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EVALUATION OF BALNEOLOGICAL TREATMENT ON PAIN, FUNCTION, AND QUALITY OF LIFE IN KNEE OSTEOARTHRITIS: A RANDOMIZED, CONTROLLED, SINGLE-BLINDED TRIAL

DİZ OSTEOARTRİTİNDE BALNEOLOJİK TEDAVİNİN AĞRI, FONKSİYON VE YAŞAM KALİTESİNE ETKİSİNİN DEĞERLENDİRİLMESİ: RANDOMİZE, KONTROLLÜ, TEK KÖR BİR ÇALIŞMA

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ABSTRACT

Objective: The study aimed to evaluate the efficacy of balneological treatment in patients with knee osteoarthritis using clinical scales and to determine its effect on pain, function, and quality of life.

Material and Method: Thirty-two patients with knee osteoarthritis were divided into two randomization groups. The patients in the study group were given a full bath for 20 min in the hydrotherapy pool at 38°C. Then, medical mud was applied to both knees at 43°C. The second group was not given any specific treatment and continued to receive routine treatment (control group). Patients completed the clinical scales with the blinded physician before treatment/day 1 (baseline), at the end of treatment/day 12, and 3 months.

Result: At the end of treatment, WOMAC total, VAS pain, and global assessment scores of patients and physicians were statistically significant improved compared with baseline and third-month controls in the study group. A statistically significant improvement occurred in the 12-d and 3-month Lequesne knee index scores compared with the baseline in the study group. A statistically significant improvement was observed in Nottingham Health Profile pain, emotional reactions, physical move-

ÖZET

Amaç: Bu çalışmada balneolojik tedavinin diz osteoartritli hastalarda etkinliğinin klinik ölçeklerle değerlendirilmesi ve ağrı, fonksiyon ve yaşam kalitesi üzerine etkisinin belirlenmesi amaçlandı.

Gereç ve Yöntem: Diz osteoartriti tanısı almış 32 hasta, randomizasyonla iki gruba ayrıldı. Çalışma grubundaki hastalara, hidroterapi havuzunda 38°C'de 20 dakika tam banyo uygulandı, ardından tıbbi çamur her iki dize de 43°C'de uygulandı. İkinci grup özel bir tedavi almadı ve rutin tedavilerine devam etti (kontrol grubu). Hastalar, tedavi öncesi/1. gün, tedavi sonu/12. gün ve 3. ayda kör bir hekimle klinik ölçekleri tamamladı.

Bulgular: Çalışma grubunda WOMAC toplam, VAS ağrı, hasta ve hekim global değerlendirme skorlarında, başlangıca göre, tedavi sonu ve üçüncü ay kontrollerinde istatistiksel olarak anlamlı bir iyileşme gözlendi. Çalışma grubunda Lequesne Diz İndeksi başlangıca göre 12. gün ve üçüncü ay skorlarında istatistiksel olarak anlamlı bir iyileşme gözlendi. Nottingham Sağlık Profili ağrı, duygusal reaksiyonlar, fiziksel hareket ve enerji skorlarında, çalışma grubunda 12. günde başlangıca istatistiksel olarak anlamlı bir iyileşme gözlendi ve bu anlamlı fark üçüncü ayda da

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ment, and energy scores in the study group on day 12 compared with baseline, and this significant difference continued in the third month for all scores, excluding the energy score. No change was observed in the control group.

Conclusion: The positive effects of balneological treatment on pain, functional status, and quality of life in knee osteoarthritis have been demonstrated.

Keywords: Hydrotherapy, peloidotherapy, knee osteoarthritis, balneotherapy

enerji skoru dışında devam etti. Kontrol grubunda herhangi bir değişiklik gözlemlenmedi.

Sonuç: Balneolojik tedavinin diz osteoartritinde ağrı, fonksiyonel durum ve yaşam kalitesi üzerinde olumlu etkileri gösterilmiştir.

Anahtar Kelimeler: Hidroterapi, peloidoterapi, diz osteoartriti, balneoterapi

INTRODUCTION

Osteoarthritis (OA) is a degenerative disease characterized by progressive cartilage destruction and osteophyte formation, especially in load-bearing joints. The incidence of OA increases with age. OA can affect all joint structures, including the cartilage, bone and synovium, and surrounding muscles (1, 2). OA is the most common form of arthritis and a leading cause of disability in >65 year old individuals (3). Pain is the most common clinical symptom and is associated with joint use. The medial tibiofemoral and patellofemoral joints are the most affected areas in the knee (4).

Definitive treatment for OA are lacking. Evidence-based approaches to the nonsurgical treatment of knee OA include a combination of pharmacological and nonpharmacological treatment methods to relieve pain, improve joint function, and change risk factors for disease progression. Balneological treatment modalities are nonpharmacological treatment methods commonly used to treat OA, because they are well-tolerated and have positive effects on pain relief, stiffness, and function (5).

Balneological treatment utilizes natural resources, such as thermal mineral-rich waters, peloids (muds), and gases, which are administered to patients through bathing, drinking, inhalation treatments, etc. (6). Hydrotherapy is a type of balneological treatment method that uses tap water. Hydrotherapy includes the external application of water using the physical characteristics of water, such as temperature, hydrostatic pressure, buoyancy, and viscosity (7). However, peloid therapy improves blood flow, connective tissue flexibility, and plasma level of β-endorphins. Peloid therapy affects the neuro–immune–endocrine system and has anti-inflammatory properties. Among the most popular treatments within the field of spa therapy, balneotherapy, hydrotherapy, and peloid therapy are usually employed in musculoskeletal conditions (8, 9). Balneological treatment modalities are a clinically effective treatment option for many low-grade inflammations, especially rheumatic conditions, due to their anti-inflammatory, antioxidant, and chondroprotective properties (10).

Our study aimed to evaluate the effects of hydrotherapy and peloid package application in hospital settings on pain, function, and quality of life in patients with knee OA via clinical scales.

MATERIAL and METHODS

Participants and Sample

Patients with knee OA who met our research criteria and were followed up in the Leucomotor System Diseases outpatient clinic of Istanbul University, Istanbul Faculty of Medicine, Department of Medical Ecology and Hydroclimatology, were included in the study. Sample size calculation on powerandsamplesize.com revealed that type 1 error was 5%, type 2 error was 20%, and power (power) was 80%. A minimal sample size of 26 patients was targeted for each group, with a difference of 15 units and a standard deviation of 20 units between the two groups. Sample size was calculated according to Fioravanti et al. (11). The files of 368 patients who applied to the Department of Medical Ecology and Hydroclimatology with complaints of knee pain were scanned and evaluated for suitability (Figure 1). Patients who were followed up in our hospital with knee OA, who met the inclusion criteria, and agreed to participate in the study, were randomly divided into two groups. Each patient was given information about the study.

Inclusion criteria: The study included patients 40–80 years of age, who were diagnosed with knee OA according to American College of Rheumatology criteria after physical examination and radiological evaluation and who scored two or three on the Kellgren and Lawrence scale.

Exclusion criteria: Patients who had decompensated organ failure, malignant disease, systemic inflammatory diseases, infectious diseases; received balneotherapy in the last year; changed their medication in the last two months; and had a history of intramuscular injection, arthroplasty, or prosthetic surgery in the knee joint in the last six months were excluded from the study.

Permissions

The study is a randomized, controlled, single-masked study according to the guidelines of the Declaration of Helsinki. The study protocol was approved by İstanbul Faculty of Medicine Clinical Research Ethics Committee, İstanbul University (Date: 21.08.2020, No: 19).

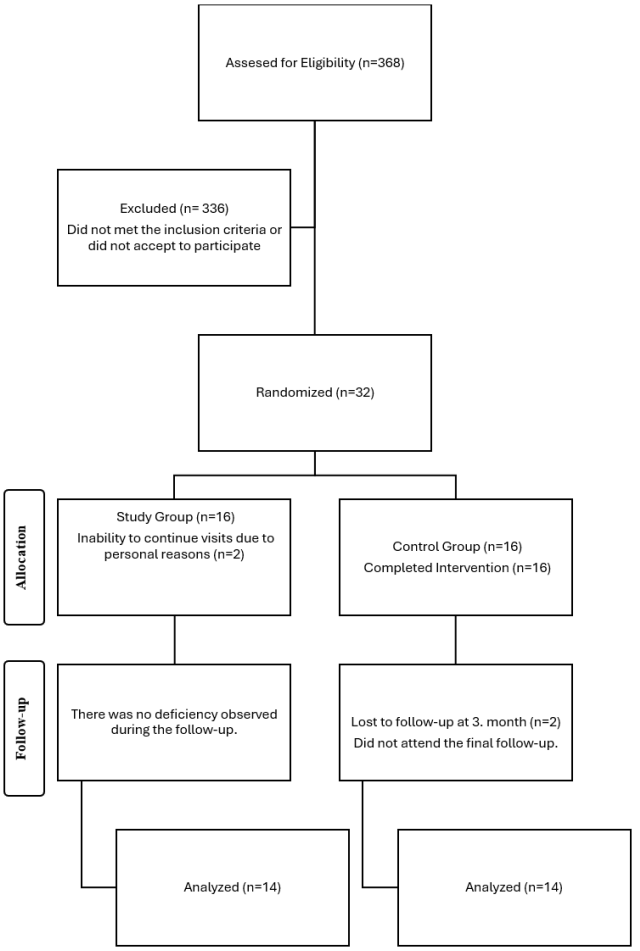

Figure 1: Flow diagram of the patients

Intervention

The patients who accepted to participate were divided into two groups, study and control, by randomization according to the computer-generated random numbers table.

Patients in the study group were given a full bath (up to shoulder level) in a hydrotherapy pool with water temperature 38°C for 20 min, once a day, five days a week, (in total 10 times in two weeks). Following the bath, the peloid was applied directly on the skin of both knee areas with a thickness of approximately 1 cm at 43°C for 20 min (Figure 2). To maintain the application temperature, the top of the peloid was first wrapped with a stretch film and then a towel. The peloid (palomino) used in the application was obtained by mixing natural substances containing 90% magnesite and 10% sepiolite with salt and mineral water. During peloidotherapy, the patients sat comfortably or lay on their backs/prone. In the hydrotherapy pool, patients sat without exercising. The dimensions of the pool were 2.25–1.30 m^2. Pool temperature was normal and was not increased for operation.

Figure 2: Peloid package application

Patients in the control group were not given balneological treatment. They were allowed to take oral paracetamol if needed (maximum 2 g/d).

In both groups, in the beginning, at the end of the treatment (day 12), and in month 3 after treatment, the visual

analog scale (VAS), which is one of the clinical scale forms, pain, general evaluation of the patient, general evaluation of the physician, Western Ontario and McMaster Universities knee index (WOMAC), Lequesne knee index, and Nottingham Health Profile (NHP) forms were filled in by the blind physician. The forms were filled by a physician blinded to the treatments and treatment groups. Blood samples were taken at baseline, after treatment, and 3 months after treatment to detect serum levels of C-reactive protein (CRP). Both groups continued their treatments for comorbidities.

Data collection tools

Patient Global Assessment-VAS: This assessment questions the patient's general well-being. The patient is asked to evaluate the effect of the disease and mark the point that is most appropriate for their condition.

Physician Global Assessment-VAS: The doctor evaluates the patient's general well-being on the same scale.

Pain Assessment-VAS: The patient assesses their pain between "no pain: 0" and "very severe pain: 10" and marks the current situation on this line.

WOMAC: This consists of 24 questions: 5, 2, and 17 in the pain, stiffness, and function sections, respectively.

Lequesne Knee Index: This is an index used in patients with knee OA. It questions pain, stiffness, and functionality. The form consists of 10 questions, including three separate titles.

NHP: This assesses the quality of life.

Laboratory: Blood samples were taken from all patients for the hemogram, erythrocyte sedimentation rate, total cholesterol, low-density lipoprotein, uric acid, creatinine, aspartate aminotransferase, alanine aminotransferase, and CRP at each control, and evaluated at the Clinical Biochemistry Laboratory of Istanbul University Faculty of Medicine on the same day.

Blinding: The clinical evaluations of the patients were made by a physician who was blinded to treatment and groups. Another physician who was blinded to treatment and groups was responsible for treatments. A biostatistician who was blinded to the study analyzed the results.

Statistical analysis

Independent sample t-test and Mann–Whitney U test were used to analyze continuous independent data. The Wilcoxon test was used to analyze dependent continuous data. The chi-square test or Fisher's exact test was used to analyze categorical independent data. SPSS program version 27.0 (IBM SPSS Corp., Armonk, NY, USA) was used for analysis.

RESULTS

Flow diagram

Because our patient population mainly consisted of older patients, 32 patients (16 each in the study and control groups) were studied study due to restrictions during the coronavirus disease 2019 (COVID-19) pandemic. The study was completed with 28 patients, 14 in the study group and 14 in the control group. In total, 11 patients received 10 sessions, two patients received 9 sessions, and one patient received 8 sessions. During treatment, no side effects were observed.

Sociodemographic data

There was no difference between the study and control groups in terms of age, body mass index, employment status, smoking and alcohol use, and comorbidity. The mean age of patients was 61.7±6.8 years in the study group and 56.6±9.7 years in the control group. The rate of female patients in the control group was significantly higher than the rate of male patients in the study group (Table 1).

Clinical evaluation criteria results

Patient VAS global assessment, physician VAS global assessment, and VAS Pain scores in the study group significantly decreased on day 12 and month 3 after treatment, compared with baseline ($p<0.005$). By contrast, VAS scores in the control group did not change significantly on day 12 and month 3 after treatment, compared with baseline ($p=0.202$) (Table 2).

In the study group, on day 12, third-month WOMAC total and Lequesne knee index score decreased significantly ($p<0.05$) compared with pretreatment. In the control group, WOMAC total and Lequesne knee index score did not significantly change compared with pretreatment on day 12 and month 3 (Table 3) (Figure 1).

In the study and control groups, CRP levels were 7.7±12.3 and 2.6±1.9 mg/L before treatment, respectively. After 3 months of treatment, CRP levels were 4.3±2.9 and 3.3±3.3 mg/L in the study and control groups, respectively. There was no significant difference in CRP value change on day 12 and month 3 in the study and control groups.

In the study group, day-12 and month-3 NHP pain score, Nottingham emotional reaction score, and Nottingham physical activity score decreased significantly ($p<0.05$) compared with pretreatment. In the study group, day-12 and month-3 Nottingham sleep score, Nottingham social isolation score, and NHP part 2 score did not change significantly ($p>0.05$) compared with pretreatment level. The Nottingham energy score on day 12 decreased significantly ($p<0.05$) in the study group, whereas that on month 3 did not change significantly ($p>0.05$) in the study group compared with pretreatment. In the control group, day-12 and month-3 Nottingham scores did not

Table 1: Comparison of the sociodemographic data of the groups

		Study group (n:16)	Control group (n:16)	p
		Mean±SD (Median) or N (%)	Mean±SD (Median) or N (%)	
Age, years		61.7±6.8 (61.5)	56.6±9.7	0.098 [t]
Sex	Female	10 (62.5)	15 (93.8)	**0.033** [X²]
	Male	6 (37.5)	1 (6.2)	
BMI, kg/m²		32.3±4.3	30.6±5.5	0.331 [t]
Working Status	Not working	8 (%50.0)	12 (75.0)	0.144 [X²]
	Working	3 (18.8)	3 (18.8)	
	Retired	5 (31.3)	1 (6.3)	
Smoking	(-)	14 (87.5)	11 (68.8)	0.200 [X²]
	(+)	2 (12.5)	5 (31.3)	
Alcohol Use	(-)	16 (100)	13 (81.3)	0.226 [X²]
	(+)	0 (0)	3 (18.8)	
Comorbidity	(-)	5 (31.3)	10 (62.5)	0.077 [X²]
	(+)	11 (68.7)	6 (37.5)	
Hypertension		8 (%50.0)	3 (18.8)	0.063 [X²]
Hypothyroidism		5 (31.3)	2 (12.5)	0.200 [X²]
Hypercholesterolemia		2 (12.5)	1 (6.3)	1.000 [X²]
DM		4 (25.0)	3 (18.8)	0.669 [X²]
Heart disease		1 (6.3)	0 (0)	1.000 [X²]
Asthma		2 (12.5)	1 (6.3)	1.000 [X²]
Depression		2 (12.5)	0 (0)	0.484 [X²]

[X²]: Pearson Ki-Square, [t]:Student's t-test, SD: Standard deviation, BMI: Body mass index, N: Count, DM: Diabetes Mellitus

change significantly (p>0.05) compared with pretreatment (Table 4).

The changes in the parameters evaluated in the study and control groups in month 3 are shown in Figure 2. A decrease was observed in the study group in all parameters. Although there was an increase in some parameters in the control group, the rate in the parameters with a decrease was higher in the study group.

DISCUSSION

Nonpharmacological interventions form the basis of OA management. Balneological treatments-one of the nonpharmacological treatments-have been a treatment option for knee OA for years (12). Balneotherapy can be a good alternative for patients who cannot tolerate pharmacological treatments or as an adjunct to pharmacological treatment for knee OA (13). Balneotherapy and physical therapy were more effective than physical therapy alone in patients with knee OA (14).

In a study comparing the effectiveness of balneotherapy with pharmacological treatment in patients with advanced knee OA, balneotherapy was superior in reducing pain and improving functional capacity in the short and medium term. Consistently, our study found the superiority of the balneological treatment group compared with the control group on day 12 and at the 3-month follow-up (15).

Another study showed that balneological treatment could be an alternative option without medication; consecutive and intermittent balneological treatment regimens were effective in patients with knee OA (16). In a study evaluating the duration of thermal spring treatment, group 1 received treatment for three weeks, and group 2 received treatment for two weeks. Patients were evaluated using VAS, WOMAC, and NHP before, after, and at 1-month follow-up. Measurements showed significant improvements in both groups compared with baseline measurements, except for the social isolation subgroup of the Nottingham Health Profile, which is consistent with our study (17). In our study, statistically significant improvements were

Table 2: General wellness in the study and control groups at the beginning, end of treatment, and month 3

	Study group (n:14) Mean±SD (Median)	Control group (n:14) Mean±SD (Median)	p
VAS global patient assessment			
Before treatment	49.4±17.4 (50.0)	52.6±20.0 (50.0)	0.890 [m]
Day 12	39.9±25.1 (47.5)	50.0±24.9 (51.0)	0.114 [m]
Month 3	32.1±24.9 (22.0)	43.9±20.6 (50.0)	0.227 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.028**[w] 19.28% ↓ Cohen d:0.43	0.780[w] 4.88% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.013**[w] 35.03% ↓ Cohen d:0.80	0.202[w] 16.43%↓	
VAS pain			
Before treatment	52.8±16.8 (50.0)	48.3±23.1 (50.0)	0.908 [m]
Day 12	41.3±21.8 (44.0)	51.8±25.4 (51.0)	0.116 [m]
Month 3	29.5± 24.9 (28.0)	43.4±21.1 (50.0)	0.195 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.037**[w] 21.83% ↓ Cohen d:0.59	0.409[w] 7.24%↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.010**[w] 44.21% ↓ Cohen d:1.09	0.443[w] 10.26% ↓	
VAS global physician assessment			
Before treatment	51.5±15.5 (50.0)	50.8±20.7 (50.0)	0.938 [m]
Day 12	39.2±22.9 (42.5)	49.8±24.0 (51.0)	0.065 [m]
Month 3	31.2±24.3 (25.0)	43.1±21.0 (50.0)	0.257 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.022**[w] 23.86% ↓ Cohen d:0.62	0.916[w] 1.85% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.01**[w] 39.51% ↓ Cohen d:0.99	0.161[w] 14.99% ↓	

[m] Mann–Whitney U test / [w] Wilcoxon test, SD: Standard deviation, VAS: Visual analog scale

observed in the study group regarding VAS pain and patient and physician global assessment scores compared with baseline at the end of treatment and 3-month follow-up. A statistically significant reduction was observed in WOMAC subgroups and WOMAC-total scores, except for stiffness, in the study group at the 3-month follow-up compared with baseline. Significant improvement was observed in the study group after treatment compared with before treatment in NHP, except for the social isolation and sleep subgroups.

In a meta-analysis evaluating the effects of balneotherapy using WOMAC scores, balneotherapy was found to be clinically effective in relieving pain and stiffness and improving functional status compared with controls, similar to our study (18). Consistently, a meta-demonstrated the beneficial effects of balneotherapy and mud therapy on pain, stiffness, and functional status in patients with knee OA (19). In a meta-analysis evaluating thermal modalities, such as balneotherapy, mud therapy, and thermal spring treatment, thermal modalities were effective in the short-term prognosis of patients with OA (20). The effects of balneotherapy are probably related to the temperature and physicochemical and microbial properties of natural mineral water. This type of therapy triggers a set of biological, physiological, and perceptional responses involved in a neuroendocrine reaction that increases serum levels of opioid peptides, such as endorphins, and changes the circulating levels of prostaglandins, leukotrienes, and metalloproteinases (21).

Studies on the long-term clinical efficacy of thermal spring treatment in knee OA are lacking. In a study to determine the clinical efficacy of thermal spring treat-

Table 3: Osteoarthritis assessment measurements at baseline, end of treatment, and month 3 in study and control groups

	Study group (n:14) Mean±SD (Median)	Control group (n:14) Mean±SD (Median)	p
WOMAC Total			
Before treatment	41.8±17.0 (46.0)	42.3±18.3 (33.0)	0.910 [m]
Day 12	35.1±21.3 (35.0)	42.1±20.3 (31.5)	0.360 [m]
Month 3	30.9±22.9 (31.0)	39.1±13.7 (29.5)	0.254 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.041**[w] 15.95% ↓ Cohen d:0.34	0.938[w] 0.3% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.039**[w] 26.04% ↓ Cohen d:0.54	0.969[w] 7.35% ↓	
Lequesne Knee Index			
Before treatment	11.3±3.5 (11.8)	11.4 ±4.6 (12.3)	0.636 [m]
Day 12	8.2±3.5 (9.0)	11.3±4.1 (11.5)	**0.021**[m] Cohen d:0.81
Month 3	7.9±4.7 (9.5)	10.7±2.8 (10.5)	0.187 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.002**[w] 27.3% ↓ Cohen d:0.88	0.959[w] 0.82% ↓	
Before treatment and month 3 intragroup exchange p-value and percent change	**0.003**[w] 29.57% ↓ Cohen d:0.82	0.729[w] 6.38% ↓	

[m] Mann–Whitney U test/[w] Wilcoxon test, SD: Standard deviation, WOMAC: Western Ontario and McMaster Universities multifunctional index

ment in the long-term prognosis of patients with bilateral knee OA, the treatment group received a combination of peloidotherapy and balneotherapy. The control group continued routine medical treatment. Follow-up was performed two weeks after treatment and at 3, 6, 9, and 12 months. VAS and WOMAC scores, which were also used in our study as primary outcome measures, were used. Consistent with our study, significant improvements were observed in the VAS and WOMAC scores of the treatment group, which continued at the 3-month follow-up. However, no significant changes were observed in the control group. Unlike our study, longer-term follow-up was performed, and the significant difference between the two groups continued until month 9 (22).

Table 4: Quality-of-life measurements at baseline, end of treatment, and at month 3 in study and control groups

Nottingham health profile	Study group (n:14)		Control group (n:14)		p
	Mean ± Sd	Median	Mean ± Sd	Median	
Pain					
Before treatment	67.10±31.17 16	74.15	58.73±24.4	54.41 16	0.34 [m]
Day 12	49.33±29.11 14	53.79	57.57±27.9 16	59.4	0.36 [m]
Month 3	45.25±28.15 14	48.91	59.74±16.77	59.4 14	0.25 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.01**[w] 26.48% ↓ Cohen d:0.59		0.78[w] 1.98% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.02**[w] 32.56% ↓ Cohen d:0.73		0.58[w] 1.72% ↑		

Table 4: Continue

Emotional reactions					
Before treatment	48.49±33.21	56.28	47.94±28.15	48.87	0.84 [m]
Day 12	30.17±32.76	13.95	41.81±27.44	40.88	0.23 [m]
Month 3	35.65±31.62	29.54	54.42±37.44	60.07	0.16 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.02**[w] 37.78% ↓ Cohen d:0.55		0.43[w] 12.79% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.04**[w] 26.46% ↓ Cohen d:0.39		0.48[w] 13.53% ↑		
Sleep					
Before treatment	36.27±26.52	39.89	42.30±19.09	43.36	0.45 [m]
Day 12	27.97±25.16	22.47	48.33±29.7	49.65	0.07 [m]
Month 3	31.94±24.81	28.67	38.66±23.75	43.36	0.39 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	0.14[w] 22.88% ↓		0.67[w] 14.25% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	0.41[w] 11.94% ↓		0.64[w] 8.63% ↓		
Physical movement					
Before treatment	49.48±15.5	53.4	43.54±16.75	41.61	0.19 [m]
Day 12	43.51±18.1	44.17	47.34±24.4	54.96	0.63 [m]
Month 3	34.65±18.7	33.53	47.94±20.2	43.15	0.11 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.03**[w] 12.07% ↓ Cohen d:0.35		0.82[w] 8.73% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	**0.001**[w] 29.97% ↓ Cohen d:0.86		0.36[w] 10.11% ↑		
Energy scores					
Before treatment	67.10±38.52	76	65.50±40.71	81.6	1 [m]
Day 12	44.40±38.96	36.8	62.50±39.52	63.2	0.19 [m]
Month 3	61.17±32.97	60.8	66.00±37.63	69.6	0.5 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	**0.02**[w] 33.83% ↓ Cohen d:0.58		0.55[w] 4.58% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	0.53[w] 8.84% ↓		0.58[w] 0.76% ↑		
Social isolation					
Before treatment	32.65±41.39	7.99	41.44±33.71	41.76	0.4 [m]
Day 12	29.00±36.57	7.99	35.59±36.16	22.01	0.45 [m]
Month 3	19.05±29.54	0	41.85±41.89	41.26	0.16 [m]

Table 4: Continue

Social isolation					
Before treatment and day 12 intragroup exchange p-value and percent change	0.72[w] 11.18% ↓		0.4[w] 14.12% ↓		
Before treatment and month 3 intragroup exchange p-value and percent change	0.34[w] 41.66% ↓		0.53[w] 0.99% ↑		
Nottingham health profile part 2					
Before treatment	1.9±2.1	1.5	1.4±1.4	1.5	0.627 [m]
Day 12	2.1±2.2	1.5	2.5±2.5	3.0	0.830 [m]
Month 3	0.9±1.8	0.0	1.6±1.4	2.0	0.109 [m]
Before treatment and day 12 intragroup exchange p-value and percent change	0.573[w] 10.60% ↑		0.106[w] 73.91% ↑		
Before treatment and month 3 intragroup exchange p-value and percent change	0.37[w] 52.36% ↑		0.491[w] 14.29% ↓		

[m]: Mann–Whitney U Test / [w]: Wilcoxon Test, SD: Standard deviation

In another study involving long-term follow-up in patients with OA, group A received peloidotherapy and balneotherapy in three cycles for one year. By contrast, group B did not receive additional treatment. The mean value reported in VAS pain assessments was significantly lower in group A than group B. After treatment, the mean scores of the Lequesne knee index in group A were lower than those of patients in group B, who did not receive therapy (23). Our study group observed statistically significant improvement in VAS pain and patient and physician global assessment scores at the end of treatment and at 3-month follow-up compared with baseline. No change was observed in the control group who did not receive treatment.

Similarly, in our treatment group (hydrotherapy + peloidotherapy), a significant decrease in the Lequesne knee index score was observed on day 12 and month 3 compared with before treatment. In the control group who did not receive treatment, there was no significant change in the Lequesne knee index score on day 12 and month 3 compared with before treatment. The decrease in the Lequesne knee index score on day 12 and month 3 was significantly higher in the study group than the control group.

In patients with knee OA, chronic pain and functional impairment significantly decrease quality of life (related to difficulty in performing daily life activities). Therefore, a systematic meta-analysis was conducted to evaluate the effects of balneotherapy and spa treatment on the quality of life of patients with knee OA. Balneotherapy and spa treatment significantly improved the quality of life of patients with knee OA, as well as reduced medication consumption and improved algofunctional indices (5). In our study group, statistically significant improvement was observed in NHP pain, emotional reactions, physical movement, and energy scores on day 12 compared with baseline, and this significant difference continued, except for the energy score in month 3. In our control group, there was no statistically significant change in scores on day 12 and month 3 compared with baseline. Our study results show that balneological treatments improve the quality of life in patients with knee OA.

Recent studies have shown that some biomarkers may be useful in predicting OA prognosis and evaluating therapeutic response. After balneological treatment, levels of proinflammatory molecules, such as tumor necrosis factor-alpha, interleukin-1 beta, prostaglandin E2, leukotriene B4, and CRP, decreased and levels of anti-inflammatory molecules, such as insulin-like growth factor 1, increased in the serum (24). Another study investigated serum human glycoprotein of cartilage (YKL-40) and hsCRP levels in patients with knee OA after mud therapy. Mean serum YKL-40 and hsCRP levels were higher in patients than healthy controls. However, no significant change was observed in hsCRP levels throughout follow-up (25). The findings show that an anti-inflammatory effect may mediate the clinical benefits of balneotherapy in patients with musculoskeletal disease. A decrease in circulating interleukin-6 levels and improvements in pain mitigation and patient functionality were observed. Circulating levels of CRP were observed after balneotherapy, with no statistically significant difference (26). In our study, no statistically significant changes were observed in CRP values in the study and control groups during follow-up.

The main limitation of this study was that we could not reach target sample size due to COVID. Another limitation was the short duration of follow-up after treatment. However, our study has several strengths. It was a prospective study with a control group during the pandemic.

CONCLUSION

Our study found that balneological treatment effectively improved pain, function, and quality of life in patients with knee OA and persisted over at least 3 months. Our results indicate benefits in all the dimensions assessed produced in the patients who underwent balneotherapy intervention both in response to the intervention and concerning control patients. Our outpatient treatment approach allowed patients to receive treatment for <1 h per day without disrupting their daily routines or requiring a change in environment. This approach enabled us to observe the effectiveness of balneological treatment in isolation, without the confounding effects of other factors, such as rest, vacation, and climatic factors. Further investigations must broaden the application of this therapeutic intervention in patients with OA, elucidate its mechanism of action, and delineate its clinical outcomes with greater clarity.

Ethics Committee Approval: The study has ethical approval from the İstanbul Faculty of Medicine Clinical Research Ethics Committee, İstanbul University (Date: 21.08.2020, No: 19)

Informed Consent: All patients signed the informed consent form.

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REFERENCES

1. Robinson WH, Lepus CM, Wang Q, Raghu H, Mao R, Lindstrom TM, et al. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. Nat Rev Rheumatol 2016;12(10):580-92. [CrossRef]
2. Hall M, Van Der Esch M, Hinman RS, Peat G, De Zwart A, Quicke JG, et al. How does hip osteoarthritis differ from knee osteoarthritis? Osteoarthritis Cartilage 2022;30(1):32-41. [CrossRef]
3. Hawker GA, King LK. The Burden of Osteoarthritis in Older Adults. Clin Geriatr Med 2022;38(2):181-92. [CrossRef]
4. Abhishek A, Doherty M. Diagnosis and clinical presentation of osteoarthritis. Rheum Dis Clin North Am 2013;39(1):45-66. [CrossRef]
5. Antonelli M, Donelli D, Fioravanti A. Effects of balneotherapy and spa therapy on quality of life of patients with knee osteoarthritis: a systematic review and meta-analysis. Rheumatol Int 2018;38(10):1807-24. [CrossRef]
6. Kocyigit BF. Spa therapy: a geriatric perspective. AAEE 2023;2(1):45-8. [CrossRef]
7. Gálvez I, Torres-Piles S, Ortega-Rincón E. Balneotherapy, Immune System, and Stress Response: A Hormetic Strategy? Int J Mol Sci 2018;19(6):1687. [CrossRef]
8. Tognolo L, Coraci D, Fioravanti A, Tenti S, Scanu A, Magro G, et al. Clinical Impact of Balneotherapy and Therapeutic Exercise in Rheumatic Diseases: A Lexical Analysis and Scoping Review. Applied Sciences 2022;12(15):7379. [CrossRef]
9. Maccarone MC, Scanu A, Coraci D, Masiero S. The Potential Role of Spa Therapy in Managing Frailty in Rheumatic Patients: A Scoping Review. Healthcare 2023;11(13):1899. [CrossRef]
10. Gálvez I, Fioravanti A, Ortega E. Spa therapy and peripheral serotonin and dopamine function: a systematic review. Int J Biometeorol 2024;68(1):153-61. [CrossRef]
11. Fioravanti A, Giannitti C, Bellisai B, Iacoponi F, Galeazzi M. Efficacy of balneotherapy on pain, function and quality of life in patients with osteoarthritis of the knee. Int J Biometeorol 2011;56(4):583-90. [CrossRef]
12. Alkan H, Ardıç F. Güncel Kılavuzlar Eşliğinde Osteoartritte Non-Farmakolojik Tedavi, In: Hepgüler AS, Osteoartrit. 1. Baskı. Ankara: Türkiye Klinikleri; 2020. p.70-7.
13. Fioravanti A, Iacoponi F, Bellisai B, Cantarini L, Galeazzi M. Short-and long-term effects of spa therapy in knee osteoarthritis. Am J Phys Med Rehabil 2010;89(2):125-32. [CrossRef]
14. Dilekçi E, Özkuk K, Kaki B. Effect of balneotherapy on pain and fatigue in elderly with knee osteoarthritis receiving physical therapy: a randomized trial. Int J Biometeorol 2019;63(12):1555-68. [CrossRef]
15. Karagülle M, Karagülle MZ, Karagülle O, Dönmez A, Turan M. A 10-day course of SPA therapy is beneficial for people with severe knee osteoarthritis. Clin Rheumatol 2007;26(12):2063-71. [CrossRef]
16. Özkuk K, Gürdal H, Karagülle M, Barut Y, Eröksüz R, Karagülle MZ. Balneological outpatient treatment for patients with knee osteoarthritis; an effective non-drug therapy option in daily routine? Int J Biometeorol 2017;61(4):719-28. [CrossRef]
17. Özkuk K, Uysal B. Is the duration of spa cure treatment important in knee osteoarthritis? A randomized controlled study. Complement Med Res 2019;26(4):258-64. [CrossRef]
18. Matsumoto H, Hagino H, Hayashi K, Ideno Y, Wada T, Ogata T, et al. The effect of balneotherapy on pain relief, stiffness, and physical function in patients with osteoarthritis of the knee: a meta-analysis. Clin Rheumatol 2017;36(8):1839-47. [CrossRef]
19. Raza HMA, Krutulyte G, Rimdeikiene I, Savickas R. Efficacy of balneotherapy and mud therapy in patients with knee osteoarthritis: a systematic literature review. Akt Rheumatol 2021;46(02):187-97. [CrossRef]
20. D'Angelo D, Coclite D, Napoletano A, Fauci AJ, Latina R, Gianola S, et al. The efficacy of balneotherapy, mud therapy and spa therapy in patients with osteoarthritis: an overview of reviews. Int J Biometeorol 2021;65(7):1255-71. [CrossRef]

21. Cheleschi S, Tenti S, Seccafico I, Gálvez I, Fioravanti A, Ortega E. Balneotherapy year in review 2021: focus on the mechanisms of action of balneotherapy in rheumatic diseases. Environ Sci Pollut Res Int 2022;29(6):8054-73. [CrossRef]
22. Fioravanti A, Bacaro G, Giannitti C, Tenti S, Cheleschi S, Pascarelli N, et al. One-year follow-up of mud-bath therapy in patients with bilateral knee osteoarthritis: a randomized, single-blind controlled trial. Int J Biometeorol 2015;59(9):1333-43. [CrossRef]
23. Fraioli A, Serio A, Mennuni G, Ceccarelli F, Petraccia L, Fontana M, et al. A study on the efficacy of treatment with mud packs and baths with Sillene mineral water (Chianciano Spa Italy) in patients suffering from knee osteoarthritis. Rheumatol Int 2011;31(10):1333-40. [CrossRef]
24. Maccarone MC MG, Solimene U, Scanu A, Masiero S. From in vitro research to real life studies: an extensive narrative review of the effects of balneotherapy on human immune response. Sport Sci Health 2021;17(4):817-35. [CrossRef]
25. Güngen G, Ardic F, Fındıkoğlu G, Rota S. The effect of mud pack therapy on serum YKL-40 and hsCRP levels in patients with knee osteoarthritis. R Rheumatol Int 2012;32(5):1235-44. [CrossRef]
26. Silva J, Martins J, Nicomédio C, Gonçalves C, Palito C, Gonçalves R, et al. A Novel Approach to Assess Balneotherapy Effects on Musculoskeletal Diseases—An Open Interventional Trial Combining Physiological Indicators, Biomarkers, and Patients' Health Perception. Geriatrics 2023;8(3):55. [CrossRef]