Z Rheumatol
DOI 10.1007/s00393-016-0176-1

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Comparison of the effectiveness of medicinal leech and TENS therapy in the treatment of primary osteoarthritis of the knee

A randomized controlled trial

Introduction

Osteoarthritis (OA) of the knee is caused by loss of hyaline cartilage along the knee joint surfaces, is a common chronic disease among older people and is a major cause of morbidity, limitation of activity and increased utilization of health services. Symptomatic knee involvement is estimated to affect as much as 10 % of the population older than age 65 years. Another major risk factor is obesity. Treatment of OA is based on patient age, demands and expectations, comorbidities and severity [1]. In the management of OA the main goals are to reduce pain and muscle spasm, alleviate the abnormal stress imposed on affected joints and enhance the overall functional status. Conservative treatment for knee arthritis includes therapeutic approaches, such as generalized conditioning programs, weight loss, knee sleeves, braces, nonsteroidal anti-inflammatory drugs (NSAIDs) and physiotherapy, including transcutaneous electrical nerve stimulation (TENS). As an invasive approach intra-articular steroid injection, such as hyaluronic acid is an effective treatment in OA of the knee and is also an effective treatment modality for patients with symptomatic knee OA [2, 3]. Surgical interventions, such as total knee arthroplasty, improve functional status and quality of life of individuals with severe knee OA [4].

Oral supplementation with glucosamine and chondroitin sulphate may also be considered but the usefulness of these approaches are limited over time by the cost and/or side effects [5, 6]. An alternative modality for the symptomatic treatment of OA of the knee with leeches has been found to be effective in different studies [7–11]. The economic impact of OA is high with costs of approximately 15,047 US dollars per patient including indirect costs resulting in lost productivity [12].

The first description of leech therapy was found in the text of Sushruta samhita (dated ca. 800 B.C.) written by Sushruta [13]. In medieval and early modern medicine, medicinal leeches were used to remove blood from patients as part of a process to balance the humors. A recorded use of leeches in medicine was also found from 200 B.C. by the Greek physician Nicander in Colophon, the medicinal use of leeches was discussed by Avicenna in The Canon of Medicine and by Abd-el-latif al-Baghdadi in the twelfth century [14].

In this study, we aimed to evaluate the effects of medicinal leech therapy (*Hirudo medicinalis*) in the treatment of knee OA in terms of duration of effectiveness and symptomatic relief and to compare these results with TENS therapy, which is currently one of the first options for the conventional treatment of knee OA [15–18].

Material and methods

Setting

This study was coordinated by Ataturk University Acupuncture and Complementary Medicine Research Centre, in Erzurum, Turkey from June 2012 to June 2013 in accordance with the Declaration of Helsinki.

Study design

This study was designed as a prospective, single center, randomized, single-blind and parallel group study.

Patients

Patients were recruited from the outpatient clinics of the Department of Family Medicine and Department of Physical Medicine and Rehabilitation

M. Isik conceived and led the investigation, developed the study protocol and guided the statistical analyses. M. Ugur performed the initial patient examination and allocation. R. S. Yakisan and T. Sari performed leech therapy, followed patients and collected data. N. Yilmaz performed the initial baseline measurement, guided the TENS therapy in the physical medicine and rehabilitation and collected data.

Published online: 17 August 2016

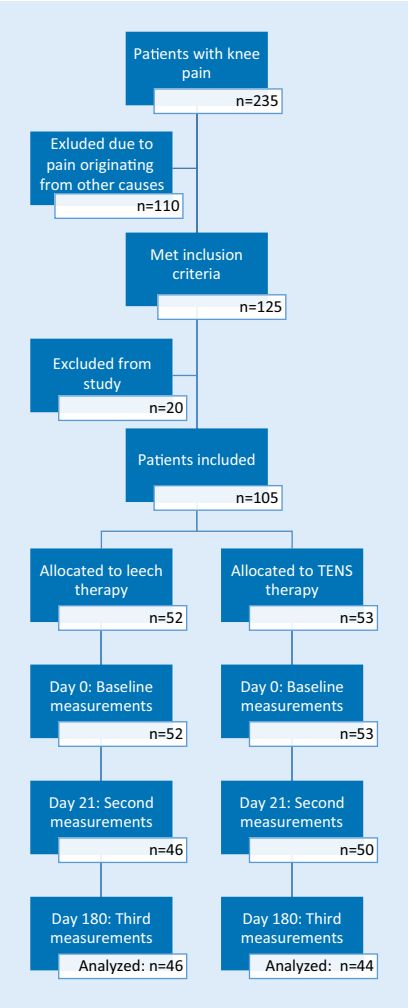

Fig. 1 ▲ Study flow diagram

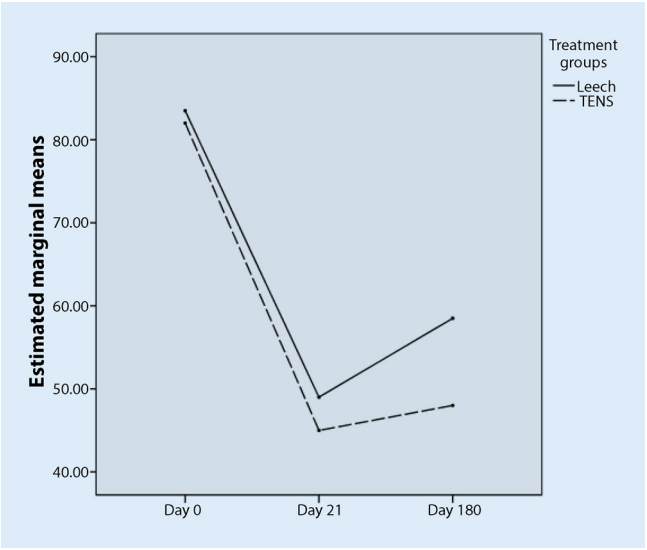

Fig. 2 ◀ Change of visual analogue scale pain score (mm) through course of study in the leech and TENS therapy groups

of Atatürk University Medical Faculty Research Hospital. All patients with a complaint of knee pain were evaluated. The first screening and selection of eligible patients among the applicants based on inclusion and exclusion criteria were carried out by a physical medicine and rehabilitation specialist. Enrolment and exclusion criteria are summarized in **Infobox 1**. In order to verify OA, selected eligible patients were invited for a study visit to have a physical examination, blood analyses and anteroposterior and lateral radiography of the affected knee (if they had not had one in last 3 months). All the patients, even those classified as grade IV according to the Kellgren and Lawrence classification system were included in the present study. The Kellgren and Lawrence system is a radiographic grading method for classification of the severity of OA of the knee (**Table 1**). During the study period a total of 235 patients with knee pain attended the physical medicine and rehabilitation clinic. Of the 235 patients 125 patients fulfilled all the study criteria and were invited to the study. Of the invited patients 8 did not want to sign the informed consent and 12 patients rejected participation for a variety of reasons. A total of 105 patients (52 to leech therapy and 53 to the TENS group) were randomized into the leech therapy group and TENS therapy group after obtaining informed consent. During the follow-up period there were 6 and 8 drop outs in the 2 groups, respectively. Detailed patient flow is given in the study diagram (**Fig. 1**).

Randomization

Patients were randomly allocated to the two groups by non-stratified block randomization with equal block lengths. Sequentially numbered envelopes containing the treatment assignment were prepared. When a patient met the inclusion criteria and consented to participation, the investigator opened the lowest numbered envelope, which determined the group of assignments. One group received leech therapy while the control group received TENS therapy.

Patients and physicians allocated to the intervention group were aware of the allocated treatment groups but the randomizer, outcome assessors and data analysts were kept blinded to the allocation. After overall assessment, written informed consent was obtained from the patients and then they were equally randomized into two groups in a 1:1 ratio: leech treatment group and TENS treatment group.

Study protocol

As the intervention was invasive it was not possible to make a double blinded study. The following measurements were carried out in each patient: for pain assessment the visual analogue scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were used. Measurements and group comparisons were carried out at 0, 21 and 180 days. One day before the appointments, patients were reminded and supported to come to the study visits in order to increase compliance with the study protocol. Laboratory investigations were performed including complete blood count, liver function tests, e.g. serum bilirubin, aspartate aminotransferase (AST), Alanine Aminotransferase (ALT) and alkaline phosphatase (ALP), serum creatinine, blood urea and uric acid, prothrombin time (PT) and partial thromboplastin time (PTT) on days 0 and 21. The study period was 3 weeks and with a follow-up at 6 months.

Enrolled patients were examined by a specialist physician who was blinded to

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Comparison of the effectiveness of medicinal leech and TENS therapy in the treatment of primary osteoarthritis of the knee. A randomized controlled trial

Abstract

Objectives. The aim of this study was to evaluate the effects of leech therapy in the treatment of knee osteoarthritis in terms of duration of effectiveness and symptom relief and to compare these results with transcutaneous electrical nerve stimulation (TENS) therapy.

Material and methods. This study was designed as a prospective, single center, randomized, single-blind and parallel group study. A total of 90 patients were included in the study, 46 in the leech group and 44 in the TENS group. Primary outcome measures were changes of the pain scores in visual analogue scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) on the measurements day 0, 21 and 180. Secondary outcome measures were the changes in the sub-groups of the WOMAC scores. Five leeches were applied to the affected knee, once every week for 3 weeks.

Results. The VAS pain score showed a similar decrease in both groups in the evaluation on day 21 ($p < 0.001$). The course of the change of the VAS pain score in both groups was similar in the comparisons between groups. Long-term benefits of the TENS therapy group were slightly more than the leech therapy group. All the sub-scores of WOMAC in both therapy groups showed a similar decrease ($p = 0.819$). Throughout the study this decrease was statistically significant in both groups ($p < 0.001$).

Conclusion. Leech therapy relieves symptoms in patients with osteoarthritis of the knee and is as effective as TENS therapy in the management of osteoarthritis of the knee. This treatment has the potential of being an additional or alternative therapy for the non-surgical management of osteoarthritis of the knee.

Keywords

Leech therapy · Osteoarthritis · Knee joint · TENS · Clinical study · Integrative medicine

Vergleich der Wirksamkeit von medizinischer Blutegel- und TENS-Therapie zur Behandlung der primären Gonarthrose. Eine randomisierte kontrollierte Studie

Zusammenfassung

Ziel. Ziel dieser Studie war es, die Wirkung der Blutegeltherapie zur Behandlung einer Gonarthrose bezüglich Wirksamkeitsdauer und Symptomlinderung zu beurteilen und diese Ergebnisse mit denen der transkutanen elektrischen Nervenstimulation (TENS) zu vergleichen.

Material und Methoden. Es handelte sich um eine prospektive, randomisierte, einfach verblindete Parallelgruppenstudie an einem Studienzentrum. Insgesamt 90 Patienten wurde in die Studie eingeschlossen, davon 46 in der Blutegelgruppe und 44 in der TENS-Gruppe. Primärer Endpunkt waren Veränderungen der Schmerzscores auf der visuellen Analogskala (VAS) und dem Western Ontario sowie dem McMaster Universities Osteoarthritis Index (WOMAC) an den Tagen 0, 21 und 180. Sekundärer Endpunkt waren Veränderungen in den Subgruppen des WOMAC-Scores. Fünf Blutegel wurden auf dem betroffenen Knie aufgesetzt, 1-mal pro Woche für 3 Wochen.

Ergebnisse. Der VAS-Schmerzscore zeigte bei der Beurteilung an Tag 21 einen ähnlichen Rückgang in beiden Gruppen ($p < 0{,}001$). Die Veränderungen des VAS-Schmerzscores zeigten im Vergleich beider Gruppen einen ähnlichen Verlauf. In der TENS-Gruppe überwogen die langfristigen Vorteile geringfügig im Vergleich zur Blutegelgruppe. Alle Subscores des WOMAC zeigten über die gesamte Studiendauer ($p = 0{,}001$) in beiden Therapiegruppen einen vergleichbaren Rückgang ($p = 0{,}819$).

Schlussfolgerung. Die Blutegeltherapie lindert die Symptome bei Patienten mit Gonarthrose und ist bei der Behandlung einer Gonarthrose genauso wirksam wie die TENS-Therapie. Diese Behandlung hat das Potenzial einer Zusatz- oder Alternativbehandlung bei der nichtoperativen Therapie der Gonarthrose.

Schlüsselwörter

Blutegeltherapie · Arthrose · Kniegelenk · TENS · Klinische Studie · Integrative Medizin

the randomization procedure and treatment modalities at the department of physical medicine and rehabilitation clinics. All measurements were done by the same physician. Before the interventions all patients were asked to perform a pain rating on VAS and complete the WOMAC inventory. Each patient asked to record any kind of adverse effects due to leech or TENS therapy. Steroids or any other kind of intra-articular medication injection were not allowed to be used during the study. The research protocol was reviewed and approved by the local Institutional Ethics Committee of Atatürk University (B.30.2.ATA.0.01.00/52).

Leech therapy

Medicinal leeches were obtained from a leech farm and kept for one week in dechlorinated tap water that is changed every other day until application.

Appointments were given to patients in the leech group once per week for 3 weeks. Therapy consisted of the application of five leeches on the affected knee, once every week for 3 weeks; 3 of the leeches were applied on the periarticular soft tissue on the medial side of the knee (mostly the maximum painful area in the examination) and 2 to the lateral side. There was no preparation of skin before application. Leeches were left in place up to 60 min and usually detached by themselves. If they did not detach by themselves in 60 min they were manually removed by scraping. Leeches were used only once and then were killed. The treated knees were then bandaged. Patients were cautioned not to be active for 12 h in order to decrease bleeding. Pa-

Table 1 Radiographic grading scheme for osteoarthritis of the knee (adapted from Kellgren and Lawrence)

Grade 0	No radiographic features of OA are present
Grade 1	Doubtful JSN and possible osteophytic lipping
Grade 2	Definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph
Grade 4	Multiple osteophytes, definite JSN, sclerosis, possible bony deformity
Grade 4	Large osteophytes, marked JSN, severe sclerosis and definite bony deformity

JSN joint space narrowing, *OA* osteoarthritis

Table 2 Baseline characteristics of study groups

		Leech group		TENS group		t-test	*p*-value
		Mean (*n*)	SD (%)	Mean (*n*)	SD (%)		
Age (years)		59.6	8.8	53.8	12.6	2.52	0.013
Sex	Women	44	95.7	36	81.8	–	0.047
	Men	2	4.3	8	18.2		
BMI (kg/m^2)		33.5	5.1	32.6	3.8	0.99	0.326
Duration of pain symptoms (years)		7.7	5.7	3.2	3.3	4.51	0.000
VAS (mm)		84	20	82	21	0.63	0.533
WOMAC pain score		66.0	16.5	59.0	19.0	–	0.819
WOMAC stiffness score		33.7	21.2	53.7	12.5	21.2	0.000
WOMAC physical function score		43.7	10.6	36.8	8.8	0.29	0.773

SD standard deviation, *VAS* visual analogue scale, *WOMAC* Western Ontario and McMaster Universities osteoarthritis index, *BMI* body mass index, *TENS* transcutaneous electrical nerve stimulation

Table 3 Changes of mean visual analogue scale scores in the course of study in therapy groups

	Therapy groups			
	Leech		TENS	
	Mean (mm)	SD	Mean (mm)	SD
Day 0	84	20	82	21
Day 21	49	33	45	31
Day 180	59	29	48	33

SD Standard deviation, *TENS* transcutaneous electrical nerve stimulation
Within groups comparison $p < 0.001$
Between groups comparison $p = 0.296$
Groups and time interaction $p = 0.356$
Comparison of day 0 and day 21 $p < 0.001$
Comparison of day 21 and day 180 $p = 0.08$

Infobox 1 Enrolment criteria.

Inclusion criteria
- Age between 40–70 years,
- Diagnosed as primary osteoarthritis of the knee according to the definition of American College of Rheumatology criteria,
- Patients from all grades of the Kellgren and Lawrence classification system.

Clinical exclusion criteria
- Diagnosis of rheumatoid arthritis and other systemic joint diseases,
- Secondary osteoarthritis,
- Arthroscopy or surgery of the knee,
- Intra-articular injection in the past 3 months,
- Physical therapy in the past 3 months,
- Skin disorders with or without exfoliation, scar or open wound on the knee,
- Comorbidities, such as blood disorders, anemia, uncontrolled diabetes, severe depression or other psychological diseases,
- Anticoagulation treatment,
- Advanced joint deformity,
- Pregnancy,
- Intercurrent disease(s) that might interfere with the free use and evaluation of the affected knee.

Laboratory exclusion criteria
- Abnormal hemogram, erythrocyte sedimentation rate, C-reactive protein (CRP) and blood biochemistry,
- ESR > 40 mm/h (Westergren method),
- CRP > 5 mg/l.

Other exclusion criteria
- Inability to give informed consent,
- Potentially noncompliant (high possibility of loss to follow-up due to personal reasons),
- Previous treatment with leeches.

tients were also asked to return to the clinic to check the treated area.

Transcutaneous electrical nerve stimulation therapy

Control group patients were hospitalized in the physical medicine and rehabilitation clinic for at least 3 weeks until 15 TENS treatment sessions had been completed. In working days, one treatment session was applied to the effected knee. Throughout the hospitalization, patients were cautioned to decrease physical activities. The TENS procedure was performed using the conventional method with a high stimulation frequency (40–150 Hz) and low intensity. Patients received dual channel TENS therapy once a day for 20 min into the affected knee(s). Electrodes of a 2-channel apparatus were placed in pairs on either side, above and below the affected knee. The TENS therapy was applied at 50 cycles/s for 20 min with an intensity so that patients could barely notice the current. No other treatment (e. g. physiotherapy exercises) was provided and treatment ended at the end of the third week.

Outcome measures

Primary outcome measures were the changes of the pain scores in VAS and WOMAC on the measurements after 0, 21, and 180 days. Secondary outcome measures were the changes in the WOMAC scores in the two groups.

Table 4 Mean WOMAC subscores throughout the therapy

		Leech group		TENS group	
		Mean	**SD**	**Mean**	**SD**
Pain	Day 0	66.0	16.5	59.0	19.0
	Day 21	38.0	29.0	36.5	18.5
	Day 180	43.0	28.0	40.0	25.0
	Within group comparison $p < 0.001$ Between groups comparison $p = 0.819$ Groups and time interaction $p = 0.133$ Comparison of day 0 and day 21 $p < 0.001$ Comparison of day 21 and day 180 $p = 0.131$				
Stiffness	Day 0	33.7	21.2	53.7	12.5
	Day 21	25.0	22.5	28.7	20.0
	Day 180	31.2	33.7	43.7	17.5
	Within group comparison $p < 0.001$ Between groups comparison $p = <0.001$ Groups and time interaction $p = 0.062$ Comparison of day 0 and day 21 $p < 0.001$ Comparison of day 21 and day 180 $p = 0.021$				
Physical function	Day 0	54.0	12.9	64.2	15.5
	Day 21	39.1	24.4	40,8	20.2
	Day 180	40.8	25.7	36.6	16.9
	Within group comparison $p < 0.001$ Between groups comparison $p = 0.509$ Groups and time interaction $p = 0.003$ Comparison of day 0 and day 21 $p < 0.001$ Comparison of day 21 and day 180 $p = 0.502$				

SD standard deviation, *TENS* transcutaneous electrical nerve stimulation

Visual analogue scale (VAS)

A VAS is a psychometric response scale. It is a measurement instrument for subjective feelings that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end points. We used a prepared 0–100 mm long standardized graphic rating scale, the ends of which were labelled as the extremes "no pain" and "pain as bad as it could be", that has a movable pointer showing the degree of the perceived pain. Numbers are provided on the back along the scale for guidance.

Western Ontario and McMaster Universities osteoarthritis index (WOMAC)

The WOMAC is a measurement to assess pain, stiffness and physical function in patients with hip and/or knee osteoarthritis. It consists of 24 items divided into 3 subscales: pain (5 items), stiffness (2 items) and physical function (17 items). We used a linguistically validated Turkish version of WOMAC LK 3.1 scale. In Likert (LK) scales, there are five alternative answers to every question (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). The maximum score in a LK scale is 20 points for pain, 8 points for stiffness and 68 points for physical function. Higher scores indicate worse symptoms, maximum limitations and poor health [19, 20].

In this study, we used a amplification procedure to correct the differences in scale length. In order to normalize the LK scale on a scale of 0–100, the following correction factors were used where S = sum of raw scores of items in dimension: pain amplification S =×5, stiffness amplification S =×12.5 and physical function amplification S =×1.47.

Sample size determination and statistical analysis

Sample size calculation was based on the main outcome of VAS. For a between-within interaction repeated measures of ANOVA with 3 repeated measurements in 2 groups, 41 patients in each treatment group (a total of 82 patients) were needed to detect a difference in the means with an effect size of 0.35, alpha error of 0.05 and a power of 80 %. In order to compensate for drop-out, we included a total of 105 patients during randomization. Stange et al. conducted a similar study where they reported mean VAS scores at day 0 for the leach and TENS groups as 5.89 ± 2.40 and 5.63 ± 2.35, respectively [21].

Data are presented as number, percentage, mean and standard deviation. Data were analyzed using the SPSS 20.0 program. Comparison of age, body mass index (BMI) and duration of illness by treatment groups were done by the t-test (independent samples t-test). The mean of dependent numeric variables was analyzed using a paired t-test, the data of repeatedly measured variables in the treatment groups in time were analyzed by repeated measures of ANOVA and *P* values less than 0.05 were considered to be statistically significant.

Results

For the measurements on day 21, 6 patients in the leech therapy group and 3 patients in TENS therapy group were absent and for the measurement on day 180, 6 patients in the TENS therapy group did not show up. A total of 90 patients completed the study, 46 patients in the leech therapy group and 44 patients in the TENS therapy group.

As shown in the **Table 2** the duration of pain symptoms in the leech group and WOMAC stiffness score in the TENS group were high ($p < 0.001$). The groups did not show any significant differences with regard to demographic variables, anthropometric and patient history as well as main outcome and secondary outcome variables ($p > 0.05$). Baseline parameters are shown in **Table 2**.

Clinical effect

After therapy in the evaluation on day 21 the mean VAS pain score showed a similar decrease in both groups ($p < 0.001$). The mean reduction in the VAS score on day 21 was 35 mm (58 %) in the leech group and 37 mm (55 %) in the

Table 5 Evaluation of blood tests in all participants in the study

	Day 0		Day 21		t-test	*p*-value
	Mean	SD	Mean	SD		
White blood cell (mg/dl)	15.1	28.6	15.2	29.9	−0.11	0.910
Hemoglobin (g/dl)	14.3	1.2	13.5	1.6	4.67	*0.000*
Hematocrit (%)	43.1	3.7	40.8	4.7	4.95	*0.000*
Platelet (100/µl)	242,300	57,300	250,500	55,400	−1.49	0.149
Prothrombin time (s)	10.7	0.8	10.4	0.7	3.06	*0.005*
Partial thromboplastin time (s)	32.3	8.6	31.8	8.5	0.48	0.635
International normalized ratio	0.98	0.06	1.0	0.07	−0.99	*0.036*
Erythrocyte sedimentation rate (mm)	21.8	12.2	26.7	14.4	−4.58	*0.000*
C-reactive protein (mg/dl)	7.8	17.6	4.2	2.4	1.15	0.259
Hemoglobin A1c (%)	6.0	0.3	5.8	0.6	1.20	0.242
Aspartate aminotransferase (U/L)	23.1	6.9	21.4	7.0	1.55	0.133
Alanine aminotransferase (U/L)	22.36	14.08	19.89	6.97	1.46	0.149
Alkaline phosphatase (U/L)	87.9	16.5	82.6	11.6	1.50	0.144
Blood urea nitrogen (mg/dl)	16.1	5.2	14.3	2.2	1.45	0.164
Creatinine (mg/dl)	0.7	0.2	0.7	0.2	0.49	0.625
Uric acid (mg/dl)	5.1	0.9	5.1	0.9	0.74	0.463
Glucose (mg/dl)	110.0	35.3	101.7	17.2	1.53	0.136
Total cholesterol (mg/dl)	222.8	43.7	220.3	42.6	0.54	0.592
High density lipoprotein (mg/dl)	48.4	10.2	49.0	8.2	−0.59	0.557
Low density lipoprotein (mg/dl)	158.9	43.4	159.8	33.9	−0.19	0.851
Triglyceride (mg/dl)	178.9	75.6	193.3	90.3	−0.96	0.345

SD standard deviation
Numbers in italics were statistically significant

TENS group, which was statistically significant ($p < 0.001$). In the comparison of the mean VAS scores on day 21 and day 180 there was a slight increase in both groups but the difference was not statistically significant ($p = 0.085$). The course of the change of the VAS pain score in both groups was similar in the comparisons between groups ($p = 0.296$, **Table 3 and Fig. 2**). In the evaluation on day 180 the therapeutic effect was still continuing in both therapy groups and remained with only a slight deterioration over 6 months in both groups. The long-term benefits in the TENS therapy group were slightly more than in the leech therapy group (**Fig. 2**).

All the subscores of WOMAC in both therapy groups decreased similarly ($p = 0.819$) throughout the study ($p < 0.001$). These decreases were similar in the group comparison ($p = 0.488$). In the evaluation of day 180 the therapeutic effects were still continuing in both therapy groups. Therapeutic benefit stayed with only slight deterioration over 6 months in both groups (**Table 4**). The long-term benefits of TENS therapy group were slightly more than the leech therapy group but the differences in between group comparison of WOMAC pain and physical function on day 21 and day 180 were not statistically significant ($p = 0.131$ and $p = 0.502$, respectively). The WOMAC stiffness score was higher in the TENS group in the group comparison on day 21 and day 180, which was statistically significant ($p = 0.021$, **Table 4**).

In order to check the effects of leech therapy on the body we performed routine blood tests on day 0 and day 21. As shown in **Table 5**, while the mean hemoglobin and hematocrit levels decreased, PT, INR and ESR values increased significantly on day 21 in the leech group.

Side effects

There were no serious side effects in both groups. In the leech therapy group there was a mild local itching and skin redness in 31 patients (12 patients required topical antihistamine therapy) and severe local itching and reddening in 3 patients (requiring oral plus topical antihistamine therapy). One of these 3 patients attended the emergency department and oral antibiotic therapy was given with the diagnosis of cellulitis. Itching generally began on the day 3 after treatment and lasted for approximately 3 days. Pain associated with the leeching procedure was rated as not severe by all patients except for two patients who rated the pain as severe and seven patients reported leech therapy as disgusting at the first session. In comparison to the TENS therapy group, hemoglobin and hematocrit levels decreased and PT, INR and ESR values increased significantly in patients in the leech therapy group after the therapy period in the measurements on day 21.

In the TENS group no side effects were reported although 21 of the patients reported the treatment as boring due to the long hospital stay. Another disadvantage may be the economic impact of TENS therapy requiring about 3 weeks hospitalization and more work compared to leech therapy.

Discussion

As long-term therapy for OA of the knee has limited options and treatment carries substantial risk for serious adverse effects of NSAIDs [22, 23] new therapeutic approaches should be considered. Throughout medical history, leech therapy has been extensively used in the treatment of many illnesses involving pain. In the last two decades studies evaluating the effectiveness of leech therapy in the management of OA of the knee, based on modern scientific contexts, have been published. In this randomized controlled trial, patients with OA of the knee who were treated with leech and as control group with TENS therapy, experienced clinically significant improvements in the self-perception of pain for a limited period. The three session application of

leeches improved pain, functional ability and joint stiffness for at least 6 months. In previous studies it was shown that a single leech therapy significantly decreased the pain-related symptoms in patients with knee OA [9, 21, 24] but a single session TENS therapy did not show significant long-term or short-term effects in patients with knee OA [21]. In the present study, we compared a three session leech therapy applied on ambulatory patients with a routinely applied full term TENS therapy which composed of 15 sessions of TENS therapy application on hospitalized patients in 3 weeks. In the evaluation of the main outcome scores on day 21, pain scores in VAS and WOMAC significantly decreased in both groups which was consistent with the literature [9, 11, 15, 21]. The leech therapy and TENS therapy provided similar therapeutic effects in the short term. In a non-randomized pilot study, Michalsen et al. compare leeches with physical therapy in 10 patients with OA of the knee [25]. Only four leeches were used here in a single application. The mean reduction of the VAS (0–10) was 3.9 units at the fourth week of the observation, which is comparable with our result of 3.7 cm after day 21 of observation. The same research group later performed a randomized controlled study with 51 patients and used topical diclofenac as control therapy instead of TENS. As outcome measures, mean of pain, function and stiffness subscores of WOMAC with group comparisons on days 3, 7, 28 and 90 were used. The mean WOMAC pain score decreased from 53.5 ± 13.7 to 19.3 ± 12.2 on day 7 in the leech therapy group. In our study the mean WOMAC pain score decreased on day 21. The finding in the present study is slightly higher than the aforementioned study that may be due to differences in patient selection criteria. All the patients, even those classified as grade IV according to the Kellgren and Lawrence classification system were included in the present study; however, the mean WOMAC pain score on day 180 slightly increased in both therapy groups and it was seen that the therapeutic effects were still continuing in both therapy groups. Therapeutic benefits remained with only slight deterioration throughout the study in both groups. The long-term benefits in the TENS therapy group were slightly more than in the leech therapy group.

The decrease in the hemoglobin and hematocrit levels is expected and may be attributed to loss of blood during leech application and leakage of blood for approximately 24 h after therapy. This situation is consistent with the literature [11].

Leech saliva contains hirudin that irreversibly binds with high specificity to thrombin. Inhibition of the thrombin may be responsible for the small increases in the PT and INR values, which might not be clinically significant. Increase of the ESR may be due to response of the immune system to leech biting and to the contents of leech saliva but we could not retrieve any literature to support these explanations. The higher mean duration of pain history in the leech therapy group was attributed to outliers who had suffered from OA for more than 20 years.

As a weakness of the present study, severity of OA was evaluated solely based on the VAS. It would be more objective to include a classification system such as that of Kellgren and Lawrence. As a potential confounder we should mention the activity status of the patients. Leech subjects were outpatients and advised to decrease activity for some days while TENS subjects were inpatients and advised to limit activity throughout the active treatment; however, even if present this effect would be in favor of the TENS group.

Conclusion

Our study has shown that leech therapy relieves symptoms in patients with OA of the knee and is as effective as TENS therapy in the management of the OA of the knee. Repeated application of the leech therapy increased the long-term therapeutic effect. In the light of our clinical findings which are consistent with previous studies, we believe that leech therapy has the potential of being an additional or alternative therapy for the non-surgical management of OA of the knee. The clinical value of the leech therapy for OA must be tested further with studies involving more patients and compared with different pain management modalities. The ideal interval between leech therapy should also be investigated in further studies.

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Acknowledgements. The authors disclose that no external writing assistance with the manuscript was received. We thank Prof. Dr. Zekeriya Akturk for support and encouragement.

Funding. This study was funded by the Scientific and Technological Research Council of Turkey (TÜBİTAK). Research protocol number: 111S387. The funding source had a role in the design and conducting of the study including statistical analysis.

Compliance with ethical guidelines

Conflict of interests. M. Isik, M. Ugur, R. S. Yakisan, T. Sari and N. Yilmaz declare that they have no conflict of interests.

All studies on humans described in this manuscript were carried out with the approval of the responsible ethics committee and in accordance with national law and the Helsinki Declaration of 1975 (in its current revised form). Informed consent was obtained from all participants in the study.

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