is to warm and tonify Heart Yang, rescue from collapse, and consolidate against collapse. The primary formula is modified Shen Fu Long Mu Rescue Decoction (Common herbs: Ginseng, Aconite, Dragon Bone, Oyster Shell, White Peony, Licorice. Modifications: For qi-yang deficiency, Du Shen Tang or Shen Fu Tang may be administered in small, frequent doses for emergency relief. For both qi and yin depletion, add Sheng Mai San to tonify qi, nourish yin, and reverse collapse. For pronounced blood stasis manifestations such as pale-blue complexion, cyanotic lips and tongue, or masses in the right hypochondrium, consider adding blood-activating herbs like Carthamus and Salvia to promote smooth blood circulation.

Symptoms of pathogenic factors invading the Jueyin channel often manifest as persistent high fever, cyanotic lips, shortness of breath, wheezing in the throat, restlessness, delirium, agitation, loss of consciousness, locked jaw and stiff neck, opisthotonos, limb convulsions, dark red tongue, fine and rapid pulse, cyanotic fingerprints, and in severe cases, fingernail bed hemorrhage. Treatment primarily focuses on calming the liver and extinguishing wind, clearing the heart, and opening the orifices. The main formula Lingjiao Gou Teng Tang (from Popular Treatise on Cold Damage) combined with Niu Huang Qing Xin Wan (from Essentials of Smallpox and Measles Treatment) is modified as needed. Key herbs include antelope horn, mulberry leaf, fritillary bulb, rehmannia root, Uncaria stem, chrysanthemum flower, poria, white peony root, licorice root, bamboo shavings, cowbane, scutellaria root, coptis root, gardenia fruit, and curcuma rhizome. Modifications: For coma with excessive phlegm, add Acorus tatarinowii rhizome, Pinellia ternata processed with bile, Bambusa vulgaris sap, or Monkey's-fist Powder to resolve phlegm and open orifices. For high fever with mental confusion and convulsions, consider adding Zixue Dan, An Guan Niu Huang Wan, or Zhibao Dan. Corresponding Chinese patent medicines include An Guan Niu Huang Wan and Zixue Dan [26].

Damp-Toxicity and Stagnation Pattern Characterized by prolonged cough with viscous, difficult-to-expectorate phlegm; absence of fever or fluctuating low-grade fever; dyspnea; cyanosis and shortness of breath; dark purple tongue with ecchymoses; thick, greasy white coating. Imaging reveals persistent atelectasis or persistent inflammatory consolidation. Primary treatment principles include clearing heat and resolving phlegm, promoting blood circulation and unblocking collaterals. Primary formula: Ganlu Disinfecting Pill (from Wenre Jingwei) combined with Qianjin Weijing Decoction (from Jingui Yaolue), with modifications. Common herbs: Talcum, Scutellaria, Yinchen, Acorus, Fritillaria, Agastache, Forsythia, Belamcanda, Phragmites rhizome, Amomum, Areca, Magnolia bark, Peach kernel. Modifications: For persistent high fever, add Gypsum and Houttuynia cordata to clear lung heat and disperse heat. For fluctuating low-grade fever, add White Peony Root and Artemisia annua. For persistent rales, add Fried Mustard Seed and Perilla Seed to warm the lungs, descend qi, and resolve phlegm. For persistent pulmonary imaging abnormalities, add Angelica sinensis and Astragalus membranaceus to tonify qi and activate blood circulation [27].

4. Summary and Outlook

In summary, traditional Chinese medicine (TCM) treatment approaches are gaining increasing attention in the field of refractory pneumonia research in children and warrant further investigation. For RMPP, the efficacy of conventional antibiotic therapy is gradually diminishing, while antibiotic resistance resulting from overuse during treatment is becoming increasingly severe. Generally, in TCM research, common patterns in pediatric refractory mycoplasma pneumonia typically include wind-heat obstructing the lungs, phlegm-heat obstructing the lungs, and wind-cold obstructing the lungs. For RMPP, while these common patterns remain predominant, severe cases may present with secondary patterns such as heart yang deficiency, pathogenic factors invading the liver meridian, or damp-toxin and blood stasis obstruction. Treatment primarily involves decoction formulas combined with TCM external therapies, with adjustments made based on the specific pattern. Additionally, integrating Western medical approaches can enhance therapeutic efficacy. Future research should therefore continue exploring the optimal combination and mechanisms of TCM treatment, as well as strategies to enhance therapeutic outcomes while reducing antibiotic usage. This requires collaborative efforts between clinicians and researchers to validate the efficacy and safety of TCM in treating MRP pneumonia through additional randomized controlled trials and long-term clinical observations.

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