

Effect of traditional Chinese medicine Zhiyi decoction and acupuncture on serum ADH & inflammatory factors in patients of enuresis

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Abstract: This study was designed to investigate the curative effect of traditional Chinese medicine Zhiyi decoction combined with acupuncture in the treatment of enuresis and its influence on serum ADH and inflammatory factors. A total of 84 enuresis patients treated were selected as cases from September 2014 to January 2017, randomly divided into study and control group with 42 cases each. The control group was treated with traditional Chinese medicine Zhiyi decoction while the study group was treated with traditional Chinese medicine Zhiyi decoction combined with acupuncture. The clinical efficacy and levels of serum ADH, serum inflammatory factors (TNF- α and IL-6) were compared between two groups before and after treatment. In study group, there were 34 cases cured and 5 cases were improved. Total effective rate was 92.9% and recurrence rate was 4%. In control group, there were 23 and 7 cases cured and improved respectively. Total effective rate was 71.4% and recurrence rate was 14.3%. The total efficiency of study group was significantly higher than that of control group ($P < 0.05$), and the recurrence rate was significantly lower than control group ($P < 0.05$). After treatment, there was no significant change in ADH level of study group at 10am and 11pm ($P > 0.05$). In control group, the level of ADH at 11pm before treatment was lower than that after treatment ($P < 0.05$) and the level of ADH at 10am before treatment was not significantly different from that after treatment ($P > 0.05$). The levels of serum TNF- α and IL-6 in study group and control group decreased at 10am and 11pm after treatment ($P < 0.05$) There was no significant difference in serum TNF- α and IL-6 levels between study group and control group before treatment ($P > 0.05$). Compared with simple acupuncture, traditional Chinese medicine Zhiyi decoction combined with acupuncture of children had more exact effect, changed enuresis symptoms effectively.

Keywords: Acupuncture, Enuresis, ADH, Osmotic pressure.

INTRODUCTION

Enuresis refers to children after age 5, wetting at night involuntarily more than 2 times/week. It can be divided into primary and secondary, simple and complex. Simple primary enuresis is most common in enuresis (Wang, 2008), refers to children who have never been successfully trained to control urination and are not associated with anatomical and functional abnormalities of urinary system and nervous system. It is a common and perplexing disease in urology (Bower *et al.*, 2012). The incidence rate varies from 2.2% to 25% of the population (Kanaheeswari, 2003). The annual self-remission rate was 15%. However, conditions of children who cannot relieve themselves aggravated with age, and are affected by both physical and mental health seriously (Al, 2012). In recent years, it has been reported (Kovacevic *et al.*, 2015) that about 70% of patients have nocturnal antidiuretic hormone deficiency. Studies have shown (Rittig *et al.*, 2008) that for some children, the pathogenesis is not the lack of antidiuretic hormone, but the deficiency of antidiuretic hormone receptor or the obstacles of signal transduction pathway. At present, the main treatment methods include behavior therapy, drug treatment, acupuncture treatment, laser irradiation of acupoints, TCM treatment and other treatment methods. However,

these therapies are still deficient (Guo *et al.*, 2009; Elnabil and Helmy, 2013). Among them, behavioral therapy is relatively stable, but parents and children need good compliance. Drug treatment is quick, but easy to recur. Any single treatment is ineffective, and combined treatment is the current mainstream of enuresis clinical research at home and abroad (Heba *et al.*, 2013). In recent years, the traditional Chinese medicine Zhiyi decoction combined with acupuncture carried out in "The First People's Hospital of Changzhou" is a new method for the treatment of enuresis. At present, there are few reports about the therapeutic effect of this therapeutic mechanism and the influence of serum ADH, hematuria, osmotic pressure and inflammatory cytokines in enuresis have not been reported yet. This study aimed to explore curative effect of traditional Chinese medicine Zhiyi decoction combined with acupuncture in treatment of enuresis and impacts on serum ADH and inflammatory factors, in order to further reveal the mechanism, and to provide a new theoretical basis for traditional Chinese medicine combined with acupuncture.

MATERIALS AND METHODS

General Information

Out of 84 enuresis patients, 50 were boys and 34 were girls. Their ages ranged from 5 to 14 years with an average of 7.5 ± 1.2 .

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Inclusion criteria

Inclusion criteria were as (1) Chronological age was at least 5 years of age. (2) Behavior was clinically significant as manifested by a frequency of twice a week. (3) Children exclude from organic lesions by examination (urine routine, kidney function, urinary system ultrasound, lumbosacral vertebra X-ray and abdominal plain film examination). (4) All of them met the diagnostic criteria primary and simple enuresis criteria.

Exclusion criteria

Exclusion criteria included (1) children suffering from other diseases, genetic disorders and mental issues were excluded from the study.

Selected cases were randomly divided into study and control group, with 45 cases in each group. The general characteristics of the patients between two groups did not differ significantly ($P>0.05$). The Hospital Ethics Committee approved this study and parents signed informed consent forms.

Treatment method

The control group had acupuncture therapy. They were treated with acupuncture at double sides of Sanyinjiao point and Yinlingquan point, Guyuan and Zongji. Retaining needle for 0.5h was appropriate. Twirling for 2 minutes at the frequency of 1 time per minute Moxibustion was taken after the withdrawal of needle. Three Moxa cone were used every time with Ginger separated moxibustion. In treating on control group, once a day, two weeks a course. Treatment effect was observed after one course, then another course given again after one-day rest.

The study group was treated with traditional Chinese medicine Zhiyi decoction on the basis of control group. The composition of decoction was Alpinia 10g, Chinese yam 10g, Sangpiaoxiao 10g, Raspberry 10g, Astragalus 10g, Lindera 10g, Radix Rehmanniae Preparata 6g, Polygala tenuifolia Willd 8g, Codonopsis pilosula 10g, Cuscuta chinensis Lam. 10g, Roasted Ephedra sinica 5g, Licorice 6g, in treating the study group, one dose per day. Each decoction was decocted twice a day.

Sample collection and index detection

Blood samples of 84 children were taken to be detected before and after treatment. No longer having diet and water after dinner (6pm), patients should urinate before sleep. 2ml venous blood was collected and centrifuged immediately at 10am and 11pm. The upper plasma was packed separately and stored at -70°C for testing. Levels of ADH at 10am and 11pm were measured by enzyme linked immunosorbent assay. Double antibody sandwich method (enzyme-linked immunosorbent assay (ABC)) was used to determine the levels of TNF- α and IL-6. The kit was provided by Shanghai science and Technology Industrial Co., ltd.

Evaluation standard of curative effect

After treatment, clinical efficacy of children was evaluated.

Cured: Enuresis disappeared, no recurrence after half a year follow-up.

Valid: The number of enuresis reduced or enuresis disappeared, but recurrence after half a year follow-up.

Invalid: Condition has no change after treatment.

STATISTICAL METHOD

All statistical analyses were performed using SPSS 20.0 software. Comparison between groups was analyzed by student's t-test or X^2 . A p-value of <0.05 was considered statistically significant.

RESULTS

Comparison of clinical efficacy between two groups

In study group, there were 34 cases cured, 5 cases improved. Total effective rate was 92.9% and recurrence rate was 4%. In control group, there were 23 cases cured, 7 cases improved. Total effective rate was 71.4% and recurrence rate was 14.3%. The total efficiency of study group was significantly higher ($P<0.05$) than that of control group, and the recurrence rate was significantly lower ($P<0.05$) than control group. The data is presented in table 1.

Comparison of ADH level before and after treatment

Before treatment, ADH level of control group at 10am was higher than that at 11pm ($P<0.05$). ADH level of study group at 10am was higher than that at 11pm ($P<0.05$). After treatment, ADH level of control group at 10am was not significantly different from that at 11pm ($P>0.05$). After treatment, there was no significant change in ADH level of study group at 10am and 11pm ($P>0.05$). In control group, the level of ADH at 11pm before treatment was lower than that after treatment ($P<0.05$). The level of ADH at 10am before treatment was not significantly different from that after treatment ($P>0.05$). In study group, the level of ADH at 11pm before treatment was lower than that after treatment ($P<0.05$). The level of ADH at 10am before treatment was not significantly different from that after treatment ($P>0.05$) as shown in table 2.

Comparison of inflammatory factors before and after treatment

The levels of serum TNF- α and IL-6 in study group and control group decreased at 10 AM and 11PM after treatment. There was no significant difference ($P>0.05$) in serum TNF- α and IL-6 levels between study group and control group before treatment. At 10 AM and 11PM after treatment, the levels of serum TNF- α and IL-6 in study group were significantly lower ($P<0.05$) than those in control group after treatment as shown in table 3.

Table 1: Comparison of clinical efficacy between two groups (n=42)

Group	Cured	Valid	Invalid	Total effective [N (%)]	Recurrence [N (%)]	Total effective [N (%)]
Control	23	7	12	30 (71.4)	6 (14.3)	30 (71.4)
Study	34	5	3	39 (92.9)	2 (4.8)	39 (92.9)
X ²	---			9.728	8.014	9.728
P	---			<0.05	<0.05	<0.05

Table 2: Comparison of ADH level between two groups before and after treatment (pmol/L)

Group	Before Treatment		After Treatment	
	Day Time (10am)	Night Time (11pm)	Day Time (10am)	Night Time (11pm)
Control group	68.5±3.1	60.4±1.7	67.9±2.4	64.6±2.1
Study group	68.3±3.4	60.2±1.5	68.4±2.2	65.7±2.8
T	0.452	0.363	0.178	0.194
P	>0.05	>0.05	>0.05	>0.05

Table 3: Comparison of Inflammatory Factors between Two Groups before and after Treatment (n=42)

Group	TNF- α (ng/L)				IL-6 (ng/L)			
	Day time (B/T)	Night time (B/T)	Day time (A/T)	Night time (A/T)	Day time (B/T)	Night time (B/T)	Day time (A/T)	Night time (A/T)
Control	32.5±2.2	32.2±1.7	29.5±3.4	29.1±4.2	39.6±3.4	39.4±3.1	30.5±4.1	30.3±3.9
Study	32.4±1.9	32.1±2.3	26.4±4.1	26.2±3.7	39.5±2.8	39.2±2.9	25.4±2.7	25.2±2.6
T	0.403	0.728	5.416	5.692	0.317	0.411	6.005	7.034
P	>0.05	>0.05	<0.05	<0.05	>0.05	>0.05	<0.05	<0.05

Where, (B/T) and (A/T) represents before treatment and after treatment respectively.

Medical record

Lee, male, 9 years old, was newly diagnosed on January 8, 2016. The physique of the child was poor at infancy, subjected to colds, enuresis at night more than 2 times, and not interested in activities. The symptoms were; poor complexion, bad appetite, clear and long urine, pale tongue, thin and white fur, powerless and weak pulse. There was no abnormality in routine urine examination, abdominal ultrasound and neurological examination. By treatment with traditional Chinese medicine Zhiyi decoction, and asking his parents to wake up the child to urinate, after a course of treatment, enuresis was significantly relieved. Then study continued to consolidate 2 courses of treatment, and follow-up showed no recurrence.

DISCUSSION

Enuresis can be divided into primary and secondary, simple and complex. The etiology of primary enuresis is still not very clear. Western medicine thinks enuresis is combined with genetic factors, arousal disorders, bladder dysfunction, psychological factors, and antidiuretic hormone (ADH) secretion abnormalities (Kosar *et al.*, 1993). Traditional Chinese medicine believes that the pathogenesis of this disease is congenital deficiency, cold lower limbs, or acquired dystrophy, caused by abnormal intake. Kidney is responsible for opening and closing and the source of gas, interacting with the bladder. Kidney-

deficiency cannot dominate the water. Weak lower limbs lead to instability of bladder and enuresis. After a long illness, lack of aftercare, Qi-deficiency of lung and spleen, bladder dysfunction will also result in enuresis. According to Viscera of traditional Chinese medical science, the kidney is the foundation of the congenital, and dominate the water. Kidney Qi has the function of stabilizing lower limbs. Kidney governs the feces and urine. Insufficiency of kidney yang, unable to maintain body temperature, incontinence of bladder will lead to clear and long urine, night urination and even enuresis. "Su inquiry, menstruation theory" says, "Kidney is the organ of water, mainly responsible for body fluid". According to "A-B classic of Acupuncture and Moxibustion"; "Deficiency is the cause of incontinence". "General Treatise on the Cause and Symptoms of Diseases" claims that "Enuresis, is due to the bladder has a cold, unable to dominate the water". Excretion and storage of urine depends on warming and gasification of Kidney Yang. Children with deficiency of kidney-qi, Yuan-deficiency, cannot raise temperature of bladder. Bladder dysfunction will not restrict the waterway, causing enuresis (Pomeranz *et al.*, 2000). Thus, the incidence of enuresis has a direct relationship with the kidney and bladder. The key pathogenesis of enuresis is caused by bladder incontinence, may be related to congenital spleen and kidney weakness, changes in diet, eating cold food in summer, injury of the spleen and kidney yang. Enrolled children's overweight burden of

study, mental stress leads to abnormality in hepatic excretion and tri-jiao, which is also a factor that could not be, neglected (Du, 2007).

In the traditional Chinese medicine Zhiyi decoction: *Alpinia fructus* is hard and warm, entering the spleen and kidney to warm the kidney and spleen cultivating lower limbs. The root of three-nerved spicebush can warm kidney and dissipate cold, used for kidney yang deficiency and enuresis caused by asthenia cold of bladder. Yam can tonify kidney to cure enuresis; *Othea mantidis*, the seed of Chinese dodder, raspberry can tonify the kidney and benefiting the essence and strengthening yang, acting on the target directly, enriching the innate essence. *Astragalus membranaceus*, prepared rhizome of rehmannia can invigorate qi and blood; licorice can free the twelve channels, tonifying qi and closing kidney. Alkaloids in honey-fried, *Codonopsis pilosula* have an excitatory effect on the central nervous system, improving the regulating effect of the cerebral corte. All the medicines warm and tonify Kidney-Yang, invigorate the spleen and benefit the lung, and better for bladder to be an effective cure for children enuresis.

The theory of traditional Chinese medical science points out that Sanyinjiao point, Yinglingquan, Guanyuan and Zhongji have the function of tonifying kidney and invigorating qi, enriching the kidney-qi, control the bladder, which can be used for the treatment of enuresis (Ge and Wang, 2007). Sanyinjiao and Yinlingquan points belong to channels of foot Taiyin spleen. The spleen meridian is mainly used for treatment on the spleen and the diseases of the heart, liver, kidney and lung, which are closely related to the spleen. Sanyinjiao is the convergent acupoint of Foot-Taiyin, Jueyin meridian and Shaoyin. "Prescriptions worth a thousand ounces of gold" says that Yinlingquan is mainly responsible for incontinence of enuresis without realizing it. These two points are invigorating the kidney and replenishing qi, used in the treatment of urinary incontinence and enuresis of kidney deficiency. Besides, Guanyuan and Zhongji belong to Ren-channel which is mainly used for the treatment of liver and kidney, spleen and stomach, related to heart and lung (Cheng *et al.*, 2010). Points below umbilicus mainly treat disease of lower energizer. Guanyuan and Zhongji are indicated for diseases of spleen, kidney and bladder. Zhongji is the Mu-front acupoint of meridian of foot-Taiyang. "A-B classic of Acupuncture and Moxibustion" says, "Guanyuan and Zhongji is the junction of foot three yin and Ren channel, the main treatment of dysuria, frequent urination, and incomplete urine (Liu, 2003).

In the present study, the total effective rate of study group was significantly higher than that of control group, and the recurrence rate was significantly lower than that of control group. The total efficiency of study group was significantly higher than that of control group, and the

recurrence rate was significantly lower than control group. After treatment, there was no significant change in ADH level of study group at 10am and 11pm. The levels of serum TNF- α and IL-6 in study group and control group decreased at 10am and 11pm after treatment. There was no significant difference in serum TNF- α and IL-6 levels between study group and control group before treatment. At 10am and 11pm after treatment, the levels of serum TNF- α and IL-6 in study group were significantly lower than those in control group after treatment.

CONCLUSION

Traditional Chinese medicine Zhiyi decoction combined with acupuncture treatment reduced the level of serum TNF- α and IL-6 more effectively than that of simple acupuncture. The reason might be that traditional Chinese medicine Zhiyi decoction combined with acupuncture played a synergistic role, which effectively alleviated the degree of inflammation in children. This study provided a new therapeutic basis for the combination of traditional Chinese medicine and acupuncture in the treatment of infantile enuresis.

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