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Traditional Chinese herbal compound as complementary treatment for nonspecific low back pain

A randomized controlled trial

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Abstract

Background: This prospective randomized controlled trial was designed to evaluate the clinical efficacy and safety of Bu Shen Tong Luo herbal compound as a complementary treatment for nonspecific low back pain (NSLBP).

Methods: A total of 76 patients with NSLBP included from January 2022 to June 2023 according to the criteria were randomly divided into Bushen Tongluo formula (BSTL) group (n = 38) and celecoxib group (n = 38). According to Traditional Chinese Medicine principles, patients of 2 groups were divided into 5 syndrome types. Celecoxib or BSTL herbal compound were used to treat NSLBP of each group for 3 weeks, every week the Visual Analog Scale (VAS), Oswestry Disability Index, and Japanese Orthopaedic Association scores of each patient was record and compared to evaluate the clinical efficacy, and adverse reaction was reported to evaluate the safety of 2 interventions.

Results: A total of 71 patients finished the follow-up, including 36 patients in BSTL group and 35 patients in celecoxib group. The result showed that within 3 weeks, both BSTL and celecoxib interventions were able to treat NSLBP, with improvements in VAS scores and waist function index. However, there were no significant differences in clinical outcomes between these 2 interventions. Then we divided the patients into 5 syndromes on the basis of traditional Chinese medicine principles and observed their clinical outcomes. We found that celecoxib had similar improvements in VAS score and waist function index for each syndrome type and most of the syndromes in the BSTL group, except for the SRBZ syndrome. In the treatment of SRBZ syndrome, BSTL prescription showed no statistically significant clinical improvement. Meanwhile, in the treatment of HSBZ syndrome of NSLBP, BSTL prescription showed better clinical results than celecoxib, although there was no difference in VAS scores between the 2 groups, patients in BSXL group had better waist function than those in celecoxib group.

Conclusion: Both BSTL herbal compound and celecoxib are effective and safe in the clinical treatment of NSLBP, and BSTL herbal compound had unique advantages in the treatment of HSBZ syndrome type of NSLBP especially in waist function improvement.

Abbreviations: BSTL = Bushen Tongluo formula, HSBZ = Han Shi Bi Zu, JOA = Japanese Orthopaedic Association scores, LBP = lower back pain, NSLBP = nonspecific low back pain, ODI = Oswestry Disability Index, QZXY = Qi Zhi Xue Yu, SAX = Shen Yang Xu, SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu, TCM = traditional Chinese medicine, VAS = Visual Analog Scale.

Keywords: celecoxib, clinical efficacy, complementary medicine, nonspecific low back pain, traditional Chinese medicine

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All participants gave their written consent prior to the start of the study and were free to retreat any time without giving any reasons.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This clinical trial protocol was approved by the Ethics Committee of Tongde Hospital of Zhejiang Province, Ethics number: 2023-113(K).

This clinical trial is registered and posted on the ClinicalTrials.gov public website, registration ID is NCT06336993.

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1. Introduction

Low back pain (LBP) is a common clinical symptom, which often leads to back pain and loss of lumbar function.[1] The average prevalence of low back pain is about 18.3%, and the real-time prevalence ranges from 6.11% to 28.5%,[2] which is comparable to hypertension and type 2 diabetes mellitus, and has become the 6th leading cause of disability.[2,3] Frequency and intensity of manual labor,[4] income level,[5] and the unhealthy lifestyle such as smoking,[6] obesity,[7] depression[8] are related to the prevalence of low back pain. Low back pain has a profound impact on an individual's quality of life and family income, and many workers have to retire early because of low back pain.[9,10] In developed countries, the direct and indirect costs of low back pain range from 1 billion to 28 billion.[2,11] Of all low back pain, 90% of patients are with nonspecific low back pain (NSLBP).[12]

The diagnosis of NSLBP means that there is no definite pathoanatomical cause of low back pain, and the source of his pain may be multifaceted.[12] Intervertebral discs, facet joints, muscles, nerves, and ligaments are all potential causes of pain, but there are no reliable diagnostic investigations trials or imaging studies that can attribute pain to these structures. A systematic review of studies investigating the accuracy of diagnostic tests available to clinicians to identify the disc, facet joint or sacroiliac joint as the source of a patient's NSLBP found that diagnostic investigations have no role in the management of NSLBP.[13] And findings from a systematic review did not show consistent associations between MRI findings and future occurrence of low back pain.[14]Therefore, the current multinational guidelines only recommend Nsaids for the treatment of NSLBP.[1,15]

In China, herbal compounds have been used to treat NSLBP for thousands of years, and traditional Chinese medicine (TCM) has a unique understanding of the diagnosis and treatment of NSLBP. According to the principals of TCM, the occurrence of LBP is caused by both the internal and external factors, the internal factor is Shen Xu, and the external cause is meridian damage caused by pathogenic factors (wind, cold, dampness, blood stasis). Bu Shen Tong Luo formula (BSTL), comprises Bai Shao, Chuan Niu Xi, Dan Shen, Di Long, Du Huo, Du Zhong, Gou Ji, Qin Jiao, Sang Ji Sheng, Xi Xian Cao, Xu Chang Qin, and Yan Hu Suo, is a complementary medical treatment to LBP. On the one hand, to get rid of the internal factor and cure LBP, this formula strengthens Shen, on the other hand, this formula has an effect of dispelling the external factors of LBP, which has achieved good therapeutic effect in clinic. Nevertheless, there are few randomized controlled studies evaluating the efficacy of BSTL in patients with NSLBP. Some studies have shown good clinical results of LBP treated by TCM formula,[16,17] and a randomized clinical trial found that BSHX improves the clinical outcomes of celecoxib in LBP patients.[18]

This randomized controlled trial aimed to explore the clinical efficacy and safety of BSTL in the treatment of NSLBP based on TCM principles and to compare the clinical outcomes of different syndromes of NSLBP with celecoxib.

2. Methods

2.1. Trial design, participants, and randomization

This randomized controlled trial aimed to evaluate the clinical efficacy of BSTL in the treatment of NSLBP. Sample size calculation was performed for the change in Visual Analogue Scale (VAS) using a non-inferiority approach.[19] Based on previous clinical observations and literature reports,[20] with a two-sided alpha of 0.05 and a power of 90%, the sample size for the BSTL group and celecoxib group is 30 for each group with an allocation ratio of 1:1. Considering a dropout rate of 25%, 80 patients in total were enrolled in the study. Patient recruitment was conducted through field recruitment in Tongde Hospital of Zhejiang Province, and when patients were diagnosed with NSLBP, the patients were introduced to this clinical trial, and informed consent was signed by those interested in participating in the trial. In accordance with the guideline of NSLBP,[12,21] the diagnostic criteria are: a. Pain and discomfort in the area below the costal margin, above the gluteal lines, and between the midaxillary lines on both sides; b. Pain caused by unknown causes other than specific spinal diseases and radicular pain; c. A duration of more than 1 week; with or without referred thigh pain (above the knee). Each patient was screened by inclusion and exclusion criteria, and the included patients were subsequently randomly assigned due to the order of recruitment based on a predefined random number table. After all, 76 patients with NSLBP were enrolled and randomly assigned to BSTL group (n = 38) and celecoxib group (n = 38). The baseline information was recorded and assessed, and the study design flow is shown in Figure 1. The medical history of each patient was obtained by a traditional Chinese practitioner, and the TCM diagnosis was made by the characteristics of the patient's pain and the types of comorbidities, and the patient was classified into the most appropriate syndrome type. According to the TCM principles and the representation of each patient, we divided NSLBP into 5 syndrome types[22]: Han Shi Bi Zu (HSBZ), Shi Re Bi Zu (SRBZ), Qi Zhi Xue Yu (QZXY), Shen Yin Xu (SIX), and Shen Yang Xu (SAX).

2.2. Inclusion, exclusion, and elimination criteria

Recruitment lasted for 17 months from January 1, 2022, to June 16, 2023, with a total of 80 patients enrolled. Each patient interested in this trial was screened by the inclusion and exclusion criteria. The inclusion criteria are: a. Patients with low back pain who were seen between January 1, 2022, and June 16, 2023, were included; b. Meet the diagnostic criteria of NSLBP; c. The age range was 20 to 90 years old; d. Agree to participate in the study and sign the informed consent; exclusion criteria are: a. Those who are unable to communicate normally, such as those suffering from mental and cognitive diseases, and cannot cooperate with the treatment; b. Pregnant or lactating women; c. Patients who are allergic to the treatment components or sulfonamides; d. Patients with a history of coronary artery bypass grafting; e. Patients with active gastrointestinal ulcer or bleeding; f. Patients with severe heart failure; g. Patients with hepatic and renal insufficiency. The shedding and elimination criteria: a. Poor compliance or serious adverse reactions or other diseases in the trial cannot continue to participate in the trial; b. Patients who voluntarily asked to withdraw from the trial and lost follow-up due to various reasons; c. Those who do not take drugs as prescribed or use other drugs in the course of treatment; d. It was found to be inconsistent with the inclusion criteria after recruiting. After screening for inclusion and exclusion criteria, 76 patients were enrolled and underwent randomization. One patient was excluded because of a history of lumbar surgery, and 3 patients did not wish to participate in the trial for personal reasons.

2.3. Intervention and follow-up

In both the BSTL group and the celecoxib group, patients could be treated, and no other treatment was allowed. In celecoxib group: Celecoxib (Ouyi Pharmaceutical Co., Ltd., H20203296) was used twice a day for 3 weeks, 200 mg/ time, to treat NSLBP; While in the BSTL group, patients were instructed to take the herbal compound twice a day for 3 weeks, 200 to 300 mL each time, the composition of herbal compound of BSTL was BaiShao 9 g, ChuanNiuXi 15 g, DanShen 15 g, DiLong 9 g, DuHuo 9 g, DuZhong 15 g, GouJi 15 g, QinJiao 9 g, SangJiSheng 15 g, XiXianCao 9 g, XuChangQin 9 g, and YanHuSuo 9 g,

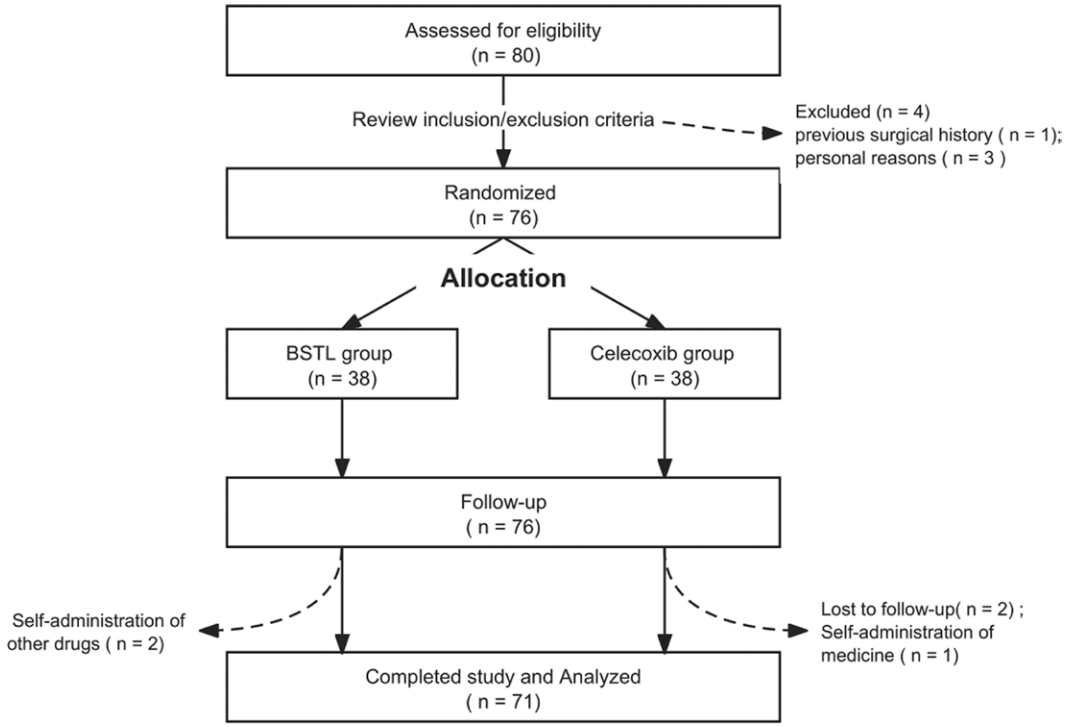

Figure 1. Flowchart of the clinical trial on BSTL in patients with NSLBP. BSTL= Bushen Tongluo formula, NSLBP = nonspecific low back pain.

and herbs were provided by the traditional Chinese medicine pharmacy of Tongde Hospital in Zhejiang Province. Based on previous studies, we determined the follow-up time to be 3 weeks.[20] Patients were advised to return to the hospital weekly for follow-up and collection of clinical data, and clinical data of Visual Analogue Scale, Oswestry Disability Index (ODI), Japanese Orthopaedic Association scores (JOA), and digestive system reaction after medication were recorded. For patients who did not attend on time, we will collect the clinical data by telephone. During the follow-up period, 2 patients in the BSTL group were kicked out from the trial due to self-administration of other drugs, 2 patients in the celecoxib group were lost, and 1 patient was kicked out due to self-administration of other drugs. After excluding the clinical data of these 5 patients, 71 patients completed the follow-up of this trial.

2.4. Observation indicators

To evaluate the safety and clinical efficacy of the herbal compound in the treatment of NSLBP, the adverse reactions digestive or systemic were used as the main safety indicators, and the subjective pain perception and changes in low back function were used as the main clinical efficacy indicators. We selected the observation indicators reliable and commonly used in majority of NSLBP trials.[23,24] VAS as a clinical outcome of the subjective pain of the patients, the patient marks on the line the point that they feel represents their perception of their current low back pain. The VAS score is determined by measuring in millimeters from the left end of the line to the point that the patient marks.[25] And ODI and JOA were used as indicators of waist function.[26,27] The ODI and JOA scores were calculated for each patient after the patient answered the questions on the scale related to low back pain by an individual unrelated to the trial, and the clinical outcomes were graded as significant, effective, and ineffective based on the improvement rate of the JOA scale, the improvement rate also corresponded to the commonly used criteria for efficacy evaluation: the improvement rate of 100% was cured, the improvement rate of >60% was significant, 25% to 60% was effective, and <25% was ineffective. Improvement rate = [pro-treat JOA score - pre-treat JOA score]/[normal - pre-treat JOA score] × 100%.

2.5. Statistical analysis

IBM SPSS Statistics 22.0 software was used for statistical analysis. The measured data were expressed as $x \pm s$. The t test was used to compare the normal distribution measurement data between the clinical data groups, and the chi-square test was used to compare the count data between the 2 groups. Fisher exact test was used when the conditions of the chi-square test were not met. Repeated measures analysis of variance was used for multiple time measurement data within the measurement group. Mauchly sphericity test was first performed to compare different time points. When the set of Mauchly sphericity test was not met, the difference was corrected by the Greenhouse–Geisser method, and $P < .05$ was considered statistically significant.

3. Results

3.1. General result of patients

During patient recruitment, 80 individuals (52 female and 28 males) with NSLBP showed interest in this clinical trial. Four patients (2 male and 2 female) were not included for previous lumbar surgical history or personal preference. Two patients were lost, and 3 patients were kicked out for self-administration of medicine in the period of follow-up. Finally, the data of 71 patients who have undergone the intervention (36 in BSTL, 35 in Celecoxib group) was calculated and analyzed. The ages of the patients ranged from 25 to 89 years. In the BSTL group, there were 12 males and 24 females, with a mean age of 54.36 ± 13.99 years. The pretreatment VAS was 4.69 ± 1.47, ODI was 0.57 ± 0.11, and JOA was 10.78 ± 2.61. While in celecoxib group, the mean age of the patients was 58.37 ± 13.9. Pretreatment, VAS was 4.63 ± 1.31, ODI was 0.56 ± 0.13, and JOA was

10.91 ± 3.09. According to the TCM principles, patients in each group were classified into 5 syndromes. Specifically, in BSTL group, there were 14 patients in HSBZ, 3 patients in SRBZ, 5 patients in QZXY, 9 patients in SIX, and 5 patients in SAX; while there were 13 patients in HSBZ, 5 patients in SRBZ, 6 patients in QZXY, 6 patients in SIX, 5 patients in SAX in Celecoxib group as Table 1 shown. The 2 groups of patients had similar distribution in age, gender, and TCM syndrome types, and the clinical data before treatment were also similar. After statistical testing, it was found that the 2 groups of patients were comparable. Then, we separately evaluated the baseline and clinical data before the treatment of patients in each syndrome group. After statistical analysis, we found that the 2 groups of patients in each TCM syndrome group were also comparable as shown in Table 2. And there were no adverse effects were reported.

3.2. VAS result

After intervention with BSTL and celecoxib, the weekly VAS scores of patients in both groups decreased, and after 3 weeks of intervention, the VAS scores of patients in BSTL group decreased from 4.69 ± 1.47 to 1.50 ± 1.18, and the VAS scores of patients in celecoxib group decreased from 4.63 ± 1.31 to 1.57 ± 1.44. The results showed that the degree of low back pain in both groups decreased significantly after 3 weeks of treatment, but there was no significant difference between the 2 interventions. The VAS scores of each syndrome of patients in the 2 groups are shown in Table 3, and the VAS scores of patients with each syndrome also decreased significantly after 3 weeks of treatment. Except for SRBZ in the BSTL group, the degree of low back pain was significantly reduced in both groups after 3 weeks of treatment, but there was no significant difference between the 2 interventions.

3.3. ODI results

After 3 weeks of intervention, most patients had felt the improvement of lumbar function. ODI scores of the 2 groups showed that ODI scores of the 2 groups decreased statistically, the ODI of patients in BSTL group decreased from 0.57 ± 0.11 to 0.24 ± 0.11, and the ODI of patients in celecoxib group decreased from 0.56 ± 0.13 to 0.28 ± 0.09, except for the SRBZ syndrome of the BSTL group, indicating that the lumbar function was improved. We then compared the 2 interventions at 3 time points, and the results showed that at 3 weeks, patients with HSBZ syndrome who received BSTL had significantly better ODI scores than those in the celecoxib group ($P = .002$), whereas patients with other syndromes had no significant differences in ODI scores at any other time point. ODI scores for each syndrome type in the 2 groups are shown in Table 3.

3.4. JOA scores results

The results of the JOA score within 3 weeks after treatment in both groups showed that the JOA scores of both groups were improved, the JOA score of patients in BSTL group decreased from 10.78 ± 2.61 to 19.67 ± 3.76, and the JOA score of patients in celecoxib group decreased from 10.91 ± 3.09 to 19.17 ± 3.08, and all other syndromes of LBP except for SRBZ type in BSTL group had statistical significance, suggesting that the lumbar function had been improved. At 3 weeks, the patients of HSBZ syndrome of BSTL group had significantly better lumbar function than those in the celecoxib group ($P = .03$), while the patients with other syndromes had no significant difference in JOA scores at any other time point. The JOA scores of the 2 groups of patients before and after treatment for each syndrome type are shown in Table 3.

According to the JOA scores of patients in the 2 groups, the clinical efficacy of patients with each syndrome in each time node of the 2 groups were calculated respectively, and a histogram was drawn as shown in Figure 2. At 1 week after treatment, 5 patients in the BSTL group were effective and 31 were ineffective. Celecoxib group has 3 patients effective and 32 ineffective. At the 2-week time, 15 people were effective and 21 were ineffective in BSTL group, while 13 were effective and 22 were ineffective in celecoxib group. And at the 3-week, the number of significant patients was 13, and the number of effective was 18, and the left 5 patients were ineffective. In the celecoxib group, 6 patients were significant, 24 were effective, and 5 were ineffective. After combining the patients of significant and effective, a four-cell table was obtained for each syndrome in the 2 groups at each time point, as shown in Table 4. The chi-square test/Fisher exact test showed that there was no statistical

Table 1

General information of the 2 groups before treatment.

		BSTL (n)	Celecoxib (n)	*P* value
Syndrome type	HSBZ	14	13	.713
	SRBZ	3	5	
	QZXY	5	6	
	SIX	9	6	
	SAX	5	5	
Sex	Male	12	10	.799
	Female	24	25	
Age (year)		54.36 ± 13.99	58.37 ± 13.9	.230
VAS		4.69 ± 1.47	4.63 ± 1.31	.843
ODI		0.57 ± 0.11	0.56 ± 0.13	.762
JOA		10.78 ± 2.61	10.91 ± 3.09	.841

QZXY = Qi Zhi Xue Yu, SAX = Shen Yang Xu, SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu, VAS = Visual Analog Scale.

Table 2

General information of each syndrome type of 2 group.

Intervention	BSTL (n)					Celecoxib (n)				
Syndrome type	HSBZ	SRBZ	QZXY	SIX	SAX	HSBZ	SRBZ	QZXY	SIX	SAX
Male	4	0	3	2	3	3	2	1	2	2
Female	10	3	2	7	2	10	3	5	4	3
Age (year)	54.5 ± 13.11	44.67 ± 12.66	46.2 ± 20.07	63.11 ± 10.89	52.2 ± 10.11	62.23 ± 8.82	51.60 ± 16.18	56.33 ± 23.23	61.83 ± 14.19	53.4 ± 7.7
VAS	4.71 ± 1.27	6.00 ± 2.65	3.40 ± 0.89	4.67 ± 1.41	5.20 ± 1.30	4.69 ± 1.03	5.40 ± 1.14	4.50 ± 1.38	3.67 ± 1.03	5.00 ± 2.00
ODI	0.58 ± 0.11	0.62 ± 0.17	0.53 ± 0.09	0.52 ± 0.09	0.63 ± 0.14	0.58 ± 0.16	0.55 ± 0.10	0.54 ± 0.08	0.51 ± 0.08	0.58 ± 0.20
JOA	10.93 ± 2.23	8.33 ± 3.06	11.40 ± 2.30	12.22 ± 2.49	8.60 ± 2.30	11.38 ± 3.33	10.00 ± 2.55	11.33 ± 2.42	11.5 ± 3.39	9.40 ± 3.78

SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu, VAS = Visual Analog Scale.

Table 3

The VAS, ODI, JOA results of the 2 groups before and after treatment.

Intervention	Syndrome type	Before treatment			1-week			2-week			3-week			*P* value		
		VAS	ODI	JOA	VAS	ODI	JOA	VAS	ODI	JOA	VAS	ODI	JOA	VAS	ODI	JOA
BSTL		4.69 ± 1.47	0.57 ± 0.11	10.78 ± 2.61	3.44 ± 1.27	0.47 ± 0.08	12.69 ± 2.30	2.53 ± 1.48	0.41 ± 0.10	14.61 ± 3.04	1.50 ± 1.18	0.24 ± 0.11	19.67 ± 3.76	.000†	.000†	.000†
	HSBZ	4.71 ± 1.27	0.58 ± 0.11	10.93 ± 2.23	3.36 ± 1.15	0.48 ± 0.06	12.14 ± 1.79	2.29 ± 1.59	0.39 ± 0.11	15.79 ± 3.09	1.07 ± 1.14	0.18 ± 0.09*	22.50 ± 2.50*	.000†	.000†	.000†
	SRBZ	6.00 ± 2.65	0.62 ± 0.17	8.33 ± 3.06	4.33 ± 2.08	0.49 ± 0.18	11.33 ± 1.53	3.33 ± 2.08	0.48 ± 0.18	11.00 ± 1.00	2.67 ± 0.58	0.32 ± 0.03	15.33 ± 1.53	.084	.082	.142
	QZXY	3.40 ± 0.89	0.53 ± 0.09	11.40 ± 2.30	2.40 ± 0.55	0.42 ± 0.06	14.60 ± 2.88	1.80 ± 0.45	0.39 ± 0.04	14.80 ± 2.95	2.40 ± 0.55	0.34 ± 0.09	16.20 ± 1.48	.007†	.008†	.073†
	SIX	4.67 ± 1.41	0.52 ± 0.09	12.22 ± 2.49	3.78 ± 1.30	0.45 ± 0.08	13.33 ± 1.80	2.78 ± 1.72	0.41 ± 0.08	13.78 ± 2.54	1.00 ± 0.87	0.24 ± 0.11	19.22 ± 3.70	.000†	.000†	.001†
	SAX	5.20 ± 1.30	0.63 ± 0.14	8.60 ± 2.30	3.60 ± 1.34	0.49 ± 0.09	12.00 ± 3.39	3.00 ± 1.00	0.45 ± 0.09	14.80 ± 3.35	2.00 ± 1.58	0.29 ± 0.10	18.60 ± 3.71	.001†	.002†	.007†
Celecoxib		4.63 ± 1.31	0.56 ± 0.13	10.91 ± 3.09	3.74 ± 1.36	0.48 ± 0.09	12.43 ± 2.85	2.74 ± 1.54	0.43 ± 0.09	14.34 ± 3.24	1.57 ± 1.44	0.28 ± 0.09	19.17 ± 3.08	.000†	.000†	.000†
	HSBZ	4.69 ± 1.03	0.58 ± 0.16	11.38 ± 3.33	3.92 ± 1.19	0.49 ± 0.10	12.62 ± 3.01	2.92 ± 1.55	0.45 ± 0.11	14.08 ± 2.99	1.31 ± 1.38	0.29 ± 0.09*	19.46 ± 4.12*	.000†	.000†	.000†
	SRBZ	5.40 ± 1.14	0.55 ± 0.10	10.00 ± 2.55	4.20 ± 1.92	0.45 ± 0.10	13.40 ± 3.78	3.60 ± 1.82	0.44 ± 0.09	14.00 ± 4.47	2.60 ± 0.89	0.32 ± 0.06	18.00 ± 2.35	.043†	.001†	.004†
	QZXY	4.50 ± 1.38	0.54 ± 0.08	11.33 ± 2.42	3.67 ± 1.21	0.50 ± 0.08	12.83 ± 1.33	2.67 ± 1.21	0.45 ± 0.08	14.67 ± 3.83	2.50 ± 1.64	0.32 ± 0.10	18.00 ± 1.79	.007†	.001†	.003†
	SIX	3.67 ± 1.03	0.51 ± 0.08	11.5 ± 3.39	2.83 ± 1.17	0.47 ± 0.07	12.33 ± 2.34	1.83 ± 1.17	0.40 ± 0.01	16.00 ± 2.19	0.83 ± 1.17	0.24 ± 0.05	20.17 ± 3.06	.000†	.000†	.009†
	SAX	5.00 ± 2.00	0.58 ± 0.20	9.40 ± 3.78	4.00 ± 1.58	0.5 ± 0.090	10.60 ± 3.58	2.60 ± 1.95	0.41 ± 0.11	13.00 ± 3.32	1.00 ± 1.41	0.21 ± 0.10	19.80 ± 1.64	.001†	.006†	.001†

QZXY = Qi Zhi Xue Yu, SAX = Shen Yang Xu, SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu, VAS = Visual Analog Scale.

*p.s. and comparison between groups with the same syndrome type, $P < .05$.

†p.s. and comparison before and after treatment, $P < .05$.

difference in the effective rate of each syndrome type in the 2 groups. Subsequently, the significant rate of each syndrome type in the 2 groups was evaluated as shown in Table 5, and the results showed that there was no statistical difference in the significant rate between the 2 groups ($P = .071$). After that, statistical analysis of the significant rate of each syndrome type was done, and it was found that the significant rate of patients with HSBZ syndrome in the BSTL group was significantly higher than those in the celecoxib group ($P = .012$). The difference was statistically significant.

4. Discussion

To our knowledge there were few randomized controlled clinical trials to evaluate herbal combination therapy for NSLBP, recently some related trials were seen frequently.[16,17,28] As the clinical trial progressed, we observed that within 3 weeks, both BSTL and celecoxib interventions were able to treat NSLBP, with improvements in VAS scores and waist function index. However, there were no significant differences in clinical outcomes between these 2 interventions. Then we divided the patients into 5 syndrome types according to TCM principles and observed their clinical improvements. We found that celecoxib had similar improvements in VAS score and waist function index for each syndrome type. The same conclusion can be drawn for the syndromes in the BSTL group as in the celecoxib group, except for the SRBZ syndrome. In the treatment of SRBZ syndrome, BSTL prescription showed a trend of improvement in VAS scores and waist function index of patients, but no statistically significant improvement could be concluded. Meanwhile, in the treatment of HSBZ syndrome of NSLBP, BSTL prescription showed better clinical results than celecoxib, although there was no difference in VAS scores between the 2 groups. However, patients in BSXL group had better waist function than those in celecoxib group. In order to explore the reasons for it, after analyzing each item of the ODI and JOA, we found that the improved waist function is mainly reflected in "personal care," "lifting," "walking," "sitting," and "standing," which may be due to the improvement of the body's muscular endurance or muscle energy supply efficiency, while in the theory of TCM, Shen Xu is the root cause of LBP, which is manifested by the decline of body function, fatigue and other manifestations, while BSTL can enhance the Shen. Therefore, it can improve waist function in the case of similar VAS scores.

At present, most NSLBP is mainly treated by conservative treatment, and there is no sufficient evidence to prove that certain fusion surgeries can treat NSLBP.[29] There is also no evidence to support interventional treatment of NSLBP, such as epidural steroid injections, lumbar facet joint injections, and cryoablation.[30,31] In this case, complementary medicine can play its unique advantages in the management of NSLBP. In China, most patients with low back pain choose some complementary medical methods such as compound Chinese herbal medicine, acupuncture, massage, and qigong, which can relieve the symptoms of patients to a certain extent.

Traditional Chinese Medicine principles consider LBP to be a disease caused by exogenous factors (Feng, Han, Shi, Re), internal factors (Shen Xu), or injury factors (Qi Zhi, Xue Yu, Tan Yin), which leads to one or both sides or in the middle as the main symptoms of a disease, many other parts can be manifested as discomfort at the same time. Based on TCM principles, Shen Xu, which leads to decreased defences against those exogenous factors, is the most important factor of LBP. Based on this, in a nutshell, with the exogenous factor of Feng, Han, Shi, making the syndrome of Han Shi Bi Zu (HSBZ); with the exogenous factor of Feng, Shi, Re, making the syndrome of Shi Re Bi Zu (SRBZ); with the injury factor of Qi Zhi or Xue Yu, making the syndrome of QZXY, with only the internal factors making the syndrome of SIX and SAX.

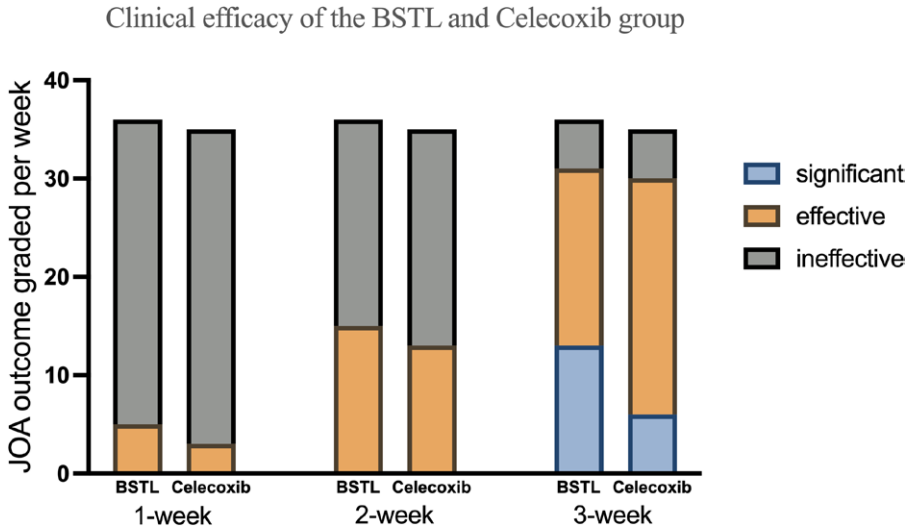

Figure 2. Clinical efficacy distribution of patients in BSTL and Celecoxib group assessed by JOA scores at each time point. BSTL= Bushen Tongluo formula, JOA = Japanese Orthopaedic Association scores.

Table 4

Therapeutic outcome of each syndrome type for 2 groups due to JOA results.

		1-week (n)			2-week (n)			3-week (n)		
Effective rate		**Effective**	**Ineffective**	***P* value**	**Effective**	**Ineffective**	***P* value**	**Effective**	**Ineffective**	***P* value**
Total	BSTL	5	31	.710	15	21	.697*	31	5	.962*
	Celecoxib	3	32		13	22		30	5	
HSBZ	BSTL	0	14	.222	8	6	.252	14	0	.098
	Celecoxib	2	11		4	9		10	3	
SRBZ	BSTL	1	2	>.999	0	3	.464	2	1	.375
	Celecoxib	1	4		2	3		5	0	
QZXY	BSTL	2	3	.182	2	3	>.999	4	1	>.999
	Celecoxib	0	6		3	3		5	1	
SIX	BSTL	1	8	>.999	2	7	.085	6	3	.604
	Celecoxib	0	6		4	2		5	1	
SAX	BSTL	1	4	>.999	3	2	.136	5	0	>.999
	Celecoxib	0	5		0	5		5	0	

SAX = Shen Yang Xu, SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu.

*p.s. and Chi-square test was used, and Fisher exact test was used for other data.

On the one hand, due to the randomized grouping in this study, the number of patients in each syndrome type was not unified for each syndrome type when the patients were enrolled, but after the patients of 2 groups were divided, then to determine whether the patients in each syndrome type of the 2 groups were comparable, so as to compare the clinical results. At the same time, from the perspective of the distribution of syndrome types, HSBZ has the most patients among all syndrome types. However, there were only 8 patients with SRBZ. Although the 2 groups of SRBZ patients were statistically comparable, it is too early to conclude that BSTL formula does not improve the clinical outcomes of NSLBP patients with SRBZ syndrome. In the future, we will standardize the number of subjects for each syndrome, so as to be able to make a unified judgment on the efficacy of BSTL formula in the treatment of NSLBP for each syndrome. On the other hand, NSLBP is a self-healing disease, especially in the early stage of symptoms, and some patients' pain symptoms and waist function may be improved within 1 or 2 weeks.[32] Therefore, the trial included patients with an onset time of more than 1 week to reduce bias. For the universality and convenience, we chose VAS, ODI and JOA as the primary observation indicators.[24] However, because these scales were filled out by patients themselves, they were subjective. Although specific evaluation criteria were given in some items, due to the differences in each individual's understanding of the criteria, different scores were given. But on the other hand, pain and functional limitations is a subjective phenomenon, so there is no better way to quantify the severity of pain and waist function. At present, NSAID drugs are the recommended medical choice for NSLBP in many national guidelines and research,[1,15,20] we believe that celecoxib, a classic NSAID, is the best pharmacological intervention for NSLBP. And this clinical trial is a non-inferior study, and the original intention of this trial was to evaluate the clinical outcomes of BSTL and celecoxib for NSLBP, considering the nocebo effect and corresponding ethical issues (Article 33 of Declaration of Helsinki) as well. Thus, this trial did not set up a blank control group or a placebo group to eliminate the interference caused by the self-healing of the disease. However, from the results, this trial could prove that BSTL prescription has similar clinical results with celecoxib in the treatment of NSLBP, and even in a special syndrome, BSTL prescription has better waist function improvement than celecoxib. In the future, if we can solve the problem of the herbal compound placebo and design the study as a double-blind trial, we will design the trial to demonstrate the outcomes of BSTL formula without the effect of self-healing nature of NSLBP.

Table 5

Comparison of significant rate of each syndrome type between the 2 groups based on JOA.

Significant rate		3-week (n)		*P* value
		Significant	Other	
Total	BSTL	13	23	.071*
	Celecoxib	6	29	
HSBZ	BSTL	10	4	.012†
	Celecoxib	3	10	
SRBZ	BSTL	0	3	>.999
	Celecoxib	0	5	
QZXY	BSTL	0	5	>.999
	Celecoxib	0	6	
SIX	BSTL	2	7	>.999
	Celecoxib	2	4	
SAX	BSTL	1	4	>.999
	Celecoxib	1	4	

SAX = Shen Yang Xu, SIX = Shen Yin Xu, SRBZ = Shi Re Bi Zu.

*p.s. and Chi-square test was used, and Fisher exact test was used for other data.

†p.s. and comparison before and after treatment, $P < .05$.

A multicenter randomized controlled clinical trial in Korea to evaluate herbal combination therapy for LBP is also expected. The protocol of this study has been published, but the results are not available at this time.[28]

A parallel double-blind randomized clinical trial by Zhan et al evaluated the efficacy and safety of the intervention on LBP by comparing the ODI, VAS, and MCID of patients with herbal compound with lumbar traction and placebo with lumbar traction. Studies have shown that herbal compound combined with lumbar traction in the treatment of LBP can more effectively relieve the symptoms of patients and improve the lumbar function, which is similar to the conclusions drawn in this paper, but this study compared herbal compound with Nsaid drugs and reached a more intuitive conclusion.[16]

5. Conclusion

Based on the clinical outcomes of this randomized controlled clinical trial, we can conclude that both BSTL herbal compound and celecoxib are effective and safe in the clinical treatment of NSLBP. After sub-grouping according to TCM principles, we found that BSTL herbal compound had unique advantages in the treatment of HSBZ syndrome type of NSLBP. Although the pain improvement of patients was similar to that of celecoxib, they could obtain better waist function after 3 weeks of treatment.

Author contributions

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