Research Paper

Effect of Shentong Zhuyu Decoction on Serum 5-Hydroxytryptamine and Prostaglandin E2 in Patients with Sciatica

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We attempt to discuss the effects of oral Shentong Zhuyu Decoction on the pain degree and serum 5-hydroxytryptophan and prostaglandin E2 of patients with sciatica caused by lumbar disc herniation. We selected 90 patients with sciatica under-treated in the orthopedics department of our hospital from March 2018 to December 2020 as the study cohort. Divided them into experimental group and control group randomly, with 45 patients in both groups and treated patients in control group with mecobalamin tablets, after receiving the same treatment in control group, treated experimental group with another Shentong Zhuyu Decoction. The traditional Chinese medicine syndrome score, visual analog scale score, Oswestry disability index score, Sciatica Bothersomeness index score and serum 5-hydroxytryptophan and prostaglandin E2 of the two groups were compared before treatment, 1 w and 28 d after treatment. 1 w and 28 d after treatment, the decline trend of traditional Chinese medicine syndrome score, visual analog scale score, Oswestry disability index score and Sciatica Bothersomeness index score in experimental group was greater than the other, they were significant different, so it possessed statistical significance ($p<0.05$). After 7 d and 28 d of treatment for both groups, 5-hydroxytryptophan and prostaglandin E2 of experimental group had a greater downward trend than the other and it possessed significant difference ($p<0.05$). The total clinical effective rate (86.67 %) of experimental group was remarkably higher than control group (68.89 %), with a remarkable difference ($p<0.05$). Shentong Zhuyu Decoction can significantly improve the pain degree and clinical effective rate of patients with sciatica caused by lumbar disc herniation and reduce their serum concentration levels of 5-hydroxytryptophan and prostaglandin E2, which is worthy of clinical promotion.

Key words: Shentong Zhuyu Decoction, sciatica, lumbar disc herniation, 5-hydroxytryptophan, prostaglandin E2

Sciatica is characterized by leg pain and changes in leg sensation and/or weakened leg sensation. It is believed to be caused by compression, inflammation and/or increased sensitivity of the lumbar/sacral nerve roots caused by lumbar disc herniation and lumbar spinal stenosis. A very small part is caused by the compression of malignant tumors. The current cause is completely clear[1]. Sciatica is different from somatic leg pain, which concerns with structures except nerve roots, such as joints, muscles and ligaments[2]. Compared with simple low back pain or somatic leg pain, sciatica can increase the severity of symptoms, cause disability and seriously affect physical health. More severe symptoms can cause loss of mobility and restricted daily activities[3]. The prevalence of sciatica is estimated to range from 1.2 % to 43 %. Although the early improvement of symptoms in most patients with sciatica is usually 2-3 mo in the early stage of onset, over time, some patients will experience intermittent or recurrent sciatica[4].

Studies have shown that sciatica is often accompanied by the increase of 5-Hydroxytryptophan (5-HT), Prostaglandin E2 (PGE2) and inflammatory mediators, and induces the development of pain and hyperalgesia[5]. In the current treatment, Shentong Zhuyu Decoction is composed of 11 kinds of Traditional Chinese Medicine (TCM), which can promote blood circulation and remove blood stasis. And there are studies which proved that it can inhibit inflammation and relieve pain[6]. The curative effect of Western medicine in treating sciatica is not clear, including conventional

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symptomatic treatment or surgical treatment when the illness is serious. The disease is prone to recurring after treatment[7]. Shentong Zhuyu Decoction has a definite effect on sciatica, but its influence on patients' serum 5-HT and PGE2 has not been studied yet. In this study, we selected 90 patients with sciatica under-treated in the orthopedics department of our hospital from March 2018 to December 2020 as the research object to explore how Shentong Zhuyu Decoction affects clinical effective rate and serum 5-HT and PGE2 of patients with sciatica.

MATERIALS AND METHODS

General information:

Collected 90 patients with sciatica under treated in the orthopedics department of our hospital from March 2018 to December 2020 as the study cohort, divided them into experimental group and control group randomly, with 45 patients in both groups respectively. 19 males and 26 females included in experimental group, ages were from 37 y to 73 y old and their average age is about (51.67±16.51) y old. 22 males and 23 females included in control group, ages were from 38 y to 74 y old and their average age is about (52.96±16.72) y old. Inclusion criteria includes nerve root pain at Lumbar 4 (L4), L5 or Sacral 1 (S1) skin; the physical examination results were consistent with the results of radicular pain, kinesiology or sensory neurology or the L4, L5 or S1 spinal nerve root reflex is weakened; straight leg elevation test was positive; leg pain aggravated when coughing, sneezing or fatigue and magnetic resonance imaging showed unilateral.

Exclusion criteria includes patients with or suspected of having severe spinal disease (such as cauda equina syndrome or spinal fracture); pregnant or breast-feeding; patients who were planning or considering spinal surgery or interventional surgery for sciatica during treatment; combined with other malignant tumors, bleeding tendency, rheumatoid arthritis or other known autoimmune diseases; focal neurological dysfunction with progressive or disabling symptoms; allergic to Shentong Zhuyu Decoction; contraindications for magnetic resonance imaging; the Visual Analogue Scale (VAS) of sciatica is <3 points and, patients gender and age possessed no statistically significant difference ($p>0.05$).

Methods:

Treated control group with Western medicine alone, they were given mecobalamin tablets (H20060865), 0.5 mg orally, Thrice in a Day (TID); after receiving the same treatment as control group, treated experimental group with Shentong Zhuyu Decoction[8]. The specific decoctions are: *Gentiana* 9 g, Ligustrazine 6 g, peach kernel 9 g, safflower 9 g, *Notopterygium* 6 g, *Angelica* 15 g, *Trogopterus dung* 6 g, *Cyperus rotundus* 6 g, *Achyranthes* 9 g, *Lumbricus* 6 g and Licorice 6 g. Both groups were required a 28 d treatment.

Observation indicators:

Detection of 5-HT and PGE2 expression levels in peripheral blood serum: Collected 5 ml of fasting elbow venous blood of both groups in the morning of 2nd d of admission and then packed them into two centrifuge tubes, 3 ml for each tube. After stewing one tube for 30 min at room temperature, then centrifuged in a 3500 r/min centrifuge at 4° for 10 min, extracted the supernatant in order to exam 5-HT and PGE2 expressions in peripheral blood serum. Adopted enzyme-linked immunosorbent assay to exam 5-HT and PGE2 expressions in the peripheral blood serum according to human 5-HT kit and PGE2 kit instructions. After 7 d and 28 d of treatment, the 5-HT and PGE2 expression levels in the patients' serum were tested again.

Clinical efficacy evaluation indicators: The significantly effective means the patient's signs and symptoms scores reduced between 70 % and 100 %; the effective means the patient's signs and symptoms scores reduced between 30 % and 70 %. The ineffectiveness means the patient's signs and symptoms scores reduced less than 30 %. The total clinical effective rate=(markedly effective+effective)/total number of cases×100 %. Compared the following indicators of both groups before and after treatment; the scores of TCM symptoms (lower limb pain, straight leg elevation test, dysfunction and lower limb numbness) before treatment and after are compared between both groups. The higher the score, the more serious the symptoms are; the patients' sciatic nerve pain is evaluated by VAS score before and after treatment. 0 is painless and 10 is the limit of pain. The higher the VAS score, the more intense the pain is; the Oswestry Disability Index (ODI) scale mainly evaluates symptoms such as leg or back pain, with a score of 0~6. 0 means basically no dysfunction and 6 means severe dysfunction; the Sciatica Bothersomeness Index (SBI) scale mainly evaluates the numbness and weakness of the feet or legs. The score is 0-6 points. A score of 0 indicates that there is basically no numbness and weakness and a score of 6 indicates that the numbness and weakness are very strong.

Statistical analysis:

Adopted Statistical Package for the Social Sciences (SPSS) 22.0 to process and analyze enumeration data and measurement data. Expressed enumeration data by constituent ratio (%), adopted χ^2 test to make comparison of both control group and experimental group. The measurement data (VAS score, TCM syndrome score and 5-HT and PGE2 expressions in peripheral blood serum) accorded with normal distribution and homoscedasticity and use mean±standard deviation ($\bar{x}$±s) to indicate it. Adopted t-test to compare control group with experimental group. $p<0.05$, indicating that the divergence possessed statistical significance.

RESULTS AND DISCUSSION

Both groups patients had no remarkable differences in age, gender, underlying diseases, etc., there was no statistical significance ($p>0.05$), they had comparability. As shown in Table 1.

Comparison of TCM syndrome scores of both groups before and after treatment was it had no significant difference in the scores of lower limb pain, straight leg elevation test, dysfunction and lower limb numbness of both groups before treatment ($p>0.05$) and they all decreased after treatment. Compared with control group, experimental group decreased more significantly and it possessed statistical significance ($p<0.05$). As shown in Table 2.

Comparison of VAS scores of both groups before and after treatment. Before treatment, both groups had no significant difference in VAS scores and it was of no statistical significance ($p>0.05$). After 3 d and 28 d of treatment, comparing the VAS scores of both groups, the decline trend of experimental group was greater than control group, with remarkable differences and it possessed statistical significance ($p<0.05$). As shown in Table 3.

Comparison of ODI scores of both groups before and after treatment. Before treatment, both groups had no significant difference in ODI scores and it was of no statistical significance ($p>0.05$). After 3 d and 28 d of treatment, comparing the ODI scores of both groups, the decline trend of experimental group was greater than control group, with remarkable differences and it possessed statistical significance ($p<0.05$). As shown in Table 4.

Comparison of SBI scores of both groups before and after treatment. Before treatment, both groups had no significant difference in SBI scores and it was of no statistical significance ($p>0.05$). After 3 d and 28 d of treatment, comparing the SBI scores of both groups, the decline trend of experimental group was greater than control group, with remarkable differences and it possessed statistical significance ($p<0.05$). As shown in Table 5.

TABLE 1: COMPARISON OF GENERAL INFORMATION OF BOTH GROUPS

	Experimental group (n=45)	Control group (n=45)	t/ ^{2}	p
Age	51.67±16.51	52.96±16.72	0.1	0.9
Gender (female)	26 (57.8 %)	23 (51.1 %)	0.1	0.8
Complications				
Hypertension	7 (15.6 %)	9 (20 %)	0.1	0.8
Diabetes	8 (17.8 %)	7 (15.6 %)	0.2	0.7
Other	3 (6.7 %)	2 (4.4 %)	0.2	0.7

TABLE 2: COMPARISON OF TCM SYNDROME SCORES OF BOTH GROUPS BEFORE AND AFTER TREATMENT

	Lower limb pain		Straight leg elevation test		Dysfunction		Lower limb numbness	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Experimental group	5.25±0.71	2.34±0.33	5.03±0.67	2.42±0.38	5.26±0.65	2.24±0.39	5.16±0.67	2.01±0.35
Control group	5.14±0.65	3.24±0.48	5.13±0.66	3.17±0.53	5.31±0.71	3.15±0.51	5.08±0.65	3.25±0.52
t	0.434	0	0.621	0.007	0.575	0.011	0.678	0.002
p	0.325	0.004	0.522	0.008	0.365	0.013	0.546	0.003

Note: TCM: Traditional Chinese Medicine

TABLE 3: COMPARISON OF VAS SCORES OF BOTH GROUPS BEFORE AND AFTER TREATMENT

Grouping	Cases	VAS		
		Before treatment	7 d after treatment	28 d after treatment
Control group	45	5.31±0.74	3.45.±0.54	3.12±0.49
Experimental group	45	5.23±0.69	3.01±0.43	2.24±0.35
t		0.566	0.047	0.002
p		0.412	0.018	0.003

Note: VAS: Visual Analog Scale

TABLE 4: COMPARISON OF ODI SCORES OF BOTH GROUPS BEFORE AND AFTER TREATMENT

Group	Cases	ODI scores		
		Before treatment	7 d after treatment	28 d after treatment
Control group	45	5.14±0.61	3.34.±0.51	3.05±0.43
Experimental group	45	5.21±0.57	2.81±0.41	2.13±0.31
t		0.761	2.81±0.42	0.003
p		0.521	2.81±0.43	0.002

Note: ODI: Oswestry Disability Index

TABLE 5: COMPARISON OF SBI SCORES OF BOTH GROUPS BEFORE AND AFTER TREATMENT

Group	Cases	SBI scores		
		Before treatment	7 d after treatment	28 d after treatment
Control group	45	5.22±0.66	3.25.±0.48	2.92±0.34
Experimental group	45	5.26±0.71	2.72±0.42	2.03±0.31
t		0.566	0.057	0.047
p		0.412	0.026	0.012

Note: SBI: Sciatica Bothersomeness Index

Comparison of inflammatory indexes (5-HT, PGE2) of both groups before and after treatment. Before treatment, both groups had no significant difference in the levels of 5-HT and PGE2 and it was of no statistical significance ($p>0.05$). After 7 d and 28 d of treatment, comparing 5-HT and PGE2 of both groups, experimental group had a greater downward trend than control group, with remarkable differences and it possessed statistical significance ($p<0.05$). As shown in Table 6.

Comparison of clinical efficacy of both groups after treatment. There were 39 markedly effective and effective patients in experimental group and 31 markedly effective and effective patients in control group. There were 39 markedly effective and effective patients in experimental group, 31 markedly effective and effective patients in control group. As shown in Table 7.

TABLE 6: COMPARISON OF 5-HT AND PGE2 SCORES OF BOTH GROUPS BEFORE AND AFTER TREATMENT ($\bar{x}\pm s$)

Group	Cases	PGE2 (pg/ml)			5-HT (μmol/ml)		
		Before treatment	7 d after treatment	28 d after treatment	Before treatment	7 d after treatment	28 d after treatment
Experimental group	45	249.68±26.67	180.23±18.86	137.42±16.04	229.15±23.46	165.56±17.17	109.85±15.23
Control group	45	250.53±25.79	201.36±20.61	168.39±17.62	231.91±22.67	198.93±18.57	165.93±16.94
t		0.14	2.57	7.45	0.02	2.75	5.79
p		0.68	0.02	0	0.96	0.01	0

Note: 5-HT: 5-Hydroxytryptamine and PGE2: Prostaglandin E2

TABLE 7: COMPARISON OF CLINICAL EFFICACY OF BOTH GROUPS AFTER TREATMENT

	Markedly effective	Effective	Ineffective	Total effective rate
Experimental group	26 (57.78 %)	13 (28.89 %)	6 (13.3 %)	39 (86.67 %)
Control group	19 (42.22 %)	12 (26.67 %)	14 (23.3 %)	31 (68.89 %)
χ^2		5.56		
p		0.03		

At present, there is a lack of accurate data on the incidence and recurrence rate of sciatica at home and abroad. Studies have shown that 5 %-10 % of patients with low back pain are often accompanied by sciatica and the lifetime prevalence of low back pain is 49 %-70 %[9]. Although sciatica can be caused by various causes, most cases (85 %-90 %) are caused by Lumbar Disc Degeneration (LDD) which results in the intervertebral disc material protruding from nucleus pulposus to epidural space and mechanical and/or chemical damage to the affected nerve roots[10]. Microdiscectomy is a minimally invasive spinal surgery for the removal of lumbar disc herniation tissue. It is only applicable to individuals with severe, progressive and persistent sciatica symptoms consistent with the location of disc herniation confirmed by radiology[11]. One of the most challenging medical problems is the treatment of sciatica symptoms. At present, it is mainly treated by Western medicine. For example, the use of glucocorticoids and Tumor Necrosis Factor (TNF) inhibitors in the treatment of sciatica may hinder the reabsorption of disc herniation and may hinder the median or long term progression of the disease[12]; Epidural Steroid Injections (ESI) have traditionally been used as an adjunct to the treatment of sciatica, with an average reported success rate of 67 %[13,14]. Because hormones and non-steroidal anti-inflammatory drugs are commonly used in the treatment of sciatica, the high cost, high recurrence rate and serious side effects bring a heavy burden to patients, and the application of TCM is gradually showing its unique advantages[15]. This study also reported that Shentong Zhuyu Decoction could significantly improve the pain symptoms of sciatica.

Shentong Zhuyu Decoction is a recorded medicine, which is mainly used to treat pain caused by blood stasis and is often used to treat low back and leg pain[16]. PGE2 is a key factor in the excessive pain sensation caused by inflammation, but we are still unclear what prostaglandins (PGs) and PG receptors mediate pain sensitization in the periphery and spinal cord, and to what extent these two loci cause inflammatory hyperalgesia[17]. It has also been reported that the perception of pain is altered by the endogenous pain suppression system, which mainly acts by reducing norepinephrine and 5-HT[18]. Studies have shown that Shentong Zhuyu Decoction can have a protective effect on nerves. In the mouse model, Shentong Zhuyu Decoction can significantly down regulate the levels of 5-HT and PGE2 in the serum of painful mice, thereby significantly alleviating the pain of mice. The specific mechanism research needs to be further carried out[19]. Shentong Zhuyu Decoction contains TCMs that promote blood circulation, remove blood stasis, dredge collaterals and relieve pain, which can significantly relieve pain[20]. This study has almost the same results as previous studies.

We studied how Shentong Zhuyu Decoction treated sciatica. The clinical effective rate of patients after the treatment with Shentong Zhuyu Decoction was remarkably higher than the other ($p<0.05$). After treatment, TCM syndromes scores such as dysfunction, lower limb pain, straight leg elevation test and lower limb numbness in experimental group decreased more remarkably than control group, which possessed statistical significance ($p<0.05$). And after 1 w and 28 d of treatment, the decline trend of VAS score, ODI score and SBI score in experimental group was greater than control group, with remarkable differences and it possessed statistical significance ($p<0.05$). The 5-HT and PGE2 of both groups decreased after 7 d and 28 d of treatment, but the decline trend of experimental group was greater than the other and it had significant difference ($p<0.05$). The total clinical effective rate of experimental group (86.67 %) was remarkably higher than control group (68.89 %), with a significant difference ($p<0.05$). It proves that Shentong Zhuyu Decoction can significantly improve the pain and discomfort symptoms of patients with sciatica, reduce 5-HT and PGE2 in the patients' serum and help improve the pain symptoms of patients, so it is worth popularizing and applying on clinic.

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Conflict of interests:

The authors declared no conflict of interest.

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