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Original Article

Blood-letting therapy combined with Master Tung's Five-tiger Point Scraping (Gua Sha) for patients with hematological malignancy and chemotherapy-induced peripheral neuritis

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Abstract: Objective: To investigate the clinical efficacy of Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping for patients with hematological malignancy and peripheral neuritis. Methods: A total of 70 patients with hematological malignancy who were admitted to Langfang TCM Hospital between January 2020 and December 2022 for treating chemotherapy-induced peripheral neuritis were enrolled retrospectively. The patients were divided into a single treatment group that received western nutritional interventions alone, and a combined treatment group that underwent additional Traditional Chinese Medicine (TCM) Shixuan and Qiduan blood-letting therapy, along with Master Tung's Five-tiger Point (11.27) Scraping. Statistical analyses were carried out to compare the clinical efficacy of the two treatment plans in the patients. Scores of sensory disturbance rating (SDR), numeric rating scale (NRS) for pain, nail fold microcirculation (NFM) of the infected extremity, and the quality of life (QoL), as well as the motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) of the median and peroneal nerves of patients in both groups were recorded and compared before and after treatment. The incidence rate of adverse events was compared between the two groups. Furthermore, the clinical outcomes of patients in the two groups were followed up and analyzed for correlated factors using univariate and multivariate analyses. Results: The clinical efficacy rate achieved by the combined therapy was 88.57%, significantly higher than 68.57% for patients undergoing single therapy (P=0.041). Moreover, the scores of SDR, pain NRS, QoL, and NFM of the affected extremity, as well as the MNCV and SNCV of patients in the two groups were all improved after treatment, with better improvements in the combined treatment group than in the single treatment group. The incidence rate of adverse events was higher in the single treatment group compared to that of the combined treatment group (17.14% vs. 11.42%) (P=0.466). In addition, during the six-month follow-up period, a total of 27 patients in both groups developed chronic neural disorders. Logistic regression analysis revealed that the MNCV and SNCV of the median and peroneal nerves, together with the duration of chemotherapy, served as independent influencing factors. Conclusion: Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping could improve the SDR and pain NRS scores, facilitate the recovery of neural functions, and advance the QoL of patients with chemotherapy-induced peripheral neuritis without increasing the risk of adverse reactions.

Keywords: Shixuan and Qiduan blood-letting therapy, Master Tung's Five-tiger Point (11.27) Scraping, chemotherapy, peripheral neuritis, clinical efficacy

Introduction

Leukemia is a malignant tumor of the blood and bone marrow. It can be classified into over 60 clinical subtypes and is characterized as acute or chronic based on its severity [1-3]. Hematological disorders often affect children. It was reported that hematological malignancy was the second largest cause of children's death in China, with a morbidity of 30-40 per million children. The morbidity and its rising incidence were both higher in China than those of the developed countries in Europe or America [4]. Clinical data analysis showed that hematological malignancy was characterized by features such as high mutation rate, repeated occurrence, complicated treatment, and difficulty in achieving full recovery, resulting in a low cure rate of affected patients [5, 6]. Currently, chemotherapy is a primary therapy for the clinical treatment of hematologic malignancy, and can increase patients' 5-year survival rate to about 50%. However, chemotherapy not only has a long duration, but is also accompanied by various complications, such as myelosuppression, nausea, vomiting, liver function injury and peripheral neuritis, the last of which has a high morbidity of 50%-90%. Patients with mild peripheral neuritis might get despondent, leading to a reduced quality of life (QoL), and those with severe peripheral neuritis might not be able to soldier through the chemotherapy process, resulting in a shortened life span [7, 8].

So far, nutritional support to maintain neural function plus the use of pain killers including antiepileptic drugs, antidepressants, selective 5-serotonin reuptake inhibitors, norepinephrine reuptake inhibitors, tricyclic antidepressants, and opioid drugs for relieving specific symptoms are primary treatment options for chemotherapy-induced peripheral neuritis, but it is still a challenge to determine the optimal dose and to prevent adverse events caused by the drugs [9]. Traditional Chinese Medicine (TCM), however, was found to have a significant importance in the treatment of peripheral neuritis. In a previous single-case study, Shixuan and Qiduan blood-letting therapy in combination with Master Tung's Five-tiger Point (11.27) Scraping was reported to have promising efficacy for peripheral neuritis, even though the results were limited by the small sample size [10]. We, therefore, explored the treatment Shixuan and Qiduan blood-letting therapy plus Master Tung's Five-tiger Point (11.27) Scraping for patients with hematological malignancy and chemotherapy-induced peripheral neuritis, aiming to offer a more evidence-based perspective for improving treatment.

General data and methods

General data

The clinical data of 70 patients with hematological malignancy who were admitted to Langfang TCM Hospital for treating chemotherapy-induced peripheral neuritis were collected retrospectively. The patients were divided into two groups according to what treatment they underwent. Patients who received Western medical treatment alone were defined as a single treatment group, and those who underwent additional Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping were defined as a combined treatment group. This research was approved by the Ethnic Committee of Langfang Hospital of Traditional Chinese Medicine (Ethics No.: 021-007).

Patients were eligible if they: i. were confirmed to have hematological malignancy by bone marrow biopsy; ii. were over 18 years; iii. were conscious in speech; iv. were confirmed with peripheral neuritis by clinical diagnosis plus the use of electromyography [11]; v. had not undergone any chemotherapy before; vi. had complete clinical data.

Patients were excluded from the study if they: i. had cognitive dysfunction before treatment; ii. had any other malignancies; iii. Were aged over 80 years; iv. had previous peripheral neuritis caused by other diseases; v. had severe cardiovascular diseases, or serious dysfunction of neural or digestive systems; vi. had disabled extremities caused by any reason; vii. could not be followed up due to poor compliance.

Treatment methods

Patients in the single treatment group received conventional nutritional support to maintain their neural functions by intravenous or intramuscular injection of methylcobalamin (500 μg per time, three times a week; Drug Approval No.: J20130076; Weicai (China) Pharmaceuti-

Table 1. Evaluation criteria of clinical efficacy

Item	Score
No symptoms	0
Occasional symptoms, but not affecting daily life	2
Frequent symptoms, affecting daily life	4
Continuously present symptoms, severely affecting daily life	6

cal Co., Ltd.), oral administration of vitamin B1 (one tablet a time, three times a day; Drug Approval No.: H42020611; Huazhong Pharmaceutical Company Limited), or B2 (5 mg a time, twice per day; Drug Approval No.: H51020831H51020831; Youhua Pharmaceutical (Leshan) Co., Ltd.), and intramuscular injection of ganglioside (20 mg; Drug Approval No.: H20051486; Qilu Pharmaceutical Co., Ltd.). Patients in the combined treatment group received additional Shixuan and Qiduan bloodletting therapy plus Master Tung's Five-tiger Point (11.27) Scraping.

For Shixuan and Qiduan blood-letting therapy: 75% alcohol was used to disinfect the bloodletting site of patients before operation. Points located at the affected extremity were selected. For instance, Qiduan points of patients with toe numbness were selected to let out blood from their toes, and points at the sole of the feet could also be pricked to release blood if numbness and pain were identified at the site. Shixuan points were chosen to let out blood if patients had pain or numbness in the fingers. The therapy was carried out in the following way. The needle of a 1 mL syringe was used to prick the points to release blood. When dark red blood was seen oozing out from the skin, two to three more drops of blood were continually squeezed out from the pricked site until the blood color turned to red, which was the cue to stop the bloodletting. Later on, a cotton swab was placed at the operation site to stop the bleeding.

Master Tung's Five-tiger Point (11.27) Scraping: Five-tiger Points, also known as Wu Hu points (11.27), is a set of acupoints located on the radial aspect of the proximal segment of the thumb on the border of the red and white skin. The points are numbered sequentially, one through five, starting from the first transverse striation and ending at the second striation, with No. 1 point being the most distal point and No. 5 point the most proximal. Anatomically, the points were surrounded by subcutaneous superficial branches of nerves, as well as spleen and renal nerves on the radial aspect of the thumb, where the scraping technique was performed. The scraping was performed once every other day, for two weeks as a course. The clinical efficacy of the therapies on patients was evaluated at the end of the first course.

Outcome measurements

To evaluate the clinical efficacy, the sensory disturbance rating (SDR) scores were compared before and after treatment to determine the sensory recovery (coldness, numbness, myrmeciasi, burning sensation) in the affected extremity of patients, then the reduction rate was calculated for a comparison of clinical efficacy [12]. See **Table 1**. The reduction rate is equal to the score margin between before and after treatment/the score before treatment *100%. Patients with a reduction rate of ≥90% were considered fully recovered, ≥70% was considered a significant improvement, between 30%-69% was considered as having an improvement in general, and <30% was deemed as no improvement at all. The total efficacy rate = (patients with full recovery + significant improvement + improvement)/35 *100%.

The numeric rating scale (NRS) [13] was applied to compare the severity of pain in the peripheral nerves of patients before and after treatment.

Nailfold capillaroscopy by ZL104 detector and imaging analyzing system was used to evaluate nail fold microcirculation (NFM) of the affected extremity [14]. Major measures include image resolution, loop, input branch diameter, crossed loop, abnormal loop, bleeding velocity and erythrocyte aggregation, and the scores of each measure were added up together in the end. The condition of the affected extremity was judged by the cumulative scores, with a score <2 considered normal, between 2 and 4 as mildly abnormal, between 4 and 8 as moderately abnormal, and >8 as severely abnormal.

To evaluate the QoL, the European Organization for Research and Treatment of Cancer (EORTC) Core Quality of Life questionnaire (EORTC QLQ-

Table 2. Comparison of general data between the two groups

Item	Single treatment group	Combined treatment group	T/χ^2 value	*P* value
Gender			0.521	0.470
Male	21	18		
Female	14	17		
Age (years)	56.7±7.2	57.3±6.9	0.774	0.442
Type of disease			1.048	0.592
Leukemia	10	11		
Lymphoma	16	12		
Myeloma	9	12		
Chemotherapy course			2.083	0.353
1-3	8	11		
4-6	15	10		
>6	10	14		
BMI (kg/m^2)	24.8±1.8	25.1±1.9	0.773	0.492
Chemotherapy plans			0.393	0.822
DA	7	9		
R-CHOP	15	13		
VAD	13	13		

Note: DA: Daunorubicin + Cytarabine; R-CHOP: Rituxima + Cyclophosphamide + Doxorubicin + Vincristine + Prednisone; VAD: Vincristine + Doxorubicin + Dexamethasone. *t* denotes for independent sample *t* test, and χ^2 for Chi square test. BMI: body mass index.

Table 3. Comparison of clinical efficacy between the two groups (n, %)

Group	Single treatment group	Combined treatment group
Clinical efficacy		
Cured	15 (42.86%)	20 (57.14)
Significantly improved	8 (22.86)	7 (20.00)
Generally improved	1 (2.85)	4 (11.43)
No efficacy	11 (31.43)	4 (11.43)
Total efficacy	24/35 (68.57)	31/35 (88.57)
χ^2	4.158	
P	0.041	

C30) was used in this study [15]. The scores were cumulative, with 30 questions in total, and each question valued from 0 to 5 points. Higher scores indicate better QoL.

For the assessment of motor nerve conduction velocity (MNCV) and sensory nerve conduction velocity (SNCV) of the median and peroneal nerves in the affected extremity, the median nerves in the affected arms and peroneal nerves in the affected legs were selected to monitor the electromyogram changes before and after treatment. The neurophysiologic detector was used to measure the SNCV of patients in the two groups.

The incidence rate of adverse events in this study included any abnormality in blood routine measures and kidney function, as well as skin rash and headache. The incidence rates of adverse events were compared between patients receiving Western medical treatment alone and those undergoing additional combined therapy.

Statistical analysis

All data were analyzed with the use of SPSS22.0 software. Measured data conforming to a normal distribution were expressed as mean ± standard deviation ($\bar{x}$ ± sd), and the between-group comparison for the measurement data was performed using independent sample *t*-test. Numeric data were expressed as n (%), and the between-group comparison for the incidence rates was carried out with Chi-square test. P<0.05 was considered a statistically significant difference.

Results

Comparison of the general data between the two groups

A total of 70 patients were included in the study, and the results showed no significant differences in general data, such as age, chemotherapy plans, type of malignancies, gender, or chemotherapy course (all P>0.05). See **Table 2**.

Comparison of the clinical efficacy between the two groups

The clinical efficacy rate of the combined treatment group was 88.57%, higher than the 68.57% for the single treatment group. The difference was statistically significant (χ^2=4.158, P=0.041). See **Table 3**.

Comparison of the NRS pain score before and after treatment

No statistical significance was found in the NRS pain scores between the two groups before

Table 4. Comparison of NRS pain scores of patients before and after treatment ($\bar{x} \pm sd$)

Group	Before treatment	After treatment	t value	*P* value
Single treatment group	3.68±1.63	1.76±0.84	6.174	<0.001
Combined treatment group	3.74±1.75	0.98±0.81	8.467	<0.001
t value	0.148	3.954	-	
P value	0.882	<0.001	-	

Note: *t* means independent sample t test for between-group comparison. NRS: numeric rating scale.

Table 5. Comparison of total NFM and QoL scores between the two groups before and after treatment

Group	Total NFM scores	QoL scores
Single treatment		
Before treatment	6.87±0.86	73.82±7.86
After treatment	4.96±0.81*	82.70±6.13*
Combined treatment		
Before treatment	6.83±0.84	72.23±4.73
After treatment	3.52±0.57*,#	87.65±7.81*,#

Note: *P<0.05 compared to before treatment; #P<0.05 when the combined treatment group is compared to the single treatment group. NFM: nail fold microcirculation; QoL: quality of life.

treatment. The NRS pain scores in the affected extremity decreased after treatment in both groups, with the score lower in the combined treatment group than that in the single treatment group (P<0.05). See **Table 4**.

Comparison of the scores of QLQ-C30 and NFM of the affected extremity between the two groups

There was no statistical significance in the scores of QoL and NFM of the affected extremity between the two groups before treatment. After treatment, the NFM total scores were decreased and the QoL scores increased in both groups, with better results achieved in the combined treatment group than in the single treatment group (P<0.05). See **Table 5**.

Comparison of the SDR scores before and after treatment

There was no statistical significance in the SDR scores between the two groups before treatment. However, the SDR scores of patients in both groups were reduced after treatment, with the score in the combined treatment group lower than those in the single treatment group (P<0.05). See **Table 6**.

Comparison of the MNCV and SNCV of the peroneal nerves and the median nerves in the affected extremity before and after treatment

No statistical significance was found in the MNCV and SNCV before treatment (all P>0.05). However, the MNCV and SNCV both increased in the two groups after treatment, with the velocities in the combined treatment group higher than those of the single group treatment (P<0.05). See **Figures 1**, **2**.

Comparison of the incidence rates of adverse reactions between the two groups

Both groups showed one case of skin rash and one case of headache, which fully disappeared after symptomatic treatment. In addition, one patient in the single treatment group developed abnormal blood routine lab values and one had abnormal liver function, while none of the patients in the combined treatment group developed hematologically-related disorders (χ^2=0.634, P=0.466).

Analysis of risk factors for chronic neural disorders

Our follow-up results showed that a total of 27 patients developed chronic neural disorders and the other 43 patients obtained favorable efficacy after treatment. The results of univariate analysis suggested that factors contributing to the development of chronic neural disorders from chemotherapy-induced peripheral neuritis included chemotherapy course, MNCV, SNCV, and treatment plan. Disease type, chemotherapy protocol, and age were not among the risk factors. Furthermore, a logistic regression analysis was carried out with the factors mentioned above as independent variables and chronic neural disorders as a dependent variable. The results indicated that disease course, MNCV, SNCV, and treatment plan were independent risk factors for chronic neural disorders. See **Tables 7** and **8**.

Table 6. Comparison of SDR scores between the two groups before and after treatment

Group	Coldness	Formication	Burning sensation	Numbness
Singe treatment group				
Before treatment	3.56±1.36	2.48±1.83	2.69±1.42	4.88±1.42
After treatment	2.59±0.48*	1.78±1.46*	1.47±1.23*	2.43±0.46*
Combined treatment group				
Before treatment	3.62±1.27	2.43±1.92	2.71±1.38	4.84±1.79
After treatment	1.53±0.66*,#	0.74±0.49*,#	0.60±0.44*,#	1.18±1.30*,#

Note: *P<0.05 compared with before treatment; #P<0.05 when the combined treatment group was compared to the single treatment group. SDR: sensory disturbance rating.

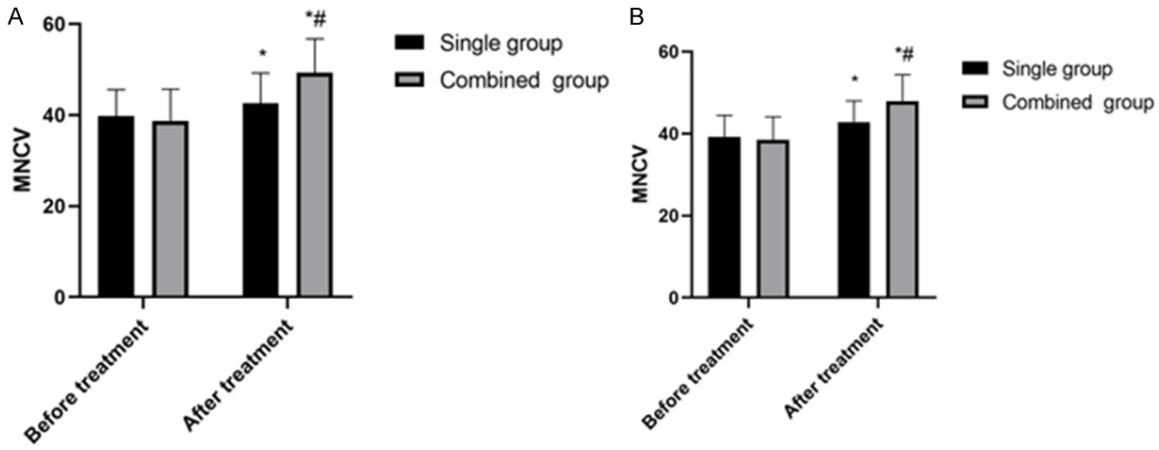

Figure 1. Comparison of the MNCV of the peroneal nerves and median nerves before and after treatment between the two groups. A: MNCV of the peroneal nerves; B: MNCV of the median nerves. *P<0.05, compared to that before treatment in the corresponding group; #P<0.05, compared to the single treatment group after treatment. MNCV: motor nerve conduction velocity.

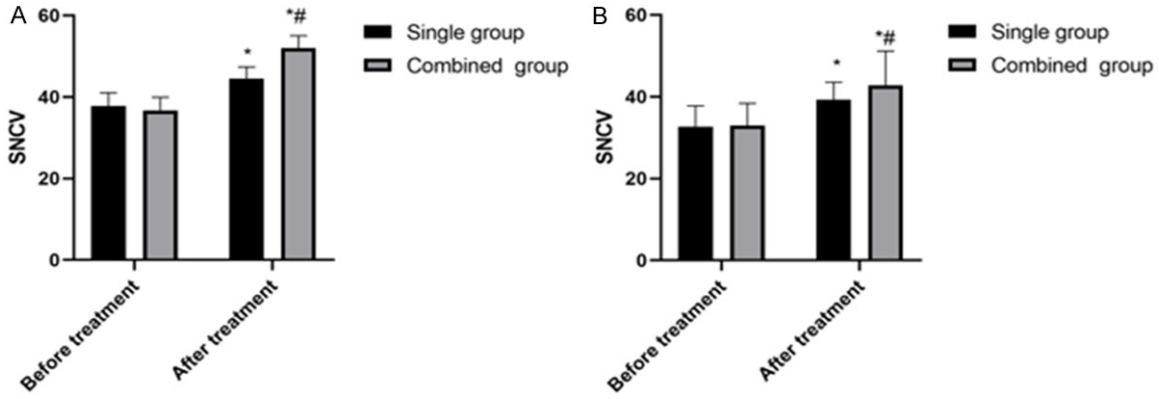

Figure 2. Comparison of the SNCV of the peroneal nerves and median nerves before and after treatment between the two groups. A: SNCV of the peroneal nerves; B: SNCV of the median nerves. *P<0.05, compared to that before treatment in the corresponding group; #P<0.05, compared to the single treatment group after treatment. SNCV: sensory nerve conduction velocity.

Discussion

Hematological malignancies are a set of diseases caused by malignant clones of hematological stem cells. Such diseases are acute in occurrence and rapid in development, with poor prognosis. They are also major threats to human health. It has been reported that the

Table 7. Univariate analysis of factors associated with chronic neural disorder

Item	Patients with chronic neural disorder (n=27)	Patients with effective treatment (n=43)	t/χ^2 value	*P* value
Age			0.161	0.688
≤65 years old	17	25		
>65 years old	10	18		
Gender			1.004	0.316
Male	15	29		
Female	12	14		
Treatment plan			9.023	0.002
Single treatment	20	16		
Combined treatment	7	27		
Chemotherapy plan			0.774	0.663
DA	9	21		
R-CHOP	10	10		
VAD	8	12		
Disease type			0.699	0.532
Leukemia	10	15		
Lymphoma	8	17		
Myeloma	9	11		
MNCN	62.5±13.5	36.8±12.4	22.558	<0.001
SNCV	59.1±10.3	41.8±11.5	11.772	<0.001
Chemotherapy course	7.4±2.5	5.8±3.0	8.440	0.034

Note: DA: Daunorubicin + Cytarabine; R-CHOP: Rituxima + Cyclophosphamide + Doxorubicin + Vincristine + Prednisone; VAD: Vincristine + Doxorubicin + Dexamethasone; MNCV: motor nerve conduction velocity; SNCV: sensory nerve conduction velocity.

Table 8. Logistic regression analysis of factors influencing chronic neural disorder

Indicator	Standardized β	OR	95% *CI*	*P*
Treatment plan	0.025	0.321	0.119-0.846	0.033
Chemotherapy course	1.246	2.767	1.025-4.642	0.005
MNCV	0.418	1.572	1.109-6.595	0.027
SNCV	0.209	1.692	1.309-7.015	0.003

Note: MNCV: motor nerve conduction velocity; SNCV: sensory nerve conduction velocity.

occurrence of hematological malignancies is showing a growing tendency year on year worldwide. The prognosis is largely age-related, worsening with older age [16]. China, with a large aged population close to 300 million, now has a high prevalence of hematological malignancies. Therefore, it is of great significance to improve diagnosis and treatment.

Although targeted therapy and immunotherapy have made continuous improvement over recent years, and have been applied for treatment of hematological diseases, chemotherapy is still the main method for relief of symptoms and prolongation of survival [17, 18]. However, various complications, such as nausea, vomiting, myelosuppression-induced infections, and risk of bleeding, occur as a consequence of systematic application of chemotherapy drugs, even though they can all be relieved by antidotes [19, 20]. Apart from nutritional intervention, so far treatment for chemotherapy-induced peripheral neuritis has few effective choices. Complications of peripheral neuritis often include numbness and pain in the fingertips, pale skin, abnormal sensation, and reduced muscule strength, greatly influencing the QoL of patients, and leading to negative emotions of anxiety and depression. Some patients even quit treatment [21, 22]. Hence, it is significant to explore treatment plans that can relieve chemotherapy-induced peripheral neuritis. Currently, treatment for the disease focuses on nutritional support using western medicine. Our study results revealed that after receiving nutritional supplementation using western medicine, several measures to assess neural functions of patients in the two groups were all improved compared with before treatment. The mechanisms behind it might be the excitability of central and peripheral neurons caused by chemotherapy-related neural injury, leading to demyelination of nerve fibers, damage to sensory neurons in the dorsal root ganglia, axonal degeneration, etc. B vitamins can supplement the energy for neuronal metabolism, thereby reducing neural injury, consistent with the results of previous studies [23].

Originating from China, TCM plays a critical role in the treatment of hematologic diseases. According to syndrome differentiation principles in TCM, peripheral neuritis is similar to the TCM syndromes that are manifested as cold coagulation, blood stasis, and malnutrition of channels. Treatment for this disorder, from the *Miraculous Pivot·Meridians*, is to "eliminate prolonged stagnation", indicating that nlocal blood-letting is an efficient therapeutic approach [24]. Therefore, Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping were selected in the study for this specific purpose. After the application of the combined therapies, the SDR, NRS pain, NFM, QoL scores, as well as MNCV and SNCV of the affected extremities of patients were all improved compared to those before treatment, which might be associated with the fact that puncture at the Qiduan and Shixuan points could alleviate symptoms of the extremities. The TCM theoretical bases applied here include: Qiduan points mainly govern numbness in the feet and toes (*Outline of Acupuncture Points and Their Application*), and Shixuan points control the upper extremities (*Compendium of Acupuncture and Moxibustion* and *Thousand Golden Prescriptions*). According to the two theories, letting blood out from the Shixuan and Qiduan points can effectively treat ailments in corresponding extremities, thus eliminating blood stagnation, regenerating blood, unblocking meridians and Qi circulation, and as a result, relieving clinical symptoms. The Five-tiger Point, as a supplementary treatment site, is effective because it is located on the radial aspect of the proximal segment of the thumb and surrounded by subcutaneous superficial branches of radial nerves, median nerves, proper palmar digital nerves, and splenic nerves, thereby governing pain in the feet and hands, which is consistent with the findings of previous studies [25-27]. Our results again confirmed the importance of TCM for treatment of peripheral neuritis and supported the conclusion that the combination of Shixuan and Qiduan blood-letting therapy and Master Tung's Five-tiger Point (11.27) Scraping could realize promising clinical outcomes, consistent with results from previous studies [28, 29]. Furthermore, statistical analysis of our follow-up results showed that chemotherapy course, MNCV, SNCV, and treatment plan were closely correlated with the long-term prognosis of patients. This suggests that combined TCM therapy can improve clinical effects, which again confirmed our results above. The prognosis of patients was suggested to be associated with their clinical features; therefore treatment plans for the patients should be chosen in accordance with their clinical features.

In this study, we observed and compared the incidence rates of complications in patients with peripheral neuritis between the two groups. Results suggested no significant difference in the incidence rates of the complications between the two groups, preliminarily indicating that Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping was safe in treating neuritis. This might be associated with TCM features such as minimal invasiveness, conforming to the previous result that TCM was highly safe in treating diseases [30].

All in all, Shixuan and Qiduan blood-letting therapy combined with Master Tung's Five-tiger Point (11.27) Scraping can improve the SDR scores, elevate MNCV and SNCV, relieve pain, and improve the QoL of patients with hematological malignancy and chemotherapy-induced peripheral neuritis without an increased risk of adverse events.

However, there are limits to the study. It is a single-centered study with a small sample size. A larger sample size should be designed to support the study results. Moreover, more objective measures should be added to consolidate the therapeutic effects of TCM treatment.

Disclosure of conflict of interest

None.

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