An Exploration of Dr. Chunying Liu's Experience in Treating Frequent Nephrotic Syndrome in Children

Yingbo Wang^{1,a}, Chunying Liu^{2,b,*}

¹Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

²Hospital of Shaanxi University of Chinese Medicine, Xianyang 712000, Shaanxi, China

^a854716791@qq.com,^bliuchy28@163.com

* Corresponding author

Keywords: Frequent nephrotic syndrome in children, Chinese medicine, Hormone

Abstract: Dr. Liu Chunying, chief physician, believes that the pathogenesis of frequent renal syndromes in children is always based on the deficiency of the lung, spleen, and kidney, with the kidney being the main cause; heat, dampness, and blood stasis are the symptoms, and the treatment is based on the balance between helping the righteous and eliminating the evil.

1. Introduction

Nephrotic syndrome is a group of syndromes characterized by massive proteinuria, hypoproteinemia, hyperlipidemia and edema as the main clinical features. Frequent nephrotic syndrome is defined as ≥2 relapses within 6 months or ≥4 relapses within 12 months after remission by hormonal therapy [1]. Most children have microscopic renal pathology, which is hormone-sensitive but prone to recurrence, resulting in recurrent large amounts of proteinuria, aggravating kidney damage and even progression to uremia at the end stage. At this stage, Western medicine mostly uses the combination of glucocorticoids and immunosuppressants. Although Western medicine alone can control the disease quickly, the disease is still prone to recurrence and can produce side effects such as respiratory infections, immune deficiency and excessive sweating, increasing the risk of recurrence. Chinese medicine has the advantage of less toxic side effects, and is characterized by a holistic concept and dialectical treatment to achieve a combination of disease and illness, effectively improving the patient's immunity and slowing down the side effects of Western medicine, The combination of Chinese and Western medicine can effectively reduce the number of disease recurrence. The experience of Chinese medicine in treating frequent nephrotic syndrome in children is summarized below.

2. Chinese Medicine Pathogenesis and Treatment Characteristics

Nephrotic syndrome belongs to the category of "edema" and "turbidity of urine" in Chinese medicine. In children, the lungs are originally weak, and when the body is deficient in external sensations, the righteousness is not able to oppose the evil, and the evil enters the lungs, causing the

lungs to fail to promote and purify, and the spleen to fail to transport and transform, and the water essence to fail to disperse, and the kidneys to fail to open and close, causing the water to stop inside, resulting in edema. The spleen loses its health, dampness and heat are injected into the kidney, and the kidney loses its The kidney loses its ability to seal the body, and a large amount of essence and microscopic material is leaked down, resulting in urinary turbidity. According to Liu, this disease is based on the deficiency of the lung, spleen and kidney, Especially the kidney is the main focus; heat, dampness, blood stasis as the standard, always belong to the original deficiency, mixed with the real, deficiency, the development of this disease. The treatment process emphasizes the co-play of helping the righteous and driving away the evil, with the main focus on helping the righteous. The treatment features of Chief Physician Chunying Liu are summarized below.

2.1 Focus on Tonifying Lung Energy and Flexible Treatment

In Chinese medicine, glucocorticoids are considered to have a Yang-heat nature, and physiological doses can make the "qi of less fire strong" and play the role of "less fire and angry". Long-term use of large doses of glucocorticoids will cause "strong fire and eating qi", resulting in "the qi of strong fire decaying", insufficient kidney yin, deficiency of Yang floating outside, deficiency of both yin and yang, loss of function of the external guard, and the presence of external evil.

In the Suwen-Heat Commentary, it is said that "where evil comes together, its qi must be deficient", i.e., the patient's positive qi is weak, the warmth is out of duty, and the external guard is not solid, so the external evil takes advantage of the deficiency and enters, and the organism is unable to resist the evil and feels the disease. Andreas E. Stuck et al [2] found an increased risk of infectious complications when prednisone was administered at doses >10 mg daily or cumulative doses >700 mg. One study found that infection was the main cause of recurrence of nephrotic syndrome and that respiratory infections accounted for 71% of cases [3]. In contrast, respiratory infections are located in the lungs and the main cause of their infection is a decrease in the immune function of the body [4]. Chinese medicine believes that children's internal organs are delicate, the lungs are often inadequate; "Su Wen - Sickness can be discussed" cloud: "the lungs, the cover of the organs also", the lungs are located in a high position, the original susceptible to evil, mostly due to inclusions, external evil invasion of the lungs. The Ling Shu - the tenth meridian: "kidney foot Shao Yin pulse contact kidney, belong to the bladder: its straight, from the kidney on through the liver and diaphragm, into the lung, follow the throat, hold the tongue this", the lung and kidney by the kidney The lung and kidney are connected by the direct pulse of the kidney, and lung disease can enter the kidney via the meridian; the kidney is the son of the lung in the five elements, the mother's disease and the son, and the lower injury to the kidney.

Liu believes that the causes of recurrence in children are mostly related to their weak lung qi and low immunity, so the treatment is based on the lung, focusing on tonifying the lung qi, emphasizing on helping the positive and driving away the evil together, with the main focus on helping the positive, throughout the treatment. Yupingfeng San is commonly used clinically to benefit the qi and fix the surface of the body, support the righteousness and drive away the evil to prevent recurrence in children. And there are modern studies that Yu Ping Feng San can improve the immunity of patients and reduce the recurrence rate [5] [6].Children are more susceptible to deficiency, the first offense is the lungs, the throat is the gateway to the lungs, evil toxins are easy to ambush in this, resulting in upper respiratory tract infections, most of the inflammatory present, such as tonsillar enlargement. Clinical applications often apply fishy grass, which has many active antiviral components^[7], As the tonsils are a local immune organ, the inflammatory response is likely to cause recurrence of the disease, so the main focus of herbal treatment at this time is to

control the infection. Upper respiratory tract infections are frequent in children in autumn and winter, and the treatment should be based on replenishing lung qi, and the dosage of Astragalus can be increased appropriately to improve the immunity of children, and modern pharmacology has confirmed ^[8] that Astragalus can reduce the incidence of infection by enhancing host humoral and cellular immunity. By tonifying the lung qi to reduce the frequency of recurrence in children, the application of hormones, which can lead to abnormal bone metabolism in children, can be effectively reduced. c ausing complications such as short stature, glucocorticoid-associated osteoporosis, and fractures^[9]. Some studies have shown that prednisone doses as low as 0.075-0.125 mg/(kg-d) can still cause growth restriction^[10].

2.2 The Main Treatment is to Benefit Qi and Warm Yang, Supplemented by Clearing Heat and Detoxifying Toxins.

During the period of hormone withdrawal, the child mostly shows weakness in the waist and knees, dizziness and tinnitus, fatigue and laziness, etc. In Western medicine, this syndrome belongs to the hormone withdrawal syndrome, because the patient has been applying large doses of hormones for a long time. In the process of hormone withdrawal, the secretion of endogenous cortisol needs to be gradually restored to normal [11], during which the child's body is in a state of hormone deficiency, which is prone to relapse of the disease. Liu believes that warm yang medicine has hormone-like effects, which can compensate for the recurrence of the disease that occurs due to the lack of hormones in the child's body, and the clinical manifestations of such children mostly belong to spleen and kidney yang deficiency evidence, so the treatment requires the application of a large number of drugs that benefit qi and warm yang to support the right qi, improve the immunity of the child and reduce recurrence, and there are modern medical research findings [12]. The drugs that warm the kidney can improve the immune function of the body by regulating the role of immune factors, commonly used clinically are bone marrow, Cuscuta, Xian Ling Spleen, Baji Tian, Cistanches, Lock Yang, etc. However, since children are pure Yang bodies, the use of large amounts of warm Yang drugs is not easily tolerated by children, so they often add heat-clearing and detoxifying drugs on top of the warm Yang. Commonly used drugs include dandelion, forsythia, honeysuckle, fishy grass, etc. These drugs have a bitter-cold nature, which can restrain the heat of the warm-yang drugs, and the two types of drugs are used together to clear heat and detoxify the body and benefit the qi and warm yang, which are opposite to each other.

3. Treating from Blood, Activating Blood Circulation and Removing Blood Stasis Throughout the Whole Process

Nephrotic syndrome is often accompanied by hypercoagulable state, one of the long-term application of a large number of hormones can lead to strong fire eating Qi, the child has more signs of Qi deficiency. Difficult Jing - 22 Difficult" said: "The main gas yawn, the main blood moisten." That is, qi can move blood, but also can produce blood, qi deficiency is weak in transporting blood, easy to cause blood stasis, blood stasis does not go to the new blood is not born, blood loss of moistening; the second edema for a long time, can block the qi, causing blood flow is not smooth, resulting in the formation of blood stasis. Blood stasis can further aggravate edema. Third, proteinuria in children is a key and difficult point in the treatment process, because proteinuria is mostly due to dampness, which stagnates and is difficult to heal. Liu emphasized that the application of blood-stasis activating drugs should be used throughout the treatment, commonly used drugs include Chuanxiong and Angelicae to achieve the function of removing blood stasis without injury and nourishing blood without congestion; Yimoucao to activate blood and at the same time to reduce swelling.

4. Chinese Medicine Regulates Yin and Yang to Increase Effectiveness and Reduce Toxicity

4.1 Insufficient Qi and Yin, Table Deficiency Spontaneous Sweating Suwen - Yin and Yang, "Yang Plus Yin is Called Sweating"

Yang steam yin to produce sweat, hormones are "pure yang" drugs, easy to cause Yang heat, resulting in Yin deficiency fire, forcing fluid to leak out, causing increased sweating. Long-term application of hormones can cause both Qi and Yin deficiency, and because of the Wei Qi for the line of Qi outside the pulse, Qi deficiency is the Wei Qi deficiency, "Ling Shu - this organ" cloud "Wei Oi, so warm flesh, fill the skin, fat couples Division open and close." If the Wei Oi is weak, the surface deficiency is not solid, and the Xuan Fu is not dense, the sweat will leak out and make it susceptible to external evil. In the Su Wen - Commentary on Heat Diseases, it is said that "sweating is the essence of qi", which means that excessive sweating can cause depletion of blood. Therefore, Liu believes that the clinical appearance of such symptoms should be intervened or protected in advance, because the patient's spontaneous sweating also further aggravates the progress of Qi deficiency, which may lead to relapse of the disease. The medical case of Ye Tianshi's "clinical evidence guide" said "Yang deficiency spontaneous sweating, the treatment should be to supplement the qi and guard the outside", Liu Shi often added on the basis of evidence to supplement the qi and astringent sweat drugs such as Wu Wei Zi, ephedra root, floating wheat, etc., of which Wu Wei Zi taste sour and salty, its sour can astringent lung, salty can nourish the kidney, in order to achieve the same treatment of lung and kidney. Therefore, Liu also emphasizes the use of blood tonic drugs, such as Chuanxiong, Angelica, etc., on top of qi tonic and sweat tonic, to prevent qi deficiency from promoting blood flow, resulting in blood not being able to glory in the tongue, resulting in pale tongue, weak pulse, and depletion of blood.

Qi and Yin deficiency, the intestinal tract is not moistened "Ling Shu - this organ" cloud "six internal organs, so transform water and grain and move fluids." The six internal organs have the function of transferring the essence and micro substances to the five organs and discharging the dregs out of the body. If the six internal organs do not work, food stagnation, the dregs do not diarrhea, then the stool does not work. Long-term constipation not only makes the body's toxin discharge obstructed, but also can cause qi stagnation, spleen and stomach lift function malfunction, resulting in malnutrition and so on. The clinical causes of constipation are mostly related to Qi imbalance and fluid depletion, while children have the physiological characteristics of "Yang is always in excess and Yin is always in deficit". In the Su Wen - Theory of Reverse Regulation, "Kidney is a water organ, master of fluids", children's yin is already relatively insufficient, plus most of these children have kidney yin deficiency as the basis, easily due to kidney yin deficiency, the intestines lose moistening, resulting in constipation, and hormones are "pure yang" drugs, the use of the initial hyper-yang, depleting yin, causing excessive heat in the stomach, further causing fluid depletion, intestines lose moistening. At this time, Liu's teacher added Yin nourishing and bowel moistening drugs such as Shengdi, Mai Dong, XuanShen, Angelica, GuaGua Ren, etc., to achieve the function of moistening the bowels and laxative, of which Angelica is warm in nature, but can nourish Yin for Yin deficiency, its taste pungent and can help Qi to descend, its taste sweet, can moisten the internal organs, to moisten the bowels. After long-term use of hormones, the "strong fire and eating gas" leads to deficiency of both qi and yin, especially the lung qi deficiency is obvious, the lung qi is deficient, the fluid propagation and dispersal to the large intestine is not enough, the lung qi purging and descending incompetence affects the large intestine fluency, together with the large intestine does not moisten, transmission is weak. The dregs stop inside, at this time Liu Shi more in nourishing Yin and moisten the intestines based on the addition of astragalus, hemp, Chen Pi and other beneficial qi spleen medicine, in order to achieve the function of nourishing the spleen and benefit the lung, moisten the intestines and laxative. At this time, Liu's master added or used rhubarb, Citrus aurantium, houpo, yu qi, tiger scepter and other drugs on top of nourishing yin and moistening intestines to regulate abdominal qi and help diarrhea to pass stools, of which rhubarb can pass dry knots and also can lead stomach qi downward.

4.2 Loss of Harmony and Descent of the Stomach, Imbalance of Ying and Wei

dysregulation "Ling Shu - Ying health will" "people receive gas in the grain, the grain into the stomach, to pass with the lungs, the five organs and six provinces, all to receive gas, the lighter for the Ying, the turbid for the Wei, Ying in the pulse, the Wei outside the pulse, Ying week does not rest, fifty and again General Assembly." In other words, Ying and Wei Qi are the essence of water and grain produced by the spleen and stomach, of which Wei Qi can "warm the flesh, fill the skin, fatten the couples, and open and close the body" (Ling Shu - The Organ) to defend the muscle surface and resist invasion of evil; Ying Qi is "transformed into blood to honor the four ends and injected internally into the five organs and six bowels" (Ling Shu - The Evil Guest) to produce blood to nourish the whole body. Most patients need to apply immunosuppressive drugs, such as cyclophosphamide, morte-macrolide, tacrolimus, etc. In the process of taking immunosuppressive drugs some patients will have clinical symptoms such as nausea and vomiting due to drug reactions. Long-term nausea and vomiting lead to insufficient yinghengheng, which reduces the body's ability to resist external evil and leads to relapse. Liu Shi believes that such symptoms are mostly due to the loss of stomach harmony and descent, and the treatment is to harmonize the stomach and lower the rebellion. Commonly used Chinese herbal medicines such as ginger, yellow sage, perilla leaf, orris, bamboo rhizome, etc., to achieve the function of regulating qi and stomach. Among them, bamboo rhizome is good at opening the stomach and lowering the rebellious qi in the stomach, and can also facilitate urination to reduce swelling; Huang Lian is cool in nature to remove the actual heat in the spleen and stomach, and can also clear the heart heat to restrain the dry heat and irritation in the stomach and intestines caused by the hormones taken by patients.

5. Example of Case Study

Shi, male, 10 years old, was admitted to our department on June 9, 2020 with the chief complaint of "recurrent edema for 8 years, cough and runny nose for 2 days", who had developed generalized edema after a "cold" in 2012 and was diagnosed with nephrotic syndrome at a hospital. He was treated with hormone therapy, which was not effective, and then successively applied hormone combined with mortification dispersible tablets, hormone combined with cyclophosphamide, etc., which did not have significant effect and then intermittently treated in several hospitals, during which he relapsed 6 times, the last relapse was on April 6, 2020, when the dosage of methylprednisolone was 24 mg, and when the amount of hormone was reduced to 16 mg on June 9, 2020. The child was admitted to our department for upper respiratory tract infection and was treated with methylprednisolone 16mg + cyclophosphamide (0.4g + 0.2g) and ceftazidime 2g in the morning and 1g in the evening for 6 days.

At the initial diagnosis, the symptoms were: shortness of breath and weakness, easy to have external sensation, easy to sweat, foamy urine, red tongue, white fur, and fine pulse. The following prescription was given.

Astragalus membranaceus 15g, Branched Atractylodes Macrocephalae 10g, Fructus Anemarrhenae 10g, Poria Cocos 10g, Radix Shi Wei 10g, Radix Achyranthes Bidentatae 10g, Dandelion 10g, Radix Polygala 10g, Radix Angelicae Sinensis 10g, Branched Citrus Aurantium 6g, Fructus Schisandrae 10g, Fructus Wheat 10g, total 14.

On July 16, the second consultation, after taking 14 consecutive doses, the patient's shortness of

breath and weakness, sweating were relieved compared to before, easily irritable, with a red tongue, thin white fur, and a stringy pulse, the treatment was changed on the basis of the original prescription, as follows: remove Shi Wei 10g, add Red Paeonia 10g, Rutabaga 10g, Fried Gorgonian 10g, total 21 doses.

On September 16, the third consultation, the patient complained of improvement of the above symptoms, no other discomfort, light red tongue, thin white fur, smooth pulse, the formula was changed on the basis of the original formula, adding warming drugs for kidney yang, the specific formula is as follows.

Astragalus membranaceus 20g, Atractylodes macrocephala 10g, Fructus Anemarrhena 10g, Poria cocos 10g, Fructus forsythia 10g, Radix Angelicae Sinensis 10g, Fritillariae Sinensis 15g, Fructus Gorgonii 10g, Dandelion 15g, Herba Epimedium 20g, Cornu Cervi Pantotrichum 10g, Radix Bacopa Monnieri 15g, Radix Paeoniae Alba 10g, total 21.

6. Comments

This child has several recurrences of nephrotic syndrome, with the following symptoms: easy to have external sensation, shortness of breath and weakness, foam in the urine, and easy to be irritable. The above formula, on the basis of benefiting Qi and fixing the surface, regulates the body's Yin and Yang. The above prescriptions regulate the yin and yang of the body on the basis of benefiting the qi and consolidating the surface, thus reducing the incidence of infection in the child and helping to maintain the stability of the disease.

7. Conclusion

The recurrent attacks of nephrotic syndrome are also aggravating the kidney damage, and as the children grow older, the demand for hormones is increasing, and the side effects brought by them are gradually becoming obvious, and the phenomenon of slowing down or stopping the height growth of children due to hormone use is gradually drawing attention.

References

- [1] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.
- [2] Stuck AE, Minder CE, Frey FJ. Risk of infectious complications in patients taking glucocorticosteroids. Rev Infect Dis. 1989 Nov-Dec;11(6):954-63. doi: 10.1093/clinids/11.6.954. PMID: 2690289.
- [3] Chen N, Liu J, Zhao ZQ. Efficacy of intravenous gammaglobulin in the treatment of recurrent nephrotic syndrome[J]. Strait Pharmacology, 2004(06):86-87.
- [4] Chadwin R M, Bain M J, Kass P H. Effect of a synthetic feline facial pheromone product on stress scores and incidence of upper respiratory tractinfection in shelter cats[J]. J the American Veterinary Medical Association, 2017, 251(4):413.
- [5] Chen C, Wang Q, Su ZQ, Peng L, Li JAL, Wang ST. Clinical observation of Yu Ping Feng granules in regulating patients with recurrent colds with Qi deficiency constitution[J]. Chinese Journal of Experimental Formulary, 2018, 24(05):182-187.
- [6] Xu L. Efficacy of adding Yu Ping Feng San during the hormone withdrawal period in the treatment of pediatric nephrotic syndrome[J]. Practical Integrative Chinese and Western Medicine Clinical, 2018, 18(03):59-60.
- [7] LIAO Jian-Ting, HAO Chen-Jing, LI Bo. Research progress on antiviral effects of Fishoilis [J/OL]. Chinese Pharmacology and Clinic:1-12 [2021-09-20].
- [8] Xiang J, Wang YB, Xu T, Fan Y, You H. The role of Astragalus polysaccharides in host resistance to Listeria monocytogenes[J]. Journal of Wuhan University (Medical Edition),2007(06):741-743.
- [9] Zhang D. H., Liu K.W. Bone metabolism-related indicators in pediatric primary nephrotic syndrome[J]. Journal of Clinical Pediatrics, 2017, 35(10):759-761.
- [10] Blodgett FM, Burgin L, Iezzoni D, et al. Effects of prolonged cortisone therapy on the statural growth, skeletal maturation and metabolic status of children[J]. N Engl J Med,1956,254(14):636-

- [11] Li JY. Hormonal withdrawal syndrome[J]. Beijing Medicine,2007(07):427-428.
 [12] Yang D D, Zhan Gramercy. Progress of molecular mechanism and gene regulation of immune regulation by kidney warming and yang tonics[J]. Jiangsu Traditional Chinese Medicine,2004(07):59-61.