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ORIGINAL RESEARCH

Comparison of Medical Treatment and Acupuncture in Treatment of Psychogenic Erectile Dysfunction: a Prospective, Randomized, Placebo-Controlled Study

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Abstract
Objective: Erectile dysfunction (ED) is the persistent inability to achieve or maintain an erection that is sufficient for satisfactory sexual performance. The aim of this study was to assess the impact of acupuncture in psychogenic ED patients, in comparison with the medical treatment.
Material-Method: A total of 60 male patients, with psychogenic ED were randomized into 4 groups as electro-acupuncture only, electro-acupuncture and oral sildenafil 25 mg, a placebo sham acupuncture and oral sildenafil 50 mg only. The treatment lasted for six weeks in all groups, and patients were evaluated with the International Index of Erectile Function (IIEF-5 scores).
Results: After the treatment, all groups except the placebo group showed a significant increase in IIEF-5 scores, without significant differences among them.
Conclusion: Acupuncture can be used in the complementary treatment of psychogenic ED patients.

Keywords: Psychogenic Erectile Dysfunction, Acupuncture, Complementary Medicine

INTRODUCTION

Erectile dysfunction (ED) is the persistent inability to achieve or maintain an erection that is sufficient for satisfactory sexual performance.[1] It is known as the most common sexual problem in men in general practice and urology.[2,3] ED incidence increases with age and seen in one out of every three men in their lifetime.[2,4]

Sexual potency is an important indicator of physical and mental well-being.[5] ED is a frequently encountered problem in primary healthcare, and it is usually a challenge requiring interdisciplinary collaboration in urology, cardiology, endocrinology, or psychiatry. ED can be connected to an organic or a psychological disorder, or both.[5]

The currently available therapies for the treatment of ED include the followings: oral phosphodiesterase type 5 [PDE5] inhibitors, intra-urethral alprostadil, intracavernous vasoactive drug injection, vacuum constriction devices and penile prosthesis implantation.[6] Also, there is growing evidence about using low-intensity extracorporeal shock wave therapy (ESWT) for ED.[6] Complementary medicine is increasingly used to treat ED.[7] Research suggests that acupuncture can influence the central nervous system activation and neurotransmitter modulation, and thus may have an impact on different health issues.[8] Therefore, in this study we aimed to evaluate the effect of acupuncture on psychogenic ED.

MATERIALS AND METHODS

This prospective, randomized, placebo-controlled study evaluated patients that were treated for ED at the urology clinic in Umraniye Education and Research Hospital, in Istanbul, Turkey, between January 2009 to June 2010. ED patients aged between 20 to 55 years, who were diagnosed with psychogenic ED – having a stable relationship with a female partner for ≥ 1 year, the International Index of Erectile Function (IIEF-5) score <21 for 3 times,[9,10] normal blood pressure, blood

glucose, creatinine, lipids, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), total T (tT), bioavailable T (bT), albumin, sex hormone-binding globulin (SHBG), total prostate specific antigen (PSA) levels were all normal, Rigiscan (Osbon Medical Systems; Augusta, GA, USA) testing erection frequency >3 times, rigidity of >70% for ≥10 minutes, expansion >2cm, Peak Systolic Velocity of the cavernosal arteries >35cms^{-1} after intracavernosal injection of Alprostadil 10µg during Penile Doppler Ultrasonography- were included in the study. Men who have any comorbidities (diabetes mellitus, hypertension, dislipidemia, hyperprolactinemia or low levels of total testosterone, etc) or medications, uncontrolled pyschiatric disorder, penile anatomic defects or spinal cord injury, history of smoking, alcohol or drug abusing, any surgery which can cause ED (radical prostatectomy or radical pelvic surgery etc) were excluded from the study. Patients were randomized into four groups of 15 patients each. The patients in Group 1 were given two sessions of electro-acupuncture per week over 6 weeks. The patients in Group 2 were given two sessions of electro-acupuncture per week with combination of sildenafil 25 mg on the same days over 6 weeks. The patients in Group 3 represent the placebo group and received two sessions of sham acupuncture per week over 6 weeks. The patients in Group 4 were given sildenafil 50 mg twice a week only over 6 weeks. All patients were given specific standardized instructions for taking the medication. Patients in the acupuncture groups were treated by the same acupuncture specialist at corresponding points for electro-acupuncture twice a week, a total of 12 sessions. Each patient was assessed by the IIEF-5 score, immediately before the treatment and at the end of the 6-week treatment. The acupuncture specialist had 16 years of experience and has gained his license from corresponding authorities of Ministry of Health in Turkey. To carry out this study, written permission was obtained from the institutions where this study was conducted, ethical approval was obtained from the Ethics Committee of the Umraniye Education and Research Hospital for the thesis of specialization in medicine which was registered at the archive of the Databases of National Thesis Center of the Council of Higher Education (No: 681667) and informed consents of the patients were obtained. The participants were informed that their names will not be specified in the survey and will be kept confidential. Trial development and reporting was guided by the Consolidated Standards of Reporting Trials (CONSORT) and The Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) statements.[8,9]

Acupuncture technique

Group 1 was acupuncture group and Group 2 was acupuncture + medical treatment group, therefore both were treated by acupuncture. Each treatment session consisted of puncture of the acupoints known to be effective for ED.[4] Electro-acupuncture was used for the following acupuncture points of the respected meridians: Bladder (BL 23, 27, 34 and 47), Kidney (K 1, 3), Conception Vessel (CV 4, 6), Stomach (St 36). In scientific studies that test the efficacy of acupuncture in the treatment of a disorder, "sham acupuncture" is used as a control and Group 3 was identified as the control group. Therefore, in the placebo group (Group 3), the needles were inserted into different points than the classical acupuncture points, and then electrical stimulation was applied. Subjects did not know whether they were getting true or sham acupuncture. The acupuncture needle (Hua Long, 0.25x25 mm Sterile Steal Acupuncture Needles, China) was inserted into certain acupoints bilaterally at the depth of 3-5 mm and then stimulated using electrodes at 2 Hz for low-frequency electro-acupuncture treatment (AGISTIM Duo, 4 channelx4 mA. max./0.1- 9.9 Hz. Lyon, France). The correct placement of the needle was performed by an experienced acupuncturist and confirmed by the characteristic but subjective needle sensation *'de qi'*. After 45 min., the electrical stimulation was terminated, and all needles were removed.

Statistical analysis

Information received from the patient was entered into an excel program of the computer (Microsoft Excel, 2007). The Statistical Package for Social Sciences (SPSS 17.0) program was used in the evaluation of findings in statistical analysis. Data were analyzed using descriptive statistical methods (mean, standard deviation, frequency). In addition, a chi-square test was used for comparison of the qualitative data. Results were evaluated with the 95% confidence interval and statistical significance was attained when a p-value is less than 0.05($p<0.05$).

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RESULTS

Sixty patients with psychogenic ED were were evaluated prospectively. The mean age was 39.6 ± 8.5 years. The distribution of age and pre-treatment IIEF-5 scores were observed homogeneous (p = 0.717; p = 0.04, respectively) between the groups evaluated. The average IIEF-5 scores before and after the treatment were shown in Table 1.

Table 1. Pretreatment and postreatment IIEF-5 scores.

	pretreatment IIEF-5 score	***postreatment IIEF-5 score***	***p value***
Group 1	13.33	20.17	0.003
Group 2	15.43	22.29	0.0018
Group 3	15.33	17.50	0.06
Group 4	15.13	22.38	0.012

IIEF: International Index of Erectile Functions.

All groups except Group 3 showed a significant increase in IIEF-5 scores. The increase was observed less in Group 3 in comparison to the other groups; between the Group 1 and Group 3: p = 0.005; between the Group 2 and Group 3: p = 0.009; between the Group 4 and Group 3: p =0.002 (Table 2). No significant differences were detected between Group 1, Group 2 and Group 4.

Table 2. Comparison of increase in IIEF scores in the groups and group 3 (placebo).

Group comparison	***p value***
Group 1 and Placebo (Group 3)	0.005
Group 2 and Placebo (Group 3)	0.009
Group 4 and Placebo (Group 3)	0.002

IIEF: International Index of Erectile Functions.

In our study, no significant side effects of sildenafil or adverse events of acupuncture therapy were observed.

DISCUSSION

With advancing age, the prevalence of organic ED is increasing; therefore, diagnosis of pure psychogenic ED is not easy in elders.[2] Vascular, neurological and psychological factors are mixed together in the elderly ED patients.[2] Therefore, in our study, patients over 55 years of age were excluded from the assessment, and the average age of the patients included was 39.6 years.

Hypertension, hyperlipidemia, diabetes mellitus and depression are prevalent in patients with ED.[11] The majority of our patients seen in the andrology clinic in our hospital were diagnosed with comorbitidies and thus were excluded from our study. Depression can cause ED and ED can cause depression.[5] Over 40 percent of male with severe depression have problems with sexual functions and almost half of the people using antidepressant medications due to a decline in sexual satisfaction.[12,13] One study even found that 82 percent of men with ED also reported symptoms of depression.[14] In our study, only psychogenic ED patients without comorbidities and hormonal imbalance were included.

In all kinds of ED patient subgroups, sildenafil was found to be most effective. The difference between any dose of sildenafil and placebo for the outcome “able to have intercourse” ranged from 36% to 76%. In eight studies, for the erectile function domain of IIEF-5, the difference from placebo ranged from 3.7 to 11. For the intercourse satisfaction domain of IIEF-5, the range between sildenafil and placebo was 1.4 to 4 in seven studies involving 1607 patients.[6] For the sildenafil patients, 55% to 89% of the patients "able to have intercourse". The erectile function domain scores of IIEF-5 was between 14 to 27.1 while the intercourse satisfaction domain scores were between 7 to 11. Baseline IIEF-5 erectile function domain scores were between 9.3 to 17.8. For the intercourse satisfaction domain, baseline scores were between 4.9 to 7.4.[6] In our study, sildenafil was used twice a week independently from the sexual intercourse. But, on demand usage of sildenafil could contribute the functions and change the results.

Since ancient times, acupuncture has been a treatment option and raised again in this context recently. In urology, acupuncture has been succesfully applied for overactive bladder, lower urinary tract symptoms, dysuria syndrome, nocturnal enuresis and renal colic.[15–20] Acupuncture has also been used in the treatment of premature ejaculation, impotence and increased or decreased libido.[21,22] According to a recent systematic review, the available evidence supporting that the efficacy of acupuncture for the treatment of ED was insufficient and the available studies failed to show the specific therapeutic effect of acupuncture.[23]

Future well-designed and rigorous randomised controlled trials with a large sample size are required**.** In a previous pilot study, the use of acupuncture as a mono-therapeutic modality, did not influence the profile of the stress and sex hormones, but did improve the quality of erection and restored the sexual activity with an overall effect of 39%.[24] Aydın et al. compared hypnosis, acupuncture, placebo and oral placebo treatments in a study done with 29 patients. The success rate for the acupuncture group was 60%, 70% for the hypnosis, 43% and 47% in the placebo groups.[25] Engelhardt et al. reported favorable results also.[4] Both studies had methodological problems, such as an unclear randomization and allocation concealment process, small sample sizes, and a lack of assessor blinding, although they adopted a sham control as placebo. Although acupuncture was not significantly superior to sham acupuncture, the 60% and 68.4% improvement reported by Aydin et al. and Engelhardt et al., respectively, might suggest that acupuncture could be a complementary treatment for psychological ED.[4,25] It is possible that the acupuncture treatment could act as a strong placebo, and it might also be meaningful for the treatment of psychological ED.[23]

Jiang et al. revealed that combining the acupuncture with psychotherapy better than psychotherapy alone, although the study had a small size and unclear risk of bias.[26] In our study, all groups showed increase in the IIEF-5 scores. However, less increase was observed in the placebo group in comparison to other groups.

The major limitation of the current study is that the number of patients in the groups is quite small. To investigate the dose-dependent efficacy of sildenafil, two different doses were used as 25 mg/day and 50 mg/day. However, the lack of a "sildenafil 25 mg only group, without sham" is another limitation. Therefore, further studies with a longer follow up data are needed.

CONCLUSION

Treatment and follow-up of ED in clinical practice requires a holistic and interdisciplinary approach as sufferers may be skeptical of pharmacological remedies. It seems that acupuncture and sildenafil together may improve psychogenic ED. Hence, for patients with psychogenic ED, acupuncture treatment can be considered as a complementary treatment. Further extensive, long-term follow-up studies are needed.

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Conflict of interest

The authors declare that they have no conflict of interest.

Disclosure of statement

No competing financial interests exist.

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ORIGINAL RESEARCH

Investigation of the Effects of Lavender Oil Aromatherapy to Prevent Preoperative Anxiety in Patients Scheduled for Tympanoplasty

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Abstract
Objective: Anxiety is a common problem before surgical procedures. The effectiveness of aromatherapy in preoperative anxiety control has been demonstrated by some studies. The aim of this study is to investigate the effects of lavender oil inhalation on anxiety levels in patients before ear surgery.
Material-Method: The study was conducted in the Otorhinolaryngology clinic of a tertiary university hospital. A total of 68 patients (34 in the study group, 34 in the control group) who were scheduled for tympanoplasty operation were included in the study. Inhalation of lavender oil was used in the patients in the study group before the operation, and liquid paraffin was used in the control group. A personal information form and State-Trait Anxiety Scale (STAI) were used to collect data.
Results: In the study group, the mean STAI pre-test and post-test mean scores were 44.50 ± 12.38 and 36.48 ± 10.73, respectively, and there was a statistically significant difference ($p < 0.05$). These values were 45.60 ± 12.35 and 41.83 ± 10.78, respectively, in the control group, and the difference was not statistically significant ($p > 0.05$). Also, when the posttest STAI mean scores were evaluated between the study and control groups, a statistically significant difference was found ($p < 0.05$).
Conclusion: Lavender oil inhalation before ear surgery has been found to reduce anxiety levels in patients.
Keywords: Inhalation Aromatherapy, Lavender Oil, Anxiety, Tympanoplasty

INTRODUCTION

Preoperative anxiety developing in patients waiting for a surgical intervention is a common problem in health centers. Surgical procedures may cause patients to be confronted with physical and psychological problems. Patients may have preoperative anxiety with emotional stress due to reasons such as fear of losing their job and the thought of burdening other family members. High preoperative anxiety levels may cause patients to feel pain in the postoperative period [1,2].

Consequently, the use of anesthetic and narcotic drugs increases, and the hospitalization period is prolonged. In addition, delayed wound healing in postoperative period and weakening of the capacity to combat with infection can be observed [3]. Therefore, it is very important to diminish the anxiety degrees of patients prior to surgical intervention.

Ear-related surgeries are frequently performed in ear, nose and throat clinics. In chronic pathologies related to the ear, which is an important sensory organ, patients who do not benefit from medical treatment may require surgery. In the postoperative period, rapid recovery is essential for the patient to return to their normal daily life. In addition to preoperative prophylactic measures, the patient should also be psychologically ready for surgery in order not to delay wound healing.

In the preoperative period, it may be difficult for the patient to control the fear of surgery on their own. For this, the effectiveness of aromatherapy before surgery has been shown in some studies [3-7]. Our study was planned to determine the outcomes of

lavender oil inhalation on preoperative anxiety in patients scheduled for tympanoplasty.

MATERIALS AND METHODS

Our experiment was begun after the approval of the local ethics committee and Republic of Turkey Ministry of Health Traditional, Complementary and Functional Medicine Practices Ethics Committee (No: 20/07 / 2020-37106781-000-199755). All the procedures were done in accordance with the ethical standards of the Sakarya University Ethics Committee on human experimentation and with the Helsinki Declaration. The research was a randomized controlled study and an experimental research design was used. The study was completed with two groups: control (placebo) and experimental (lavender oil) groups.

Population, sampling and procedure

The population of this study was composed of patients who were diagnosed with chronic otitis media (COM) in the Ear Nose and Throat (ENT) Diseases Clinic of Sakarya University Training and Research Hospital and who were planned for tympanoplasty surgery and were hospitalized in the ENT service for this reason. G*Power 3.1.9.4 program was used to calculate the number of samples predicted for the study. In the calculation, the sample size was determined as 34 persons for each group with the assumption of 0.5 effect value at 95% confidence interval. In the study, a randomization method was used for the assignment of participants to the control and experimental groups.

Inclusion criteria

- Being over the age of 18,
- Tympanoplasty operation planned with the diagnosis of COM,
- Not having cognitive, verbal and auditory problems that may affect communication,
- Not been diagnosed with psychiatric illness,
- Being able to smell odors and have no problem with smell,
- Patients who are not allergic to odors were included in the study.

Exclusion criteria from the study

- Younger than 18 years of age,
- Having a problem in communicating,
- Having a diagnosis of psychiatric illness and a history of sedative drug use,
- Having a pathology in the nose that prevents smelling,
- Patients who did not sign a voluntary consent form and did not want to attend to the experiment were excluded from the research.

The implementation phase of the research

Preparation phase

Before starting our experiment, placebo solution and lavender oil to be used in the study were prepared by a pharmacist in the form of 68 similar bottles with labels A (34) and B (34). In the study, liquid paraffin (100% purity) was used in the placebo group and lavender oil (100% pure *Lavandula angustifolia* diluted with distilled water at a ratio of 1:10) was used in the experimental group. Throughout the study, the contents of the prepared solutions were not known by the participants or the researcher and statistician who would carry out the study, and the unbiased evaluation of the study was provided by triple blinding.

Implementation of the research

In the implementation phase of the study, patients who were diagnosed with COM and hospitalized for tympanoplasty operation in the ENT Diseases Clinic of Sakarya University Training and Research Hospital were determined and the compliance of the patients with the inclusion and exclusion criteria in the study was ascertained. Participants were instructed about the purpose, duration and scope of the study, and informed consent was obtained, stating that their participation was voluntary. In order to predict the allergic responses of the participants who were eligible for inclusion and volunteering to participate in this study, a sufficient amount of placebo and lavender oil in a dropper bottle were applied to the inner side of the forearm and this was observed in terms of allergic conditions such as rash, fever and itching. Sociodemographic findings of the participants who did not develop an allergic reaction were recorded, and the "State-Trait Anxiety Inventory" (STAI), which is frequently used in the literature regarding anxiety and defined by Spielberger et al., was applied 2 hours before the operation [8]. After the scale was completed, 5 drops of lavender oil or liquid paraffin for placebo were dropped onto a 5x5 cm sterile gauze and the participants were asked to smell this for 5 minutes from a distance of 8-10 cm. 20 minutes after the end of the sniffing process, the STAI scale was applied again and the values were recorded (Figure-1).

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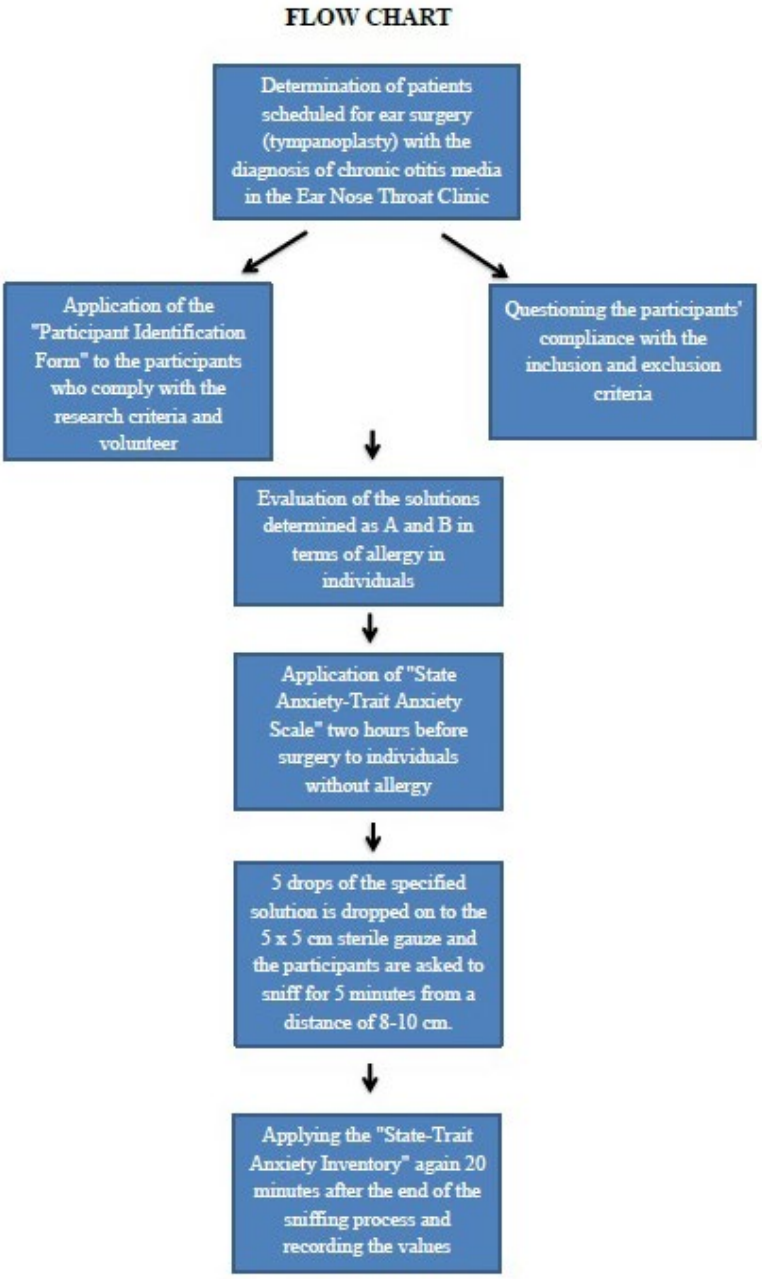

Figure 1. Flow chart for the implementation of the research

Participant identification form

This form was composed of questions regarding age, gender, height, weight, marital status, educational status, occupation, economic status, hospitalization history, surgery history and aromatherapy use history of the participants.

State-trait anxiety inventory (STAI)

One of the most frequently used anxiety inventories in psychological research is STAI. It has two sub-inventories; each containing 20 items. The initial sub-inventory determines state anxiety (S-STAI) showing how a person is feeling at that time. The second sub-inventory determines trait anxiety (T-STAI) showing how they usually feel. Sub-inventory scores range of 20 to 80. High points for the all two sub-inventories show a higher level of anxiety. A cut-off score of 39-40 points has been proposed for STAI to distinguish clinically compelling manifestations.

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Evaluation of data

SPSS for Windows v 22.00 (IBM Co., Armonk, New York, USA) program was used for statistical analysis and the evaluation of the data obtained. Descriptive statistics were mean ± standard deviation for continuous data and numbers and percentages for discrete data. The suitability of normal distribution was evaluated with the Kolmogorov-Smirnov test, and correlations between two groups were performed with t-test or Mann Whitney U test in independent groups and paired sample tests for the same group according to the normal distribution of variables. $p < 0.05$ was accepted as statistically significant.

RESULTS

Data associated with gender, age, marital condition, employment condition, place of residence, surgery history and aromatherapy experience of the patients are given in Table-1. Considering demographic characteristics, there was no statistically significant difference between the control and study groups.

Table 1. Demographic characteristics of the patients included in the study

	Study group (n=34) Mean ± Std	Control (n=34) Mean ± Std	Analysis (p)
Age	48.02±15.38	42.54±11.42	0.314
Gender, N (%)			
Female	15 (%44)	13 (%40)	0.855
Male	19 (%56)	21 (%60)	0.783
Marital Status, N (%)			
Married	25 (%73)	26 (%76)	0.765
Single	9 (%27)	8 (%24)	0.615
Employment Status, N (%)			
Yes	27 (%79)	25 (%73)	0.416
No	7 (%21)	9 (%27)	0.187
Place of residency, N (%)			0.565
Rural	2 (%6)	1 (%3)	
Town	7 (%20)	9 (%26)	
City center	25 (%74)	24 (%71)	
Surgery History, N (%)			0.725
Yes	14 (%41)	16 (%47)	
No	20 (%59)	18 (%53)	
Aromatherapy History, N (%)			0.284
Yes	2 (%6)	1 (%3)	
No	32 (%94)	33 (%97)	

N= number; Mean ± Std = Mean value ± standart deviation

Table-2 exhibits the values of the upper and lower degrees of STAI in the pre-test and post-tests of the patients in two groups. Although mean pre-test and post-test STAI points in the study group were 44.50 ± 12.38 and 36.48 ± 10.73, respectively, and the difference was statistically significant (p=0.007), it was 45.60 ± 12.35 and 41.83 ± 10.78 in the control group, respectively, and there was not a statistically significant difference (p=0.215).

Table 2. The lowest and highest values according to the State-Trait Anxiety Inventory (STAI) pre- test and post-test results applied to the patients in the study and control groups

		Pre Test		Post Test	
Sub-scale	**Highest and Lowest Ranks in the Questionnaire**	**Study group**	**Control**	**Study group**	**Control**
State Anxiety (S-STAI)	20-80	20-72	20-70	20-65	20-69
Trait Anxiety (T-STAI)	20-80	27-66	25-60	–	–

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Mean pre-test STAI scores were 44.50 ± 12.38 in the study group and 45.6 ± 12.35 in the control group, and no statistically significant difference was found between the groups (p=0.658).

However, the mean post-test STAI scores were 36.48±10.73 in the study group and 41.83±10.78 in the control, and the difference was statistically significant between two groups (p=0.015)(Table-3).

Table 3. Comparison of S-STAI pre-test and post-test mean scores within and between groups

	Study group (n=34) Mean±Std	Control (n=34) Mean±Std	Analysis (p)
S-STAI pre-test	44.5± 12.38	45.6± 12.35	0.658
S-STAI post-test	36.48± 10.73	41.83± 10.78	**0.015**
Analysis (p)	**0.007**	0.215	

STAI = State-Trait Anxiety Inventory; n = number; Mean±Std = Mean value ± standard deviation

DISCUSSION

The outcomes of our study, whose goal is to investigate the responses of lavender oil on the anxiety levels of patients before tympanoplasty operation, are reviewed with the literature. In some previously published studies, it has been reported that patients experience anxiety while waiting for the surgical intervention. In their experiment, where Foley et al. explained various treatment options and surgical steps using the Apple iPad application in the preoperative period and investigated the effects of being informed about the basis of breast cancer, it was found that anxiety levels in patients were greater before and urgently after the surgery [9]. Fındık and Topçu [10] examined the effect of the way of preparing the patient for surgical operation on the pre-operative anxiety degree and reported that the patients' anxiety levels fell before the surgery while waiting. Alike, in an experiment conducted by Şıvgın et al. [11], the impact of psychological and pharmacological premedication on pre-operative anxiety degree during elective operation were investigated and the outcomes indicated that patients had anxiety before surgeries. In the light of previous studies on preoperative anxiety, the average anxiety points of the questionnaires conducted in this period were found to be higher.

Lavender oil has in recent times been frequently used in inhalation aromatherapy and massage therapy [12]. There are many types of lavender. Among these species, *Lavandula officinalis* and *Lavandula angustifolia* have medicinal effects and are often used. With their inhalation, linalyl acetate and linalool are released in the body, thereby suppressing anxiety [13]. For this reason, lavender oil is used to diminish pain, reduce concern and depression levels, and relieve preoperative anxiety.

Toda and Morimoto studied the effectiveness of lavender aromatherapy on chromogranin and cortisol degrees in the body and found that lavender had a stress-reducing effect on the body [14]. In the experiment conducted by Lehrner et al. [1] related to the effectiveness of lavender oil and orange on concern degrees in patients before dental procedures, they concluded that lavender oil reduced anxiety. Umezu et al. [15] examined the effects of the ingredients in lavender oil aromatherapy on anxiety and concluded that this effect was with the help of linalool. Shiina et al. [16] studied the effectiveness of lavender oil aromatherapy on blood circulation and concluded that aromatherapy with lavender oil affects serum cortisol levels and thus reduces stress. In another experiment by Franco et al. [17] investigating the effectiveness of aromatherapy applying lavender oil before breast cancer operation on concern degrees, it was found that the reduction in anxiety levels in the preoperative period in the group that received lavender oil aromatherapy was statistically significant. In the review conducted by Boehm et al. [18], the effectiveness of adjuvant aromatherapy on cancer patients were investigated, and the authors concluded that cancer patients' anxiety was significantly reduced after aromatherapy. Similarly, in another study exploring the anxiolytic effects of aromatherapy massage in patients with breast cancer, it was reported that a significant reduction in anxiety levels was found in patients who received aromatherapy massage for 4 weeks (30 minutes for twice in a week) [19]. In conclusion, studies in the literature show that lavender oil applied by inhalation has the effect of reducing preoperative anxiety levels of patients. The results of our experiment revealed that either study or control group experienced parallel levels of anxiety in the preoperative period, but it was found that there was a significant difference between the pre-test and

post-test state anxiety levels of the participants in the experiment group (p = 0.007). The increase in the post-test anxiety score average of the participants in the control group suggests that the anxiety levels in this group increased as the time of surgery approached. All results support the hypothesis that aromatherapy with essential oil inhalation reduces pre-operative anxiety levels. As a conclusion of our study managed to investigate the effect of lavender oil on preoperative anxiety levels of participants undergoing tympanoplasty surgery, it was concluded that aromatherapy with lavender oil inhalation had a positive effectiveness on preoperative anxiety control.

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ORIGINAL RESEARCH

Prolotherapy Method in Treatment of Chronic Low Back Pain

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Abstract

Objective: The aim of this study is to evaluate the effectiveness of 5% dectrose prolotherapy on low back pain in patients with chronic low back pain without neurological deficits.

Material-Method: Prolotherapy with 5% dextrose was applied to patients with localized low back pain, hip pain, spreading pain in the legs for more than six months. Stretching exercises were recommended after prolotherapy and an analgesic containing paracetamol (500 mg) + codeine phosphate (10 mg) + caffeine (30) mg was used for analgesia for the first 3 days. Prolotherapy was planned 3 times with an interval of twenty days.

Results: Thirty patients between the ages of 24-73 were included in the study. Eighteen patients received 3 sessions whereas twelve patients received 2 sessions of prolotherapy. Visual analogue scale (VAS) pain scores of all patients decreased. The mean pre-treatment VAS score was 8.43 and it decreased to 2.41 after the treatment. None of the patients had side effects that would terminate the treatment.

Conclusion: The data obtained in the study show that prolotherapy is effective in treating chronic low back pain. We did not conduct long-term follow-up in our study. After three sessions and between sessions, we assessed the current state of well-being. More extensive studies will guide clarification of its place in the treatment of long-term low back pain.

Keywords: Low Back Pain, Prolotherapy, Visual Analogue Scale

INTRODUCTION

Low back pain is a common medical complaint. It affects more than 5 million people in the United States. In industrialized countries, it has been the most commonly reported disease in human life after influenza[1].

With the development of imaging methods, it is thought that a large part of low back pain is due to disc herniations. However, ligament injuries are also an important cause of low back pain[2]. Prolotherapy is an injection method designed to promote healing[3].

With prolotherapy, proliferating substances are applied with a purpose of creating microtraumas in the desired anatomical regions. Different proliferating agents and cells can be applied. For example, 5% dextrose, mannitol, sodium morrhuate, platelet-rich plasma[4]. With the use of 5% dextrose in prolotherapy treatment the patients feel less pain after the procedure. For this reason, we did our study with 5% dextrose as a proliferating agent.

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MATERIALS AND METHODS

We started our study after receiving the ethics committee approval numbered 2020-98 from the Gebze State Hospital. We conducted a retrospective study with 30 patients aged between 24-73, who had applied to the traditional and complementary medicine outpatient clinic in 2019 and had had low back pain for more than six months. Patients with sequestered and extruded disc herniations according to the magnetic resonance imaging were not included in this study.

According to the examination of the iliolumbar ligament, facet joint and transverse ligaments, 1 cc 5% dextrose prolotherapy was applied to the sensitive structures with a 23 gauge 0.6x80 mm needle. After prolotherapy, waist stretching exercises were given designed by physiatrists. The given exercises were recommended to be performed with 10 repetitions twice a day, in the morning and in the evening. After the injection, an analgesic containing paracetamol (500 mg) + codeine (10 mg) + caffeine (30 mg) was given for the first 3 days.

Patients who did not take their medication regularly and did not do stretching exercises regularly were excluded from the study. Prolotherapy was applied 3 times in total with an interval of 20 days. If there was 80% or more reduction in pain after the first or second injection, the treatment was terminated.

Statistical analysis

SPSS 15.0 for Windows was used for statistical analysis. Descriptive statistics were given as numbers and percentages for categorical variables; average, standard deviation, minimum, maximum for numerical variables. As the differences of numerical variables in dependent groups did not meet the normal distribution condition, repeated measurement analyzes were performed with Friedman Analysis.

Subgroup analysis were performed with Wilcoxon test and interpreted with Bonferroni correction. Comparisons of numerical variables between two independent groups were made with Student's t-Test, when they met the normal distribution condition, and with Mann Whitney U test, when they did not meet the normal distribution condition.

Relationships between numerical variables were analyzed with Pearson Correlation Analysis, when the parametric test condition was met, and with Spearman Correlation Analysis, when the parametric test condition was not met. Statistical alpha significance level was accepted as $p<0.05$.

RESULTS

Patients with persistent pain for more than six months were included in the study. None of the patients had previously received a similar or different injection therapy. Patients with sequestered or extruded disc herniations according to the lumbar magnetic resonance imaging were not included in the study.

The characteristic features of the patients are shown in Table 1. The decrease in the evaluated VAS scores of the patients was found statistically significant ($p<0.001$) (Table 2). The results of the VAS scores before and after the prolotherapy session by gender are shown in Table 3.

The results of the pretreatment and posttreatment VAS scores by gender are shown in Table 3. Three sessions of prolotherapy were applied to 18 patients. Through the VAS score of 12 patients decreased by 80% or more after 2 sessions of prolotherapy treatment, the third session of prolotherapy was not performed. Ligament and joint examinations were performed at each session. Painful and tender ligaments were detected and these ligaments were injected. Non-painful ligaments were not treated.

Table 1. Demographic table of patients based on gender and age.

		Mean±SD	**Min.-Max.**
Age (year)		49.0±12.5	24-73
		n	**%**
Gender	**Male**	9	30.0
	Female	21	70.0

Table 2. Changes in VAS score before and after treatment

		Mean±SD	**Min.Max.**
VAS	Pre-treatment	8.43±1.07	6-10
	After the 1st session	4.27±1.23	2-7
	After the 2st session	3.40±1.94	0-8
	After the 3st session	2.41±1.58	0-5
	p	<0.001	

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Table 3. Results of mean VAS scores before and after treatment by gender

		Male		Female		
		Mean±sD	**Min.-Max.**	**Mean±SD**	**Min.-Max.**	**p**
VAS	Pre-treatment	8.11±1.05	7-10	8.57±1.08	6-10	0.215
	After the 1st session	4.22±0.67	3-5	4.29±1.42	2-7	0.900
	After the 2st session	2.56±1.13	1-5	3.76±2.12	0-8	0.081
	After the 3st session	1.50±1.00	1-3	2.69±1.65	0-5	0.197

DISCUSSION

It was shown that there were no significant difference between the two groups in a study examining the long-term efficacy of surgical and conservative treatments in patients with acute sciatica who do not have an absolute surgical indication[5]. Considering the risks of surgical treatment, the importance of conservative treatments such as prolotherapy becomes even more prominent.

It has been stated that 70% of low back pain cases occur due to ligament injuries. The sacroiliac ligament is the most commonly injured ligament. Pain as a result of damage to this ligament is reflected in the lateral of the leg and in the posterior thigh[6].

We found that all of our patients included in the study had tenderness in this ligament. We performed the iliolumbar ligament injection in all our patients especially in patients who had pain in the groin and lateral leg. There was a significant reduction in their pain after this injection.

The lumbar vertebrae and pelvis are held together by the lumbosacral and iliolumbar ligaments. The spinous processes are connected to each other by interspinous and supraspinous ligaments. Supraspinous ligaments strengthen the interspinous ligaments[7].

As a result of injury and instability in the ligaments, the facet joint and disc in the relevant segment cannot be protected and excessive pressure occurs on it. It is the most common site of injury between the lumbar vertebra and the sacrum. The lumbosacral ligament is the ligament between the 5th lumbar vertebra and the sacrum. Injury and instability in this ligament predisposes to herniation.

The iliolumbar, interspinous and supraspinous ligaments are other ligaments that protect from intervertebral disc herniation. If the separation in the spinal processes is excessive, disc herniation occurs[9].

In this study, we also examined the iliolumbar ligament, transverse ligament and facet joint in each prolotherapy session and injected 1 cc 5% dextrose into the sensitive structures.

Disc degeneration is so common that it is considered as a part of the normal aging process. As a natural course of aging, the disc loses its flexibility[8]. The first onset of a disc herniation is usually extremely painful. In approximately 10% of patients, pain and muscle spasms may continue and develop into chronic pain. Pain may persist for a long time after disc herniation due to weakened ligaments and unhealed connective tissue support[9].

We aimed at initiating regeneration with prolotherapy in the weakened ligaments, to strengthen them and increase the support of the connective tissue in patients with chronic pain.

Prolotherapy can be used in many musculoskeletal disorders, such as pain of knee, shoulder, low back and neck, osteoarthritis, tennis and golfer's elbow, tendinopathy.

The inflammation process begins with prolotherapy. With inflammation, fibroblast activation occurs, growth factors and collagen synthesis increase in the region. It activates tissue repair. Thus, the weakness of ligaments and tendons decreases.

Prolotherapy can be done when the pain first starts, or it can be used at any time after the pain onset[10]. Also, we did our study with patients whose low back pain has been going on for more than six months and with pain that spreads to the buttocks and legs.

Prolotherapy, also known as regenerative injection therapy, triggers local inflammation by stimulating collagen production at the injection site. As a result, the growth of new ligament and tendon tissue is believed to relieve pain[11].

Merriman determined in his study with 15000 patients that the success rate of the conservative method of prolotherapy in chronic low back and sciatic pain is between 80% and 90%, and the side effects are very low compared to surgery[12]. We did not see any side effects in our study.

In a study conducted with 145 people with chronic low back pain, where the mean VAS score of the patients before the prolotherapy session was 5.6, and the mean VAS score was 2.6 after the prolotherapy. 80% of patients reported that the improvement in pain levels was still ongoing one year after treatment[13].

We also obtained similar results after three sessions of prolotherapy in our study. While the mean VAS score of our patients was 8.43 before the treatment, it decreased to 2.41 after the treatment.

In the study of Hauser et al., more than 80% of the patients showed improvement in mobility (walking and daily activities), exercise ability, anxiety and depression states. After one year of follow-up from the last prolotherapy session, it was observed that the well-being continued[13]. The lack of long-term follow-up of the patients in our study is one of the limitation of our study.

Maniquis-Smigel et al. reported clinically significant improvement in pain for 12 months when they administered repeated caudal injections of 5% dextrose to patients with chronic low back and hip pain. This study shows that dextrose has a potential sensorineural effect on neurogenic pain[14]. In our study, we benefited from the analgesic and proliferative properties of 5% dextrose.

In a study of 366 patients with chronic low back pain, prolotherapy was found to reduce chronic low back pain when it was combined with spinal manipulation, exercise, and other adjunctive interventions[15]. In our study, our patients used an analgesic for 3 days containing paracetamol + caffeine + codeine after prolotherapy and we warned them that they should definitely do stretching exercises.

In a study by Solmaz et al., they applied prolotherapy with 5% dextrose to 79 patients whose pain persisted after unsuccessful low back surgery. Oswestry Disability Index and VAS scores of the patients were examined before and after prolotherapy and significant results were obtained[16]. According to this study, prolotherapy may be an appropriate treatment option for chronic pain before revision surgery.

CONCLUSION

In this study, we found a significant reduction in the pain of the patients with prolotherapy treatment who had chronic low back pain. Therefore, with the available data, we have determined that prolotherapy is a safe, economical and effective method, and 5% dextrose prolotherapy can be safely used for low back pain.

In our study, we did not perform long-term pain control of the patients. Randomized controlled trials with more patients and long-term follow-up are needed on this subject.

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ORIGINAL RESEARCH

Instant Effect of Chiropractic Upper and Middle Thoracic Zone Manipulations on Autonomic Nervous System

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Abstract

Objective: This study aims to compare the instantaneous effects of chiropractic upper and middle thoracic manipulations on the autonomic nervous system.

Material-Method: The study included 30 healthy volunteers aged 18-45 years. Manipulation was applied to the upper thoracic (T1-4) area (n=15, 8 female, 7 male) and to the middle thoracic (T6-9) area (n=15, 7 female, 8 male). Before the application, heart rate, body temperature and skin conductivity (EDA) measurements were performed using the Empatica E4 wristband device. Thoracic HVLA (high velocity low amplitude) manipulation was performed in the supine position. After the application, the measurement made with the Empatica E4 device was repeated. The mean body temperature and skin conductivity values were calculated for the analysis of the data. Heart rate data were evaluated using Kubios heart rate variability (HRV) standard program. Detailed information about the effects of upper and middle thoracic area manipulation on the autonomic nervous system was obtained according to the analysis results of the data obtained before and after manipulation. Correlation analysis of pre- and post-manipulation data and difference analysis between the two groups were performed based on significance level $p<0.05$.

Results: As a result of the research, no significant changes in parasympathetic nervous system values such as RMSSD, pNN50, PNS Index and sympathetic nervous system values such as Stress Index and SNS Index were observed after upper thoracic manipulation. After middle thoracic manipulation, significant decreases occurred in sympathetic nervous system values such as Stress Index, SNS Index, while significant increases occurred in parasympathetic nervous system values such as RMSSD, pNN50, PNS Index. It was observed that there was no significant change in temperature and EDA.

Conclusion: As a result of our measurements and analyzes, it was seen that chiropractic upper and middle thoracic manipulations had different instantaneous effects on the autonomic nervous system.

Keywords: Chiropractic, Autonomic Nervous System, Heart Rate Variability, Body Temperature, Skin Conductivity

INTRODUCTION

Although the physiological mechanisms underlying spinal manipulative techniques are still unknown, several hypotheses have been put forward that offer mechanical, neurophysiological and psychological reasons. The mechanical force used during manipulation has a direct effect on the central nervous system, creating positive neurophysiological responses. The effects of manipulation are only beyond biomechanical changes. It has both somatic and autonomic effects on the nervous system. The somatic and autonomic regulatory areas in the central nervous system usually respond to the same type of afferent inputs [1].

It is difficult to directly observe the effect of manual therapy on the central or peripheral nervous system. In the absence of direct observation, conclusions are drawn from neurophysiological responses indirectly associated with specific mechanisms. Studies measured the associated responses of hypoalgesia and sympathetic activity to form a mechanism

mediated by periaqueductal gray matter [2] and the dorsal horn of the spinal cord [3]. In cases where direct observations are not possible, directly measurable associated responses are used to demonstrate specific neurophysiological mechanisms. [1]

Chiropractors have suggested the positive effects of manipulation on the musculoskeletal system and internal organ health[4]. Although various studies have associated chiropractic vertebral subluxation and manipulative therapy in the spine with autonomic function, few studies have been conducted to link specific results to manipulated specific levels. [5,6]

Despite limited evidence that changes in autonomic activity are associated with chiropractic manipulation, autonomic-mediated reflex responses, including changes in heart rate, blood pressure, pupil diameter, and skin temperature, as well as endocrine and immune system effects, have been clearly demonstrated. [4]

Some of the findings, such as heart rate, blood pressure, and skin temperature, are consistent with chiropractors' observations about the relationship between spinal dysfunctions and visceral disorders. [7]

Our aim in the study is to determine the instantaneous effect of chiropractic upper and middle thoracic manipulations on the autonomic nervous system by looking at body temperature, skin conductivity and heart rate variability.

MATERIALS AND METHODS

The study was planned in accordance with the Helsinki Declaration Principles. It is a clinical study involving the pre- and post-test model.

In the laboratory of Yeditepe University Physical Therapy and Rehabilitation Department, 30 healthy volunteers aged 18-45 years with no limitation of movement in the thoracic area and without pain in their daily lives or during palpation were included in the study.

In addition to chronic discomfort and regular drug use, history of trauma or surgery in the thoracic area was questioned. The positive ones were not included in the study. Pain was evaluated by palpation for volunteers who met the inclusion criteria and stated that they did not have pain affecting their daily lives in the thoracic areas. Then, the range of motion of the joint in the direction of flexion, extension and lateral flexion was measured for the thoracic area using the inclinometer. Seven out of 37 people with pain and/or limited movement were excluded from the study and 30 people were randomly divided into 2 groups. It was paid attention that the numbers of men and women in the groups were proportional. Both groups were named as the research group and spinal manipulation was applied in the supine position in the upper thoracic (T1-4) and middle thoracic (T6-9) areas. The time required for each person to participate in the study was calculated as a total of 15 minutes, 5 minutes pre-manipulation measurement, 5 minutes application and 5 minutes post-manipulation measurement. Application is for one time only and no follow-up process is planned.

Before the application, heart rate, body temperature and skin conductivity measurements were performed using the Empatica E4 device. The device was placed on the left wrist and the data were recorded for 5 minutes and the measurement was repeated after the application. The average of recorded body temperature (Temp) and skin conductivity (EDA) data was calculated. HRV data (RMSSD, PNS index, Stress index, SNS index, pNN50, Power LF, Power HF and LF/HF ratio) were obtained by transferring to Kubios program and calculating the parameters of heart rate variability.

Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of the variables was measured by Kolmogorov Simonov test. Independent sample t test and Mann-Whitney u test were used in the analysis of quantitative independent data. Matched sample t test and Wilcoxon test were used in the analysis of dependent quantitative data. Chi-squared test was used for the analysis of qualitative independent data. Analysis of data has been conducted with SPSS 26.0 program.

Permissions

Approval was obtained from Yeditepe University, Clinical Researches Ethics Board on 17.06.2020 with the decision number 1241.

RESULTS

Ages of the patients in the middle and upper segment groups ($p=0.445$) and gender distribution ($p=0.715$) did not differ significantly ($p > 0.05$) (Table 1).

In the middle and upper segment groups, the mean EDA ($p=0.052$) value before manipulation did not differ significantly ($p > 0.05$). In the middle and upper segment groups, the mean EDA ($p=0.152$)

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value after manipulation did not differ significantly (p > 0.05). In the middle segment group, the mean EDA value after manipulation (p=0.798) did not differ significantly from the pre-manipulation value (p > 0.05). In the upper segment group, the mean EDA value after manipulation did not differ significantly (p > 0.05) from the pre-manipulation (p=0.410). The mean EDA change (p=0.740) after manipulation did not differ significantly (p > 0.05) in the middle and upper segment groups (Table 2).

Table 1. Distribution of age and gender

		Middle Segment		Upper Segment		P
		Mean±*sd.*/ %n	Median	Mean±*sd.*/ %n	Median	
Age		32.8±7.2	32.0	30.3±10.4	26.0	0.445 [t]
Gender	Female	7 %46.7		8 %53.3		0.715 x^2
	Male	8 %53.3		7 %46.7		

[t] Independent sample t test / X^2 Chi-Square test

Table 2. Comparison of EDA values by upper and middle segments

	Middle Segment		Upper Segment		P
	Mean ±sd.	Median	*Mean* ±sd.	Median	
Mean EDA					
Pre-manipulation	1.42±1.45	0.93	0.83±1.46	0.36	0.052[m]
Post-manipulation	1.39±1.23	1.17	1.06±1.77	0.51	0.152[m]
Pre-manipulation / Post-manipulation Change	-0.04±1.01	0.07	0.23±0.61	-0.02	0.740[m]
Intra-Group Change P	0.798[W]		0.410[W]		
Max EDA					
Pre-manipulation	2.05±1.97	1.53	1.15±2.04	0.43	0.051[m]
Post-manipulation	2.03±1.79	2.07	1.62±2.75	0.66	0.130[m]
Pre-manipulation / Post-manipulation Change	-0.02±1.55	0.05	0.47±1.14	0.05	0.561[m]
Intra-Group Change P	0.910[W]		0.280[W]		
Min EDA					
Pre-manipulation	0.93±1.30	0.39	0.46±0.63	0.26	0.152[m]
Post-manipulation	0.86±0.90	0.53	0.61±0.86	0.26	0.229[m]
Pre-manipulation / Post-manipulation Change	-0.07±0.94	0.10	0.16±0.41	0.00	0.934[m]
Intra-Group Change P	0.691[W]		0.421[W]		

[m] Mann-Whitney u test/ [w] Wilcoxon test

In the middle and upper segment groups, the pre-manipulation max EDA (p=0.051) value did not differ significantly (p>0.05). Max EDA (p=0.130) value after manipulation did not differ significantly (p > 0.05) in the middle and upper segment groups. In the middle segment group, the post-manipulation max EDA (p=0.910) value did not differ significantly from the pre-manipulation value (p > 0.05). In the upper segment group, the post-manipulation MAX EDA (p=0.280) value did not differ significantly from the pre-manipulation value (p > 0.05). The amount of change in max EDA (p=0.561) after manipulation in the middle and upper segment groups did not differ significantly (p > 0.05) (Table 2).

In the middle and upper segment groups, the pre-manipulation min EDA (p=0.152) value did not differ significantly (p > 0.05). MIN EDA (p=0.229) value after manipulation did not differ significantly (p > 0.05) in the middle and upper segment groups. In the middle segment group, the min EDA value after manipulation (p=0.691) did not differ significantly from the pre-manipulation value (p > 0.05). In the upper segment group, the min EDA value after manipulation (p=0.421) did not differ significantly from the pre-manipulation value (p > 0.05). The amount of min EDA (p=0.934) change after manipulation in the middle and upper segment groups did not differ significantly (p > 0.05) (Table 2).

In the middle and upper segment groups, the mean Temp (p=0.055) value before manipulation did not differ significantly (p > 0.05). The mean Temp (p=0.065) value after manipulation did not differ significantly (p > 0.05) in the middle and upper segment groups. In the middle segment group, the mean Temp value after manipulation (p=0.409) did not differ significantly from the pre-

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manipulation ($p > 0.05$). In the upper segment group, the mean Temp value after manipulation ($p=0.508$) did not differ significantly from the pre-manipulation ($p > 0.05$). The mean change in Temp ($p=0.808$) after manipulation in the middle and upper segment groups did not differ significantly ($p > 0.05$) (Table 3).

In the upper segment group, the pre-manipulation max Temp ($p=0.036$) value was significantly lower than the middle segment group ($p < 0.05$). Max Temp ($p=0.026$) value was significantly lower in the upper segment group after manipulation than in the middle segment group ($p < 0.05$). In the middle segment group, the post-manipulation max Temp value did not differ significantly from the pre-manipulation value ($p > 0.05$). In the upper segment group, the post-manipulation max Temp value did not differ significantly from the pre-manipulation value ($p > 0.05$). The amount of max Temp change after manipulation in the middle and upper segment groups did not differ significantly ($p > 0.05$) (Table 3).

In the middle and upper segment groups, the pre-manipulation min Temp value did not differ significantly ($p > 0.05$). Min Temp value after manipulation did not differ significantly ($p > 0.05$) in the middle and upper segment groups. In the middle segment group, the min Temp value after manipulation did not differ significantly from the pre-manipulation ($p > 0.05$). In the upper segment group, the min Temp value after manipulation did not differ significantly from the pre-manipulation ($p > 0.05$). The amount of min Temp change after manipulation in the middle and upper segment groups did not differ significantly ($p > 0.05$) (Table 3).

Table 3. Comparison of temp values according to the upper and middle segments

	Middle Segment		Upper Segment		P
	Mean ±sd.	Median	*Mean* ±sd.	Median	
Mean Temp					
Pre-manipulation	25.6±1.3	25.9	24.4±1.8	24.3	0.055[t]
Post-manipulation	25.4±1.4	25.8	24.3±1.7	24.4	0.065[t]
Pre-manipulation / Post-manipulation Change	-0.2±0.7	-0.2	-0.1±0.5	-0.1	0.808[t]
Intra-Group Change P	0.409[E]		0.508[E]		
Max Temp					
Pre-manipulation	25.9±1.3	26.0	24.7±1.7	24.7	**0.036[t]**
Post-manipulation	25.9±1.4	26.4	24.6±1.6	24.8	**0.026[t]**
Pre-manipulation / Post-manipulation Change	0.0±0.8	-0.1	-0.1±0.6	-0.3	0.748[t]
Intra-Group Change P	0.946[E]		0.509[E]		
Min Temp					
Pre-manipulation	25.2±1.4	25.6	24.1±1.9	24.1	0.076[t]
Post-manipulation	24.9±1.5	25.6	24.0±1.7	24.0	0.145[t]
Pre-manipulation / Post-manipulation Change	-0.3±0.7	-0.2	-0.1±0.6	-0.2	0.362[t]
Intra-Group Change P	0.111[E]		0.666[E]		

[t] Independent sample t test / [E] Paired sample t test

The pre-manipulation RMSSD ($p=0.018$) value was significantly higher in the upper segment group than in the middle segment group ($p< 0.05$). The RMSSD ($p=0.115$) value after manipulation did not differ significantly ($p > 0.05$) in the middle and upper segment groups. In the middle segment group, the RMSSD value after manipulation ($p=0.001$) increased significantly compared to the pre-manipulation ($p < 0.05$).

In the upper segment group, the RMSSD value after manipulation ($p=0.125$) did not differ significantly from the pre-manipulation ($p > 0.05$). The RMSSD value decreased after manipulation in the upper segment group and increased in the middle segment group and the amount of change ($p=0.000$) showed a significant difference ($p < 0.05$) (Table 4).

In the middle and upper segment groups, the pre-manipulation PNS ($p=0.052$) index did not differ significantly ($p > 0.05$). PNS ($p=0.136$) index after manipulation did not differ significantly ($p > 0.05$) in the middle and upper segment groups. The PNS ($p=0.000$) index value increased significantly ($p < 0.05$) in the middle segment group after manipulation compared to the pre-manipulation value. In the upper segment group,

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the post-manipulation PNS (p=0.347) index value did not differ significantly from the pre-manipulation value (p > 0.05). The amount of PNS (p=0.000) index change after manipulation was significantly lower in the upper segment group than in the middle segment group (p < 0.05) (Table 5).

Table 4. Comparison of RMSSD values according to upper and middle segments

	Middle Segment		Upper Segment		P
	Mean ±sd.	Median	*Mean* ±sd.	Median	
RMSSD					
Pre-manipulation	36.0±14.5	31.0	48.6±14.1	53.2	**0.018**[m]
Post-manipulation	54.9±22.4	58.3	44.1±21.0	37.9	0.115[m]
Pre-manipulation / Post-manipulation Change	18.9±17.6	12.1	-4.4±13.0	-5.4	**0.000**[m]
Intra-Group Change P	**0.001**[W]		0.125[W]		

[m] Mann-whitney u test/ [W] Wilcoxon test

The pre-manipulation stress index (p=0.074) did not differ significantly (p > 0.05) in the middle and upper segment groups. The post-manipulation stress index (p=0.724) did not differ significantly (p > 0.05) in the middle and upper segment groups. In the middle segment group, the post-manipulation stress index (p=0.074) value decreased significantly compared to the pre-manipulation value (p < 0.05). In the upper segment group, the post-manipulation stress index (p=0.330) value did not differ significantly from the pre-manipulation value (p > 0.05). The difference in post-manipulation stress index in the upper and middle segment groups (p=0.004) was found to be significant (p < 0.05) (Table 5).

Table 5. Comparison of PNS ındex, stress ındex and SNS ındex values according to upper and middle segments

	Middle Segment		Upper Segment		P
	Mean ±sd.	Median	*Mean* ±sd.	Median	
PNS Index					
Pre-manipulation	-1.1±0.7	-1.2	-0.6±0.5	-0.5	0.052[t]
Post-manipulation	-0.3±0.9	-0.3	-0.8±0.8	-0.8	0.136[t]
Pre-manipulation / Post-manipulation Change	0.8±0.6	0.7	-0.1±0.5	-0.3	**0.000**[t]
Intra-Group Change P	**0.000**[E]		0.347[t]		
Stress Index					
Pre-manipulation	15.0±5.4	14.3	12.0±3.3	11.7	0.074[t]
Post-manipulation	12.2±2.9	11.5	12.7±4.3	11.8	0.724[t]
Pre-manipulation / Post-manipulation Change	-2.8±3.4	-2.3	0.7±2.7	0.9	**0.004**[t]
Intra-Group Change P	**0.006**[E]		0.330[E]		
SNS Index					
Pre-manipulation	2.2±1.5	1.8	1.5±1.0	1.3	0.121[t]
Post-manipulation	1.3±1.0	1.1	1.6±1.1	1.7	0.361[t]
Pre-manipulation / Post-manipulation Change	-1.0±0.7	-0.8	0.1±0.6	0.2	**0.000**[t]
Intra-Group Change P	**0.000**[E]		0.448[E]		

[t] Independent sample t test / [E] Paired sample t test

The pre-manipulation SNS index (p=0.121) did not differ significantly (p > 0.05) in the middle and upper segment groups. The SNS index after manipulation (p=0.361) did not differ significantly (p > 0.05) in the middle and upper segment groups. In the middle segment group, the SNS index (p=0.000) value decreased significantly (p<0.05) after manipulation compared to the pre-manipulation value.

The SNS index after manipulation (p=0.448) value in the upper segment group did not differ significantly from the pre-manipulation value (p > 0.05). The change in SNS index (p=0.000) after manipulation in the upper and middle segment groups was found to be significant (p < 0.05) (Table 5).

In the upper segment group, the pre-manipulation pNN50 (p=0.025) value was significantly higher

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than the middle segment group ($p < 0.05$). In the middle and upper segment groups, pNN50 ($p=0.141$) value did not differ significantly ($p > 0.05$) after manipulation. In the middle segment group, the pNN50 ($p=0.001$) value increased significantly after manipulation compared to the pre-manipulation value ($p < 0.05$). In the upper segment group, the pNN50 ($p=0.100$) value after manipulation did not differ significantly from the value before manipulation ($p > 0.05$). The post-manipulation pNN50 ($p=0.000$) change difference in the upper and middle segment groups was found to be significant ($p < 0.05$) (Table 6). In the middle and upper segment groups, the pre-manipulation power LF ($p=0.950$) value did not differ significantly ($p > 0.05$). Power LF ($p=0.422$) value after manipulation did not differ significantly ($p > 0.05$) in the middle and upper segment groups. In the middle segment group, the post-manipulation power LF ($p=0.917$) value did not differ significantly from the pre-manipulation value ($p > 0.05$). In the upper segment group, the post-manipulation power LF ($p=0.229$) value did not differ significantly from the pre-manipulation value ($p > 0.05$). In the middle and upper segment groups, the amount of power LF ($p=0.517$) change after manipulation did not differ significantly ($p > 0.05$) (Table 6).

In the middle and upper segment groups, the pre-manipulation power HF ($p=0.548$) value did not differ significantly ($p > 0.05$). In the middle and upper segment groups, power HF ($p=0.361$) value after manipulation did not differ significantly ($p > 0.05$). In the middle segment group, the power HF value after manipulation ($p=0.156$) did not differ significantly from the pre-manipulation ($p > 0.05$). In the upper segment group, the post-manipulation power HF ($p=0.125$) value did not differ significantly from the pre-manipulation value ($p > 0.05$). In the middle and upper segment groups, the amount of power HF ($p=0.576$) change after manipulation did not differ significantly ($p > 0.05$) (Table 6).

In the middle and upper segment groups, the pre-manipulation LF/HF ratio ($p=0.548$) did not differ significantly ($p > 0.05$). The LF/HF ratio ($p=0.290$) after manipulation did not differ significantly ($p > 0.05$) in the middle and upper segment groups. In the middle segment group, the post-manipulation LF/HF ratio ($p=0.394$) did not differ significantly from the pre-manipulation ($p > 0.05$). In the upper segment group, the post-manipulation LF/HF ratio ($p=0.156$) did not differ significantly from the pre-manipulation ($p > 0.05$). The amount of LF/HF ratio ($p=0.633$) after manipulation did not differ significantly in the middle and upper segment groups ($p > 0.05$) (Table 6).

Table 6. Comparison of pNN50, power LF, power HF and LF / HF ratio values by upper and middle segments

	Middle Segment		Upper Segment		P
	Mean ±sd.	Median	*Mean* ±sd.	Median	
pHH50 %					
Pre-manipulation	12.2±10.2	6.1	22.0±14.7	23.0	**0.025**^{m}
Post-manipulation	25.6±15.2	25.4	19.3±16.9	12.2	0.141^{m}
Pre-manipulation / Post-manipulation Change	13.4±12.4	9.4	-2.7±9.0	-2.6	**0.000**^{m}
Intra-Group Change P	**0.001**^{W}		0.100^{W}		
Power%LF					
Pre-manipulation	60.8±15.3	64.4	61.2±12.4	63.9	0.950^{t}
Post-manipulation	61.4±14.5	60.1	65.8±15.1	71.0	0.422^{t}
Pre-manipulation / Post-manipulation Change	0.5±19.4	4.0	4.6±14.2	1.6	0.517^{t}
Intra-Group Change P	0.917^{E}		0.229^{E}		
Power % HF					
Pre-manipulation	25.5±11.4	26.6	24.2±14.6	23.0	0.548^{m}
Post-manipulation	21.9±11.7	20.2	19.7±12.9	13.8	0.361^{m}
Pre-manipulation / Post-manipulation Change	-3.6±12.4	-4.1	-4.6±12.2	-7.8	0.576^{m}
Intra-Group Change P	0.156^{W}		0.125^{W}		
Min EDA					
Pre-manipulation	3.3±2.6	2.3	4.1±3.7	3.1	0.548^{m}
Post-manipulation	3.9±2.9	3.2	5.3±3.6	5.2	0.290^{m}
Pre-manipulation / Post-manipulation Change	0.6±2.5	0.3	1.1±3.0	1.4	0.633^{m}
Intra-Group Change P	0.394^{W}		0.156^{W}		

^{E} Paired sample t test / ^{m} Mann-whitney u test/ ^{t} Independent sample t test / ^{W} Wilcoxon test

DISCUSSION

In our study, we aimed to measure the instantaneous effect of chiropractic upper and middle thoracic manipulations on the autonomic nervous system. The study was conducted in a controlled and prospective manner on 30 individuals aged 18-45 years. HVLA manipulation used in our study is generally used in pain treatment, movement limitations, postural disorders and joint dysfunctions. When the sources related to the chiropractic method are examined, it is seen that this interaction is generally ignored although information about the autonomic nervous system is given.

While RMSSD, pNN50, HF Power, which are heart rate variability parameters, reflect parasympathetic nervous system activity, LF Power, Stress Index are values related to sympathetic nervous system activity.[8] PNS Index and SNS Index are the results related to parasympathetic and sympathetic activities specified in Kubios software.[9] As a result of the research, no significant change was observed in parasympathetic nervous system values such as RMSSD, pNN50, PNS Index and sympathetic nervous system values such as Stress Index and SNS Index after upper thoracic manipulation. After middle thoracic manipulation, significant decreases occurred in sympathetic nervous system values such as Stress Index, SNS Index, while significant increases occurred in parasympathetic nervous system values such as RMSSD, pNN50, PNS Index. It was observed that there was no significant change in temperature, EDA, HF Power, LF Power and HF/LF Ratio values. There is no study using exactly the same parameters in the literature review.

In a study conducted by Budgell and Polus on 28 individuals aged 18-45 years, the effect of thoracic HVLA manipulation on heart rate variability (HRV) in healthy adults was investigated. [10] In this study, it was reported that thoracic HVLA manipulation on HRV resulted in short-term changes and although there was no statistically significant effect, it could partially affect the autonomic system.

In the study conducted by Welch and Boone, the effect of chiropractic manipulation of cervical and thoracic joint dysfunctions on the autonomic nervous system was investigated.[11] Blood pressure and heart rate were measured in all individuals between the ages of 25-55. In the study, it was found that cervical manipulation was statistically effective on blood pressure, while thoracic manipulation was not statistically effective.

Çakır et al. investigated the instantaneous effect of chiropractic thoracic manipulations on the autonomic nervous system.[12] In this study, only HRV measurement was performed in people with dysfunction in the thoracic region. Segments to be manipulated have been determined according to movement limitation. They reported a decrease in parasympathetic nervous system data and an increase in sympathetic nervous system data.

The review of the effects of spinal mobilization on the sympathetic nervous system by Kingston et al. was conducted in asymptomatic individuals.[13] In these studies, it was concluded that spinal mobilizations had an effect on the sympathetic nervous system. Segments have not been evaluated in this study. Welch and Boone (2008) reported that the cervical area exhibited parasympathetic stimulation while the thoracic area exhibited sympathetic stimulation. However, none have been subjected to HVLA manipulation. [7]

Win et al. investigated the effects of upper (C1 - C2) and lower (C6-C7) cervical spinal manipulation on blood pressure and heart rate variability in individuals with neck pain.[14] The study was conducted on 20 people between the ages of 19 and 23 years. As a result of the study, it was concluded that manipulation of the upper cervical area increased parasympathetic activity while manipulation of the lower cervical area increased sympathetic activity.

Sillevis et al. examined the instantaneous effects of thoracic spine manipulation on the autonomic nervous system with pupil diameter measurements. 101 people aged between 18-65 years were included in the study provided that they had dysfunction at T3-T4 levels and compared the effects of placebo and HVLA manipulation. They stated that pupil diameter did not change after manipulation and that there was no sympathetic or parasympathetic response.[15] The possible cause of the discrepancy with our study may be the measurement methods.

In a study conducted by Zhang et al., they examined the effects of chiropractic treatment on HRV and pain. In the study, 96 chiropractic practitioners were given HRV measuring devices and 10 patients were asked to record their pre- and post-application data for 4 weeks. When the one-time measurements were removed, the study was carried out in 539 people. Chiropractic applications showed a significant

improvement in HRV at week 1 and week 4.[16]

Grimm et al. stated that the correction of dysfunctions in the musculoskeletal system also had an effect on the autonomic nervous system in chiropractic applications. However, in this study, no distinction was made between area, application and measurement and a general opinion was mentioned.[17]

Picchiottino et al. investigated the instantaneous effect of joint manipulative treatments on the autonomic nervous system and stated that mobilizations had an effect on the sympathetic activity of the skin and were ineffective on HRV, and that HVLA manipulations could have an acute effect on cardiovascular autonomic activity and various parameters of autonomic activity. [18]

Our study was limited to 30 asymptomatic individuals. Applications were performed on different segments of the thoracic area and instant measurements were taken. Autonomic nervous system results obtained by different measurement methods and evaluating long-term effects may vary. As a result of the study, it was observed that upper thoracic manipulation had no effect on the autonomic nervous system. This may be due to the initially high levels of parasympathetic activity such as RMSSD and pNN50% in the upper thoracic group. The fact that the values such as Stress index and SNS index did not decrease in the upper thoracic group compared to the middle segment group may be due to the sympathetic innervation of the heart originating from the upper thoracic segments. Since middle thoracic manipulations increase parasympathetic activity and decrease sympathetic activity, it can be associated with vagal control, but this should be supported by studies evaluating other parameters as it is a multifactorial condition. This study does not explain why mid-thoracic manipulation increases parasympathetic or vagal activity. Studies involving more participants, using different techniques and investigating longer-term effects are important in terms of explaining the relationship between chiropractic manipulations and the autonomic nervous system. The results of studies evaluating lower thoracic and lumbar area manipulations with similar protocols and methods may shed light on our understanding of the effect of the level of chiropractic applications on the autonomic nervous system.

CONCLUSION

As a result of our measurements and analyzes, it has been observed that chiropractic upper and middle thoracic manipulations have different instantaneous effects on the autonomic nervous system. While HVLA manipulation in the upper segments of the thoracic area does not lead to a significant change in the autonomic nervous system, HVLA manipulation in the middle thoracic segments causes an increase in parasympathetic nervous system values and a decrease in sympathetic nervous system values. There is a need for more comprehensive research to examine this difference in healthy people as a result of upper and middle thoracic manipulation.

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ORIGINAL RESEARCH

Views of Healthcare Professionals to Traditional and Complementary Medicine

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Abstract

Objective: Although its roots go back centuries, there is still a demand for traditional medicine practices and it is important to know the opinion of the society and healthcare professionals about the subject. Our study aims to determine the attitudes of healthcare professional and non-healthcare hospital staff about traditional medicine.

Material-Method: A two-stage questionnaire, a demographic information section, and the Complementary, Alternative, and Conventional Medicine Attitudes Scale (CACMAS) was used to collect the data. Descriptive statistics, Kolmogorov Smirnov, Mann-Whitney U, Kruskal Wallis and chi-square tests were used to analyze the data.

Results: A total of 681 staff of nine public and private hospitals participated in the study. 65.4% (n=439) of the participants were healthcare professionals, 34.6% (n=232) were non-healthcare professionals. The mean scores of the healthcare professional respondents were 92.6 (±16.7), of the non-healthcare professional respondents were 126.1 (±11.7).

Conclusion: In our study, it was found that healthcare professionals' attitudes towards traditional medicine practices were more negative than non-healthcare professionals. However, as according to the current legislation in many countries around the world, only physicians who receive standard training and other healthcare professionals under their supervision are authorized to perform traditional medicine practices in Turkey. As a result of our study, it was determined that the attitudes of healthcare professionals and other segments of the society should be observed about traditional medicine practices and that measures should be taken to bring together the supply and demand for traditional medicine on a legal basis.

Keywords: Traditional Medicine, Attitude, Health Personnel, Hospital Staff

INTRODUCTION

Traditional medicine emerged with human history and has been the only treatment alternative for humans for centuries. Although traditional treatment methods vary according to the culture, religious beliefs and traditions of societies, some of them have survived to this day. Although modern medicine has made relatively great progress until today, traditional treatment practices are carried out in daily life in order to maintain health and treat diseases because people want to try all possibilities to protect or restore their health. Therefore, interest in traditional and complementary medicine practices continues. The use of traditional medicine methods is widespread worldwide. Reasons for being preferred include being easy to access, culturally acceptable, reliable by many people and cost-effective. Regardless of the reasons for its preference, it is seen that interest in traditional and complementary therapies is increasing worldwide and it is thought that it will continue to increase[1]. Legal regulations on traditional and complementary medicine practices date back to ancient times in some countries, while in some countries it is seen that they have been made in recent years[2]. What these legal regulations generally have in common is that traditional and complementary medicine is foreseen to be practiced by people who have been trained in the subject area. Turkey is one of the countries where legal regulations on traditional and complementary medicine practices have been made in recent years. According to the current legislation in Turkey, only health professionals who are certified by training are allowed to practice traditional and complementary medicine.

In this respect, it is very important to know the attitudes of health professionals about traditional and complementary medicine practices. However, the literature research has shown that there are few comprehensive studies on the attitudes of health professionals in Turkey regarding traditional and complementary medicine practices, perhaps because the legal regulations have just been made.

As it is known, health professionals such as physicians, nurses, etc. and non-health professionals such as cleaning staff, office employees, etc. work together in hospitals. In our study, it was aimed to determine the attitudes of health professionals and non-health professionals working in nine different hospitals, five being public and four being private, about traditional and complementary medicine practices. Thus, it was aimed to make future inferences by comparing the traditional and complementary medicine perspectives of non-health professionals with health professionals.

Traditional and complementary medicine in Turkey

There is no complete consensus on the naming and definition of traditional medicine and it is defined in many different ways[3]. For example, according to the National Center for Complementary and Alternative Medicine in the United States, traditional and complementary medicine is a group of medical and health systems, practices, and products which are considered as a part of the traditional medicine[4].

The Turkish Ministry of Health has adopted the definition made by the World Health Organization (WHO) in past years. Accordingly, traditional and complementary medicine is a whole of knowledge, skills and practices based on theories, beliefs and experiences indigenous to different cultures, that can be explained or not explained, that are used to prevent, diagnose, improve or treat physical and mental diseases, as well as to maintain health well[5].

The first legal regulation in Turkey is the "Regulation of Acupuncture Practices" published in 1991. However, the first comprehensive legal regulation is the "Regulation on Traditional and Complementary Medicine Practices" published in 2014. In this regulation, acupuncture, apitherapy, phytotherapy, hypnosis, leech therapy, homeopathy, chiropractic, cupping therapy, larval therapy, mesotherapy, prolotherapy, osteopathy, ozone therapy, reflexology and music therapy are listed as traditional and complementary medicine practices. Those who want to perform these practices are required to participate in the trainings to be organized by the bodies authorized by the Turkish Ministry of Health, to successfully complete the training and obtain certificates According to that regulation, traditional and complementary medicine is allowed to be practiced only by certified medical doctors or dentists. Healthcare professionals who have basic medicine training are allowed to participate in the practices under the supervision of certified medical doctors[6].

MATERIALS AND METHODS

This study is a descriptive and cross-sectional research which has been conducted in Kırklareli, in June, 2021. Kırklareli is a city with around 360.000 habitants in northwestern Turkey.

Target population of our research consists of 2.277 hospital employees recruited in nine hospitals in Kırklareli, five hospitals being public and four being private. We have used stratified random sampling method. We have calculated the sampling size as 658 by using the Epi-info-7 StatCalc Program, with the values of 2.277 population, 95% confidence interval, 5% acceptable margin of error and 50% expected frequency and by taking the design effect as 2. Considering that all employees who received the survey may not respond, we aimed to reach out to 724 participants by increasing the sampling by 10%. Target population was considered to consist of nine strata, each hospital being one stratum. We categorized hospital employees based on occupational groups. We sent a survey to the participants randomly selected based on the occupational groups' frequency within the strata. Criteria for participating in the survey were being employed by a hospital in Kırklareli and filling out the survey form with free will. 671 survey forms meeting the mentioned criteria returned, thus the response rate is 92.7%.

A two-stage questionnaire, a demographic information section developed by the researchers, and the Complementary, Alternative, and Conventional Medicine Attitudes Scale (CACMAS) was used to collect the data. CACMAS was developed in 2010 by McFadden et al[7]. The adaptation study of the scale into Turkish was conducted by Köse et al. in 2016[8].

CACMAS consists of 27 items in total. Each item was measured with 7-point scale, 1 corresponding to "I strongly disagree" and 7 corresponding to "I

strongly agree". Therefore, it is possible for a participant to score at least 27 and at most 189 points on the scale. The scale consists of 22 positive and 5 negative (1, 4, 8, 9, 26.) items. During the analysis, items consisting of negative statements were scored in reverse (7-6-5-4-3-2-1). The CACMAS includes three subscales as philosophical congruence with complementary and alternative medicine (5, 7, 9, 18, 19, 21, 22, 24. items), dissatisfaction with conventional medicine (1, 4, 8, 11, 14, 16, 17, 20, 26, 27. items) and holistic balance (2, 3, 6, 10, 12, 13, 15, 23, 25. items). It is stated that the CACMAS does not have a specific cut-off point, and higher scores on the scale indicates the participant's attitude towards traditional medicine is more positive.

SPSS 22 (Statistical Program for Social Sciences) software was used in analyzing the survey data. Descriptive statistics are presented in form of numeric value, percentage, standard deviation and average. Data distribution was verified by using Kolmogorov-Smirnov and Shapiro Wilk tests. Chi-square, Mann Whitney U and Kruskal Wallis tests were used in analyzing the data which were not normally distributed. Findings were evaluated at 95% confidence interval and results with <0.05 p value were regarded as statistically significant.

Ethical approval

Our study was conducted with the permission of Kırklareli Provincial Health Directorate Research Applications Examination and Evaluation Commission (dated April 14, 2020, and numbered 2020/26) and Kırklareli University Institute of Health Sciences Ethics Committee (dated April 06, 2020, and numbered 2020-04). In addition, permission was obtained from Köse for the use of the CACMAS Turkish form.

RESULTS

The sample of the study consists of 671 hospital workers at the age from 21 to 67 (M = 36.6, SD = 9.4) and 66.5% were female (n=446) and 33.5% were male (n=225). 83.0% (n = 557) of the participants stated that they work in shifts and 17.0% (n = 114) of them work only in the daytime. The distribution of the participants according to their institutions and job titles is shown in Table 1.

Table 1. The distribution of the participants according to their institutions and job titles.

Job Titles	Public Hospital		Private Hospital		Total	
	n	%	n	%	n	%
Physician	63	9.4	38	5.7	101	15.1
Health Personnel*	245	36.5	93	13.9	338	50.4
Health Professionals (Subtotal)	**308**	**45.9**	**131**	**19.5**	**439**	**65.4**
Office Staff**	56	8.3	29	4.3	85	12.7
Auxiliary Services Staff***	98	14.6	49	7.3	147	21.9
Other Health Workers (Subtotal)	**154**	**23.0**	**78**	**11.6**	**232**	**34.6**
Total	**462**	**68.9**	**209**	**31.1**	**671**	**100.0**

* Nurses, midwives, medical technicians
** Secretary, accountant, administrative manager, etc.
*** Cleaning staff, driver, security, technical staff, etc.

The mean CACMAS score of our study group was 104.2 (± 21.7). Mean scores of CACMAS subscales were calculated as 27.9 (± 9.4) for the Philosophical Congruence with Complementary and Alternative Medicine subscale, 30.0 (± 10.5) for Dissatisfaction with Conventional Medicine and 46.3 (± 4.1) for the Holistic Balance subscale. The comparison of the mean scores of the CACMAS with some sociodemographic characteristics of the respondents is shown in Table 2. There is no statistically significant difference in the total scores of general practitioners or specialist physicians within the physician group (U=939.000, z= -0.631, p=0.528). However, there is a significant difference between the CACMAS scores of the participants healthcare and non-healthcare professionals (U=2417.000, z= -20.326, p<0.001). Similarly, it was found that there is a significant difference between physician and other healthcare professionals' CACMAS scores (U=830.000, z= -14.548, p<0.001). The distribution of CACMAS scores of the participants according to the subscales is shown in Table 3.

Table 2. The comparison of the mean scores of the CACMAS with some sociodemographic characteristics of the respondents.

Various Characteristics of The Respondents	n	%	Min	Max	Mean Rank	p
Gender*						
Female	446	66.5	42	144	333.6	0.657
Male	225	33.5	43	141	340.7	
Age**						
29 Years and Under	189	28.2	56	144	245.3	<0.001
30 - 39 Years	219	32.6	42	135	315.9	
40 - 49 Years	198	29.5	60	138	401.7	
50 Years and Over	65	9.7	59	142	467.4	
Marital Status*						
Married	340	50.7	42	142	365.1	<0.001
Not Married (Single, Widow, Divorced etc.)	331	49.3	57	144	306.1	
Job Titles**						
Physician	101	15.1	42	138	65.3	<0.001
Health Personnel***	338	50.4	61	144	273.4	
Office Staff	85	12.7	62	130	477.5	
Auxiliary Services Staff	147	21.9	65	142	584.2	
Institution Type*						
Public Hospital	462	68.9	42	144	337.6	0.753
Private Hospital	209	31.1	43	142	332.5	
Education Status*						
Vocational School and below	238	35.5	65	142	475.4	<0.001
University and Above	433	64.5	42	144	259.3	
Perceived Economic Status**						
Very Bad - Bad	206	30.7	65	144	402.5	<0.001
Middle	348	51.9	42	142	343.6	
Good - Very Good	117	17.4	43	138	196.2	

* Mann Whitney U test was used.
** Kruskal Wallis test was used.
*** Nurses, midwives, medical technicians

Table 3. The distribution of CACMAS scores of the participants according to the subscales.

Job Titles	Subscales	n	Min.	Max.	Mean ± SD
Physician	Subscale 1	101	8	43	12.51 ± 5.03
	Subscale 2		10	37	14.80 ± 4.19
	Subscale 3		17	62	40.29 ± 5.05
	CACMAS		42	138	67.60 ± 11.57
Health Personnel*	Subscale 1	338	10	41	26.40 ± 3.96
	Subscale 2		11	53	27.26 ± 4.989
	Subscale 3		39	51	46.37 ± 2.47
	CACMAS		61	144	100.03 ± 7.54
Office Staff	Subscale 1	85	10	43	33.59 ± 6.75
	Subscale 2		11	42	35.94 ± 5.27
	Subscale 3		41	55	47.74 ± 3.36
	CACMAS		62	130	117.27 ± 10.52
Auxiliary Services Staff	Subscale 1	147	10	44	38.38 ± 4.92
	Subscale 2		11	54	43.33 ± 6.71
	Subscale 3		44	54	49.44 ± 1.97
	CACMAS		65	142	131.16 ± 9.09

Subscale 1: Philosophical Congruence with Complementary and Alternative Medicine
Subscale 2: Dissatisfaction with Conventional Medicine
Subscale 3: Holistic Balance
CACMAS: Complementary, Alternative, and Conventional Medicine Attitudes Scale

* Nurses, midwives, medical technicians

As seen in Table 3, 59.6% of physicians' CACMAS score averages originate from the holistic balance subscale. This rate is 46.4%, 40.7% and 37.7% in health staff (nurses, midwives, and medical technicians), office staff and auxiliary services staff, respectively. The Cronbach's alpha reliability coefficient of the CACMAS was calculated as 0.928 in our study.

DISCUSSION

Traditional medicine is as old as human history, but discussions about traditional medicine are just as old. The number of healthcare professionals around the world who describe traditional medicine methods as "quackery" is too much to underestimate[9-12]. For this reason, it is important to know the attitudes of those who receive or provide traditional medicine services. Among the participants of our study, there were both healthcare professionals and non-healthcare professionals who worked in a hospital. In this respect, it was possible to evaluate and compare both groups simultaneously in our study.

Although our study was conducted in two different types of hospitals, public and private, no statistically significant difference was found between the participants' CACMAS scores in terms of the institution type. In this respect, it can be said that different hospital staff that consist our study group have similar attitudes about traditional medicine practices.

For the CACMAS, the researchers who developed the scale stated that it had three subscales[7]. In a study conducted in 2014 using CACMAS, it was stated that it could have four subscales[13]. When the CACMAS was adapted to Turkish in 2016, it was found that it had three subscales[8]. In another study conducted in Turkey in 2019, it has been reported that the items of the scale could be collected in two subscales[14]. In our study, the data were analyzed in three subscales, adhering to the original version of the CACMAS and its Turkish version.

It has been observed that healthcare professional and non-healthcare participants got similar scores in the "Holistic Balance" subscale. There is a more significant difference mainly between responses of medical doctors and social workers to the statements about "Philosophical Congruence with Complementary and Alternative Medicine" and "Dissatisfaction with Modern Medicine" subscales.

A study on the sociodemographic determinants of the use of traditional and complementary medicine throughout Europe reports that in general women use it more than men[15]. According to the same study, people with higher education and higher income use traditional and complementary medicine more frequently. As to our study, a statistically significant difference in terms of CACMAS total scores based on gender has not been observed. Nevertheless, it is observed that as our participants' level of education and economic conditions increase, their CACMAS score decreases. In addition, the positive view of our healthcare professional participants on traditional and alternative medical practices is significantly lower than the one of non-healthcare participants. These findings suggest that the attitude of healthcare professionals towards traditional and alternative medical practices is more negative compared to the general public. Some of the studies conducted at different places of the world support that suggestion whereas some others report that healthcare professionals have a positive view on traditional and alternative medical practices[16-19].

In our study group, the most positive attitude towards traditional medicine was found in auxiliary services personnel and the most negative attitude was found in physicians. In a study conducted with healthcare professionals working in two different public hospitals in Istanbul using a different scale in 2019, no significant difference was found between gender, education status and whether they were physicians or not in terms of the attitudes of the participants towards traditional medicine[20]. Although our findings are not compatible with this study, there are also studies with similar results to ours. For example, in a study conducted in Mexico, it was reported that physicians' attitudes towards traditional medicine practices were more negative than other healthcare professionals[21]. In a systematic review examining the attitudes of healthcare professionals about traditional medicine practices in cancer treatment, it was found that doctors displayed more negative attitudes than other professionals[22]. However, according to current legislation in Turkey and many countries around the world, traditional medicine practices can be performed only by certified physicians or dentists or by other healthcare professionals with basic medical training under the supervision of certified physicians or dentists[8]. When our findings are evaluated in the light of this information, it is understood that if traditional medicine practices are to be widespread, studies that will positively change the attitude of healthcare professionals are required. Otherwise, the demand against traditional medicine practices in the

society may be abused by malicious persons who are uneducated, prioritizing their own benefit instead of the patient's health[10]. Another risk is that patients who notice the negative attitude towards traditional medicine of healthcare professionals who treated them, resort to traditional medical practices that may have cross-interactions with their treatments and hesitate to inform their physicians about this. Thus, in a study conducted in 2018, it was reported that the majority of the participants applied for traditional medicine methods without a physician's recommendation and did not inform their physicians after the practices[23].

In order to determine their attitudes towards traditional medicine of pediatrics nurses, in a study conducted in Turkey in 2019 using CACMAS like ours, average of total scores was reported as 112.01 ± 20.07[24]. In our study group, average of total scores in the healthcare personnel group, including nurses, midwives, medical technicians was 100.03 (±7.54). This result suggested that the increase in the number of similar studies is important in determining the general tendency about traditional medicine.

Köse et al., who made the Turkish adaptation of the CACMAS we used in the study, reported the Cronbach's alpha reliability coefficient of the Turkish form as 0.808[8]. In our study group, Cronbach's alpha reliability coefficient was calculated as 0.928. This finding has once again confirmed that the Turkish form of CACMAS is valid and reliable.

Our study also has some limitations. Firstly, the entire population could not be reached. Another limitation is that our study group consists of only the staff working in hospitals, so it does not reflect the general opinion of healthcare professionals about traditional medicine.

CONCLUSION

In our study, the attitudes of healthcare and non-healthcare professional personnel working in nine different hospitals about traditional medicine practices were evaluated. The most negative attitude towards traditional medicine practices was determined in physicians. In terms of negative attitude, healthcare personnel such as nurses, midwives, medical technicians, etc. come second. In other words, the attitude of healthcare professionals towards traditional medicine practices was more negative than non-healthcare hospital staff. However, similar to many countries, according to the legislation in force in Turkey and many countries in the world, traditional medicine practices should be performed by only healthcare professionals. It is understood that this contradiction should be eliminated if it is aimed to meet the demand from the society about traditional medicine practices in accordance with legal regulations. As a result of our study, it was determined that the attitudes of healthcare professionals and other segments of the society should be observed about traditional medicine practices and that measures should be taken to bring the supply and demand for traditional medicine together on a legal basis. If traditional and complementary medical services are required to be delivered by healthcare professionals, studies which help them to adopt a more positive view of the matter are needed. For this purpose, complementary and traditional medicine practices should be provided with scientific evidence and practices without scientific basis should not be allowed.

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ORIGINAL RESEARCH

Determination of Knowledge, Attitudes and Behaviors towards Traditional and Complementary Medicine in Patients Applying to Pamukkale University Medical Faculty Hospital Polyclinics

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Abstract

Objective: The aim of research was to investigate the attitudes and behaviors towards traditional and complementary medicine methods, the use of which has increased in recent years, in individuals admitted to the hospital.

Material-Method: The descriptive study was performed by applying a questionnaire to 276 people. The questionnaire included questions about the sociodemographic characteristics of the participants, their knowledge, attitudes and behaviors about traditional complementary medicine methods, and the Complementary, Alternative, and Conventional Medicine Attitude Scale. Data were analyzed with the Statistical Package for the Social Sciences version 15. Chi-square test, Mann-Whitney U and Kruskall-Wallis H tests were used in the comparison of traditional and complementary medicine attitudes and behaviors with sociodemographic characteristics. $p<0.05$ was considered significant.

Results: 33% of respondents had applied at least one traditional complementary medicine method. The most commonly used methods were cupping (n=40), phytotherapy (n=34) and acupuncture (n=17). The mean score of scale was found to be 109.05±15.44. The mean score of the individuals aged 45 and over is higher than the other ages and is 102.7±17.2 ($p<0.048$). A statistically significant difference was found between the use of at least one traditional and complementary method and the variables of age, marital status, place of residence for the longest time, and perceived health ($p<0.05$).

Conclusion: TCM methods are known to the majority of people who visit polyclinics. Their attitudes towards traditional and complementary medicine are quite close to positive. Physicians should question whether their patients use traditional methods.

Keywords: Complementary Medicine, Traditional Medicine, Knowledge, Attitudes, Practice

INTRODUCTION

According to World Health Organization (WHO), traditional medicine is the sum total of the knowledge, skill and practices based on the beliefs, beliefs and experiences traditional to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illnesses. WHO has defined complementary medicine as: ‘a broad set of healthcare practices that are not part of that country’s own tradition or conventional medicine and are not fully integrated into the dominant healthcare system[1,2]. As a result of the discussions, it was decided that these methods could not be an alternative to medicine, but could only be complementary to the treatment, and the definition of "traditional and complementary medicine" came to the fore, based on the definition of WHO[3]. Traditional and complementary medicine (TCM) methods are classified as "alternative whole medical systems" (homepathy, acupuncture, etc.), "mind-body interventions" (hypnotherapy, yoga, etc.), "biological-based therapies" (probiotics, antioxidants, herbs), "manipulative body-based methods" and "energy therapies" [4,5].

Although the clinical efficacy of many TCM methods is controversial because of a lack of scientific evidence, the use of TCM has increased significantly worldwide, especially in the last 20 years [6,7]. Studies show that the frequency of TCM use varies between 9.8-76% worldwide [7]. Many individuals resort to TCM methods for the treatment of serious physical and mental diseases,

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especially diabetes, hypertension, cancer, musculoskeletal system diseases and dermatological problems [6,8]. Sometimes patients may prefer these methods first without going to the health institution, and sometimes they turn to these methods to support their medical treatment[8]. The fact that TCM methods are individual-oriented and their holistic approach, which takes into account not only physical health but also mental and social well-being, has made these methods trustworthy by the society [4]. The WHO supports the integration of proven TCM methods into national health systems [9]. The frequency of use of TCM in Turkey has been reported as 22.1%, and these methods have not yet been integrated into the national health system [10]. TCM services are carried out by physicians and dentists (only in the field of dentistry) who have practice certificates in practice centers authorized by the Ministry. Health professionals with basic education can participate in the practice under the supervision of certified physicians. With the Regulation on Traditional and Complementary Medicine Practices by the Ministry of Health, the principles of the practices, who can do it, the qualifications of the places where the practice will be made, the drugs that must be kept in the practice centers and the inspection principles have been determined [11].

The factors affecting the use of TCM are various. Sociodemographic factors, income level, type and severity of the disease, dissatisfaction with modern medicine, limited health care access, cultural beliefs, long-term use of TCM methods, perceived usefulness and safety of these methods, accessibility of TCM methods and being affected by social networks are considered among the reasons why TCM methods are preferred [4,6,7,8,12]. In the literature, the main reasons that keep individuals from using these methods are reported as lack of scientific evidence for TCM methods, disbelief in their effectiveness and safety, and not performing the applications under hygienic conditions [7]. The reasons for using TCM vary from country to country, while Western societies use these methods to keep their health under control, these methods are used in African countries due to the problems experienced in accessing professional health personnel and the affordability and accessibility of TCM methods. Asian societies are influenced by social networks and turn to TCM methods. Dissatisfaction with conventional medicine in South American countries is the main reason for using TCM [7,9]. There are many studies to determine the frequency of use of these methods in specific disease conditions and the knowledge and attitudes of health professionals about TCM. The number of studies investigating the knowledge, attitudes and behaviors of people applying to a health institution towards TCM applications is limited.

The aim of this study is to determine the knowledge, attitudes and behaviors of people who applied to selected polyclinics of a university hospital towards TCM.

MATERIALS AND METHODS

This research is a descriptive type epidemiological study. The population of the study consisted of individuals who applied to four selected polyclinics (internal diseases, family medicine, physical therapy and rehabilitation and dermatology) of the Pamukkale University Medical Faculty Hospital. According to the sample size calculation formula of the Open Epi program, the population size of which is unknown, the frequency was accepted as 50% and the type 1 error level was 5%, and the sample size to represent the universe was calculated as 384 with 80% power and 95% confidence interval (p=0.50, alpha=0, 05, d=0.05). The research was carried out between January 30-February 26, 2019. The data collection tool of the research is a questionnaire consisting of 59 questions, created by the researchers by scanning the literature. In the questionnaire form, there are 9 questions about the sociodemographic characteristics of the participants, 6 questions about the general health characteristics, 17 questions about the level of knowledge and behavior of traditional and complementary medicine. In the survey, the practices mentioned in the Regulation on Traditional and Complementary Medicine Practices published in the Official Gazette No. 29158 on 27.10.2014 were questioned, while other traditional methods used among the public were not included. There are 15 TCM methods whose implementation principles are determined by the relevant regulation. These are acupuncture, apitherapy, phytotherapy, hypnosis, leech therapy, homeopathy, chiropractic, cupping, maggot debridement therapy, mesotherapy, prolotherapy, osteopathy, ozone application, reflexology and musicotherapy (11). The data of the research were collected between 1-15 February 2019 by filling in the questionnaire form

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by people who volunteered to participate in the research. The Complementary, Alternative, and Conventional Medicine Attitude Scale (CACMAS) consisting of 27 questions was used to determine the attitudes of the participants towards traditional and complementary medicine. The scale consists of 3 sub-factors: Philosophical congruence with complementary and alternative medicine, dissatisfaction with conventional medicine, and holistic balance. The scale is 7-point Likert type (1 = I strongly disagree, 7 = I strongly agree). Questions 1, 4, 8, 9 and 26 are reverse coded. A score between 27-189 can be obtained from the scale. A high score from the scale indicates a positive attitude towards traditional and complementary medicine. The Turkish validity and reliability study of the scale developed by McFadden et al. was performed by Köse et al. [13] (Cronbach's alpha: 0.808). Ethical approval for this study was obtained from Pamukkale University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee for the study. Required institutional permission has been obtained. Verbal consent was obtained from the participants.

Statistical analysis

Statistical Package for the Social Sciences (SPSS) version 17 was used for data analysis. Descriptive statistics are given by calculating mean, standard deviation, frequency and percentage. The compatibility of continuous variables with normal distribution was evaluated with Kolmogorov-Smirnov and Shapiro Wilk Tests. Since the normal distribution conditions were not met, Mann-Whitney U test and Kruskal-Wallis H test were used to compare the scale means. Factors associated with performing at least one traditional application were compared using the Pearson Chi-square test. Statistical significance level was considered significant if $p<0.05$.

RESULTS

Overall 276 (72.0%) people participated in the research. The mean age of the participants in the study was 37.6±14.1 years. 58.9% of the participants were women, while 83.7% of the participants had a high school or higher education level and 36.7% of the participants had a chronic disease. The sociodemographic characteristics of the participants in the study are shown in Table 1.

Table 1. Sociodemographic characteristics of the participants

		n	%
Age	18-24	72	26.1
	25-44	112	40.6
	≥45 years	92	33.3
Gender	Female	162	58.9
	Male	113	41.1
Education level	Middle school and below	45	16.3
	High school and above	231	83.7
Income	Income less than expenses	83	30.5
	Income equals expense	135	49.6
	Income more than expenses	54	19.9
Marital status	Married	119	43.1
	Single	131	47.5
	Divorced/Widowed/Separate	26	9.4
Family type	Nuclear family	230	83.9
	Extended family	31	11.3
	Broken family	13	4.7
Longest lived place	Province	186	67.6
	District	67	24.4
	Town/Village	22	8.0
Perceived health	Excellent/Very good	88	31.9
	Good/Medium	186	67.4
	Bad	2	0.7
Chronic disease	Yes	101	36.7
	No	174	63.3
Outpatient clinic applied	Internal medicine	88	31.9
	Family medicine	23	8.3
	Dermatology	71	25.7
	Physical therapy and rehabilitation	94	34.1

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The frequency of participants who heard TMC modalities was 85.9%; 40.4% of participants got information about TCM; source of information was television/radio/internet with a frequency of 28.3%. The participants stated that TCM applications were beneficial with a frequency of 36.6%. They stated that they applied at least one TCM method with a frequency of 33.0%. It was found that the purpose of the applications was relaxation with a frequency of 66.3% and treatment with a frequency of 25.8%; 18.0% of participants who had TCM application stated that they benefited completely, 71.9% benefited partially, 10.1% had no benefit from the application. The knowledge, attitudes and behaviors of the participants towards TCM applications are shown in Table 2. The methods most frequently applied by the participants of the study are cupping method (n=40), phytotherapy (n=34) and acupuncture (n=17).

Table 2. Participants' knowledge, attitude and behavioral characteristics towards TCM applications

		n	**%**
Hearing the methods	Yes	237	85.9
	No	39	14.1
Getting information about TCM modalities	Yes	111	40.4
	No	164	59.6
Information source*	Specialist doctor	14	5.1
	Family doctor	2	0.7
	Pharmacist	2	0.7
	Nurse	1	0.4
	Television/Radio/Internet	78	28.3
	Book/Magazine/Newspaper	37	13.4
	Neighbor/Relative/Frien	60	21.7
Thoughts on the usefulness of TCM	Beneficial	100	36.6
	Damaging	14	5.1
	Neither beneficial nor harmful	69	25.3
	No idea	90	33.0
Useing at least one of the TCM modalities	Yes	91	33.0
	No	185	67.0
The purpose of applying TCM	Cosmetic	5	5.6
	Protection	2	2.2
	Relaxation	59	66.3
	Treatment	23	25.8
Application time	Before going to the doctor	63	71.6
	After going to the doctor	25	28.4
Place of application	Public hospital	3	3.4
	Private hospital	5	5.7
	Private health institution	18	20.7
	House	53	66.7
	Other	3	3.4
Person making the application*	Doctor	13	4.7
	Nurse/Midwife	2	0.7
	Pharmacist	0	0.0
	Transfer	6	2.2
	By himself/herself	34	12.3
	Other	10	3.6
Post-application health problem	Yes	2	2.3
	No	86	97.7
Benefit from the application	Complete	16	18.0
	Partial	64	71.9
	None	9	10.1
Repeating application	Yes	52	59.1
	No	36	40.9
Recommending the app	Yes	66	76.7
	No	20	23.3

*More than one option ticked. Percentage is taken over the total number.

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The CACMAS mean score of the participants was found to be 109.05±15.44 (Table 3). Distribution of people using TMC according to the treatment modality they use is shown in Figure 1.

Table 3. The mean and standard deviation of the participants' scores on the Complementary, Alternative, and Conventional Medicine Attitude Scale (CACMAS)

	Mean ± standard deviation
Scale total score	109.05±15.44
Philosophical congruence with complementary and alternative medicine	46.57±8.11
Dissatisfaction with conventional medicine	26.28±9.73
Holistic balance	26.18±9.78

When the scores of the participants from the CACMAS were analyzed according to their sociodemographic characteristics, the mean score of the scale was 97.4±17.4 in individuals aged 18-24, 97.0±18.7 in individuals aged 25-44, and 102.7±17.2 in individuals aged 45 and over (p=0.048). There was no statistically significant difference between gender, educational status, perceived income, marital status, family type, perceived health, presence of chronic disease and scale score (p>0.05). When the sociodemographic variables associated with performing at least one application were compared, it was found that 29.2% of the participants aged 18-24, 24.1% of the participants aged 25-44, and 46.7% of the participants aged 45 and above performed at least one TCM application. (p=0.002). 28.5% of the participants whose place of residence was most of time city center for the longest time and 42.7% of those whose place of residence was most of time the county-town-village for the longest time stated that they used at least one TCM method (p=0.019). There was no statistically significant difference between the characteristics of the participants such as gender, educational status, income, family type, and presence of chronic disease and use of at least one TCM method (p>0.05). The comparison of the participants' sociodemographic characteristics and their behaviors and attitudes towards TCM applications is given in Table 4.

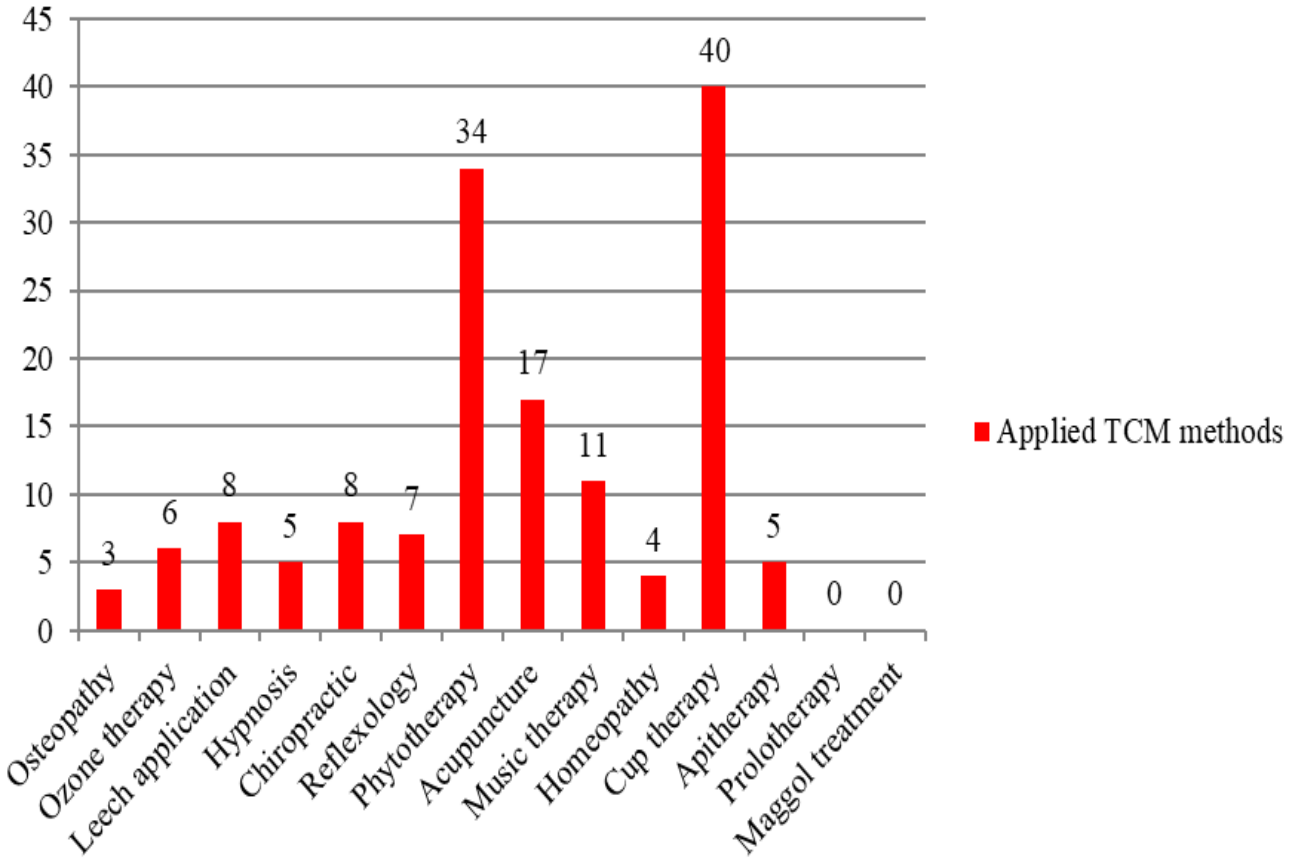

Figure 1. Distribution of people using TMC according to the treatment modality they use**.**

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Table 4. Comparison of the sociodemographic characteristics of the participants and their behaviors and attitudes towards TMC applications

Variables		Scale total score	TCM	
			Applying	Not applying
Age	18-24	97.4±17.4	21 (29.2)	51 (70.8)
	25-44	97.0±18.7	27 (24.1)	85 (75.9)
	≥45 years	102.7±17.2	43 (46.7)	49 (53.3)
		p=0.048	**p=0.002**	
Gender	Female	99.83±18.04	57 (35.2)	105 (64.8)
	Male	97.88±18.11	33 (29.2)	80 (70.8)
		(p=0.380)	p=0.298	
Education level	Middle school and below	98.28±17.34	17 (37.8)	28 (62.2)
	High school and above	99.19±18.19	74 (32.0)	157 (68.0)
		p=0.772	p=0.453	
Perceived income	Income less than expenses	99.72±16.10	31 (37.3)	52 (62.7)
	Income equals expense	98.45±19.10	40 (29.6)	95 (70.4)
	Income more than expenses	100.37±18.57	20 (37.0)	34 (63.0)
		p=0.770	p=0.414	
Marital status	Married	100.4±17.8	50 (42.0)	69 (58.0)
	Single	97.7±18.5	33 (25.2)	98 (74.8)
	Divorced/Widowed/Separate	99.3±16.5	8 (30.8)	18 (69.2)
		p=0.483	**p=0.018**	
Family type	Nuclear family	98.63±18.00	74 (32.2)	156 (67.8)
	Extended family	102.16±19.23	10 (32.3)	21 (67.7)
	Broken family	98.92±17.69	5 (38.5)	8 (61.5)
		p=0.597	p=0.895	
Longest lived place	Province	99.02±17.82	53 (28.5)	133 (71.5)
	District/Town/Village	99.14±18.65	38 (42.7)	51 (57.3)
		p=0.959	**p=0.019**	
Perceived health	Excellent/Very good	97.3±20.1	21 (23.9)	67 (76.1)
	Good/Medium/Bad	99.8±16.9	70 (37.2)	118 (62.8)
		p=0.291	**p=0.028**	
Chronic disease	Yes	98.97±16.45	40 (39.6)	61 (60.4)
	No	99.02±18.96	51 (29.3)	123 (70.7)
		p=0.852	p=0.080	
Outpatient clinic applied	Internal medicine	101.35±16.41	29 (33.0)	59 (67.0)
	Family medicine	100.11±19.62	10 (43.5)	13 (56.5)
	Dermatology	106.00±20.46	25 (35.2)	46 (64.8)
	Physical therapy and rehabilitation	99.04±18.03	27 (28.7)	67 (71.3)
		p=0.010	p=0.556	

DISCUSSION

This research was conducted to determine the knowledge, attitudes and behaviors of people who applied to the polyclinics of a university hospital towards TCM methods. In the study, it was determined that the majority of the participants had heard of TCM methods, nearly half of them were informed about the methods, and one third of them applied at least one method while 85% of the participants have heard of TMC methods. In the study conducted by Sensoy et al. [14] among those who applied to a university hospital, 95% of the participants were aware of TCM practices, while in the study conducted by Ozer et al. [3] 68.5% of the patients were knowledgeable about TCM methods[3].

In the present study, the most common source of information about TCM was television/radio/internet; it was determined that neighbor/friend/relative is in the second rank. It is thought-provoking that the frequency of obtaining information from health personnel is quite low. Similar to our research finding, in the study conducted by Odabas and Agadayi[15], it was the media from which participants get the most information with a frequency of 64%, and the least information from the doctors. In the study conducted by Sensoy et al. [14], participants received information from their close circles with a frequency of 76.9% and from the media with a frequency of 15.9%. According to the study conducted by Karatas et al. [16], the most common source of information about the TCM

methods of the participants during the Covid 19 pandemic process is social media (52.4%), while the second most frequent is close relatives, friends and neighbors (27.5%). The reason for the low frequency of obtaining information from health personnel may be negative reactions and disapproval [3,17]. Information about the correct application of TCM methods, interactions with ongoing medical treatment, and whether the method is suitable for the patient should be obtained from the doctor[7].

It can be said that the attitudes of the individuals participating in our research towards alternative medicine methods are moderately positive according to the scale score average. It can be stated that the participants of the research approached complementary medicine practices cautiously.

In the study conducted by Ozer et al. [3], on patients who applied to the internal medicine outpatient clinic using CACMAS, the mean score of the scale was found 115.78±18.81, and it was stated that the participants' attitudes towards TCM were moderately positive. The average score (29.52±5.70) obtained in the study conducted by Sensoy et al. [14], using the Attitude Scale to Integrative Complementary and Alternative Medicine (ICTAS) indicates that the participants' attitudes towards traditional and complementary medicine are moderately positive. In the study conducted by Dursun et al. [18], the mean CACMAS score was found to be 103.99 ± 22.03, similar to our study.

In this study, it can be said that the attitudes of people aged 45 and above more positive towards TCM methods than those in the other age groups. In the study conducted by Ozer et al. [3], no significant correlation was found between the CACMAS score and age.

Most of the people with chronic diseases in Turkey use at least one TCM method and the most commonly used methods are herbal therapy, massage and acupuncture [17]. In the study, one third of the participants used at least one TCM method and the most used methods as cupping, phytotherapy and acupuncture. Dursun et al. [18] reported that the frequency of using traditional complementary medicine in individuals aged 18-65 who applied to the family health center was 39.3%, similar to our study. The most commonly used methods in this study are herbal therapy, massage, and cupping. In the study conducted by Odabas and Agadayi [15], on patients who applied to the family health center, 14.8% of the participants used at least one TMC method, the most common being mug, leech and acupuncture. According to the research conducted by Ozer et al. [3], 56.5% of the participants used at least one TCM method. Avci [19] reported that 46.4% of diabetic patients who applied to university hospital outpatient clinics used at least one TCM method.

In a study evaluating data from 32 countries, the frequency of use of TMC has been reported as 33.2% in the USA, 0.3-86.0% in Europe, 76.0% in Japan, 71.3% in South Korea, and 22.1% in Turkey. TCM is applied the most in China (50.7%) and the least in Poland (6.1%) [10]. 30% of cancer patients in Europe and 33.4% in Norway reported using TMC in the last one year [20].

In the present study, it was found that the participants used TCM methods with a frequency of 66.3% for relaxation. In the study conducted by Ozer et al. [3], TCM methods were most frequently used to support a conventional treatment (28.3%), and in the study conducted by Odabas and Agadayı [15], 76.3% used TCM to alleviate musculoskeletal pain.

In recent years, when chronic diseases have come to the fore and the proportion of the elderly population has increased, TCM applications could be the first treatment method applied [21]. As a matter of fact, TCM methods are mostly applied before visiting a doctor, though the use of TCM methods as an alternative to conventional medicine and the use of these methods without consulting a physician may cause delay in diagnosis and treatment [21, 22].

In our study, it was found that 66% of the people who are using TCM perform the application in their home environment and mostly apply it to themselves. In the study conducted by Odabas and Agadayi [15], 60.5% of those who had TCM had this application done at home. The application of these applications by people who have not been trained in TCM methods with unsuitable materials and under bad conditions may cause serious side effects [22]. With the "Regulation on Traditional and Complementary Medicine Practices", the principles of application, the situations in which the method should be applied, the characteristics of the practitioner, the medical materials and devices used during the treatment were determined [11].

According to the research, the majority of the participants (97.7%) did not experience any side effects after the application, 71.1% benefited partially from the application, 59.1% repeated the application and 76.7% recommended the application to others. In the study conducted by Ozer et al. [3],

58.9% of the participants recommend the method they use to others. In the study conducted by Avci [19], 48.6% of diabetic patients did not report any side effects regarding the method they used, and 66.4% did not complain about the method they used. In the study conducted by Odabas and Agadayi [15], 70.3% of the participants stated that they benefited from their practice. Accordingly, it can be said that the majority of people who apply TCM find the methods useful and reliable, and are satisfied with the methods they use.

TCM methods are mostly applied by people aged 45 and over, married, living in rural areas, and people who do not consider their health as excellent or very good. It was found by Avci [19] that diabetes patients aged 65 and over use TCM methods more frequently. In the study conducted by Karatas et al. [16], people aged 40 and over and married people use these methods more frequently, similar to our research finding. In the study conducted by Otegen et al. [23], people aged 40 and over use the interventional TCM method more. According to studies, TCM applications are more preferred by people who are elderly, live in rural areas, and have diseases that are difficult to treat and last for a long time [22].

Limitations and strengths of the research

The research was conducted among patients who applied to selected polyclinics of a university hospital with various health problems and their relatives. Since it is a hospital-based study, the data do not fully reflect the attitudes and behaviors of the society towards traditional and complementary medicine. Despite this, revealing the knowledge, attitudes and behaviors of individuals who apply to a health institution providing tertiary treatment services towards traditional and complementary medicine methods can be a guide for health service providers. Attitudes of the participants were measured with a scale with proven validity and reliability. 72.0% of the sample size determined at the beginning of the research has been reached.

CONCLUSION

TCM methods are known to the majority of people who visit selected polyclinics of an university hospital and are applied by one third of them. Individuals generally apply these methods without consulting health personnel but with the information which they receive from the media and their close circles. The attitudes of the participants towards TCM applications are quite close to positive. Physicians should question the TCM methods used by patients to prevent undesirable interactions before prescribing medication. Health professionals should provide counseling to individuals who apply to them about TCM.

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ORIGINAL RESEARCH

Efficacy of Prolotherapy with Periarticular 5% Dextrose in the Treatment of Knee Joint Osteoarthritis

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Abstract

Objective: Determination of the effectiveness of periarticular 5% dextrose prolotherapy in the treatment of knee pain due to osteoarthritis.

Material and Methods: The clinical results of prolotherapy with 5% periarticular dextrose in adult female and male patients with knee pain and complaints related to osteoarthritis were evaluated retrospectively. During the examination, we identified the sensitive ligaments in the knee and injected 1 cc of 5% dextrose with a 0.6 * 60 mm sterican needle. In routine practice, stretching exercises are recommended to patients after prolotherapy and for analgesia, a combined analgesic containing paracetemol 500mg + codeine phosphate 10mg + caffeine 30mg is given for the first 3 days. In addition to the initial application, prolotherapy is performed 3 times with an interval of 20 days, and when the Visual Analogue Scale (VAS) score decreases by 80% or more after the first or second injection, prolotherapy is terminated.

Results: 30 patients aged between 36-70 years were included in the study. Patients' mean age was 52,9±9,0 years. Nineteen patients received 3 sessions and 11 patients received 2 sessions of prolotherapy. A significant decrease was achieved in VAS scores of all patients except one patient. The VAS score was 2.9 at the end of the third session meanwhile the initial VAS average was 8.4. None of the patients had any side effects that would terminate the treatment.

Conclusion: The data obtained in the study show that prolotherapy with periarticular 5% dextrose is effective in the treatment of knee pain and complaints related to osteoarthritis. However, more comprehensive studies will be guiding the clarification of its place in the osteoarthritis' treatment.

Keyword: Prolotherapy, Knee, Osteoarthritis, Periarticular 5% Dextrose, Visual Analog Scale

INTRODUCTION

Osteoarthritis is a painful, degenerative disease that causes dysfunction in the joints. Osteoarthritis of the knee is a common, chronic, non-inflammatory arthritis that causes joint pain and disability[1]. Knee osteoarthritis is mostly age-related and approximately 30% of the population over the age of 65 has osteoarthritis[2]. Knee osteoarthritis is an important public health problem because of its high prevalence, besides causing loss of workforce and expensive treatment methods[3]. The mechanism of pain and functional impairment in osteoarthritis is complex. There are genetic, biochemical, biomechanical and psychosocial factors. The fact that patients respond differently to different treatments, suggests that there is no common pain mechanism in knee osteoarthritis[4]. Although exercise and weight loss are effective in knee osteoarthritis, they are often

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not sufficient[5]. Complementary treatments such as physiotherapy, analgesic drugs, acupuncture and herbal therapy have also been shown to be effective in patients with knee osteoarthritis[6,7]. Current guidelines suggest that a multidisciplinary approach should be followed in the treatment of knee osteoarthritis, including non-pharmacological, pharmacological, surgical and complementary therapies[8]. In advanced knee osteoarthritis, knee replacement is a highly effective but costly treatment. Therefore, the development of a safe and effective treatment option that complements the current conservative treatment remains a priority in clinical trials[9].

Prolotherapy is a regenerative and complementary treatment method. With prolotherapy, proliferating substances are applied with a purpose of creating microtraumas in the desired anatomical regions. Different proliferating agents and cells can be applied in this process. For example, dextrose solutions, mannitol, sodium morrhuate, platelet-rich plasma and stem cells are a few of them[10,11]. Dextrose solutions are mostly used as 12.5-25% periarticular and articular hypertonic solutions. In vitro studies show that dextrose solutions can have similar histological and molecular effects at lower levels[12]. The clinical results of our prolotherapy applications with 5% dextrose periarticular injections to patients with knee joint osteoarthritis were retrospectively evaluated in this study.

MATERIALS AND METHODS

We started our study after receiving ethics committee approval from the Gebze State Hospital with protocol number 2019-42. In this study, the records of 30 patients; who applied to the Traditional and Complementary Medicine Polyclinic with knee pain due to osteoarthritis and were treated with 5% dextrose periarticular prolotherapy; were reviewed and the data obtained were retrospectively evaluated. Informed consent was obtained from each patient.

Our patients were asked to consult their physical therapy and rehabilitation physicians before injection.

Inclusion criteria

Patients with stage 2 and stage 3 according to the Kellgren Lawrence classification were included in the study. Before the injection, the painful ligaments of the knee were identified and 1 cc of 5% dextrose was injected into each painful and tender ligament. Patients were monitored during the injection. Saturation values and peak heart rate were followed during the injection and observed after the injection.

The prolotherapy application process

In our outpatient clinic, prolotherapy is not applied to patients with rheumatological disorders, bleeding disorders, and needle phobia. During this application, it is recommended to do stretching exercises after prolotherapy and an analgesic containing paracetamol 500 mg + codeine phosphate 10 mg + caffeine 30 mg is given for the first 3 days. In our polyclinic, after the initial application of prolotherapy, 3 more sessions are performed with an interval of 20 days.

Pain severity was assessed by Visual Analogue Scale (VAS) scoring at baseline and at each session. If the patient's VAS score decreases 80% or more after the first or second injection, the treatment is terminated.

Statistical analysis

SPSS software (IBM SPSS, Version 22.0, IBM Corporation, Armonk, NY, USA) was used for data analysis. Data were presented as mean and standard deviation. T and repetitive ANOVA tests were used to compare VAS scores between sessions. $P<0.05$ was considered significant.

RESULTS

30 patients were included in the study in total. Among them, 5 (16.7%) were male and 25 (83.3%) were female. The mean age of the patients was 52.9±9.0 (minimum-maximum values: 36-70). All patients got 2 sessions of prolotherapy meanwhile only 19 patients got their 3rd session of prolotherapy. The mean VAS scores of the patients, measured at the beginning and during the sessions, are shown in Figure 1.

The mean of VAS score measured during the 1st, 2nd and 3rd session were all significantly lower than the mean of the initial VAS score. (4.7±1.5, 3.1±1.8, and 2.9±1.8 vs. 8.4±1.1; $p<0.05$). The mean VAS scores measured during the 2nd and 3rd sessions were significantly lower than the mean of the VAS scores measured during the 1st session (3.1±1.8 vs. 2.9±1.8 vs. 4.7±1.5; $p <0.05$). The mean VAS scores measured during the 2nd and 3rd session were found to be similar ($p>0.05$)(Figure 1).

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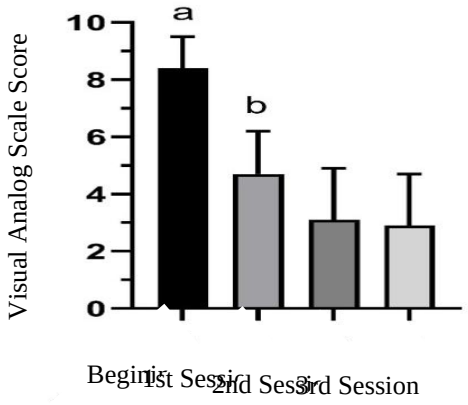

Figure 1. Visual analog scale (VAS) scores measured at baseline and in the 1st, 2nd and 3rd sessions.

The VAS scores of male and female patients measured at baseline and during sessions are shown in Figure 2. In male patients, the mean VAS score measured in the 3rd session was lower than that measured at the beginning (7±1.4 vs. 8.8±1.3). In women, the mean VAS scores measured in the 1st, 2nd and 3rd sessions were found to be significantly lower than the baseline (4.6±1, 3.1±1.3, 2.4±1 versus 8.4±1, 1; $p<0.05$). The mean VAS scores measured in the 2nd and 3rd sessions were found to be significantly lower in women compared to the 1st session (3.1±1.3 and 2.4±1 versus 4.6±1; $p<0.05$), but the mean VAS scores measured in the 2nd and 3rd sessions were similar ($p>0.05$).

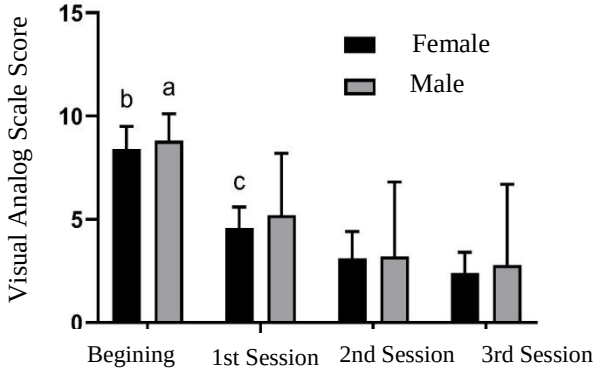

Figure 2. Visual analog scale (VAS) scores of female and male patients measured at the beginning and 1st, 2nd and 3rd sessions.

There was no significant difference between the mean VAS scores of male and female patients measured at baseline and between sessions (Figure 2).

DISCUSSION

In this study, 5% dextrose periarticular injections of prolotherapy which were applied 3 times with an interval of 3 weeks for the first time, were more successful in patients with knee osteoarthritis especially in female patients. Less post-injection pain at periarticular injection sites increased the patient's satisfaction and adherence to treatment.

Osteoarthritis, the most common form of arthritis, is an important disease of western societies, primarily affecting the knee joint and causing progressive loss of function, pain and stiffness[13].

Osteoarthritis has the potential to worsen progressively by affecting the extra-articular structures as well as the degeneration of intra-articular cartilage, bone and synovial tissues.

Because of the lack of successful and easy-to-apply treatment options for knee joint osteoarthritis, a continued research is required on new treatment applications. Various non-invasive and minimally invasive methods are used in the treatment of pain associated with knee osteoarthritis.

The most common treatments are physical therapy, the use of nonsteroidal anti-inflammatory drugs, and if these methods are ineffective, intra-articular injection of hyaluronic acid, corticosteroid and platelet-rich plasma as well as prolotherapy are used[13, 14].

Factors such as the individual and social burden of osteoarthritis, the damage it causes to work life, and the overuse of health services by the patient can significantly impair the quality of life of individuals. Some important risk factors have been identified for the development of osteoarthritis, which can be seen in 10% of populations over the age of 50.

While some of these risk factors are demographic factors such as age, female gender, being overweight and having a family history of osteoarthritis depending on the structural characteristics of the person, many of them may be due to lifelong local and unwanted mechanical traumas that disrupt the joints[15]. 83% of the cases included in our study were female.

The risk factors mentioned above and the different pathogenesis of osteoarthritis are important in terms of offering alternative methods such as

prolotherapy in addition to the traditional medical and surgical treatments used in the treatment of this disease.

Prospectively managed research results with new studies in cases of osteoarthritis developed due to different mechanisms will be useful in terms of understanding the clinical efficacy of prolotherapy and in which osteoarthritis types it is more effective[13]. Since 83% of the cases included in our study were female and the sample size of female was sufficient, the success of prolotherapy was clearly observed in female patients. Due to the small number of male patients (17%), some of the differences in VAS scores did not reach significance.

The mechanism of action of prolotherapy is multifaceted. Fibroblast and vascular proliferation, intense collagen deposition and stimulation of cartilage growth are some of them. In addition, elevated levels of extracellular dextrose hyperpolarize the nerves through a different mechanism. Activation of potassium channels by dextrose leads to increased potassium conductivity and consequent neuronal hyperpolarization. The analgesic effect of hyperpolarization with dextrose injection has been proven. With dextrose prolotherapy, neurogenic inflammation is prevented and thus pain is reduced[17, 18].

In a study comparing periarticular prolotherapy and intraarticular prolotherapy, it was found that the VAS score was lower in the periarticular prolotherapy group. Improvements in walking on level ground, climbing stairs, and morning stiffness were similar in both groups, and positive responses were obtained. Intra-articular injections are used in the treatment of arthritis, but this method is still discussed among many clinicians because of the needle penetration into the joint capsule and possible side effects.

Periarticular injections are more safety than intraarticular injections. It can give similar or even better results[19]. In our study, we performed periarticular dextrose injection and found significant decreases in VAS values.

Seven et al. investigated the efficacy of exercise and ultrasonography-guided prolotherapy in patients with chronic pain associated with a rotator cuff lesion. It has been observed that the success of treatment generally increases with prolotherapy[20]. In our study, we applied 5% dextrose periarticular prolotherapy and gave stretching exercises to the patients. We believe that prolotherapy combined with exercise therapy will be more effective.

The difference of prolotherapy from other regenerative injection treatments is that it is not injected with biological material as in platelet-rich plasma and stem cell injections. 5% dextrose and hypertonic glucose are preferred in prolotherapy applications because they are cheap, easily available and safe[11]. For these reasons, we used 5% dextrose in our study, which is effective, inexpensive, easy to access and has few side effects.

As an alternative method in the treatment of knee osteoarthritis cases, intra-articular prolotherapy with hypertonic glucose is also being investigated increasingly[21, 22].

Sit et al. compared intra-articular hypertonic dextrose prolotherapy administered 4, 8 and 16 weeks after the initial application with normal saline injections over a period of one year[21].

Rabago et al. tested the efficacy of extra-articular 15% hypertonic dextrose and intra-articular 25% dextrose in the treatment of patients with knee osteoarthritis. Prolotherapy has produced beneficial results in terms of pain and mobility in patients with moderate and severe knee osteoarthritis. Our study is on extra-articular prolotherapy and we concluded that prolotherapy is an effective treatment for pain[22].

This study had some limitations. Relatively lack of number of the patients included in the study, the fact that the disorders in the joints have not been determined objectively, and probably the fact that the studies are conducted in cases with osteoarthritis of different severity require a cautious approach to the statistical results. Functional changes were not examined in our study. This is a limitation of our study. Randomized-controlled studies with more patients are needed in the future.

CONCLUSION

The result of this study supports that prolotherapy performed with a similar method can be applied as an alternative method in the treatment of knee osteoarthritis. Prolotherapy using periarticular 5% dextrose is a good option in patients with knee osteoarthritis. Periarticular 5% dextrose application by prolotherapy specialists in similar clinical situations can positively affect patient satisfaction and treatment success. Keeping detailed clinical information of the patients, performing prolotherapy with a similar protocol to the patients, interpreting the treatment results based on similar and objective criteria and keeping records of possible unexpected

situations by physicians who practice prolotherapy in patients with knee osteoarthritis may provide a more established treatment for patients with osteoarthritis.

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ORIGINAL RESEARCH

The Effect of Aromatherapy Application on the Vital Signs of Intensive Care Patients

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Abstract
Objective: This study aims to examine the effect of aromatherapy application on vital signs in intensive care patients.
Material-Method: This study was carried out as a nonrandomized controlled experimental trial. The population consisted of inpatients in the internal medicine intensive care unit of a research and training hospital located in southeastern Turkey. The sample of the study consisted of 100 patients. The data were collected between July 2018 and February 2019 using patient identification and monitoring forms. Descriptive statistics, t-test, chi-squared test, analysis of variance and post-hoc test were used in the analysis of the data.
Results: The mean age of the experimental group patients was 66.84±20.53, 54.0% of them were female, 92.0% were married, 28.0% were literate, 78.0% were unemployed, and 74.0% had not been subjected to aromatherapy before; The mean age of the control group patients was 61.30±22.67, 52.0% of them were female, 82.0% were married, 30.0% were high-school graduates, 66.0% were unemployed, and 64.0% had not been subjected to aromatherapy before. It was found that the mean respiratory rate of the patients in the experimental group decreased significantly ($p<0.05$).
Conclusion: It was determined that aromatherapy applied on the intensive care patients was not effective on their pulse rate, systolic blood pressure, diastolic blood pressure or partial oxygen pressure, but it was effective in reducing their respiratory rate.
Keywords: Aromatherapy, Intensive Care, Nursing, Patient, Vital Signs

INTRODUCTION

Intensive care units are the places where the life functions of patients with serious physical conditions are supported, special treatment methods are applied and at the same time, patients' vital signs are monitored throughout 24 hours[1-4]. When their life functions are severely impaired, patients need to be treated in intensive care units (ICUs) to receive the special treatment they require[5-9]. For this reason, complementary treatment should be provided as well as medical treatment to control the impaired vital functions of patients in the ICU. The purpose of these treatments is to support the care of patients in addition to their medical treatment[10, 11]. The complementary treatment creates a relaxant effect in intensive care patients and may be effective in improving patients' impaired physiological signs and preventing complications related to intensive care[10-12].

In aromatherapy, which is a complementary treatment method, elements of essential oils that are available in the stems, roots and flowers of natural plants are used[12, 13]. Aromatherapy may be applied in various forms such as massage, inhalation, and compression. Aromatherapy is used to calm the mind, body and spirit the patients[13-15]. The use of aromatherapy has been increasing lately around the world and in Turkey[16-21]. Patients admitted to the ICU require higher levels of nursing care. Aromatherapy is used in nursing as a holistic intervention to improve patient care and quality of

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life. The focus of holistic treatments is symptom control rather than treatment[17-19]. Nurses apply aromatherapy to increase quality of sleep[17], reduce stress[11], anxiety[10,16], reduce pain[22], promote relaxation[23] and improve the well-being of patients[24]. Aromatherapy applications, therefore, have an effective role in healing patients in the physical, psychological, social, emotional and spiritual sense[24, 25]. Therefore, it is important to combine aromatherapy with pharmacological methods in symptom management in intensive care patients. Clinicians and nurses should be aware of potential drug interactions when applying essential oils together with medication. In the literature, many studies conducted in intensive care units have revealed that aromatherapy application positively affects vital signs[12, 14]. In their nonrandomized and controlled experimental study carried out in adult ICU patients, Cho et al. (2017) found that aromatherapy application led to a decrease in the patients' pulse and blood pressure values[11]. In the randomized controlled study by Ltyle et al., it was determined that aromatherapy application was effective in reducing blood pressure values[12]. This study was carried out to examine the effect of aromatherapy application on the vital signs of intensive care patients. In line with the results obtained, information will be provided to healthcare professionals and nurses in ICU about complementary treatments to be used to improve the holistic wellbeing of patients.

MATERIALS AND METHODS

Research type

This study was carried out as a nonrandomized controlled experimental study.

Place and time of research

The study was conducted between the dates of July 2018 and February 2019 in an internal medicine ICU of a research and training hospital located in southeastern Turkey.

Research population and sample

The population consisted of inpatients in the internal medicine ICU of a research and training hospital located in southeastern Turkey. The sample was composed of a total of 100 patients based on power analysis, in a 95% confidence interval and with 80% power (50 in the experimental and 50 in the control group). Patients included in the study were among the ones who received the same treatment and patients with the same settings in the ICU. Systolic blood pressure (SBP), diastolic blood pressure (DBP), partial oxygen pressure (SPO2), pulse and respiratory rate measurements were taken every hour in same intervals.

Inclusion criteria: (1) Patients aged over 18, (2) patients who were conscious, (3) patients who were able to verbally communicate, (4) patients who had no allergy to lavender oil, (5) patients staying in the ICU for more than 5 nights, (6) patients whose general condition was stable (Figure 1).

Exclusion criteria: (1) Having a mental illness, (2) have side effects or allergies to essential oils (Figure 1).

Data collection forms

Patient identification form: The patient identification form was created from questions prepared by the researcher containing demographic information such as the age, sex, educational status and marital status of the patients[10-16].

Patient monitoring form: In the pretest-posttest data collection processes of the patients in both groups this form was used to collect information about the patients' SBP, DBP, SPO2, pulse and respiratory rate.

Nursing interventions: Standard treatment and care protocols were followed for all patients, and these protocols did not affect the outcome measures. Aromatherapy was applied to the experimental group patients. Stimuli such as noise arising from the physical environment of the ICU and interventions applied to patients during this process could affect the physiological parameters of the patients. For this reason, aromatherapy application hours were chosen as the hours when patients did not have intervention procedures in the ICU. Data were collected first from the control group and then from the experimental group in order to prevent contamination between the groups.

Application of aromatherapy: The intervention was applied 1 hour after the routine drug treatment of the patients**.** SBP, DBP, SPO_2, pulse and respiratory rates were measured before applying aromatherapy intervention on the experimental group patients. In the literature, it has been stated that, when lavender oil is administered by inhalation, it acts quickly, with an inhaled application of 10-15 minutes. Thus, it shows its effect in a short time by the respiratory tract[14-16,25,26]. Since the patients hospitalized in the ICU were mostly given a supine position, in this study, 5 drops of lavender oil were dropped on a sterile gauze cloth

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and the patients were asked to inhale the lavender oil for 15 minutes. Then, five drops of lavender oil were dropped onto a gauze patch and placed onto the patients' chest. After the application, the measurements were repeated for a total of 4 times at 30-min intervals. Lavender oil was applied on the patients only once. No intervention was made on the control group, only the measurements were taken and recorded before applying the nursing intervention of the patients.

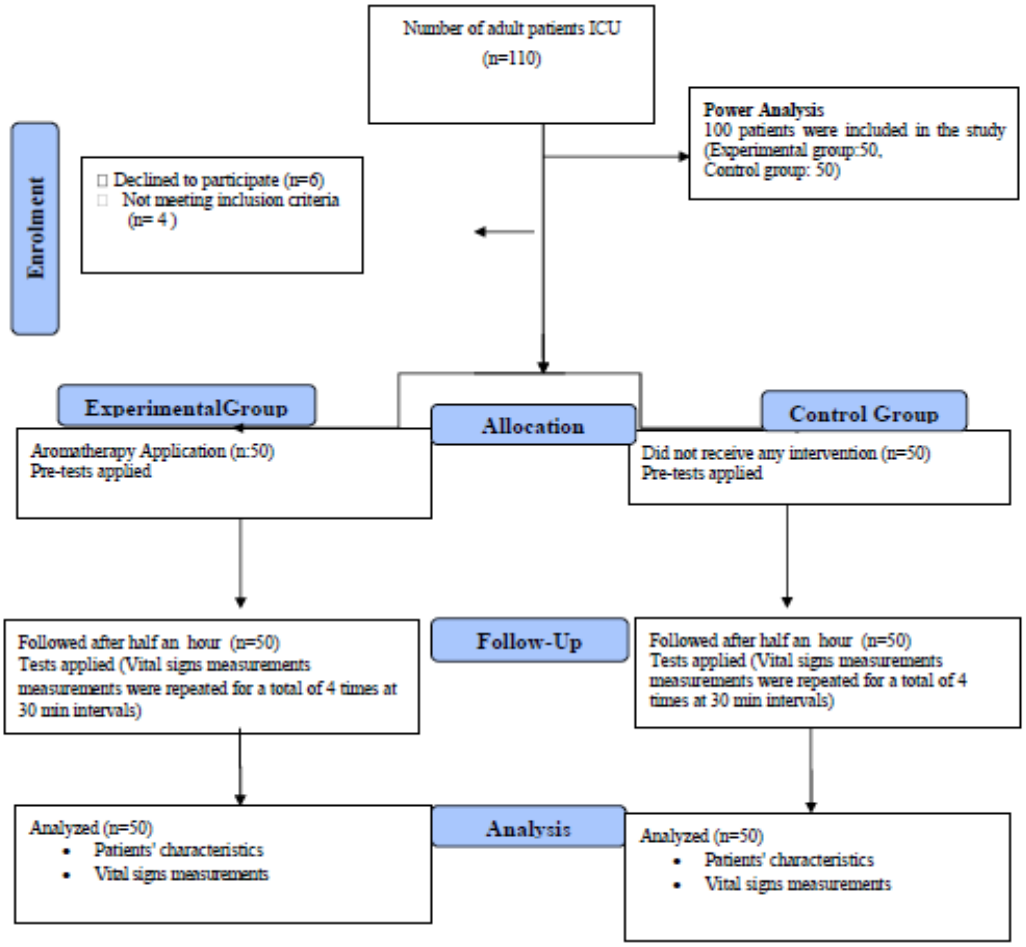

Figure 1. Flowchart of the study participants

Data analysis

For the analysis of the data, the SPSS 22.0 package program was used. In the analysis of the demographic data, descriptive statistics were used. Kolmogorov-Smirnov test, t test, Anova, post hoc test analysis were used to evaluate the data. All findings were tested on the significance level of 0.05. Before starting the study, no statistically significant difference was found between the patients' groups in terms of their introductory characteristics ($p>0.05$) (Table 1).

Ethical aspect of research

Prior to the study, written approval was obtained from the Non Invasive Clinical Research Ethics Committee of a University on 06.07.2018 (Decision Number: 128). Written permission was obtained from the University, and the patients who participated in the study.

RESULTS

The distribution of the patients included in the study based on their descriptive characteristics is given in Table 1. The mean age of the experimental group patients was 66.84±20.53 and the mean age of the control group patients was 61.30±22.67. When the other descriptive characteristics of the patients were examined, it was determined that, among the

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patients in the experimental group, 54.0% were female, 92.0% were married, 28.0% were literate, 78.0% were unemployed and 74.0% had not previously received aromatherapy. It was found that, of the patients in the control group, 52.0% were female, 82.0% were married, 30.0% were high school graduates, 66.0% were unemployed, and 64.0% had not previously received aromatherapy (Table 1). The difference between the control group and the experimental group in terms of the control variables was not statistically significant (p>0.05) (Table 1).

Table 1. Comparison of control variables between experimental and control groups

Descriptive characteristics	Experimental group		Control group		Test and Significance
	S	%	S	%	
Sex					
Female	27	54.0	26	52.0	x^2 =0.040
Male	23	46.0	24	48.0	p =0.841
Marital Status					
Married	46	92.0	41	82.0	x^2 =2.210
Single	4	8.0	9	18.0	p =0.137
Education Status					
Illiterate	11	22.0	10	20.0	x^2 =4.665 p =0.323
Literate	14	28.0	12	24.0	
Primary School	12	24.0	6	12.0	
High School	8	16.0	15	30.0	
Undergraduate-Postgraduate	5	10.0	7	14.0	
Working Status					
Employed	11	22.0	17	34.0	x^2 =1.786
Unemployed	39	78.0	33	66.0	p =0.181
Have You Ever Received Aromatherapy?					
Yes	13	26.0	18	36.0	x^2 =1.169
No	37	74.0	32	64.0	p =0.280
Age	$mean \pm sd$		$mean \pm sd$		t=-1.281
	66.84±20.53		61.30±22.67		p =0.203

The pretest-posttest vital sign mean scores of the experimental group are given in Table 2. It was found that there was no significant change in the mean respiration over time (p=0.040). The mean 60th-minute respiratory rate was 20.20±3.60 and the mean 120th-minute respiration rate was 18.40±4.02. This difference was found to be statistically significant (p<0.05) (Table 2).

Table 2. Comparison between pre-test and post-test mean vital sign scores in the experimental group

Vital Signs	Pre-test $\bar{x} \pm sd$	Post-test				Test and Significance
		30th min $\bar{x} \pm sd$	60th min $\bar{x} \pm sd$	90th min $\bar{x} \pm sd$	120th min $\bar{x} \pm sd$	
Pulse rate (per min)	92.54±15.96	93.30±16.43	92.28±17.21	93.00±15.42	89.72±14.60	F=2.315 ***p*** =0.091
SBP	121.30±24.51	121.18±23.60	121.56±24.41	118.54±24.76	120.82±22.42	F=0.921 p =0.437
DBP	69.96±11.77	72.64±14.00	71.38±12.78	70.26±12.82	71.94±12.16	F=1.033 ***p*** =0.387
SPO_2	94.98±2.71	94.80±2.67	94.76±2.53	95.08±2.77	94.70±2.96	F=0.733 ***p*** =0.550
Respiration	19.60±4.44	19.28±4.26	20.20±3.60*	18.76±3.89	18.40±4.02*	F=2.777 ***p* =0.040**

The pretest-posttest vital sign mean scores of the control group are given in Table 3. It was found that there was a significant change in the mean SPO2 values over time (p=0.006). The mean 30th-minute SPO2 value was 95.66±3.25 and the mean 30th-minute SPO2 value was 94.40±4.25. This difference was statistically significant (p<0.05) (Table 3).

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Table 3. Comparison between pre-test and post-test mean vital sign scores in the control group

Vital Signs	Pre-test $\bar{x} \pm sd$	Post-test				Test and Significance
		30th min $\bar{x} \pm sd$	60th min $\bar{x} \pm sd$	90th min $\bar{x} \pm sd$	120th min $\bar{x} \pm sd$	
Pulse rate (per min)	92.36±22.08	92.02±21.79	90.08±22.18	89.42±21.54	89.76±20.79	F=1.999 p =0.120
SBP	129.76±30.10	130.42±27.87	129.32±29.35	127.76±25.71	126.26±25.97	F=1.642 p =0.176
DBP	74.74±15.64	76.70±14.52	74.46±15.91	73.46±16.08	72.90±14.29	F=1.890 p =0.133
SPO_2	95.66±2.72	95.66±3.25*	95.30±3.24	95.16±3.33	94.40±4.25*	F=4.607 **p =0.006**
Respiration	21.16±4.80	21.34±4.68	21.44±4.97	21.32±6.26	20.26±5.54	F=0.607 p =0.602

*indicates the difference.

Table 4. Comparison of pretest mean vital signs between experimental and control groups

Groups	Vital Signs (Mean±SD)				
	Pulse Rate	SBP	DBP	SPO_2	Respiration Rate
Experimental Group	92.54±15.96	121.30±24.51	69.96±11.77	94.98±2.71	19.60±4.44
Control Group	92.36±22.08	129.76±30.10	74.74±15.64	95.66±2.72	21.16±4.80
Test and Significance	t=-0.047 p=0.963	t=1.541 p=0.127	t=1.727 p=0.088	t=1.254 p=0.213	t=1.688 p=0.095

As seen in Table 4, the intergroup difference in the pretest vital signs was not statistically significant (p>0.05) (Table 4).
As seen in Table 5, the intergroup differences in the 30th-minute and 90th-minute respiration rates were found to be statistically significant (p=0.016). The intergroup differences in the other vital signs were not statistically significant (p>0.05) (Table 5).

Table 5. Comparison of posttest mean vital signs between experimental and control groups

Vital Signs	Groups	Min			
		30th min $\bar{x} \pm sd$	60th min $\bar{x} \pm sd$	90th min $\bar{x} \pm sd$	120th min $\bar{x} \pm sd$
Pulse rate (per min)	**Experimental**	93.30±16.43	92.28±17.21	93.00±15.42	89.72±14.60
	Control	92.02±21.79	90.08±22.18	89.42±21.54	89.76±20.79
Test and Significance		t=-0.332 p=0.741	t=-0.554 p=0.581	t=-0.956 p=0.342	t=-0.011 p=0.991
SBP	**Experimental**	121.18±23.60	121.56±24.41	118.54±24.76	120.82±22.42
	Control	130.42±27.87	129.32±29.35	127.76±25.71	126.26±25.97
Test and Significance		t=1.789 p=0.077	t=1.437 p=0.154	t=1.826 p=0.071	t=1.121 p=0.265
DBP	**Experimental**	72.64±14.00	71.38±12.78	70.26±12.82	71.94±12.16
	Control	76.70±14.52	74.46±15.91	73.46±16.08	72.90±14.29
Test and Significance		t=1.423 p=0.158	t=1.067 p=0.289	t=1.100 p=0.274	t=0.362 p=0.718
SPO_2	**Experimental**	94.80±2.67	94.76±2.53	95.08±2.77	94.70±2.96
	Control	95.66±3.25	95.30±3.24	95.16±3.33	94.40±4.25
Test and Significance		t=1.447 p=0.151	t=0.929 p=0.355	t=0.131 p=0.896	t=-0.410 p=0.683
Respiration	**Experimental**	19.28±4.26	20.20±3.60	18.76±3.89	18.40±4.02
	Control	21.34±4.68	21.44±4.97	21.32±6.26	20.26±5.54
Test and Significance		**t=2.302 p=0.023***	t=1.428 p=0.157	**t=2.457 p=0.016***	t=1.922 p=0.058

* indicates the difference.

DISCUSSION

In this study, it was found that the aromatherapy intervention had a statistically significant effect on the mean respiratory rate scores of the patients. In the study by Goepfert et al., aromatherapy application was found to be effective on respiratory parameters[27]. Karaman Özlü and Bilican determined, that aromatherapy changed the respiratory rate of patients[19].

In this study investigating the effect of aromatherapy application on vital signs in intensive care patients, it was determined that aromatherapy applied on the experimental group had a significant effect on the patients' mean respiratory rates, whereas the mean SPO_2 of the control group patients significantly decreased in time, on the other hand, the differences between the experimental and control groups were not significant in terms of their pulse, SBP and DBP values. In line with the findings of this study, in the study by Cho et al. (2013) examining the effect of lavender essential oil and aromatherapy application in intensive care patients, it was found that there was no significant difference in the systolic and diastolic blood pressure values of the patients[10]. Unlike the findings of this study, in their studies investigating the effect of aromatherapy applied on patients treated in intensive care units after open-heart surgery on these patients' vital signs, Salamati et al. determined that aromatherapy had an impact on pulse rate and blood pressure values and brought these values to a normal level[26]. Ltyle et al. reported, that aromatherapy application was effective on blood pressure values and brought these values to a normal level[12]. In their inhalation aromatherapy study with lavender essential oil, Bikmoradi et al. found that aromatherapy had no effect on patients' vital signs, other than their systolic blood pressure[14]. In other studies, aromatherapy application was found to be effective in lowering patients' systolic and diastolic blood pressure values[12,21,26-30].

In contrast to this study, in the study by Goepfert et al., administration of lavender oil was found to reduce the heart rate of patients[27]. Other studies have shown that application of lavender oil reduces the heart rate of patients[11,28-30].

As opposed to the case in this study, the study by İlter et al. found that inhaler aromatherapy administration during port catheter insertion in patients diagnosed with cancer resulted in an increase in the oxygen saturation levels in patients[30]. Another study found similar results[27].

It was found that the results of this study regarding vital signs were similar to those reported in some studies, but they differed with those in other studies. This situation may have been caused by the descriptive characteristics of the patient groups or differences in variables such as the duration, frequency, type and method of aromatherapy.

In terms of the posttest vital signs of the groups, the difference between the groups in terms of their mean 30th-minute and 90th-minute respiratory rates was statistically significant; however, in other vital signs, the difference between the groups was not statistically significant. According to the comparison of the posttest mean scores between the groups, the application of aromatherapy positively affected the respiratory rates of the patients.

CONCLUSION

In this nonrandomized controlled trial, it was determined that the aromatherapy intervention applied on the ICU patients was not effective on these patients' pulse, SBP, DBP and SPO_2 values, but it was effective in reducing their respiratory rates. The results showed differences in the respiratory rates between the experimental group that received the aromatherapy treatment and the control group that did not. Therefore, aromatherapy may be used as an independent nursing intervention. However, regarding the long-term effects of aromatherapy applications, more studies are recommended to be carried out.

Limitations of the study

Since this study included only inpatients in an intensive care unit, the results may only be generalized to this group. The data were collected in the intensive care unit of a research and training hospital affiliated to the Ministry of Health of Turkey. Its generalizability, therefore, is limited. Another limitation was, on the other hand, that only one aromatherapy method was used in the study. Additionally, a limitation of this study was that it was performed only in the internal medicine intensive care unit and the patients were not separated based on their medical diagnoses.

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Declaration of conflicting interests
The authors declare no potential conflicts of interest regarding the research, authorship and/or publication of this article.

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ORIGINAL RESEARCH

Evaluation of Knowledge and Attitudes about the Traditional and Complementary Medicine Practices of the Patients with Neuropatic Pain Who Applied to the Physıcal 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 ligament 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 α=0.05 error and adding 20% to allow for patient loss. Statistical

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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)	
Male	40(33.6)	42(32,1)	0.79
Marital Status			
Married	76(63.9)	95(72.5)	
Widowed/Divorced	34(28.6)	22(16.8)	
Single	9(7.6)	14(10.7)	0.07
Education Status			
Illiterate	25(21)	42(32.1)	
Primary Education	52(43.7)	51(38.9)	
High School	30(25.2)	29(22.1)	0.24
Univercity	12(10.1)	9(6.9)	
Profession			
Employee (Worker,tradesman..etc)	40(33.6)	92(70.2)	
Unemployed (Retired,House wife ..etc)	79(66.4)	39(29.8)	0.51
Location			
City center	64(53.8)	59(45)	
Suburb	33(27.7)	42(32.1)	
Village	22(18.5)	30(22.9)	0.37
Monthly Income			
<1500 ₺	42(35.3)	46(35.1)	
1500-3000 ₺	59(49.6)	60(45.8)	
>3000 ₺	18(15.1)	25(19.1)	0.68
Social Security			
General Security	48(40.3)	65(49.6)	
Green Card	55(46.2)	48(36.6)	
Private	9(7.6)	15(11.5)	
None	7(5.9)	3(2.3)	0.13
Chronic Disease			
Yes	73(61.3)	86(65.6)	
No	46(38.7)	45(34.4)	0,48
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
Cardiovasculer 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

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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 alprazolon/ 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 was 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)	
Polyneuropathy	22(18.5)	22(16.8)	
Para/tetraplegia	25(21)	19(14.5)	
Multiple Sclerosis	16(13.4)	18(13.7)	
Peripheral nevre İnjury/Neuropathy	5(4.2)	9(6.9)	
Reflex Sympathetic Dystrophy	6(5)	5(3.8)	
Other*	1(0.8)	5(3.8)	0.53
Neuropathic Pain Duration			
<5 years	53(44.53)	53(40.45)	
>5 years	66(55.47)	78(59.55)	
			0.04
Neuropathic Pain Area			
Lumbar/Dorsal	44(37)	37(28.2)	
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)	
			0.21
Current Medicine			
Pregabalin	27(22.7)	27(20.6)	
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)	0.09
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)	
No	46(38.7)	28(21.4)	**0.003**

*Mann Whitney U test

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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 patienst, 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
İnternet	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(641)	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$^{\alpha}$**			
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)	

$^{\alpha}$*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]

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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 peformance 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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REVIEW

Natural Preservatives

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Abstract
Preservatives are used in cosmetics, pharmaceuticals, food and industrial products to prevent deterioration of the product and to prolong its use. Preservatives are classified into two groups as natural and synthetic according to their source. However, the interest in natural preservatives has increased due to the negative effects of synthetic preservatives on health and the increasing concerns about their safety. Plants have been used in many fields such as medicine, food, perfume and cosmetics since ancient times, and they are important as natural preservatives. There are studies in which the antioxidant, antibacterial and antifungal effects of essential oils, extracts prepared from herbal drugs with various solvents, and herbal active substances purified and isolated from these extracts are investigated and significant results are revealed. For this reason, it is thought that they can be used as preservatives in the cosmetics, pharmaceutical and food industries due to their antimicrobial and antioxidant effects. In this study, plants, drugs, and herbal active substances that are used or can be used as preservatives of herbal origin with regards to their antimicrobial effects were examined.

Keywords: Natural Preservatives, Antimicrobial Effects, Cosmetic Products, Food Industry

INTRODUCTION

Preservatives are substances used in cosmetics, pharmaceuticals, food and industrial products to prevent deterioration of the product and to prolong its use. Deterioration occurs with the effect of light, air, humidity and the effect of microorganisms. Preservatives are generally used with antioxidant, antimicrobial and chelating effects. Preservatives are classified as natural or synthetic based on their source. Due to the negative effects of synthetic preservatives on health, which has been much discussed recently, natural preservatives have started to gain more importance today. Plants are important among natural preservatives.[1] In this study, plants, drugs and active substances that can be used as natural preservatives, whose antimicrobial effects are the most studied, were examined. Preservatives are substances used in cosmetics, pharmaceuticals, food and industrial products to prevent deterioration of the product and to prolong its use. Deterioration occurs with the effect of light, air, humidity and the effect of microorganisms. Preservatives are generally used with antioxidant, antimicrobial and chelating effects. Preservatives are classified as natural or synthetic based on their source. Due to the negative effects of synthetic preservatives on health, which has been much discussed recently, natural preservatives have started to gain more importance today. Plants are important among natural preservatives.[1] In this study, plants, drugs and active substances that can be used as natural preservatives, whose antimicrobial effects are the most studied, were examined.

Rubus rosaefolius Smith

The effectiveness of *Rubus rosaefolius* leaves as a preservative in gel and emulsion formulations was evaluated. For this purpose, 0.2% ethanol extract of *Rubus rosaefolius* leaves was prepared and this extract was used in gel and emulsion formulations for *Pseudomonas aeruginosa* (ATCC 9027), *Burkholderia cepacia* (ATCC 25416), *Staphylococcus aureus* (ATCC 6538), *Escherichia coli* (ATCC 10536) and *Aspergyllus brasiliensis* (ATCC 16404) growth in microorganisms was controlled (Tables 1 and 2). As a result of the

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study, it was determined that the ethanol extract did not show any effect against fungi, but showed a significant lethal effect on bacteria. The results meet the criteria of the American Pharmacopoeia, the European Pharmacopoeia, and the Japanese Pharmacopoeia Antimicrobial Efficacy Test [2]

There are different *Rubus* species (*Rubus caesius, Rubus anatolicus, Rubus idaeus*) in Turkey. According to the results of the above study, it may be possible to benefit from these species with their protective effects in the food and pharmaceutical industry. [2,3]

Table 1. Results of antimicrobial activity test (CFU/gram) in emulsion formulations using 0.2% *Rubus rosaefolius* leaf extract.

Time (Day)	0	2	7	14	21	28
***Escherichia coli* ATCC 10536**	6.17	<1	<1	<1	<1	<1
Physiological saline	6.36	6.59	5.5	5	4.71	5.78
***Pesudomonas aeruginosa* ATCC 9027**	6.07	<1	<1	<1	<1	<1
Physiological saline	6.27	6.28	6.53	6.15	6.59	6.64
***Burkholderia cepacia* ATCC 25416**	5.62	<1	<1	<1	<1	<1
Physiological saline	5.59	6.11	6.48	6	6.54	6.36
***Staphylococcus aureus* ATCC 66538**	5.99	<1	<1	<1	<1	<1
Physiological saline	6.3	5.99	6.49	6.85	6.77	6.61
***Candida albicans* ATCC 10231**	4.72	4.64	4.43	4.87	4.92	5.04
Physiological saline	4.72	5.41	5.41	5.62	4.72	4.53
***Aspergillus brasibensis* ATCC 16404**	5.54	5.4	4.84	4.17	4.18	3.81
Physiological saline	5.4	5.4	5.7	5.04	5.65	5

Table 2. Antimicrobial activity test results (CFU/gram) in gel formulations using 0.2% *Rubus rosaefolius* leaf extract.

Time (Day)	0	2	7	14	21	28
***Escherichia coli* ATCC 10536**	6.18	<1	<1	<1	<1	<1
Physiological saline	6.36	6.59	5.5	5	4.72	5.78
***Pesudomonas aeruginosa* ATCC 9027**	6	<1	<1	<1	<1	<1
Physiological saline	6.28	6.28	6.53	6.15	6.59	6.64
***Burkholderia cepacia* ATCC 25416**	5.83	<1	<1	<1	<1	<1
Physiological saline	5.59	6.11	6.48	6	6.54	6.36
***Staphylococcus aureus* ATCC 66538**	6.32	<1	<1	<1	<1	<1
Physiological saline	6.3	5.99	6.49	6.85	6.77	6.61
***Candida albicans* ATCC 10231**	4.61	4	1.84	3.81	Could not be counted	6.04
Physiological saline	5.77	5.41	4.8	5.62	4.72	4.53
***Aspergillus brasibensis* ATCC 16404**	5.48	5.48	4.74	4.7	4.18	4.18
Physiological saline	5.4	5.4	5.7	5.04	5.65	5

Lippia origanoides Kunth

The protective effect of *Lippia origanoides* leaves in cream, syrup and shampoo formulations has been investigated. In the study, the antimicrobial effect of the essential oil obtained from the leaves of the plant on microorganisms (*Aspergillus brasiliensis, Candida albicans, Escherichia coli, Pseudomonas aeruginosa and Staphylococcus aureus*) was investigated. In the same study, the protective effect of the essential oil of the plant was evaluated by controlling the microbiological growth in cream, syrup and shampoo formulations in which essential oil was used (Table 3).[4] The protective efficacy test results of the formulations were evaluated according to the acceptance criteria of the American Pharmacopoeia (USP, 2010). According to these results, *Lippia origanoides* essential oil showed fungicidal activity against *Candida albicans* in the syrup formulation, while it showed fungistatic effect against *Aspergillus brasiliensis*. The essential oil in the cream formulation was not effective against bacterial strains. The essential oil in shampoo and syrup formulations, on the other hand, is effective against microorganisms and meets the requirements of the American Pharmacopoeia.[4] The major compounds responsible for the antimicrobial activity of *Lippia origanoides* essential oil are thymol and carvacrol; minor compounds are also thought to affect the activity synergistically.[5] Studies with the same plant species show the presence of thymol,

carvacrol, thymol/carvacrol, α and β-phellandrene/p-cimene/limonene and (E)-methyl cinnamate /(E)-nerolidol chemotypes. The chemical content of the plant and the essential oil obtained from the plant should be determined before using it in industrial processes, since the differentiation of chemical content will also cause a change in biological activity.[4] *Lippia canescens* and *Lippia nodiflora* species found in Turkey can also be evaluated in terms of their antimicrobial activities. [6,7]

Table 3. Microbiological growth in cream, syrup and shampoo formulations in which essential oil obtained from *Lippia origanoides* leaves is added as a preservative.

Formulation	Microorganisms	0. day	7. day	14. day	28. day
Cream + Essential Oil + Polysorbate 80	*Aspergillus brasiliensis*	5.9	5.4	5.2	5.1
	Candida albicans	5.6	5.6	5.8	5.8
	Escherichia coli	6.0	6.2	6.2	6.4
	Pseudomonas aeruginosa	6.2	6.0	6.4	6.6
	Staphylococcus aureus	6.0	5.7	6.3	6.2
Syrup + Essential Oil + Polysorbate 80	*Aspergillus brasiliensis*	5.0	5.4	5.3	4.5
	Candida albicans	5.6	0	0	0
	Escherichia coli	5.0	4.0	0	0
	Pseudomonas aeruginosa	5.6	4.9	0	0
	Staphylococcus aureus	5.9	4.8	4.1	0
Shampoo+Essential Oil+Polysorbate 80	*Aspergillus brasiliensis*	5.3	0	0	0
	Candida albicans	5.9	0	0	0
	Escherichia coli	6.0	0	0	0
	Pseudomonas aeruginosa	6.0	0	0	0
	Staphylococcus aureus	6.0	0	0	0

***Syzygium aromaticum* L., *Cinnamomum* Schaeff spp.**

An outbreak of listeriosis caused by *Listeria monocytogenes* has been associated with the consumption of pasteurized milk. As a result, pasteurized milk has been evaluated as a medium risk product by the FDA (US Food and Drug Administration). Based on this information, in the study where the antibacterial effect of *Syzygium aromaticum* buds and essential oils obtained from the leaves and bark of *Cinnamomum* spp. against *Listeria monocytogenes* bacteria for 14 days was examined, *Cinnamomum* spp. essential oil showed strong bactericidal activity. However, it has been noted that higher concentrations of essential oils from *Syzygium aromaticum* and *Cinnamomum* species are required to completely inhibit the growth of Listeria monocytogenes. These results show that essential oils obtained from *Syzygium aromaticum* and *Cinnamomum* species can be used as natural preservatives in dairy products.[8] The major compounds responsible for the antimicrobial effect of Syzygium aromaticum essential oil are eugenol, eugenyl acetate and β-caryophyllene.[9,10] The compounds responsible for the effect of *Cinnamomum* spp. essential oil are cinnamaldehyde, which is the major compound, and l-linalool, p-cimen, and eugenol, which are minor compounds.[10]

In a study on cinnamaldehyde, one of the major components of *Cinnamomum* species, cinnamaldehyde showed an antimicrobial effect against *Salmonella* and *Escherichia coli* microorganisms. *Salmonella* and *Escherichia coli* are risky microorganisms that reproduce especially in animal foods and water sources. Therefore, it has been noted that cinnamaldehyde could be evaluated to control foodborne pathogens.[11]

***Citrus bergamia* Risso&Poiteau, *Citrus limon* (L.)Burm.f., *Citrus sinensis* (L.) Osbeck**

In a study in which the ethanol extract of bergamot peels was tested against Gram (-) bacteria (*Escherichia coli, Pseudomonas putida, Salmonella enterica*), and Gram (+) bacteria (*Listeria innocua, Bacillus subtilis, Lactococcus lactis* ve *Saccharomyces cerevisiae*), it was noted that bergamot fractions showed antimicrobial effect only against Gram (-) bacteria among the tested microorganisms.[12] In another study, the inhibitory effect of essential oils obtained from *Citrus bergamia, Citrus limon, Citrus sinensis* on the growth of *Listeria monocytogenes*,

Staphylococcus aureus, Bacillus cereus, Escherichia coli and *Campylobacter jejuni* bacteria was investigated in cabbage leaves and chicken skin. The highest inhibitory effect was observed in *Citrus bergamia* species. The results of the study were close to the results of another study investigating the inhibitory effects of citral and linalool.[13]

***Vaccinium macrocarpon* Aiton, *Rubus chamaemorus* L., *Rubus idaeus* L., *Fragaria ananassa* Duch., *Vaccinium myrtillus* L.**

In a study, were investigated the antimicrobial effects of *Vaccinium macrocarpon, Rubus chamaemorus, Rubus idaeus, Fragaria ananassa, Vaccinium myrtillus* fruits against microorganisms *Helicobacter pylori, Listeria monocytogenes, Salmonella, Staphylococcus aureus, Escherichia coli* and *Campylobacter* spp. and it was found that the fruits inhibited the growth of microorganisms. The effect is thought to be due to phenolic compounds such as phenolic acids, condensed tannins, proanthocyanidins, anthocyanins, flavonoids, and organic acids.[10]

***Humulus lupulus* L.**

The antibacterial effects of bitter substances such as lupulon and humulon in the resin obtained from *Humulus lupulus* L. flowers against *Streptococcus* spp., *Escherichia coli, Listeria monocytogenes* microorganisms were investigated and it was determined that the hydrophobic parts of these substances inhibit the growth of Gram (+) bacteria as a result of interaction with the cytoplasmic membrane of the bacteria. In the study examining the antimicrobial effect of Humulus lupulus L. essential oil and chloroform extract, antimicrobial activity was observed against Gram (+) bacteria; No antimicrobial activity was observed against Gram (-) bacteria and *Candida albicans*.[10]

***Olea europaea* L.**

In order to determine the antimicrobial activity of *Olea europaea* due to its high phenolic content, many studies have been carried out against various bacteria and fungi in recent years and it is thought that it can be used as an alternative natural preservative.[15,16] While the antimicrobial effects of crude extracts prepared with different solvents were investigated in the first studies, studies to determine the compounds responsible for the antimicrobial effect have increased in recent years and effective compounds such as oleorepine, ligstroside, tyrosol, hydroxytyrosol and elenoic acid have been identified.[10,15] Elenoic acid and its derivatives, oleacein and oleocanthal compounds have been proven to have significant antibacterial activity. Although significant antimicrobial activity potentials of *Olea europaea* L. extracts and effective compounds isolated from the extracts have been demonstrated, more research is needed on their use in the food industry and their application routes.[15]

Some species in the Brassicaceae family

There are studies reporting that glucosinolate derivative allyl isothiocyanates found in the (*Brassica oleracea* L.var. *capitata, Brassica oleracea* L. var. *botrytis, Brassica rapa* L. subsp. *rapa., Brassica nigra* L., *Brassica oleracea* L. var. *italica*) seeds of species belonging to the Brassicaceae family have an antimicrobial effect.[10,17,18] According to the results of the study, isothiocyanates showed antimicrobial effect a broad spectrum in nanogram amounts on Gram (+) (*Listeria monocytogenes, Staphylococcus aureus*) and Gram (-) bacteria (*Escherichia coli* O157:H7, *Pseudomonas corrugata, Salmonella* spp.) and yeast (*Endomyces fibuliger*) and fungi (*Aspergillus flavus, Aspergillus niger, Cladosporium cladosporioides, Penicillium citrinum, Penicillium commune*) and were showed a broad spectrum antimicrobial effect in nanogram amounts. showed.[10] The very low amount required to inhibit microorganisms suggests that it can be used as a microbial preservative in the food industry.[19]

***Allium* spp.**

Allium cepa L. and *Allium sativum* L. inhibit the growth of *Bacillus cereus, Clostridium botulinum* type A, *Escherichia coli, Lactobacillus plantarum, Salmonella, Shigella* spp., *Staphylococcus aureus, Aspergillus niger, Candida albicans* and many microorganisms and inhibit toxin production.[19] The antimicrobial effect of allicin is due to the chemical reaction of thiosulfinates with some enzymes containing thiol groups.[20] It has been determined that allicin has an inhibitory effect against microorganisms in processed meat and meat products.[10] There is no fresh allicin in the *Allium sativum* plant. Allicin is formed by the interaction of alliin with the alliin alkyl sulfonate lyase enzyme when the garlic clove is crushed.[21]

A similar phenomenon occurs in onions in the presence of substrate (S-(1-propenyl)-L-cysteine sulfoxide) and thiopropanal-S-oxide, one of the major compounds, is formed. These compounds (allicin and thiopropanal-S-oxide) occurring in garlic and onions are responsible for both antimicrobial effect and flavor and odor.[10]

In another study, flower extracts of *Allium*

scabriscapum Boiss. &Kotschy, *Allium iranicum* (Wendelbo)Wendelbo, *Allium atroviolaceum* Boiss., *Allium shelkovnikovii* Grossh. species showed antimicrobial activity against pathogenic microorganisms such as *Klebsiella pneumoniae, Bacillus subtilis, Bacillus cereus, Staphylococcus aureus* and *Escherichia coli* and it was determined that the effect was caused by the tannin compounds found in the flowers.[22]

***Melaleuca alternifolia* (Maiden &Betche) Cheel**

In a study examining the antimicrobial activity of *Melaleuca alternifolia* essential oil and its major components in oil-based personal care products, MIC values were recorded as 0.4% for *Escherichia coli* and *Bacillus subtilis* and were found to be as effective as parabens in the 0.08%-0.8% concentration range. According to this result, it was determined that it would be appropriate to add tea tree oil as a natural antimicrobial preservative in oil-based formulations.[23] The essential oil obtained from *Melaleuca alternifolia* showed significant antimicrobial activity against the microorganisms of *Candida albicans, Pseudomonas aeruginosa, Staphylococcus spp. Aspergillus niger*.[19,24] *Melaleuca alternifolia* essential oil as major components 35-40% terpinen-4-ol, 4% 1,8-cineol, 2-5% p-cymene; it also contains linalool, α-terpinene, γ-terpinene, α-terpineol and terpinolene as minor components.[19] While the compound responsible for the effect against *Pseudomonas aeruginosa* is p-cymene; the compounds responsible for the action against *Candida albicans* are terpinen-4-ol and p-cymene compounds.[24,25]

***Cupressus sempervirens* L.**

According to the results of the study (MIC, MBC, Disk Diffusion Method) in which the antimicrobial activity of *Cupressus sempervirens* essential oil and methanol extract were evaluated, it was determined that the methanol extract showed strong antibacterial activity against bacteria, while the essential oil showed lower antibacterial activity. However, it was determined that both the essential oil and the methanol extract did not have antifungal activities against *Candida albicans*. Based on this study, antibiofilm activity against *Klebsiella pneumoniae* was determined and it was noted to have a strong effect.[26] α-pinene (48.6%), δ-3-carene (22.1%), limonene (4.6%) and α-terpineol (4.5%) compounds are responsible for the antibacterial activity in the essential oil; phenolic compounds are responsible for the antibacterial activity and the antibacterial activity of the methanol extract. [26, 27] Since *Cupressus sempervirens* essential oil and methanol extract have strong antimicrobial potential, it is thought that they can be used to increase the shelf life of products industrial and can be evaluated as a natural antimicrobial preservative.[26]

***Coriandrum sativum* L.**

The fixed oil obtained from the seeds of *Coriandrum sativum* has significant antimicrobial activity against fungi, some yeasts and Gram (+) and Gram (-) bacteria. This effect is found in the composition of the fixed oil, linalool (57-72%), terpinen-4-ol (0.1-0.5%), γ-terpinene (4.2-9.3%), p-cymene (1.12-4%), limonene (% 0.3-3.7), α-pinene (1.63-4.81%) and minor β-pinene, myrcene, camphene, linalyl acetate, sabinene and geranyl acetate compounds.[27] It has been noted that there are various applications in the food industry in the storage and packaging stages in order to extend the shelf life of the product and to prevent the growth of pathogenic bacteria.[28,29]

***Origanum* L. spp**.

The major components of the essential oil from *Origanum* species are thymol and carvacrol; compounds responsible for antimicrobial activity.[30] The activity is due to interactions of thymol and carvacrol with the biological membrane of bacteria or fungi.[31] According to the results of the study, when the essential oil is applied to products in the food industry in different concentrations, it can increase the shelf life of the product by preventing or slowing down microbial spoilage.[30]

***Thymus vulgaris* L.**

The essential oil obtained from *Thymus vulgaris* showed antibacterial activity against *Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis* and *Pseudomonas aeruginosa* microorganisms. Thymus vulgaris essential oil inhibited microbial growth in cream-gel formulations.[32]

Thymol, carvacrol and caryophyllene oxide as major compounds; terpinen-4-ol, γ-terpineol, borneol, geraniol. as minor compounds in the composition of essential oil obtained from *Tyhmus vulgaris.* [34] While it is possible to use essential oil in the food industry and nutraceutical products; The addition of herbal preservatives to topical formulations in the cosmetic industry can also be a good alternative to synthetic preservatives.[33]

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Table 4. The relationship of different *Origanum* species and chemical components with their antimicrobial activities is shown.

***Origanum* spp.**	**Major Compounds**	**Microorganism**
Origanum. vulgare L.	*Carvacrol* *Thymol* *Cymene* *α-pinene* *Cymenol*	*Salmonella enteridis* *Bacillus. cereus, Bacillus. subtilis* *Escherichia coli* *Listeria. monocytegenes* *Candida albicans* *Pseudomonas aeruginosa*
Origanum acutidens (Hand.-Mazz.) Letsw.	*p-cymene* *Carvacrol* *Borneol* *B- caryophyllene*	*Pseudomonas vulgaris* *Staphylococcus aureus* *Escherichia coli* *Klebsiella pneumoniae*
Origanum compactum Benth.	*Carvacrol* *Thymol* *Terpinene* *p-cymene*	*Pseudomonas aeruginosa* *Staphylococcus aureus*
Origanum. majorana L.	*Terpinene-4-ol* *Thymol* *4-thujanol* *Cis-sabinene hydrate* *p-cymene* *γ-terpinene*	*Pseudomonas aeruginosa* *Staphylococcus aureus* *Bacillus subtilis, Bacilus cereus* *Escherichia coli* *Klebsiella pneumoniae* *Candida albicans* *Listeria. monocytegenes*

***Rosmarinus officinalis* L.**

In the study in which the antimicrobial activity of the essential oil obtained from the leaves of *Rosmarinus officinalis* was determined, it was found that the essential oil showed significant antibacterial activity against *Klebsiella pneumoniae* and *Escherichia coli* microorganisms.[34] In another study evaluating the antimicrobial activity of Rosmarinus officinalis ethanol extract on foodborne microorganisms, the MIC values for Gram (+) bacteria were 1% for Leuconostoc mesenteroide, 0.5% for *Listeria monocytogenes*, 0.5% for *Staphylococcus aureus*, 0.13% for *Streptococcus mutans* and *Bacillus cereus*. While it was found as 0.06%, no activity was observed on Gram (-) bacteria (*Escherichia coli*, *Salmonella enteritidis* and *Erwinia carotovora*) and yeasts (*Rhodotorula glutinis* and *Cryptococcus laurentii*). It has been reported that phenolic diterpenes are responsible for the effect. It is thought that it can be used in the food industry, especially in pasteurized products.[35]

In a study in which ointment formulations containing 2% and 4% *Rosmarinus officinalis* essential oil were applied topically to the wound formed on the skin of rats, the status of the infection caused by *Candida albicans* and the number of microorganisms on the wound were examined. As a result, it was observed that the number of *Candida albicans* and infection were much lower in the wounds of the rats in which 4% essential oil formulation was applied, compared to the wounds of the rats who were treated with 2% essential oil-containing ointment formulation and without the ointment formulation. This study suggests that an ointment containing rosemary essential oil on *Candida albicans* infected wounds can accelerate wound healing and can be added as a natural preservative to wound healing formulations.[36]

***Quillaja saponaria* Molina and *Yucca schidigera* Roezl**

Saponins show an antimicrobial effect by reducing glucose utilization and enzyme activities of bacteria, suppressing protein synthesis, and interacting with fatty acids and sterols in the bacterial cell wall.[37,38] *Ouillaja saponaria* and *Yucca schidigera* extracts, which are rich in saponins, have been approved by the FDA for use as emulsifiers and flavorings in foods and beverages. Therefore, considering its antimicrobial effects, it can be considered as a natural antimicrobial preservative.[38]

***Equisetum arvense* L.**

When the antimicrobial effects of *Equisetum*

arvense water and ethanol extract against *Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus saprophyticus* and *Enterococcus faecalis* microorganisms were examined, it was found that both extracts showed inhibitory effects against all microorganisms.[39]

It has been stated that 4% aqueous extract of *Equisetum arvense* plant in cream formulations inhibits the growth of *Staphylococcus aureus* and *Escherichia coli* microorganisms, therefore the aqueous extract can be used as a preservative in topical formulations. Phenolic compounds are the compounds responsible for the activity in the plant.[40]

In a study investigated the antibacterial and antifungal effects of *Equisetum arvense* essential oil, diluted 1:10 against *Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella enteritidis, Aspergillus niger* and *Candida albicans* microorganisms, a broad-spectrum antibacterial activity was observed.[40]

***Argemone mexicana* L.**

In a study investigating the antibacterial and antifungal activities of methanol and ethanol extracts of *Argemone mexicana* plant and cream and ointment formulations prepared from these extracts against *Staphylococcus aureus, Pseudomonas aeruginosa, Candida albicans* and *Aspergillus niger* microorganisms, ethanol extract showed stronger antibacterial effects than methanol extract; It was determined that methanol extract showed stronger antifungal effect than ethanol extract. Based on this study, it is thought that *Argemone mexicana* extracts can be included in cream and ointment formulations as natural preservatives.[41]

***Eupatorium glandulosum* Michx**

In the study, in which the antimicrobial activity of the gel formulation prepared with the methanol extract of the *Eupatorium glandulosum* plant for wound healing purposes was evaluated on albino mice, it was found that it had a strong inhibitory effect against *Staphylococcus aureus* and *Escherichia coli* bacteria. Thus, it has been stated that it can be evaluated as a natural preservative in the cosmetics and pharmaceutical industries.[42]

CONCLUSION

In this review, the effects of plants, drugs, active substances, which are used or can be used as preservatives of natural origin today, are revealed with the results of antimicrobial activity against various microorganisms. Its usability in the food industry and cosmetics industry has been evaluated according to the results of the research. Although the degree of usability as a preservative for plants, drugs and plant-derived active substances with antimicrobial activity cannot be determined precisely, MIC values are determined by some researchers. Based on MIC values, a classification was made as strong activity (up to 0.5 mg/ml), moderate activity (0.51-1.0 mg/ml), weak activity (more than 1.1 mg/ml).[27]

When we consider that there are many plant species with antimicrobial effect, there are many plants, drugs and herbal active ingredient options that can be used as preservatives. As a result of the review, it has been revealed that it is possible to use *Rubus rosaefolius, Lippia origanoides, Melaleuca alternifolia* and *Equietum arvense* especially in cosmetic preparations; *Coriandrum sativum, Szyzgium aromaticum, Cinnamomum* spp, cinnamaldehyde, allicin, *Cupressus sempervirens* as natural preservatives in the food industry. In addition, it has been determined that *Origanum* spp., *Rosmarinus officinalis* and *Thymus vulgaris* are valuable as natural preservatives in both the food industry and cosmetics sectors. In this short review, only studies on plants, herbal extracts or herbal substances which were concluded to be used as a preservative were included not all antimicrobial studies. When we consider the potential of herbs with regards to their antimicrobial activity there is a need for more specific and detailed studies on the use of herbs as preservatives.

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