

# *Research Progress of Chinese Medicine in the Treatment of Diabetic Neurogenic Bladder*

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**Abstract:** The etiology of diabetic neurogenic bladder is not very clear. The main manifestations are frequent urination, urgency, inadequacy and bladder urine retention, and even renal dysfunction. It seriously affects the quality of life of DNB patients. The treatment of DNB should be combined with other schemes on the basis of blood glucose control. The effect of Western Medicine on DNB is not obvious. In traditional Chinese medicine, DNB belongs to the category of "Xiaoke" and "dysuria". It is considered that its etiology and pathogenesis are mostly kidney qi deficiency and stagnation of blood stasis. The disease is treated by means of traditional Chinese medicine, acupuncture, moxibustion, acupoint application, traditional Chinese medicine package, ear acupoint application and so on. The total effective rate of the treatment group is  $\geq 80\%$ , which is significantly higher than that of the control group. Therefore, traditional Chinese medicine has a good curative effect on DNB.

## 1. Introduction

Diabetic neurogenic bladder (DNB) is an easily neglected disease in the later stages of diabetes mellitus, mainly manifesting as frequent urination, urgent urination, incomplete dripping and bladder urine retention, while prolonged urine retention can cause urinary tract infection, urinary tract infarction, and even renal function damage, the initial symptoms of patients are not obvious, but with the development of the disease will appear a series of the above symptoms, the incidence of this disease in the diabetic complications is 25%-85% [1]. The exact pathological mechanism of DNB is not yet clear, but it is closely related to whether diabetes is combined with peripheral neuropathy, but not significantly related to the gender and age of the patient.

## 2. Modern Research

### 2.1. Modern medical understanding of the disease

The etiology of DNB is complex, and research has focused on neuropathy, alterations in the detrusor muscle, changes in the uroepithelium, morphological and functional changes in the urethra,

oxidative stress injury, and the role of bladder Cajal interstitial cells (ICC) [2]. Due to the combined effects of diabetic osmotic diuretic effect, metabolic disorders, peripheral microvascular damage and diabetic neuropathy, the dysfunction of the forceps cells, urinary epithelial cells and nerve conduction structures is caused. In the early stage of the disease, the main manifestation of bladder dysfunction due to overactivity of the forceps muscle is storage phase symptoms, such as urinary frequency and urge incontinence. In the late stage of pathogenesis, excessive accumulation of oxidative stress and endoplasmic reticulum stress reaction products and massive apoptosis of the detrusor muscle cells lead to a further decrease in detrusor contractile function, mainly manifesting as symptoms of bladder hypermobility, such as urinary retention, dysuria, and filling incontinence, and secondary to different degrees of upper urinary tract damage, eventually leading to chronic renal insufficiency.

## **2.2. Western medical treatment**

Based on general treatment such as controlling blood sugar and instructing patients to urinate on time, DNB patients are given pharmacological treatment as well as non-pharmacological treatment [3-4]. Pharmacological treatments include drugs that increase the release of cholinergic neurotransmitters, aldose reductase inhibitors,  $\alpha$ 1-adrenoceptor blockers, 5-hydroxytryptamine (5-HT) receptor agonists,  $\alpha$ -lipoic acid, and new target drugs. Non-pharmacological treatment includes catheterization, cytotherapy, surgery, gene therapy, neuromodulation and electrical nerve stimulation, etc. Intermittent clean catheterization can improve the quality of life of patients [5]. In conclusion, there are various Western medical treatments, but the clinical efficacy is not obvious.

## **3. Traditional Research**

### **3.1. Chinese medicine understanding of diabetic neurogenic bladder**

Compared with modern medicine, there is no clear record of the name of DNB in Chinese medicine, and modern doctors mostly classify this disease as "thirst" combined with "retention of urine" according to its clinical manifestations. It is believed that the disease is mainly located in the kidney and bladder, and is closely related to the lung, spleen, liver, heart, small intestine and Sanjiao. Sheng Ji General Record" pointed out that "thirst for a long time, kidney gas injury, kidney main water, kidney gas failure, abnormal gasification, opening and closing adverse."The Suwen - Wu Chang Zheng Da Lun said, "The disease of retention of urine is caused by the evil that injures the kidneys." It clearly states that the occurrence of retention of urine is related to the kidney. It can be seen that thirst for a long time and damage to kidney energy are the internal causes of the disease. Chen Hang et al. [6] concluded that the pathogenesis of this disease is due to the imbalance of the kidney's water-drinking function, blood stasis and water stagnation, and internal obstruction of the bladder. Thirst for a long time, body weakness and weakness of Qi, the inability to promote blood flow, long-stopped into stasis, long-term disease and kidney, kidney Yang deficiency, the vital gate fire failure, bladder gasification without the right, and drowning cannot come out, blood stasis and water stopping that is born. At the same time, thirst for a long time, injury and depletion of qi, qi and yin deficiency, qi deficiency is unable to push the blood to run, yin deficiency blood stagnation, can make the blood to run unfavorably, the formation of blood stasis. Therefore, the pathogenesis of this disease is based on kidney deficiency and blood stasis as the symptom. Pan Qiu [7] treated elderly DNB patients from the theory of "phase fire" and concluded that the pathogenesis lies in the loss of vital energy, deficiency of vital yang, and the prevalence of water-cold, forcing the fire to cross over to the upper floating level, with the yang floating over and the yin fire leaving the position, resulting in the bladder not being able to qi-chemistry, and the deficiency of middle qi, and

the failure of astringency or transportation, resulting in the development of the disease due to unfavorable water channels.

## 3.2. Chinese Medicine Treatment

### 3.2.1. Traditional Chinese medicine prescription treatment

Wang Cai-di [8] studied 80 patients with DNB with deficiency of kidney yang and divided them into two groups of 40 cases each. In addition to the individually applicable conventional treatment for diabetes, the study group was given Fu Ling Si Wei Tang (Poria 30g, Ginseng tablet 10g, Radix et Rhizoma 10g, Dried ginger 10g, Roasted licorice 10g). One dose was given daily, and 300mL was decocted routinely and taken orally in 2 doses; the control group was given methylcobalamin tablets orally, 0.5mg each time, 3 times daily. The total effective rate after 2 months of treatment was 79.5% in the study group and 55.3% in the control group.

Fu Yang-Xi [9] studied 60 patients with DNB and divided them into 2 groups according to Dolls clinical case randomization table, 30 cases in each group. Under the premise of giving the basic treatment of diabetes, the control group was given methylcobalamin capsule orally, 0.5 mg, 3 times daily. In the treatment group, zhuling soup with added flavor was given on the basis of the treatment of the control group. One dose was taken daily, and 300mL of juice was decocted in water and taken in 2 warm doses. After taking the medicine for 1 month, the pre- and post-treatment comparison of the Chinese medical evidence efficacy was 93.3% for the treatment group and 83.3% for the control group, and the pre- and post-combined efficacy ratio was 93.3% for the treatment group and 80.0% for the control group.

Wang Haojie et al. [10] used a randomized parallel controlled study method to randomly divide 64 patients with DNB with kidney deficiency and blood stasis into a control group and a treatment group of 32 patients each, according to the order of enrollment. In the control group, under the premise of diabetic lifestyle intervention, oral medication or insulin subcutaneous injection was chosen to control blood glucose in the ideal range, and methylcobalamin tablets, 500 µg/d, 3 times/d, were given orally. In the treatment group, on top of the treatment in the control group, deer antler formula (Medicinal deer antler slices, saltbush, roasted astragalus, raw groundnut, codonopsis, motherwort, hyssop, cistanches) with the effect of tonifying the kidney and activating blood was given. After 8 weeks of continuous treatment with the drug, the total effective rate of the treatment group reached 90.6%, compared with 62.5% in the control group.

According to academician Tong Xiaolin [11], the treatment of DNB requires "promoting qi, promoting water, and promoting stasis", of which the most important is promoting qi. The use of orange kernels, lychee kernels, and sedum powder in treating various stages of DNB is exactly in line with the basic pathogenesis of DNB, and can be used as a basic medicine regardless of heat or cold. The efficacy of applying this medicine in the treatment of DNB is satisfactory and the quality of life of patients has been improved.

Professor Zhu Zhizhang [12], based on the Taiyin root and supporting the Shaoyin yuan-yang, took the spleen and stomach as the entry point, and used the method of pungent opening and bitter lowering to treat DNB patients with the addition and subtraction of Banxia Diarrhea Heart Soup (Banxia, Scutellaria baicalensis, Huanglian, Ginger, Cinnamon, Chrysanthemum, Astragalus, Radix Bupleurum, Chaihu, Pueraria lobata, Bupleurum, Radix et Rhizoma, Fritillariae, Che Qianzi, Dandelion, Radix et Rhizoma, Mai Dong) with remarkable efficacy.

### 3.2.2. Acupuncture Treatment

Chang Mingkong [13] divided 60 patients into two groups using a randomized grouping scheme.

In both the treatment and control groups, under the premise of general treatment of diabetes, the treatment group was treated with snap acupuncture, acupuncture points Renyu Shuang, Tai Xi Shuang, Guan Yuan, Qi Hai, Zhong Ji, once every other day; Combined with the ginger twisted end along the Governor's vein evenly spread out, the ginger spread with moxa, once every other day, a 30-minute moxibustion, 7 days for a course of treatment, 2 consecutive courses of treatment to observe the efficacy; The control group was treated with methylcobalamin injection 500ug, 1 time/day by sedation, and 14 days as a course of treatment. After 28 days of treatment, the total effective rate of the study group reached 90%, while the control group was only 67%.

Chen Cuizhi et al. [14] randomly divided 100 patients with DNB into 2 groups, and the control group was given methylcobalamin injection 0.5 mg by static push once a day with no change in basic treatment. In the treatment group, on the basis of methylcobalamin injection treatment, acupuncture point moxibustion treatment was given, taking Guan Yuan and Zhong Ji acupoints, each acupuncture point moxibustion 15mins, to the extent that the skin appeared flushed and the patient felt warm and comfortable. Each person was treated with acupuncture point moxibustion once a day, and the course of treatment was 1 week. After 14 d of treatment, there were 28 cases with significant effect, 17 cases with effective effect and 5 cases with ineffective effect, with a total efficiency of 90%; in the control group, there were 21 cases with significant effect, 14 cases with effective effect and 15 cases with ineffective effect, with a total efficiency of 70%.

Gao Caixia [15] selected 66 patients with type 2 DNB urinary retention and randomly divided them into 33 cases in the trial group and 33 cases in the control group. All patients in the test and control groups were given basic diabetes treatment to keep their blood glucose under better control. In the test group, on the basis of the control group, heat-sensitive moxibustion was performed on water channel, Qihai, Guanyuan and Zhongji as the main points, and additional points were added according to the type of evidence (For deficiency of middle qi, add zu sanli; for deficiency of kidney yang, add tai xi; for dampness and stagnation, add xuehai; for liver depression and qi stagnation, add yanglingquan; for damp-heat infiltration, add san yin jiao). The total effective rate after treatment was 93.3% in the test group and 46.7% in the control group.

### **3.2.3. Acupuncture combined with herbal hot compress treatment**

Luo Li [16] selected a total of 70 patients with diabetic neurogenic bladder disease and divided them into 2 groups according to the random number table method, with 35 cases in each group. Patients in the control group were given conventional drug therapy. (1) blood glucose control; (2) voiding training; (3) giving Micropol 500 µg for intramuscular injection once a day for 15 d of treatment. The observation group added acupuncture combined with herbal hot compresses on top of that. (1) Acupuncture. Select Sanyinjiao, Guanyuan, Shen Shu, Shui Dao, Bladder Shu, Qi Hai, Zhongji and Yinlingquan for acupuncture, and retain the needles for half an hour after obtaining Qi, and perform acupuncture every 10 min, once a day for 15 d. (2) Hot compresses. (Curcuma longa 20g, Salvia miltiorrhiza 10g, Radix ginger 30g, Rhizoma Chuanxiong 10g, Rhizoma aromaticum 10g, Hesperidin 50g, Rhizoma alba 50g, Rhizoma hemipterocarpus 50g, Radix ginger 10g, Cinnamon 10g, Radix angelicae 10g, Radix cinnamomi 10g, Radix astragali 10g, Rhizoma ephedra 10g, Bupleurum 10g, Glycyrrhiza glabra 20g.) The above herbs are powdered and used as one dose every 2d. After mixing with 200 ml of yellow wine in 2 bags, steaming hot before each use and wrapped with towel, placed on the bladder area with hot compress, so that the skin is slightly red but not hot, for 1h each time, twice a day for 15d. The total effective rate after treatment was 94.29% in the test group and 74.29% in the control group.

### 3.2.4. Acupuncture combined with internal Chinese medicine treatment

Li Zhenqiang [17] selected 60 patients with neurogenic bladder disease with diabetic neurogenic bladder and divided them into 30 cases each in the observation and control groups. Patients in both groups were given basic treatment of diabetes, and the control group was given western medicine mosapride and pancreatic kininogenase on the basis of basic treatment, using pancreatic kininogenase for intramuscular injection, 40U/time, 1 time/d, and then changed to pancreatic kininogenase enteric soluble tablets for oral treatment after 1w, 40U/time, 3 times/d, and continuous medication for 2w; Moxaburi was used for oral treatment, 5mg/dose, 3 times/d, for 3w. The observation group was treated with acupuncture and moxibustion combined with Chinese herbal medicine Yi kidney soup (formula: Astragalus membranaceus 20g, Yam, Radix Rehmanniae 15g each, Poria, Cinnamon, Zelig, Cornus officinalis, Polygonum officinale 10g each) on the basis of basic treatment. One dose a day with water decoction was taken for three weeks. Acupuncture points were selected according to different types of evidence: for patients with Lung and Kidney Qi deficiency, the main points were Wei Yang, Shui Dao, Qi Hai, and Zhao Hai, supplemented by Lung Shu and Da Zhu; for patients with Kidney Yang deficiency, the main points were Guan Yuan, Ming men, Wei Yang, Shui Dao, Qi Hai, and Zhao Hai; for patients with Spleen Qi deficiency, the main points were Guan Yuan, Qi Hai, and Sanyin Jiao, supplemented by Spleen Shuhu and Zu San Li; the treatment course was 3 w. After 21 days of treatment, the total effective rate of the observation group was 96.67%, which was significantly higher than that of the control group (76.67%).

Wang Wei [18] selected 66 patients with early diabetic neurogenic bladder randomly divided into two groups, and both groups were given insulin hypoglycemia, hypotension, lipid regulation and other conventional treatments. The treatment group added self-formulated formula for warming Yang, benefiting Qi and strengthening the spleen (formula is Astragalus membranaceus 30g, Radix Aconiti 10g, Cinnamon 10g, Cornu Cervi Pantotrichum 10g, Poria 10g, Rhizoma Atractylodis Macrocephalae 20g, Rhizoma Atractylodis Macrocephalae 20g, Semen Cuscutae 15g, Rhizoma Bupleurum 20g, Plantago ovata 10g, and add or subtract with evidence). Combined moxibustion (select points Guan Yuan, Zhong Ji, Qi Hai, Bladder Shu, Kidney Shu, and Shui Dao, and suspend the points with moxa sticks to the extent that the patient's local skin is flushed and feels warm and comfortable.). In the control group, methylcobalamin dispersible tablets of 0.5 mg each time, 3 times a day, were added and taken orally. Both groups took 4 weeks as a course of treatment, and a total of 2 courses of treatment. After two courses of treatment, the efficiency of the treatment group was 86.7%, and that of the control group was 63.3%.

### 3.2.5. Moxibustion combined with western medicine treatment

Wang Wen [19] randomly divided 72 patients with diabetic neurogenic bladder into a control group and an observation group, 36 cases in each group. The control group was treated with daily intravenous drip of Danhong injection 20 ml, Prostil 10 µg, and methylcobalamin 500 µg. The observation group was treated with acupuncture points such as Zhibian, Qihai, Guangyuan, Kidney Shu, Spleen Shu, and Sanjiao Shu on this basis for 2 weeks. After 14 days of treatment, the effective rate was 94.4% in the observation group and 77.7% in the control group.

### 3.2.6. Chinese herbal hot compress combined with western medicine treatment

Li Qiaoyun [20] randomly divided 60 patients with type 2 diabetic neurogenic bladder into 31 cases in the observation group and 29 cases in the control group. The control group was treated with a conventional Western medical regimen of lipoic acid 0.6 g combined with 0.9% NaCl solution 250 ml intravenously once daily, and oral medication or insulin was chosen to control blood glucose

according to the condition. In the observation group, on the basis of the control group, Chinese herbal medicine was given to seal the treatment (15g each of clove and Chuanpu, 10g each of frankincense, myrrh, Cornus officinalis, cumin, astragalus, poria, codonopsis, zedoary, psyllium, 3g of ice chips and 5g of licorice). After 2 weeks of treatment, 22 cases were effective, 7 cases were effective, and 2 cases were invalid, with a total efficiency of 93.55%; 14 cases were effective, 8 cases were effective, and 7 cases were invalid in the control group, with a total efficiency of 75.86%.

### 3.2.7. Other treatment modalities

Ji Hongyu [21] used herbs that tonify the temperature and yang to patch Guan Yuan, Kidney Yu, and Bladder muscle Yu (patching herbs: Shu Di 30 g, Cinnamon 15 g, Huang Qi 30 g, Cornu Cervi Pantotrichum 15 g, Gunpowder 15 g, and Huai Niu Knee 15 g) to treat DNB patients, and after 15 days, the effective rate of the treatment group was as high as 93.3%, which was significantly higher than that of the control group 80.0%.

Other methods such as auricular pressure beans [22] and acupressure were used to treat DNB with significant effects, and the efficiency of the treatment groups were all significantly higher than that of the control group.

## 4. Discussions

In summary, although the pathogenesis of DNB is not very clear, there is no side effect-free and efficient treatment plan for the time being, except for blood sugar control, urinary training and exercise guidance, while TCM can be guided by the basic theory of TCM, combining evidence-based treatment and disease-specific treatment, and then using Chinese herbal soup for internal use, acupuncture, moxibustion, acupuncture point application, Chinese herbal hot compress, ear acupuncture, and other treatment methods, and these methods have precise efficacy and basically no side effects. However, there are many shortcomings in this study. Although the above Chinese medical treatments are effective in treating DNB, the criteria for determining the effectiveness are not uniform, and the number of cases in some clinical observation samples is small, lacking further statistical statistics to elaborate on which specific treatment is more concise and effective. It is hoped that with the deepening of TCM research, future scientific studies will be more complete and clearer.

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