

Research Progress on the Diagnosis and Treatment of Nephrotic Syndrome Edema Based on the Theory of Huangdi Neijing Integrating Traditional Chinese and Western Medicine

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Abstract: *Huangdi Neijing, honored as the “Origin of Medicine,” is the foremost of the four major classic texts in traditional Chinese medicine. Nephrotic syndrome (NS) is a clinical syndrome caused by various etiologies, characterized by massive proteinuria, hypoalbuminemia, varying degrees of edema, and/or hyperlipidemia. Edema typically manifests as swelling of the head, face, eyelids, limbs, and abdomen/back. Modern medicine primarily employs diuretic methods for treating NS edema, but these approaches have contraindications and limited efficacy in patients with underlying conditions or severe edema. In contrast, traditional Chinese medicine (TCM) demonstrates unique advantages in treating NS edema and can effectively improve patient prognosis. This paper, based on the theoretical framework of Huangdi Neijing and its fundamental treatment principle for water disorders—“opening the ghost gate, cleansing the pure mansion, and removing stagnation”—and integrating modern medical theories such as the “underfill” and “overfill” hypotheses, systematically reviews the research progress in the diagnosis and treatment of NS edema using integrated Chinese and Western medicine. The aim is to provide more comprehensive theoretical foundations and practical guidance for clinical practice.*

Keywords: Huangdi Neijing, Nephrotic Syndrome; Edema; Integrated Chinese and Western Medicine Diagnosis and Treatment.

1. Introduction

Nephrotic syndrome (NS) is a clinical syndrome comprising a group of glomerular diseases that share similar clinical manifestations but differ in aetiology and pathological changes. Its fundamental characteristics are marked proteinuria (24-hour urine protein excretion exceeding 3.5 g), hypoalbuminaemia (plasma albumin levels below 30 g/L), hyperlipidaemia, and oedema of varying severity [1]. Epidemiological studies indicate that the prevalence of chronic kidney disease among adults in China is on the rise; as a significant component of this condition, the prevalence and incidence of nephrotic syndrome have also shown an upward trend in recent years. Furthermore, it may be accompanied by a range of complications, including infections, thromboembolism and acute kidney failure, which may ultimately result in poor clinical response to drug treatment, high recurrence rates and poor long-term outcomes [2]. Based on current medical research, the primary clinical treatments typically involve the use of hormones and immunosuppressants, among other agents; these drugs may cause adverse reactions of varying severity. Consequently, as modern medical practices continue to evolve, healthcare professionals are exploring ways to improve treatment outcomes for patients, minimise the occurrence of adverse reactions, and reduce associated risks. Traditional Chinese Medicine offers a comprehensive system for the management of nephrotic syndrome, covering everything from diagnosis and treatment to the prevention of relapse and the management of long-term outcomes. It aims not only to treat the physical symptoms of the disease but also to address the patient's emotional well-being, ensuring a holistic approach that addresses both body and mind. In recent years, many practitioners, through continuous study of classical TCM texts and integration with clinical practice, have achieved excellent

results in treating oedema associated with nephrotic syndrome. Consequently, we have recognised the importance of integrated traditional Chinese and Western medicine (TCM-WM) treatment approaches, which have demonstrated significant efficacy. In particular, they are superior to the use of a single treatment modality in many respects, including reducing the recurrence of the condition, enhancing patients' immunity, significantly reducing proteinuria, improving renal function, and minimising the side effects associated with medication [3][4]. Therefore, this paper aims to review recent advances in the integrated TCM-WM treatment of oedema associated with nephrotic syndrome, based on the theories of the Huangdi Neijing.

2. Overview of Nephrotic Syndrome

The diagnostic criteria for nephrotic syndrome are: urinary protein excretion ≥ 3.5 g/24h; plasma albumin ≤ 30 g/L; edema; hyperlipidemia. The first two are essential criteria [5]. Primary glomerular diseases constitute a significant portion of NS. Domestic reports indicate around 40%, while international data suggests a higher prevalence. The disease spectrum shows considerable regional variation, likely related to factors such as age, environment, ethnicity, and renal biopsy indications. Multiple factors including genetics, immunity, infection, drugs, and environment can influence the onset and progression of NS. NS can be classified as primary or secondary, with primary NS being predominant. The fundamental pathological change is damage to the glomerular filtration barrier, and increased permeability to proteins leads to massive proteinuria [6]. The most prominent clinical feature of NS is massive proteinuria. The selective permeability of the glomerulus is maintained by its three-layer filtration membrane structure. Damage to the glomerular filtration membrane's charge and size barrier alters its

selective permeability, ultimately resulting in massive proteinuria and the potential development of NS.

From extensive TCM literature, it is evident that NS does not have a single corresponding disease name. Based on its varying clinical manifestations, it can be categorized under “edema” (shui zhong), “turbid urine” (niao zhuo), “consumptive disease” (xu lao), or “lumbar pain” (yao tong). Among these, edema is the most characteristic symptom. In TCM classics, discussions on edema primarily originate from Huangdi Neijing (referred to as Neijing), which is divided into two parts: Lingshu and Suwen. This medical classic has exerted immense influence on physicians throughout history and maintains high guiding value today, earning its title as the “Origin of Medicine” and the foremost of the four major classics. It offers unique expositions on the etiology, pathogenesis, symptoms, treatment, and prevention of edema. Even regarding the disease name, Neijing contains numerous descriptions such as “kidney wind” (shen feng), “wind water” (feng shui), “stone water” (shi shui), “welling water” (yong shui), and “overflowing fluid retention” (yi yin). The canonical texts discuss it as follows: Suwen·Ping Ren Qi Xiang Lun states: “Pulsation of the neck vessels with panting and coughing indicates water; slight swelling of the eyelids resembling the shape of a resting silkworm indicates water”; “Facial swelling is called wind, swelling of the shins and feet is called water.” Suwen·Shui Re Xue discusses: “The kidney is a female organ... lodging in the subtle pores, traveling within the skin, transmitting to become pedal swelling, its root lies in the kidney, named wind water.” Lingshu·Xie Qi Zang Fu Bing Xing Pian mentions: “The kidney pulse... if very large, indicates impotence; if moderately large, indicates stone water.” Suwen·Qi Jue Lun states regarding edema: “When cold shifts from the lung to the kidney, it becomes welling water.” Although there are many names for edema, all originate from the stagnation and overflow of water-humor, spreading to the skin and muscles, thereby producing swelling. Beyond numerous classical references to the disease name, Neijing also describes the symptoms of edema. Lingshu·Shui Zhang describes: “At the onset of water, there is slight swelling of the upper eyelids, like the appearance of someone newly risen from sleep. The neck vessels pulsate, there is occasional coughing, coldness in the inner thighs, swelling of the shins and feet, and the abdomen becomes large—this indicates water has formed. Pressing the abdomen with the hand, it rises with the hand’s release, like the shape of wrapped water—these are its signs.” Suwen·Shui Re Xue Lunsays: “[Water] overflows up and down to the skin, therefore causing pedal swelling; pedal swelling is the gathering of water that gives rise to disease.” From the above original texts, the main characteristics of edema can be deduced as swelling of the head, face, eyelids, limbs, and abdomen/back.

3. Pathogenesis of Nephrotic Syndrome Edema

The pathogenesis of NS edema is complex, involving multiple pathophysiological links. From a modern medical perspective, massive proteinuria leads to loss of plasma albumin, decreased plasma colloid osmotic pressure, and fluid leakage from blood vessels into the interstitial space, forming edema. Concurrently, reduced effective circulating blood volume activates the renin-angiotensin-aldosterone system (RAAS),

and water-sodium retention further aggravates edema. Additionally, primary renal sodium retention, abnormal antidiuretic hormone secretion, and disturbances in the natriuretic peptide system also contribute to edema formation. Edema can present as pitting edema of the eyelids and lower limbs; in severe cases, it may manifest as generalized edema, pleural and peritoneal effusions, or even pericardial effusion, not only affecting quality of life but also increasing the risk of complications like infection and thrombosis. TCM holds that the pathogenesis of NS edema involves a deficiency root and excess manifestation. Deficiency of the spleen and kidney constitutes the root, while dampness, damp-heat, and blood stasis are the manifestations. The spleen governs transportation and transformation of water-dampness; the kidney governs the steaming and transformation of water fluids. Dysfunction of spleen and kidney leads to water accumulation. Prolonged illness can cause dampness to stagnate and transform into heat, or chronic disease entering the collaterals to form blood stasis, making the condition lingering and difficult to cure. Modern physicians, inheriting traditional theories and combining them with clinical practice, have formed a more comprehensive system of pattern differentiation and treatment. Specifically, the mechanism of edema is analyzed from both Western and TCM perspectives.

From a Western medical perspective, edema results from the accumulation of intravascular fluid in the interstitial spaces. Edema causes an imbalance in body fluid homeostasis due to decreased plasma colloid osmotic pressure, increased capillary hydrostatic pressure, increased capillary wall permeability, and impaired lymphatic drainage. Currently, two hypotheses explain the occurrence of edema. The first is the traditional “underfill” hypothesis: hypoalbuminemia leads to decreased plasma colloid osmotic pressure, fluid leaks from blood vessels into the interstitium, reducing effective circulating blood volume. This in turn activates the RAAS system and increases antidiuretic hormone (ADH) secretion, while decreasing atrial natriuretic peptide (ANP) secretion, ultimately leading to increased renal reabsorption of sodium and water, thereby worsening edema. The second is the modern “overfill” hypothesis: this theory posits that sodium and water retention caused by decreased glomerular filtration rate and increased tubular reabsorption are key factors aggravating NS edema. Studies indicate that overactivation of the epithelial sodium channel (ENaC) in renal tubular cells plays a significant role in this process. Thus, edema formation is not static but a dynamic process; both hypotheses may play a role at different stages or in different patients. Edema often manifests in dependent areas of the body, closely related to posture. In a supine position, sacral edema is more noticeable; in a standing position, edema is more apparent in the lower limbs, ankles, and feet. The edema is pitting and typically milder in the morning after rest, worsening in the afternoon and evening after activity. Severe cases may present with pleural, peritoneal, pericardial, or mediastinal effusions, and can even lead to acute pulmonary edema. For instance, patients with ascites may experience abdominal distension, nausea, and vomiting.

Traditional Chinese medicine has a long-standing understanding of oedema associated with nephrotic syndrome, and medical practitioners throughout the ages have accumulated a wealth of experience in its diagnosis and

treatment. Analyzing from the perspective of Neijing, the etiology and pathogenesis of edema include water-dampness overflow, dysfunction of the zang-fuorgans, as well as external contraction and internal damage. The core pathogenesis lies in the dysfunction of the lung, spleen, and kidney, leading to abnormal water metabolism in the triple burner (sanjiao). Discussions related to edema diseases are scattered throughout various chapters. Suwen·Shui Re Xue Lun states: “The kidney is the gate of the stomach.” “Its root is in the kidney, and its branches are in the lung.” Specifically, the kidney, as the water organ, governs water metabolism and is the root of edema occurrence; the lung, as the upper source of water, governs diffusion, depurative down bearing, and regulating the water passages, and is the external manifestation (branch) of edema. This clearly points out the key role of the kidney in water metabolism. Zhang Jiebin further elaborated: “Lung deficiency leads to qi failing to transform essence but transforming into water; spleen deficiency leads to earth failing to control water but being counter-restrained; kidney deficiency leads to water having nothing to govern and moving recklessly.” This explains the important role of lung, spleen, and kidney dysfunction in causing edema. It is concluded that the occurrence of edema is closely related to dysfunction of the lung, spleen, kidney, and other organs, and abnormal water metabolism in the triple burner. Neijing also contains related descriptions, such as spleen disease edema: Suwen·Mai Yao Jing Wei Lun says: “The spleen pulse... if soft and scattered, with dull complexion, the disease will be swelling of the feet, resembling a water condition.” This suggests the role of impaired spleen transportation in edema formation. Additionally, there are discussions on yang deficiency edema, e.g., Suwen·Sheng Qi Tong Tian Lun states: “Swelling due to qi, with the four limbs alternating [in swelling], yang qi is exhausted.” Suwen·Shui Re Xue Lun also mentions: “The qi ascending from the earth belongs to the kidney and generates water fluids”; “The kidney is the gate of the stomach; if the gate does not function properly, water gathers accordingly.” These explain the complex pathogenesis of edema from different angles. In cases of yang deficiency edema, symptoms such as aversion to cold, cold limbs, clear and copious urine, pale tongue with white coating appear. For damp-heat edema, symptoms include irritability, thirst, scanty and dark urine, red tongue with yellow greasy coating. Such diseases require regulating yin and yang to resolve swelling and achieve a cure.

4. Integrated Chinese and Western Medicine Treatment for Nephrotic Syndrome Edema

4.1 Western Medical Treatment

Currently, in Western medicine, oedema associated with nephrotic syndrome is predominantly treated with diuretics. For most patients, the standard approach to reducing oedema involves restricting salt and fluid intake and bed rest to alleviate sodium and water retention; if this proves ineffective, diuretics are prescribed. Commonly used diuretics currently include thiazide diuretics, potassium-sparing diuretics, loop diuretics and osmotic diuretics [7]. Mild edema often uses thiazides and/or potassium-sparing diuretics; loop diuretics are usually chosen for moderate to severe edema. If efficacy is poor, combination with thiazides can achieve better results.

Furosemide is the most common loop diuretic, which can be administered orally or intravenously, requiring monitoring of electrolytes to avoid side effects like hypokalemia and hyponatremia. Osmotic diuretics like dextran-40 (low molecular weight dextran) [8] can increase plasma colloid osmotic pressure and expand blood volume to achieve diuresis, but caution is needed to avoid inducing acute kidney injury. For refractory edema, other drugs like tolvaptan, although not primarily indicated for NS edema, can promote water excretion by antagonizing antidiuretic hormone receptors without affecting electrolytes, showing good efficacy and safety, and have been found clinically effective for NS edema [9]. For hypoalbuminemia, intravenous human albumin can be administered, but only in cases of severe hypoalbuminemia (serum albumin <20g/L) with refractory edema or acute complications, and should be combined with diuretics to avoid volume overload. For the underlying cause of NS, corticosteroids and immunosuppressants are often needed to control proteinuria.

4.2 Traditional Chinese Medicine Treatment

From Neijing, it can be deduced that the treatment for edema involves methods to regulate qi and move water. The treatment principle is “regulating and smoothing qi movement” and “warming yang to transform water.” For zang-fu pattern differentiation: treating the spleen — Suwen·Zhi Zhen Yao Da Lun Pian states: “All dampness, swelling, and fullness belong to the spleen”; emphasizing the importance of the spleen governing transportation of water-dampness. Treating the spleen commonly uses methods to fortify the spleen and disperse water or warm yang and fortify the spleen. Treating the lung—there is the saying “the lung governs moving water”; treating the lung can treat water. By diffusing lung qi and regulating the water passages, the effect of “lifting the lid of the pot” is achieved. Treating the kidney—the kidney is the water organ; the kidney qi’s “opening” and “controlling” govern the storage, distribution, and excretion of water within the body. “Opening” and “controlling” mainly depend on the coordinated function of kidney yin and kidney yang; treating the kidney treats the root. The triple burner is the official of the ditches; treating the triple burner means regulating the water passages. The overarching principle of TCM treatment for edema is harmonizing yin and yang, warming yang, supplementing yang, and freeing yang to restore zang-fu function. Huangdi Neijing provides the theoretical outline for edema treatment. The specific treatment principle is from Suwen·Tang Ye Lao Li Lun: “Qibo said: [The treatment should] balance and weigh [the condition], remove stagnation and accumulation, gently move the four extremities, keep warm clothes, use even needling at the affected area to restore the body’s form. Open the ghost gate, cleanse the pure mansion, essence is taken timely, the five yang [qi] are spread, and the five zang are cleansed.” “Balancing and weighing” is the general principle for treating edema, weighing the severity and urgency of the condition. “Removing stagnation and accumulation” encompasses both attacking and expelling water and removing stagnant blood. “Opening the ghost gate” refers to promoting sweating; “cleansing the pure mansion” refers to promoting urination. The overall treatment principle is to warm yang, regulate qi, and move water. Zhang Zhongjing in Jinkui Yaolue also proposed the treatment principle: “For all those with water, if

swelling is below the waist, promote urination; if swelling is above the waist, promote sweating to cure,” laying the foundation for the later method of separating and dispersing [pathogens] for discharge. Regarding research on single formulas and empirical prescriptions, various Chinese medicinal herbs and their active components have shown good effects in disinhibiting water and reducing swelling. Astragalus (Huangqi), as an important herb for supplementing qi and disinhibiting water, its active component astragaloside IV can exert diuretic effects by regulating aquaporin expression and inhibiting RAAS activity. Combining diuretic and dampness-percolating herbs like Poria (Fuling), Alisma (Zexie), and Polyporus (Zhuling) can enhance glomerular filtration rate and promote sodium and water excretion. Tripterygium glycoside tablets, a commonly used Chinese patent medicine, have dual immunomodulatory and anti-inflammatory effects, demonstrating definite efficacy in reducing proteinuria and eliminating edema, but their reproductive toxicity and effects on liver and kidney function require monitoring. Additionally, Rheum (Dahuang), through its purgative, accumulations-removing, and blood-activating, stasis-dispelling effects, can improve renal microcirculation and delay glomerulosclerosis progression.

Modern physicians also have unique insights into external TCM treatments for edema. For example, buckwheat pack external application on both lower limbs is considered an ideal external application material [10]; Bingxiao San (Ice-Niter Powder) can also be an effective supplementary treatment for NS edema, improving patient quality of life [11]; regarding acupuncture treatment for edema, the “fifty-seven water points” mentioned in Suwen-Gu Kong Lun and Suwen-Shui Re Xue Lun also have good therapeutic effects for edema; Chinese herbal fumigation and steaming therapy utilizes the warming effect and pharmacological action of medicinal steam, opening the skin’s interstices through sweating to resolve water-dampness pathogens, especially suitable for cases with pronounced upper body edema; standardized application of thunder-fire moxibustion on points like Yongquan (KI1), Zusanli (ST36), and Shenshu (BL23) can enrich yin and down bear fire, disinhibit water and reduce swelling, and enhance spleen-stomach transportation capacity, but care must be taken to avoid adverse risks and burns [12]; the five-phase generation and restriction needling method can also improve NS edema through the relationships of the five phases [13]; acupoint application as an auxiliary treatment method, such as applying Guben Peiyuan Xiaoshui Gao (Consolidate the Root and Foster the Source Reduce Water Paste), also shows certain efficacy for patients and can help minimize organ damage [14][15]. These external treatment methods are simple to operate, have few side effects, and when used synergistically with oral medications, can enhance overall efficacy.

4.3 Integrated Chinese and Western Medicine Treatment

In recent years, research on integrated Chinese and Western medicine treatment for NS edema has made numerous advances. The aim is to combine strengths and compensate for weaknesses, improve efficacy, and reduce side effects. Regarding pattern differentiation, most physicians classify it into root patterns and manifestation patterns. Common root patterns include lung-spleen qi deficiency, spleen-kidney

yang deficiency, liver-kidney yin deficiency, and qi-yin deficiency. Manifestation patterns include water-dampness, damp-heat, blood stasis, and external contraction. Treatment emphasizes supporting the healthy qi and dispelling pathogens simultaneously, applied flexibly according to the urgency of root and manifestation. For different stages of corticosteroid therapy, Chinese medicine can play a “toxicity-reducing and efficacy-enhancing” role, adopting a staged treatment strategy: during the initial high-dose stage, patients often manifest yin deficiency with fire effulgence, treated by enriching yin and down bearing fire with formulas like modified Zhibai Dihuang Wan (Anemarrhena, Phellodendron, and Rehmannia Pill), which can mitigate corticosteroid side effects like Cushing’s syndrome and hyperglycemia; during the dose-reduction stage, spleen-kidney yang deficiency is common, treated by warming and supplementing the spleen and kidney with modified Shi Pi Yin (Bolster the Spleen Decoction) or Zhen Wu Tang (True Warrior Decoction), which can prevent disease relapse; during the maintenance stage, the focus is on supplementing qi and nourishing yin to consolidate efficacy. This dynamic pattern differentiation approach effectively alleviates corticosteroid side effects and improves patient sensitivity to corticosteroids. While using Western diuretics, combining Chinese herbs that disinhibit water and percolate dampness or warm yang and disinhibit water can enhance diuretic effects and reduce electrolyte disturbances. Clinical studies show that integrated treatment plans are superior to Western medicine alone on multiple indicators. A randomised controlled trial involving 240 patients with primary nephrotic syndrome showed that the complete remission rate in the group receiving combined traditional Chinese and Western medicine was 68.3%, significantly higher than the 51.7% observed in the group receiving Western medicine alone. The recurrence rate was reduced by approximately 15%, and the incidence of complications such as infections was significantly lower. For refractory NS, integrated strategies provide new treatment options by regulating immune status, improving corticosteroid resistance, and protecting residual renal function. For pathological types like membranous nephropathy and focal segmental glomerulosclerosis, adding blood-activating, stasis-dispelling, and softening-hardness, scattering-nodulation herbs based on TCM pattern differentiation can improve pathological remission rates. Beyond oral medications, combining external treatments like Chinese herbal external application, moxibustion, and acupoint application can eliminate local edema more rapidly and safely, improving patient quality of life.

5. Conclusion and Prospects

In modern clinical practice, doctors analyse each patient’s specific circumstances and apply a syndrome-differentiation approach based on classical theories. Nephrotic syndrome is a clinical syndrome characterised by multiple symptoms and a wide variety of pathological types, and it poses a significant risk to patients. Extensive clinical experience has demonstrated that relying solely on medication or a single therapeutic approach is unlikely to yield optimal results. Only by combining multiple therapeutic modalities—leveraging their respective strengths to compensate for their weaknesses and complement one another—can one achieve twice the result with half the effort. Modern medical technology

provides a solid foundation for understanding the mechanisms by which Traditional Chinese Medicine (TCM) acts on the body, offering scientific evidence for clinical application and serving as a valuable reference for clinicians seeking to understand TCM. Compared to TCM, Western medical treatments tend to be more limited in scope and may be associated with adverse reactions and poor prognoses. TCM treatments are currently undergoing continuous development and offer a diverse range of therapeutic approaches with unique advantages. Consequently, the management of oedema associated with nephrotic syndrome through modern medicine should incorporate a variety of effective therapeutic strategies.

Although the integrated treatment of nephrotic syndrome oedema using both traditional Chinese and Western medicine has achieved significant results, a number of issues remain to be addressed. Currently, most clinical studies are single-centre, small-scale trials, and there is a lack of high-quality, evidence-based medical data from large-scale, multi-centre, randomised, double-blind trials; the criteria for TCM pattern differentiation have not yet been fully standardised, and the system of efficacy evaluation indicators requires further standardisation; the targets and molecular mechanisms of action of the active components in Chinese herbal medicines still need to be elucidated in greater depth; Establishing individualised and precision-oriented integrated treatment regimens represents a key direction for future research. With the application of new methodologies such as systems biology and network pharmacology, research into the mechanisms underlying the integrated treatment of oedema associated with nephrotic syndrome will become more in-depth, offering the prospect of providing optimised treatment strategies for clinical practice. The integrated treatment of diseases through a combination of traditional Chinese and Western medicine aims to enhance patients' quality of life, improve their prognosis, achieve optimal therapeutic outcomes, and treat both the physical and mental aspects of the patient, thereby achieving the goal of holistic health.

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