

ORIGINAL RESEARCH

Evaluation of Knowledge and Attitudes about the Traditional and Complementary Medicine Practices of the Patients with Neuropathic Pain Who Applied to the Physical Medicine and Rehabilitation Clinic

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Abstract

Objective: To evaluate the frequency of traditional and complementary medicine (TCM) use, the variety of applications, the sociodemographic and clinical characteristics of patients with neuropathic pain, and their knowledge and attitudes about TCM practices

Material and Methods: A total of 250 patients with neuropathic pain were included in this, cross-sectional study. The patients were divided into two groups: medication only (group 1, n=119) and medication with TCM practices (group 2, n=131). Questionnaires were completed by the patients in face-to-face interviews by a blinded physician.

Results: The mean age of the patients in group 2 (50.68±16.39) was found to be higher than in group 1 (p=0.043). In terms of chronic diseases, hypertension, cardiovascular diseases, and other diseases were found to be more common in group 2 than in group 1 (p<0.05). The number of patients with duration of neuropathic pain more than 5 years, the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and the Neuropathic Pain 4 (DN4) scale scores were found to be higher in group 2 than in group 1 (p<0.05). At least one TCM is known by %78.6 of group 2 and 61.3% of group 1 (p=0.003). The three most commonly used TCM practice in group 2 were wet cupping/cupping therapy (24%), leeches (22.8%), and acupuncture (11.6%).

Conclusion: It was determined that the mean age of patients who used medication with TCM practices together for the treatment of neuropathic pain was higher, neuropathic pain severity was higher, and neuropathic pain duration was longer than patients who used medication only for the treatment of neuropathic pain.

Keywords: Neuropathic, Pain, Traditional, Complementary, Medicine

INTRODUCTION

Neuropathic pain is defined by the International Association for the Study of Pain as pain resulting from a lesion or disease in the somatosensory system.

¹ Neuropathic pain is one of the main symptoms of a group of diseases such as diabetic neuropathy, trigeminal neuralgia, postherpetic neuralgia, radiculopathy, plexopathy, polyneuropathy or spinal cord injury.²

Pain due to a lesion or dysfunction affecting the central or peripheral nervous system is called central or peripheral neuropathic pain.³ It is often described

by patients as burning, tingling, numbness, and stabbing pain.³ Its prevalence is estimated to be between 1-1.5% in studies.^{4,5} First-line treatment includes tricyclic antidepressants, serotonin reuptake inhibitors, and calcium channel alpha 2 delta ligand inhibitors.⁶ However, neuropathic pain is slow to heal, difficult to treat, and similar to other forms of chronic pain. It also negatively affects the patient's psychological, social, and health-related quality of life.⁷ Opioids prescribed to patients with neuropathic pain may have undesirable effects, such as the risk of



addiction or insufficient reduction in pain.⁸ Not only in the opioid group but also anticonvulsant and antidepressant group drugs used in treatment can cause undesirable adverse effects or problems of lack of effect, make it difficult for patients to comply with treatment.⁸

Inadequacy and difficulties in the treatment of patients with neuropathic pain due to the diversity of underlying diseases make traditional and complementary medicine (TCM) applications an alternative treatment option for these patients. TCM practices are frequently used in the prevention and treatment of many diseases, and TCM practices in Turkey are regulated by the "Traditional and Complementary Medicine Regulation" published in the Official Gazette (Date: 27.10.2014, Number: 29158). The number of applications that can be applied in centers is limited to 15.⁹

There are limited data on the variety and frequency of TCM practices used in the treatment of neuropathic pain in the world and our country.^{10,11} In this study, we aimed to evaluate the frequency of use of TCM practices, the variety of applications, and the perspective and attitudes of patients with neuropathic pain to TCM practices. This study is the first study in Turkey to investigate TCM practices that are more frequently preferred by patients with neuropathic pain.

MATERIALS AND METHODS

Materials

This cross-sectional study was conducted between January 2nd, 2020, and June 2nd, 2020, in the Department of Physical Medicine and Rehabilitation of Kafkas University. A total of 250 patients with neuropathic pain were included in the study, and the patients were divided into two groups: medication only (n=119) and medication with TCM practices together (n=131). Patients aged between 30-60 years, female or male, who scored >12 points on the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scale, >4 points in the Neuropathic Pain 4 (DN4) scale, with the cognitive capacity to understand the questions, an underlying disease supporting the diagnosis of neuropathic pain, without drug or substance addiction, without a diagnosed psychiatric disease, and who used regular medication with the diagnosis of neuropathic pain for at least 1 year were included in this study.

Methods

Ethics committee approval (No: 80576354-050-99/15) was obtained from the Non-Invasive Ethics Committee of the Faculty of Medicine of Kafkas University to collect the data of the study. Before administering the questionnaire, the content of the study and the TCM practices listed in the study were

verbally explained to the patient. Written informed consent was obtained from all patients participating in the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

For the research, a questionnaire consisting of 30 questions was designed from past example studies.^{12,13} The prepared questionnaire was applied as a preliminary test on 12 volunteer participants. The questions that could not be understood by the participants were rearranged and the questionnaire was finalized. The 12 participants who volunteered for the pretest were excluded from the study. The form included questions about sociodemographic characteristics (10 questions), neuropathic pain (6 questions), and the use of TCM for neuropathic pain (2 questions). In the study, 15 TCM practices were listed. If there were TCM practices not included in the list but used by the participants, they were investigated in the form of open-ended questions. Questionnaires were administered to the patients in face-to-face interviews by a blinded physician. Three stages were followed to confirm the diseases causing pain in patients diagnosed as having neuropathic pain. Physical examinations, muscle strength, sensory and motor examinations, and deep tendon reflex examinations were performed by a physician. In addition, the diagnosis of the patients was confirmed by supportive imaging methods [magnetic resonance imaging (MRI) electromyography (EMG)] in the E-Pulse system. Finally, the DN4 questions and LANSS scale were administered to the participants via face-to-face interviews for the confirmation of neuropathic pain. Patients who scored more than 4 points in the DN4 and 12 points on the LANSS scale were classified as having neuropathic pain. Regular medication use for the treatment of neuropathic pain in the last 1 year was determined as having visited the relevant physician to prescribe minimum one drug for at least 3 months. Physician visits and prescriptions were checked from e-pulse and med-pharmacy systems. Patients whose cognitive capacity was not sufficient to answer the questions, who did not use regular medication for the treatment of neuropathic pain in the last 1 year, who achieved insufficient scores from only one questionnaire, and who had one or more TCM practices in the last 1 year for a purpose other than neuropathic pain treatment were excluded from the study.

Statistical analysis

The sample size of the study was calculated using the G*Power 3.1 program. For the study to reach 80% power, 250 patients were planned to be included in the study with the standard deviation data obtained from the previous study^{12,13}, by determining $\alpha=0.05$ error and adding 20% to allow for patient loss. Statistical

analysis and coding of the data were evaluated in the Statistical Package for the Social Sciences (SPSS) 18.0 package program. Conformity of continuous variables to normal distribution was checked using the Shapiro-Wilk test. Descriptive statistical methods were used in the evaluation of the data: frequency, percentage, mean and standard deviation. Mann-Whitney- U test was used in comparisons of numerical data because the data did not show normal distribution. Categorical variables were expressed as ratios and the Chi-square test was used in comparisons and $p < 0.05$ was accepted as the level of statistical significance.

RESULTS

Two hundred fifty patients aged 30-60 years (mean±SD: 48.54±16.15) years were included in the

study; 168 (67.2%) were female and 72 (32.8%) were male. One hundred seventy-one (68.4%) were married, 56 (22.4%) were single, and 23 (9.2%) were widowed/divorced. One hundred sixteen (46.4%) were housewives, 79 (31.6%) were working, and 40 (16%) were students/not working. Of all participants, 73.2% had primary/secondary/high school or university education. One hundred twenty-three (49.2%) lived in the city centers, 75 (30%) lived in suburbs, and 52 (20.8%) lived in villages. Almost all (96.4%) of the participants had social security. The monthly income level of 162 (64.8%) patients was found to be above 1500 ₺/month. It was found that 159 (63.6%) of the patients had a chronic disease; hypertension was the most common, found in 62 (24.8%) patients.

Table 1. Demographic characteristics of the groups

	Group 1 (n=119)		Group 2 (n=131)		χ^2
	n(%)	mean±SD	n(%)	mean±SD	
Age	46.18±15.62		50.68±16.39		0.043**
Gender					
Female	79(66.4)		89(67.9)		0.79
Male	40(33.6)		42(32.1)		
Marital Status					
Married	76(63.9)		95(72.5)		0.07
Widowed/Divorced	34(28.6)		22(16.8)		
Single	9(7.6)		14(10.7)		
Education Status					
Illiterate	25(21)		42(32.1)		0.24
Primary Education	52(43.7)		51(38.9)		
High School	30(25.2)		29(22.1)		
Univercity	12(10.1)		9(6.9)		
Profession					
Employee (Worker, tradesman..etc)	40(33.6)		92(70.2)		0.51
Unemployed (Retired, House wife ..etc)	79(66.4)		39(29.8)		
Location					
City center	64(53.8)		59(45)		0.37
Suburb	33(27.7)		42(32.1)		
Village	22(18.5)		30(22.9)		
Monthly Income					
<1500 ₺	42(35.3)		46(35.1)		0.68
1500-3000 ₺	59(49.6)		60(45.8)		
>3000 ₺	18(15.1)		25(19.1)		
Social Security					
General Security	48(40.3)		65(49.6)		0.13
Green Card	55(46.2)		48(36.6)		
Private	9(7.6)		15(11.5)		
None	7(5.9)		3(2.3)		
Chronic Disease					
Yes	73(61.3)		86(65.6)		0.48
No	46(38.7)		45(34.4)		
Chronic Disease*					
Hypertension	25(21)		37(28.2)		0.08
Hyperlipidemia	12(10.1)		16(12.2)		0.59
Diabetes Mellitus	16(13.4)		19(14.5)		0.81
Osteoporosis	12(10.1)		14(10.7)		0.87
Osteoarthritis	13(10.9)		17(13)		0.61
Cardiovascular disease	17(14.3)		9(6.9)		0.04
Asthma	9(7.6)		8(6.1)		0.80
Canser	15(12.6)		9(6.9)		0.13
Other	12(10.1)		25(19.1)		0.04

*More than 1 option is marked

**Mann Whitney-U test

One hundred nineteen patients using medication only were classified as group 1, and 131 patients using medication with TCM practices were classified as group 2.

When the distribution of diseases that caused neuropathic pain in all patients was examined, disc herniation (n=97, 38.8%) was the most common disease. The number of patients in all group who had duration of neuropathic pain less than 5 years was 106 (42.4%), and more than 5 years in 144 (57.6%) patients. When the distribution of all patients according to the localization of pain was examined, pain was in the lomber/dorsal in 81

(32.4%), the lower limb in 57 (22.8%), the upper extremity in 44 (17.6%), the head in 20 (8%) and 48 of the patients (19.2%) was more than one area. When the medications used for the treatment of neuropathic pain were evaluated, it was determined that 71 (28.4%) patients used duloxetine, 54 (21.6%) used pregabalin, 40 (21.6%) used gabapentin, 85 (34%) used alprazolom/ amitriptilin/ NSAID/ more than one medication. The number of patients with duration of neuropathic pain more than 5 years, the LANSS pain scale and DN4 questions scores were statistically significantly higher in group 2 compared with group 1 (p<0.05).

Table 2. Characteristics of Neuropathic Pain in Groups

	Group1 (n=119)	Group 2 (n=131)	χ^2
	n(%) mean±SD	n(%) mean±SD	
Diseases Associated With Neuropathic Pain			
Disc Hernia	44(37)	53(40.5)	0.53
Polyneuropathy	22(18.5)	22(16.8)	
Para/tetraplegia	25(21)	19(14.5)	
Multiple Sclerosis	16(13.4)	18(13.7)	
Peripheral nevre Injury/Neuropathy	5(4.2)	9(6.9)	
Reflex Sympathetic Dystrophy	6(5)	5(3.8)	
Other*	1(0.8)	5(3.8)	
Neuropathic Pain Duration			
<5 years	53(44.53)	53(40.45)	0.04
>5 years	66(55.47)	78(59.55)	
Neuropathic Pain Area			
Lumbar/Dorsal	44(37)	37(28.2)	0.21
Lower Limb	30(25.2)	27(20.6)	
Upper Extremity	16(13.4)	28(21.4)	
Head/Neck	6(5)	12(9.2)	
More then one area	23(19.3)	27(20.6)	
Current Medicine			
Pregabalin	27(22.7)	27(20.6)	0.09
Gabapentin	22(18.5)	18(13.7)	
Duloksetin	39(32.8)	32(24.4)	
Amitriptilin	17(14.3)	20(15.3)	
Alprazolom	3(2.5)	9(6.9)	
NSAID	7(5.9)	10(7.6)	
More then one	4(3.4)	15(11.5)	
LANSS score			
	14.59±2.31	17.76±2.29	0.03*
DN4 score			
	6.43±1.35	8.90±1.42	0.048*
Having knowledge about at least 1 TCM practice			
Yes	73(61.3)	103(78.6)	0.003
No	46(38.7)	28(21.4)	

*Mann Whitney U test

The knowledge of all patients about TCM practice is shown in Table 3.

Table 3. The state of knowledge about applications (n=250)

	Yes* n(%)	No * n(%)
Wet Cupping/Cupping Therapy	132(52.8)	118(47.2)
Leech Therapy	130(52)	120(48)
Ozon Therapy	75(30)	175(70)
Acupuncture	64(25.6)	186(74.4)
Apitherapy	62(24.8)	188(75.2)
Phytotherapy	37(14.8)	213(85.2)
Hypnosis	36(14.4)	214(85.6)
Reflexology	31(12.4)	219(87.6)
Mesotherapy	24(9.6)	226(90.4)
Prolotherapy	23(9.2)	227(90.8)

*More then 1 answer

Of the 250 patient, 176 patients (70.4%) knew at least one type of TCM practice. The most commonly known methods were wet cupping/cupping therapy (52.8%), leeches (52%),

and ozone (30%) None of the patients knew caryopraxia, osteopathy, and homoeopathic larval treatment.

33.6% of patients in group 1, and 40.5% of patients in group 2 obtained information about TCM practice from herbalists. When the attitudes towards the information about TCM practice presented in TV programs were examined, 26.1% of the patients in group 1 and 44.3% of the patients in group 2 thought that it was very useful.

It was determined that linden was consumed the most in both groups as a herb/tea derivative among the TCM practice (Table 4).

Before using TCM, 53 patients (40.5%) in group 2 were admitted to one branch physician, and 78 patients (59.5%) were admitted to more than one branch physician for neuropathic pain treatment. Of the patients in group 2, 109 (43.6%) stated that they would use TCM practice again, 70 (28%) stated that they would not use them again, and 71 (28.4%) were undecided. When the reasons of 70 patients who stated that they would not use TCM practices again were examined 35 patients (50%) due to extra financial cost, 22 patients (31.4%) did not benefit from the treatment, 13 patients (18.5%) had difficulty in reaching the health center; stated that they would not prefer TCM practices again.

Table 4. Media attitudes of groups about TCM practices and used herbal medicine

	Group 1 n=119 n(%)	Group 2 n=131 n(%)	χ^2
Sources of information *			
Herbalist	40(33.6)	53(40.5)	0.26
Internet	47(39.5)	50(38.2)	0.83
Book or Brochure	38(31.9)	40(30.5)	0.81
Family, Friend	35(29.4)	27(20.6)	0.10
Media (Television, radio or newspaper)	25(21)	28(21.4)	0.94
Medical Doctor	17(14.3)	31(23.7)	0.06
Market	16(13.4)	22(16.8)	0.48
Attitudes towards TV programs			
Very usefull	31(26.1)	58(44.3)	0.03
Trickery	77(64.7)	52(39.7)	<0.01
Hesitation	67(56.3)	84(64.1)	0.20
Making monet method	48(40.3)	73(55.7)	<0.01
Need for specialist consultation	38(31.9)	60(45.8)	0.02
Dont watch these programs	20(16.8)	20(15.3)	0.74
Mostly Used Herbals^{a**}			
Linden	16(13.4)	18(13.7)	0.32
Green tea	9(7.6)	11(8.4)	0.73
Tea	11(9.2)	8(6.1)	0.62
Mint	8(6.7)	12(9.2)	0.26
Chamomile	5(4.2)	10(7.6)	0.14
Oregano	6(5)	8(6.1)	0.05
Rosemary	2(1.7)	11(8.4)	0.42
Other ^{**}	32(21.3)	32(21.3)	

^a**More than one answer

** Carnation, Quince, teff, Cinnamon, Pomegranate, Sage

The three most commonly used TCM practices were wet cupping/cupping therapy (24%), leeches (22.8%), and acupuncture (11.6%). Reflexology, larva therapy, karyopraxia, osteopathy were not known or used by any patient. When examining who performed TCM, it was determined that wet cupping/cupping therapy, leech, phytotherapy and acupuncture were performed by non-physicians (14.4%, 12.4%, 2%, and 0.8%, respectively).

Table 5. Distribution of used TCM practices of Group 2 (n=131)

	Group 2 n=131 n %
Methods	
Wet cupping/Cupping therapy	60(45.8)
Leech therapy	57(43.5)
Acupuncture	29(22.1)
Ozone therapy	23(17.6)
Prolotherapy	13(9.9)
Mesotherapy	12(9.2)
Phytotherapy	6(4.6)
Hypnosis	1(0.8)
Caryopraksia	0
Reflexology	0
Apitherapy	0
Osteopathy	0
Person applying the method	
Wet Cupping/Cupping therapy	
Physician	23(17.6)
Non Physician	36(27.3)
Leech Therapy	
Physician	26(19.8)
Non Physician	31(23.7)
Acupuncture	
Physician	26(19.8)
Non Physician	2(1.5)
Ozone therapy	
Physician	23(17.6)
Non-physician	0(0)
Prolotherapy	
Physician	13(5.2)
Non-physician	0(0)
Mesotherapy	
Physician	11(8.4)
Non-physician	0(0)
Hypnosis	
Physician	1(0.8)
Non-physician	1(0.8)
Reasons For using TCM Practices*	
Conventional therapies don't work	38(29)
Conventional therapies have side effects	42(32.1)
No belief in conventional therapies	27(20.6)
Preferring holistic approach	16(12.2)
Desire to control the treatment process	8(6.1)
Financial Cost	
Individual payment	52(43.7)
Half health insurance	34(28.6)
Whole health insurance	33(27.7)

* More than one answer

DISCUSSION

In this study, it was determined that the mean age of patients who used medication with TCM practices together for the treatment of neuropathic pain was higher, the severity of neuropathic pain was higher, and duration of neuropathic pain was longer than patients who used medication only for the treatment of neuropathic pain.

When the reasons for preferring TCM practices are examined in the literature, among the most common reasons are the inadequacy of conventional medicine in treating patients with chronic conditions, the discomfort felt due to treatment failure with conventional medicine, and the perception that TCM practices are not harmful to health.^{14,15} In addition, the adverse effects of drug therapy and prejudice against excessive drug use leads patients to use TCM practices.¹⁶

The use of TCM practices in society varies according to social, cultural, and economic conditions.¹⁷ In our study, there was no statistically significant difference between the groups. The fact that the group that used medication and TCM practices was older in our study might be related to the higher incidence of neuropathic pain in older people. Neuropathic pain is caused by pathologic disorders in both the peripheral and central nervous systems (e.g. diabetic neuropathy and postherpetic neuralgia).¹⁸ Pharmacologic drugs act on somatic pain (physiologic and emotional), and non-pharmacologic treatment methods have effects on the emotional, cognitive, behavioral, and sociocultural processes of pain.¹⁹ It was suggested that this might be the reason for the non-pharmacologic treatment choice of the older population.¹⁹

The prevalence of TCM practices in the world varies between 40-80%, the rate is highest in African countries and lowest in Colombia. In other studies in the literature, rates ranging from 68% to 87% have been reported.²⁰⁻²³ The use of TCM also varies according to disease types.²⁴ For example, a low prevalence is observed in some cancer types, and high rates are observed in diseases such as brain tumors, multiple sclerosis, Parkinson's disease, and headache.²⁵⁻²⁹

The trend towards the use of TCM practices in patients with chronic pain is becoming more common. In a study conducted in patients using opioids for chronic pain, it was reported that the rate of use of TCM in the last 1 year was 44%.³⁰ In a study in which various chronic pains were included, the rate of use of TCM varied between 35-63%.³¹⁻³⁴

In our study, the most common chronic disease in the group that had neuropathic pain and received TCM with medication together were hypertension and cardiovascular disease.

Hypertension is a very common chronic disease all over the world. Its prevalence was found as 33.7%, 31.8%, and 31.8% in studies conducted in our country.^{35,36} Although it was not clear in the literature why patients with hypertension used TCM practices, Toprak and Demir concluded that 63.9% of patients chose to use supportive treatments when their blood pressure increased. However, no data were found regarding their neuropathic pain, and in this respect, there is a need for studies involving larger numbers of patients that highlight and distinguish neuropathic pain causes.³⁷

When we looked at the causes of neuropathic pain, there was no statistically significant difference between the group that received medication and the group that used both medication with TCM practices in terms of having diseases such as disc herniation, polyneuropathy, para/tetraplegia, and multiple sclerosis, but the duration of neuropathic pain that preferred TCM practices was found to be longer than 5 years in group 2

In the literature, it is emphasized that as the duration of neuropathic pain increases, the quality of life of the patient deteriorates and they have difficulty in social life, and the frequency of adverse effects of pharmacologic agents increases. It has been noted that the rate of pain reduction in patients with neuropathic pain who use drugs is approximately 30%. Based on this, as the duration of neuropathic pain increases, patients may prefer different treatment strategies.^{38,40}

The fact that the number of patients with high LANSS scale and DN4 scores were higher in the group using medication together with TCM may be related to the duration of neuropathic pain and the older population.

When we looked at the trend of use of TCM practices in the world, in a study conducted in the United States of America, the 10 most used complementary health approaches were listed as natural products (other than intensive use of vitamins and minerals) (17.7%), deep breathing (10.9%), yoga, Tai Chi or Qi Gong (10.1%), chiropractic or osteopathy manipulation (8.4%), meditation (8%), massage (6.9%), special diets (3%), homoeopathy (2.2%), progressive relaxation exercises (2.1%), and daydreaming (1.7%).^{41,42}

In our study, when the knowledge of TCM practices

was questioned in group 2, it was found that they had the most information about cupping, leeches, and ozone therapy, and it was determined that the patients did not know about caryopraxia, osteopathy, and homoeopathy.

In our study, when attitudes towards information about TCM practices presented on TV programs were examined, there was a significant difference between the groups. It was found that those who found it useful were those who used TCM practices. In addition, the fact that those who used TCM practices had higher income may be an indication that the patients in group 1 experienced financial difficulties while obtaining these methods.

Under the Ministry of Health, the Department of Traditional, Complementary and Alternative Medicine Practices was established, affiliated to the General Directorate of Treatment Services, and the "Traditional and Complementary Medicine Practices Regulation" was published in October 2014.⁴³ In this regulation, TCM practices other than acupuncture were defined for the first time, and it was determined who would perform these methods and which methods could be used in which diseases. The training of the people who would perform them and the characteristics of the health institutions that would provide them were also defined. In this respect, it was clearly stated that methods such as cupping and leeches should be performed by physicians. Although not significant, the high rate of performance of cupping and leeches by non-physician personnel was one of the remarkable results of our study.

Study Limitations

This was a cross-sectional study that examined the knowledge, attitudes, and behaviors of patients with neuropathic pain who used medication, about the use of TCM practices, and correlated TCM practices with neuropathic pain severity and duration. The lack of a control group consisting of healthy adults without neuropathic pain, the insufficient number of patients due to its single-center nature, and the inability to exclude individuals who had symptoms but were not diagnosed psychiatrically during the survey, were limitations of the study.

CONCLUSION

As a result, individuals with neuropathic pain showed similar behaviors to individuals with other chronic diseases and developed the behavior of using TCM practices. We think that patients using TCM practices tend to this behavior due to factors such as having a longer duration of disease, older age, and the adverse

effects or ineffectiveness of other pharmacologic agents. We believe that multicenter randomized controlled prospective studies with a larger patient population are needed to support this view.

On the other hand, it should be emphasized that the level of knowledge of the patients on TCM practices should be increased and the practices should be performed by physicians or health personnel who comply with legislation.

In addition, considering the financial evaluations of patients with neuropathic pain who use TCM practices it may be possible that these methods can

be used with the financial support of social security institutions if the effects of TCM practices are clearly revealed on the basis of disease.

Declarations

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Conflict of Interest

The authors have no conflict of interest.

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