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Experience in Treatment of Hepatitis B-related Nephritis with Integrated Traditional Chinese and Western Medicine

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Abstract
The traditional Chinese medicine treatment of hepatitis B-related nephritis should adhere to the concept of "concurrent treatment of liver and kidneys," with "reinforcing kidneys and regulating the liver" as the main strategy and "detoxification and collateral dredging" as the auxiliary strategy. Clinicians must also pay much attention to and prevent the occurrence of "*guan* (urinary obstruction)" and "*ge* (vomiting)" in patients. Modern medical treatment should keep the hepatitis B virus under control to avoid further damage to the liver and kidneys. In addition, avoiding drugs and behaviors that may damage the liver and kidneys should not be neglected.
Keywords: Hepatitis B-related nephritis; Concurrent treatment of liver and kidneys

Background

Hepatitis B-related nephritis (HBV-GN) is a major extrahepatic pathology after hepatitis B virus (HBV) infection. Hematuria, proteinuria, edema, and positive HBV markers are the main clinical features, and the disease can even progress to terminal renal failure. At present, there is no mature treatment strategy for this disease.

Based on modern research and many years of clinical experience, the author has some thoughts on the treatment of hepatitis B-related nephritis with integrated traditional Chinese and Western medicine, which are organized as follows:

1. Traditional Chinese medicine treatment of HBV-GN

1.1 Taking "reinforcing kidneys and regulating the liver" as the main strategy and adhering to the concept of "concurrent treatment of liver and kidneys."

"Treating liver diseases by reinforcing the kidneys" is one of the author's academic ideas. Zhong Jing's view that "once a liver disease is discovered, it should be known that the liver disease will be transmitted to the spleen, so the spleen should be reinforced first" is well known, but the author values the view that "once a liver disease is discovered, its origin must be in the kidneys, so the kidneys should be reinforced first" even more. Kidney reinforcement includes kidney *qi* (vital energy) reinforcement, kidney *jing* (essence) reinforcement, kidney *yin* reinforcement, and kidney *yang* reinforcement, etc. Common kidney reinforcement medications include: Kidney *qi* reinforcement: Liu-Wei-Di-Huang decoction combined with Panax quinquefolium or Radix Pseudostellariae, etc.; kidney jing reinforcement: Cynomorium songaricum, Rosa laevigata, etc.; kidney *yin* reinforcement: Ligustrum lucidum, Corni Fructus, etc.; kidney *yang* reinforcement: Cuscuta chinensis, Herba Epimedii, etc.

HBV-GN is a refractory disease. Why should we adhere to the concept of the "concurrent treatment of liver and kidneys"? There are three reasons [1]: First, the development and persistence of chronic liver diseases are caused by deficiency of kidney *jing*, due to congenital deficiency, weakness of the body, or deficiency of *jing* and blood resulting from chronic disease and body weakness, or from excessive labor or sexual indulgence, leading to imbalance between *yin* and *yang*, a decline in the body's disease resistance and inability to eliminate pathogenic factors, thus resulting in disease development. Second, the liver and kidneys are all located in the lower *jiao* and originate from *jing* and blood. The liver and kidneys show close interactions like mother and child, and their pathological changes will inevitably affect each other. Chronic liver diseases are caused by deficiency of kidney

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jing, as well as liver deficiency due to the lack of nourishment by (original essence). After developing the disease, pathogenic factors remain stagnant for a long time, which can also affect the kidneys, causing damage to kidney *yin* and kidney *yang*, resulting in a situation of "concurrent liver and kidney diseases." Third, HBV is a pathogenic factor characterized by damp-heat and epidemic toxin, and has a trend of downward transmission. It can also directly damage kidney *yin* and kidney *yang* (just like the pathogenesis of HBV-GN), so it is more appropriate to refer to it as "simultaneous liver and kidney diseases." In summary, because of "simultaneous liver and kidney diseases," "concurrent treatment of liver and kidneys" is necessary.

"Harmonizing the blood and regulating the liver" has always been the author's basic idea for treatment to inhibit the progression of liver cirrhosis. Although "static blood blocking the collaterals" is the core pathogenesis of liver cirrhosis, static blood cannot be treated simply by removing blood stasis. Instead, it should be based on the idea of "harmony," i.e., blood circulation should be promoted on the basis of enriching and nourishing blood. As the saying goes, "if you want to dredge it, you must first enrich it." This is the essence of harmonizing the blood and regulating the liver. To harmonize the blood, Tao-Hong-Si-Wu decoction or Salvia miltiorrhiza, Panax notoginseng, Radix Paeoniae Rubra, etc., are commonly used.

1.2 While "reinforcing kidneys and regulating the liver," "detoxification and collateral dredging" should not be neglected.

Hepatitis B is caused by toxic pathogens and is bound to enter the collaterals if the infection persists for a long time. Therefore, the treatment must be supplemented by the method of detoxification and collateral dredging. Common antidotes include Forsythia suspensa, Vigna umbellata, and Phyllanthus urinaria. Commonly used collateral-dredging drugs include Curcuma zedoaria, Fructus Polygoni Orientalis, and Euonymus alatus. Among them, the author gained the experience of administering Forsythia suspensa and Vigna umbellata from Yao Zhengping, a nephrologist at the Beijing Traditional Chinese Medicine Hospital, during the author's early years of practice. Yao believed that stranguria is related to prolonged accumulation of damp-heat. Therefore, to achieve detoxification, heat clearance and dampness elimination should not be neglected. Vigna umbellata can clear heat, expel carbuncles, and disperse extravasated blood and has the propensity to alleviate water retention. Forsythia suspensa has the effects of heat clearing and detoxification, promotes qi circulation, and enters the heart channel (the heart and small intestine share an internal-external relationship). Therefore, the combined use of these two medicines produces a good detoxification effect. Curcuma zedoaria and Fructus Polygoni Orientalis are a drug-pair routinely used by the author. The author gained the experience of administering Fructus Polygoni Orientalis from Yuan Shuzhang, a pediatrician and senior traditional Chinese medicine practitioner, during the author's early years of practice. Yuan developed "Yang-Xue-Rou-Gan Pills (blood-nourishing and liver-emolliating pills)" for the treatment of pediatric liver cirrhosis. He once said, "The miracle of the Yang-Xue-Rou-Gan Pills lies in Fructus Polygoni Orientalis." This medicine is effective in promoting blood circulation and diuresis. The author often pairs it with Curcuma zedoaria as the first choice for dredging collaterals.

1.3 It is also necessary to stay alert to the occurrence of "*guan*" and "*ge*" syndromes at all times to prevent deterioration of the disease.

In the whole treatment process of HBV-GN, clinicians must always be vigilant to and prevent the occurrence of "*guan ge*" syndrome. "*Guan*" and "*ge*" are the main syndromes in the uremic phase of chronic renal insufficiency. The book *Shoushi Baoyuan* (*Protection of Vital Energy for Longevity*) states, "Urinary obstruction … makes people vomit. This is called *guan ge*." *Zhubing Yuanhou Lun* (*Treatise on the Causes and Manifestations of Diseases*) states, "Those with guange cannot die a natural death." It can be seen that the appearance of these two syndromes is a sign of deterioration of the disease and must be suppressed as early as possible.

The specific treatment approaches are as follows: At the onset of the ge syndrome, anorexia, epigastric discomfort, and relatively strong mouth odor are common. The treatment approaches of "harmonizing the stomach and calming down the adverse rising of stomach *qi* and dredging hollow organs and suppressing turbidity" should be urgently applied, with prescription of Xiao Banxia Jia Fuling decoction and Tiao-Wei-Cheng-Qi decoction [2]. At the beginning of the guan syndrome, it is common that the total urine volume in 24 hours exceeds 3000 ml, i.e., the uremic oliguric phase will be preceded by a period of polyuria. The treatment approaches of "tonifying kidneys, reducing urination, and restoring the urinary bladder *qi*" should be urgently applied, with prescription of a combination of Suo Quan pills

and Sang Piao Xiao powder.

2. Key points and precautions in modern medical treatment of HBV-GN

2.1 Controlling HBV and avoiding further damage to the liver and kidneys are key points in modern medical treatment.

For the treatment of HBV-GN, there are two main clinical concerns: Antivirus and immunosuppression. Antiviral drugs mainly include interferons and nucleoside analogues. Since antiviral treatment can inhibit HBV replication and reduce proteinuria, it has been recommended for the treatment of HBV-GN clinically in Western medicine. The author strongly agrees with the application of antiviral drugs for the following reasons: The fundamental cause of HBV-GN is that the immune complex formed by the binding of HBV with the corresponding antibodies produced by the body is deposited in glomeruli, thus causing a series of pathological changes in the kidneys. This disease is chronic and persistent. If glomeruli are continuously damaged, it will eventually lead to chronic renal insufficiency. Therefore, effective control of HBV and prevention of further damage to the liver and kidneys are the top priorities for the treatment of the disease.

There are still many disputes about the application of hormones and immunosuppressants [3]. Traditional Chinese medicine has unique advantages in relieving HBV-GN symptoms and controlling disease progression. Combined with the application of antiviral drugs, the treatment of HBV-GN by integrated traditional Chinese medicine and Western medicine has achieved significant effects. Therefore, the author does not support hormones and immunosuppressants as the first choice.

2.2 Drugs and behaviors harmful to the liver and kidneys should be avoided.

When using nucleosides to treat HBV-GN, attention should be paid to the potential renal damage that may be caused by nucleosides. Since adefovir dipivoxil is potentially nephrotoxic and should be avoided, lamivudine and entecavir are the preferred antiviral drugs for HBV-GN. Another example is that the intermediate metabolite of alcohol may cause hepatotoxicity and will increase burden on kidneys. Therefore, to prevent liver damage by alcohol intoxication, no alcoholic beverages can be drunk. In addition, frequent sexual activities can hurt one's health, and contraceptive failure will further aggravate the condition in female patients, so special caution should be taken.

3. Case example

The patient Meng, a 42-year-old male, paid his first visit to the hospital on March 12th, 2015. Hepatitis B infection was detected during a health examination 25 years ago and was not treated. In the past month, the patient experienced recurrent waist soreness, fatigue, and edema of both lower limbs. Renal biopsy supported the diagnosis of "hepatitis B-related nephritis." After treatment with various drugs, the effect was not significant, so he visited the author's clinic for diagnosis and treatment.

Signs and symptoms at the time of consultation: Waist soreness, weakness, and edema of both lower limbs. The patient defecated once daily or every other day, with normal stool texture. The tongue was light red, with thin and white coating, and the pulse was sunken and thin. Family history of hepatitis B: (-). Physical examination: The patient showed normal blood pressure, mental exhaustion, dark complexion, no yellow staining on skin or sclera, soft abdomen, impalpable liver and spleen, no tenderness or rebound tenderness, shifting dullness (+). Pitting edema of both lower limbs (+). Auxiliary examination: HBsAg(+), HBeAg(+), anti-HBc(+), HBV-DNA 2.1×10^6 copies/ml, ALT 88 U/L, TP 63 g/L, ALB 41.2 g/L, BUN 3.7 mg/dl, urine protein (++), occult blood (+), 24-hour urine protein quantification 0.359 g/24 h, and HGB 88 g/L. B-mode ultrasonography: Liver cirrhosis and splenomegaly. Renal biopsy report: Glomerulosclerosis, moderate diffuse proliferation of glomerular mesangial cells and matrix, HBsAg(+), and HBeAg(+); combined with the clinical manifestations, the findings are consistent with hepatitis B-related nephritis. Western medicine diagnosis: Hepatitis B-related nephritis, hepatitis with hepatic cirrhosis, decompensated phase of hepatitis B. Traditional Chinese medicine diagnosis: Edema and tympanites. Syndrome differentiation: Deficiency of liver and kidneys and incomplete elimination of stasis and toxin. Treatment: Tonifying liver and kidneys, detoxification, and dredging collaterals. Prescription: 1) Ligustrum lucidum 15 g, Fructus corni 10 g, Cuscuta chinensis 15 g, unprepared Radix Astragali 30 g, Angelica sinensis 15 g, Forsythia suspensa 15 g, Vigna umbellata 30 g, Salvia miltiorrhiza 20 g, Phyllanthus urinaria 30 g, and Hedyotis diffusa 30 g. A total of 14 doses were prescribed, to be decocted in water, with one dose to be consumed every two days; specifically, half a dose is to be taken at

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one hour after breakfast every day. 2) Entecavir is recommended as the antiviral therapy.

On April 9th, 2015, the patient paid his second visit. The waist soreness and fatigue had alleviated, and the edema of both lower limbs had improved. The patient could sometimes detect mouth odor. The urine was slightly yellow. The patient defecated once daily or every other day, with dry stools. The tongue and pulse findings remained the same. Examinations: Urine protein (+), occult blood (+), and 24-hour urine protein quantification 0.288 g/24 h. The above treatment was continued with the addition of Radix et Rhizoma Rhei preparata 8 g and Radix Paeoniae Rubra 15 g. A total of 14 doses were prescribed, to be decocted in water, with one dose to be consumed every two days; specifically, half a dose is to be taken one hour after breakfast every day.

According to the patient's condition, one dose every day was applied when the condition was acute and severe, and one dose every other day or one dose every three days was applied when the condition was mild. While adhering to the therapeutic principles of "regulating and nourishing the liver and kidneys, and detoxification and dredging collaterals," close attention was paid to whether the patient developed early manifestations of "*guan ge*." By paying special attention to the presence of symptoms such as "strong mouth odor, nausea, vomiting, and anorexia" and the urine volume, corresponding approaches were taken according to the syndrome, including harmonizing the stomach and calming down adverse rising of stomach *qi*, dredging hollow organs and suppressing turbidity, tonifying kidneys, and reducing urination. The patient's condition had been stable and had not evolved into chronic renal insufficiency. His last visit was on September 12th, 2019. Signs and symptoms: The patient could detect mouth odor and could easily sweat without cause. The urine volume was normal. The tongue color was light, the coating was thin and yellow, and the sublingual vessels were normal. The pulse was sunken and thin. Physical examination: The blood pressure was normal, the abdomen was soft, and no edema was observed in either lower limb. Auxiliary examination: Hepatitis B with positive results for HBsAg, HBeAb, and anti-HBc, HBV-DNA(-). The hepatic and renal functions were normal, and 24-hour urine protein quantification was 0.19 g/24 h. Blood routine: HGB 95 g/L. Abdominal B-mode ultrasonography: Liver cirrhosis and splenomegaly. The treatment approaches of regulating and nourishing liver and kidneys, and detoxification and dredging collaterals were continued. At the same time, Quattuor Immortales Usti and unprepared and prepared Rheum officinale were added to strengthen the effect of dredging hollow organs and suppressing turbidity. Prescription: Ligustrum lucidum 20 g, unprepared Radix Astragali 30 g, unprepared Rehmannia glutinosa 20 g, Angelica sinensis 15 g, Radix Paeoniae Alba 20 g, Radix Salviae Miltiorrhizae 20 g, Quattuor Immortales Usti materials, unprepared Rheum officinale 6 g, prepared Rheum officinale 6 g, Semen Persicae 12 g, Carthamus tinctorius 6 g, and Cortex Moutan 15 g. A total of 20 doses were prescribed, to be decocted in water, with one dose consumed every two days; specifically, half a dose is to be taken one hour after breakfast every day.

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