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ORIGINAL ARTICLE

A 10-day course of SPA therapy is beneficial for people with severe knee osteoarthritis

A 24-week randomised, controlled pilot study

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Abstract The objective of this study was to test if spa therapy can play a role in the management of severe knee osteoarthritis (OA). Twenty patients with radiologically and clinically severe knee OA were randomly assigned into spa and drug therapy groups. Spa group (n=10) traveled to a spa town and stayed at a hotel for a 10-day spa therapy course. They followed a balneotherapy regimen including thermal pool baths at 37°C for 20 min two times daily. Drug therapy group (n=10) stayed at home and followed their individually prescribed drug therapy (NSAIDs and paracetamol). Patients were assessed at baseline (week 0), after spa therapy at 2 weeks (week 2) and during follow-up period at 12 (week 12) and 24 (week 24) weeks by a blinded investigator. Patients assessed with Lequesne algofunctional index (LAFI), pain (visual analogue scale, VAS), patient's and investigator's global evaluation (VAS), ten-stairs stepping up and down time, 15 m walking time and three times squatting up and down time. Significant improvement in pain and LAFI scores were found at week 2, week 12 and week 24 in the spa therapy group compared to baseline. Comparing the two group differences, spa therapy was superior to drug therapy in pain reduction and in physician's global assessment at all time points. This superiority was also found in LAFI scores and patients' global assessments at week 12 and week 24. A 10-day course of spa therapy may be beneficial in short- and medium-term up to 24 weeks by reducing pain and improving functional status and overall well-being in patients with severe knee OA and may be considered as an effective therapeutic tool for such patients in countries like Turkey where it is widely available and (at least partly) reimbursed.

Keywords Balneotherapy · Drug therapy · Knee osteoarthritis · Lequesne algofunctional index · Pain · Spa therapy

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Introduction

Osteoarthritis (OA) is the most common form of arthritis, and the knee is the most commonly affected joint, with more than four million new patient visits annually in the US for knee pain [1]. As estimation, 10% of people older than 55 years have disabling knee symptoms, and nearly 25% of them are severely disabled [2]. According to WHO report on global burden of disease, knee OA is likely to be one of the most important global causes of disability in the society; fourth most important in women and eighth most important in men [3]. There is no known curative therapy for OA; a variety of pharmacologic and non-pharmacologic modalities are recommended aiming to reduce pain, maintain and improve joint mobility and limit functional impairment [4]. Spa therapy was recently included among the non-pharmacologic interventions selected for assessment by EULAR Task Force aimed to reflect an evidence-based approach to key clinical questions concerning the treatment of knee OA [5]. Turkey has many thermal springs and spas where treatments are applied with a predominantly empiric and intuitive character [6]. This tradition of spa therapy

involves residential stay at a spa resort and is very popular with patients who have musculoskeletal problems including knee OA [7, 8]. Balneotherapy (thermal mineral water immersion) is the main intervention of usual spa therapy protocols in Turkish spas [6, 7]. In traditional way, balneotherapy is often given daily, two thermal water baths at temperatures 36–38°C up to 40°C during a spa therapy course which lasts usually 10 to 15 days. Mostly, balneotherapy is the sole intervention, but in some spas, mud applications, massage and hamam (Turkish bath) are combined with balneotherapy [6, 7].

The definition and classification of spa water (thermal mineral water) are based on chemical composition and temperature. The total of mineral content of a mineral water should exceed 1 g/L. The adjective "thermal" requires that the temperature of the natural spring or welled water is at least 20°C. Mineral water is classified based on the concentrations of the cations of Na, Ca, and Mg and the anions of SO_4, Cl and HCO_3 exceeding 20% milival. Some elements such as sulfur, fluoride, bromine and iodine require contents of 1 mg/L or more and radon radioactivity over 666 Bq/L and NaCl concentration over 1.5% [9].

Spa therapy is also used for treating painful conditions in southern and central countries of Europe where it is a part of conventional medical care and totally or partly reimbursed [10, 11]. In Japan, spas are a part of routine daily life and intensively visited by local people for health purposes [12–14]. The Dead Sea area is a unique health resort in Israel where many spa hotels and clinics are located and host local as well as foreign patients with rheumatic diseases seeking relief of their symptoms [15–17]. There is increasing and encouraging evidence—although inconclusive yet—that spa therapy and balneotherapy may be effective for treating a variety of rheumatic diseases, i.e. ankylosing spondylitis [18–21], rheumatoid arthritis [22, 23], fibromyalgia [24, 25] and low back pain [26, 27].

We have recently reviewed published Turkish studies on the efficacy of spa therapy for rheumatic conditions. Nearly all of these publications reported positive effects. Because of the heterogeneity in design and outcome measures, lack of randomisation and blinding and possibly publication bias (to publish trials with positive results), it was impossible to reach a definitive conclusion [8]. So far, two systematic reviews on balneotherapy for osteoarthritis [28] and knee OA [29] have been published. The authors of the knee OA review concluded that balneotherapy in the form of combination baths have short-term benefits for pain relief, function improvement and quality of life in knee OA [29]. But their common conclusion is that more randomised controlled studies are needed for stronger evidence. We have published uncontrolled or non-randomised controlled studies reporting beneficial effects of spa therapy on patients with knee osteoarthritis [30, 31]. We planned a pilot randomised controlled trial as a model of a further full study to perform evaluating the effects of 10-day spa therapy in patients with severe knee osteoarthritis.

Materials and methods

Patients At the beginning of the study, 100 patients who had the diagnosis of knee OA according to the American College of Rheumatology ACR criteria [32] were recruited from Outpatient Clinic for Rheumatic Diseases at the Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty. The patient selection for the study is based on the radiological manifestations of their knee joints (at least in one side) grade 2+ according to Kellgren and Lawrence radiological grading system for osteoarthritis (grade 0=none, grade 1=doubtful, grade 2=minimal, grade 3=moderate and grade 4=severe) [17] and algofunctional status scores 8+, assessed using LAFI for knee osteoarthritis (minor=1–4, moderate=5–7, severe=8–10, very severe=11–13, extremely severe=>14) [33, 34], aiming to include the patients with radiologically and functionally severe knee OA. The selected patients had not taken balneotherapy in the previous year and did not have any changes in their pharmacological therapy within 2 months and had no injections in knee joints within 6 months before the study. They did not have any other condition that may affect the study results, like cancer, heart or lung disease. Thirty-seven patients with symptomatic knee OA fulfilled the selection criteria, 17 of them refused to participate, and finally, 20 patients gave informed consent and were enrolled in the study. These patients were randomised using a computer-generated random number list and allocated to either spa therapy or drug therapy (control) arms of the study (10/10) by an investigator who was not informed which number belongs to which group. Another investigator managed to form the study groups accordingly. A written informed consent was obtained from all patients according to the Declaration of Helsinki [35]. The design of the trial planned in accordance with the currently applied good clinical practice standards in Turkey [36]. The patients only paid for the traveling costs and stayed at the spa hotel full board free. Patients were not blinded because of the character of the active and control treatment modalities. The health and administrative personnel of the spa resort were not included in the study; they followed the study protocol. It was not possible to blind them because of the nature of the provided spa therapy. The patients who were allocated to the drug therapy group did not have to pay any treatment costs, including physician visits and drugs, during the study period. Patients' preference of the type of therapy was also noted.

Interventions The patients in the spa group traveled together to a spa town, Alaçatı near Izmir, stayed at a seaside resort hotel (Süzer Paradise) with thermal facility and spent 10 days there (11–20 December 2002). They followed a traditional spa therapy regimen consisting of two thermal water baths (at 38±1°C for 30 min) everyday, one in the morning and one in the afternoon. If they wished, the patients also could take a therapeutic massage. Massage sessions have been controlled and recorded by the spa physician. After spa treatments either in the morning or in the afternoon, patients might just rest and relax or take part in free outdoor activities such as walking or spending time in the seashore, enjoying the convenient spa environment with temperate marine climate in wintertime during the study period. These factors were uncontrolled providing the holiday atmosphere of spa therapy. Any medication including pain killers and NSAIDs is not prescribed. But patients were told to feel free to continue the NSAIDS and pain medication from home whenever they felt it necessary and were asked to record this use. The patients in the control group stayed in their hometown of Istanbul and continued their pharmacological therapy (NSAIDs and paracetamol) as individually prescribed. After the spa therapy period, the spa group patients returned home. The patients from both groups have been instructed to continue their pharmacologic therapy *whenever they felt it necessary.* Basic difference between the treatment group and the control group was the spa therapy period. The local natural thermal mineral water which is used in balneotherapy at the spa facility contains predominantly sodium chloride (approximately 3% NaCl) and is classified as brine (Table 1).

Table 1 The ingredients of spa water used in the study

Ingredients	Spa water (mg/L)
pH	6.78
Conductivity (EC)	55000 µS/cm
NH_4^+	0.624 mg/L
Na^+	11495.000 mg/L
K^+	347.990 mg/L
Ca^{2+}	1458.912 mg/L
Mg^{2+}	845.988 mg/L
Fe^{2+}	0.340 mg/L
Al^{3+}	0.920 mg/L
Mn^{2+}	0.000 mg/L
Zn^{2+}	0.020 mg/L
Cl^-	20662.400 mg/L
I^-	0.020 mg/L
Br^-	15.000 mg/L
F^-	1.910 mg/L
SO_4^{2-}	3100.000 mg/L
NO_3^-	1.200 mg/L
NO_2^-	0.000 mg/L
HPO_4^{2-}	1.484 mg/L
CO_3^{2-}	0.000 mg/L
HCO_3^-	292.800 mg/L
S^{2-}	0.028 mg/L
HBO_2	18.254 mg/L
H_2SiO_3	30.281 mg/L
CO_2	52.800 mg/L
Total mineral	38273.171 mg/L

Assessments All patients were assessed at baseline (week 0) after spa therapy at 2 weeks (week 2) and during follow-up period at 12 weeks (week 12) and 24 weeks (week 24) in the outpatient clinic. All assessments were performed by the same investigator who was blinded to which study arms the patients belong. Blinding of the investigator was achieved by assessing both groups of patients at the same time point and at the same place (at the department polyclinic). The patients were also firmly instructed, being aware that the investor did not and must not know which group they belonged.

Outcome measures LAFI for knee osteoarthritis, pain (visual analogue scale, VAS), patient's and physician's global assessment of disease activity and a group of functional measurements, the ten-stairs stepping up and down time, 15 m walking time and the three times squatting up and down time were used as outcome measures and recorded in seconds. LAFI directly aggregates symptoms (pain, discomfort or difficulty) and function which are not graded separately. The index is an interview which includes three sections, with a total of ten questions and takes few minutes to score answers correctly and to count total scores. The total score is interpreted as follows; 1–4 minor, 5–7 moderate, 8–10 severe, 11–13 very severe, more than 14 extremely severe [37]. Pain, patient's and physician's global assessments were evaluated with 10-cm VAS where 0 indicates no pain or best, whereas ten intractable pain or worst.

Statistical analysis Due to the distribution characteristics, the data were evaluated using non-parametric statistical methods. Comparison of several paired groups (baseline and follow-up measurements) was performed using Friedman's test. Study groups were compared using Mann–Whitney *U* test. Only the baseline characteristics of the study groups were compared using paired *t* test, as related data distributed normally. All patient data were included in the analyses in an intent-to-treat fashion. Last observations of three patients (one patient in the spa treatment group and two in the drug treatment group) were carried forward and used in the analyses. All statistical calculations were performed using microprocessor and commercially available statistical software packages by two investigators who were not blinded to the groups. Alpha value was set to 0.05 in all calculations, and calculated *p* value less than 0.05 was accepted as statistically significant.

Table 2 Baseline characteristics of the patients

	Spa therapy Group (n=10)	Drug therapy Group (n=10)	p (Paired t test)
Age Mean (SD)	57.3 (11.2)	62.7 (8.4)	0.33
Gender			
Female/male	8/2	9/1	–
Pain (VAS)	50.0	44.5	0.64
Mean (SD)	(28.1)	(24.7)	
Kellgren–Lawrence	II (six patients)	II (seven patients)	0.10[a]
Radiological grade	III (four patients)	III (three patients)	
Lequesne algofunctional index	12.2	11.2	0.22
Mean (SD)	(2.4)	(3.5)	

VAS Visual analogue Scale, *SD* standard deviation
[a] Chi square test

Results

The baseline characteristics of the patients in the treatment and control groups are summarised in Table 2. At baseline, there was no statistically significant difference between the characteristics of two study groups. As shown in the study diagram (Fig. 1), nine patients completed the study in the spa group; one patient is lost at week 12 and week 24 follow-up due to family problems, and eight patients completed the study in the control group; two patients are lost at week 24 follow-up, one moved to another city, and one underwent surgery. Four patients had a total of 20 baths, four patients had 19 baths, and two patients had 18 baths. Four patients had no massage, three patients had five times, and three patients had only once. Two patients declared drug use, one in the second day of their stay as 2×250 mg aspirin and one in the third day Naproxen 2×500 mg. These patients had transient pain increase without causing any further problems. The other patients did not experience any adverse events or side effects.

Lequesne algofunctional index Patients in the spa group reported significant decrease in LAFI scores during the whole follow-up period (Table 3). In the control group, there were no significant changes (Table 4). Comparing the index scores of study groups (in terms of differences from the baseline), the spa group showed a significant superiority at week 12 that lasted till week 24 (Table 5).

Pain The pain scores were significantly lower in the spa therapy group during the follow-up period as compared to baseline (Table 3). In the control group, there was no significant change (Table 4). Pain score changes were also superior in the spa therapy arm than the control arm in all

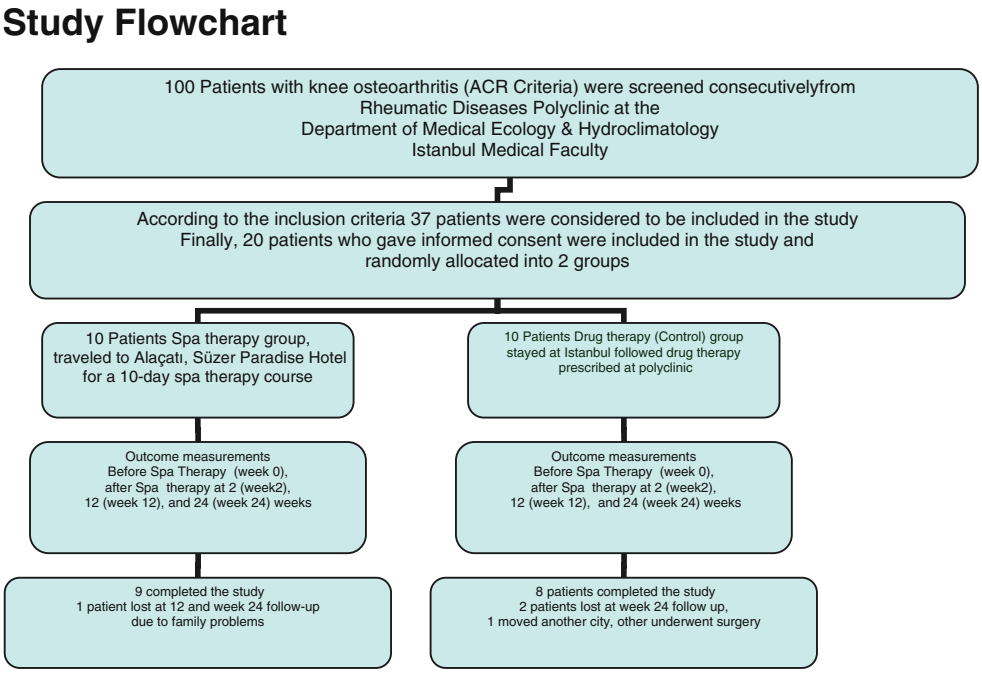

Fig. 1 Flowchart of patients selection and assessment process

Table 3 Comparisons of the pre treatment (week 0), post-treatment (week 2) and follow-up (week 12 and week 24) evaluation in spa group using Friedman's test

	Week 0 (min–max)	Week 2 (min–max)	Week 12 (min–max)	Week 24 (min–max)	χ^2	*p*
LAFI	11.50 (8–16)	7.50 (4–15)	9.50 (5–15)	8.50 (4–13)	16.344	0.001[a]
Pain (VAS)	70.00 (20–100)	33.50 (12–55)	30.00 (0–58)	17.50 (5–67)	8.694	0.034[a]
Ten-stair go up and down time	24.00 (14–37)	17.00 (11–40)	18.50 (12–35)	16.50 (10–60)	3.710	0.295
15 m walking time	17.50 (14–32)	15.50 (13–25)	15.60 (13–23)	15.00 (11–37)	7.602	0.055
Three squatting time	11.00 (8–27)	8.00 (6–26)	9.50 (6–20)	8.50 (5–23)	2.882	0.410
Patient's global assessment (VAS)	62.50 (43–90)	49.00 (5–80)	39.00 (0–80)	34.00 (10–43)	10.052	0.018[a]
Investigator's global assessment (VAS)	70.00 (51–85)	42.50 (10–68)	34.00 (0–70)	32.00 (15–44)	16.531	0.001[a]

Data represented as median (minimum–maximum)
VAS Visual analogue scale, *LAFI* Lequesne algofunctional index for knee osteoarthritis, χ^2 chi square value, *p* *p* value
[a] Significantly different than the baseline at 0.05 level

time points assessed (Table 5). When the differences in pain scores were compared to the initial values, the spa arm was found significantly superior to the control arm during whole 24 weeks follow-up period (Table 5).

Functional measurements The improvements of functional measurements (15 m walking time, ten-stair going up and down time, three squatting time) showed minor improvement without statistical significance. The spa therapy group showed superiority in terms of ten-stair going up and down time at the end of therapy and 15 m walking time at 12 weeks assessment (Table 5).

Patient's and physician's global assessments In the spa group, statistically significant improvements were observed both in patient's and physician's global assessments lasting until 24 weeks (Table 3). There were no significant changes in the control group. When the differences in both assessment scores were compared, the spa group was found superior to the control group.

Table 4 Comparisons of the pre treatment (week 0), post-treatment (week 2) and follow-up (week 12 and week 24) evaluation in drug therapy group using Friedman's test

	Week 0 (min–max)	Week 2 (min–max)	Week 12 (min–max)	Week 24 (min–max)	χ^2	*p*
LAFI	10.25 (8–16)	12.50 (5–16)	12.25 (8–16)	11.50 (8–15)	2.576	0.462
Pain (VAS)	50.00 (25–80)	52.00 (20–91)	59.00 (35–100)	53.00 (20–100)	4.728	0.193
Ten-stair go up and down time	23.50 (12–40)	27.00 (18–45)	24.50 (20–45)	26.50 (15–65)	1.517	0.678
15 m walking time	18.50 (14–24)	18.00 (15–25)	22.00 (15–27)	21.50 (15–27)	3.239	0.356
Three squatting time	14.50 (11–43)	15.50 (10–120)	18.00 (8–32)	11.00 (8–32)	3.138	0.371
Patient's global assessment (VAS)	55.50 (23–81)	65.50 (17–95)	65.00 (30–100)	60.00 (30–95)	4.582	0.205
Investigator's global assessment (VAS)	58.50 (20–80)	57.50 (23–82)	61.00 (32–85)	58.50 (32–72)	1.261	0.738

Data represented as median (minimum–maximum)
VAS Visual analogue scale, *LAFI* Lequesne algofunctional index for knee osteoarthritis, χ^2 chi square value, *p* p value

Table 5 Comparisons of spa and control groups in terms of differences from the baseline

	Week 0–week 2	Week 0–week 12	Week 0–week 24
Pain (VAS)	0.011[a]	0.017[a]	0.006[a]
LAFI	0.123	0.002[a]	<0.000[a]
10 stair go up and down time	0.015[a]	0.075	0.165
15 meter walking time	0.075	0.009[a]	0.123
3 squatting time	0.796	0.604	0.606
Patient's global assessment (VAS)	0.123	0.002[a]	<0.000[a]
Investigator's global assessment (VAS)	0.002[a]	0.002[a]	<0.000[a]

Mann–Whitney *U* test is used. Data represented as *p* value
VAS Visual analogue scale, *LAFI* Lequesne algofunctional index for knee osteoarthritis
[a] Significantly different change in favour of spa therapy at 0.05 level

Discussion

This study is a pilot study designed to assess if spa therapy may have a role in the management of a disabling condition, severe knee osteoarthritis. To our knowledge, it is the first of its kind aimed to evaluate the efficacy of such therapy in radiologically and clinically severe knee OA. We have found that a 10-day spa therapy consisting of balneotherapy (two pool baths everyday in thermal water), on request massage sessions and free-time activities decreases pain and improves functional capacity in patients with severe knee osteoarthritis in short and medium term. The observed beneficial effects lasted up to 24 weeks, whereas the usual drug therapy with NSAIDs and acetaminophen did not show such an efficacy.

Previously, in an uncontrolled study, we have observed beneficial effects of spa therapy on knee osteoarthritis [30]. Later, in a controlled study, we also found that traditional spa therapy (daily combination of mud and thermal water baths or twice daily thermal water baths) was effective in reducing pain and improving functional status [31]. But these earlier studies had no follow-up periods, and disease severity was not included in the patients' selection criteria and the controlled trial had not a drug control group, but compared two different spa therapy regimens. The present study showed similar positive results not only in short but also in medium term, up to 24 weeks after spa therapy in patients who had worse functional index and radiological grades indicating the severity of their osteoarthritis. So far, no randomised controlled trial is published evaluating the efficacy of spa therapy in radiologically and functionally severe knee OA compared to usual care. In this case, spa therapy as a non-pharmacologic modality may be seen an alternative to pharmacologic measures rather than an adjunct to them. Or vice versa, pharmacological therapy should be an adjunct to spa therapy [38].

In the last decade, several randomised controlled studies have been published in English in peer-reviewed rheumatologic journals that reported beneficial effects of balneotherapy and spa therapy in short and long term in patients with osteoarthritis including knee OA [39–42]. Also, in the international literature, there are few published randomised controlled trials evaluating the effects of spa or balneotherapy on knee osteoarthritis [43–48]. Spa or balneotherapy interventions that were used in these studies were mostly found to be effective, although application varies (such as duration and modality types of spa therapy and frequency and kind of balneotherapeutic applications) between the studies. However, none of these trials recruited patients with severe knee OA. Furthermore, they have been carried out in different spa resorts at different spa atmospheres and employed different spa therapy programs. So, in this context, the results of our study could hardly be compared with the results of these studies.

Balneotherapy (passive immersion in warm natural mineral water) was the sole common intervention that was employed in all of these trials. It is perhaps the oldest treatment modality for rheumatic conditions and is still unique and plays a central role in the effects of any spa therapy course. It uses the buoyancy, assistance and resistance of warm mineralised water to relieve pain, induce muscle relaxation and unload the lower limbs [9, 10, 49]. It was presumed that most mineral ingredients would be absorbed through the skin during a balneotherapeutic immersion, but to date, this has not been fully confirmed, and controversy exists between pros and contras of balneotherapy [50, 51]. The local mineral water, which was used in the spa resort in our study, is different from the spa waters of the aforementioned studies. It is classified as brine or saline water (3% NaCl solution) and supposed to exert additional specific chemical effects. Saline spa waters are mainly used in dermatological pathologies such as psoriasis, and their anti-psoriatic effect when combined with phototherapy has been shown [52–54].

It has been shown in experimental model of arthritis that brine or salty water baths have anti-inflammatory effect as well [55]. The sedative and analgesic effects of soaking in warm tap water are well known [9]. Analgesic effect of brine baths is also investigated in a randomised controlled study; chronic low back patients who immersed in brine and tap water baths experienced the same relaxing and pain-relieving effect, without significant difference in

between them [56]. So, beneficial affects seen in the spa and balneotherapy studies on knee OA, including the present one, seem less linked to chemical composition of the waters, which differ chemically from each other considering the information given in the aforementioned articles.

Besides balneotherapy with spa water, other "spa therapy" factors are likely to play a role in the efficacy observed in this study (and other spa studies). The non-specific and uncontrolled factors such as journey to spa resort and change of milieu and routine life (absence of daily routines) and pleasant scenery, being in a non-competitive atmosphere with fellow patients, rest in a holiday environment and massage and regular daily free activities are very likely to play a role as a whole [22, 28, 29]. But the observed persisting effect after months when the patients had returned to their routine life can be hardly explained by these factors, as the effect of these factors are expected to be favourable in the short term. We may speculate that these non-specific effects of spa therapy may have a contribution to the beneficial effects of balneotherapy in short term, but the maintained beneficial effect in long term probably depends on the balneotherapy. Recent studies evaluated the factor "spa water" rather than the factor "spa therapy" and reported results that may support this hypothesis [20, 21, 25, 46, 48]. So, the statement that the beneficial effect is less linked to chemical composition of the water is debatable. Of course, further studies are required to assess the biological effect of hot mineral water, in combination or not with other therapies, on clinical status of patients with knee OA.

We are aware of the main limitations of our study. Firstly, this is a pilot study including a small number of patients aimed to compare the effect of spa therapy and drug therapy in patients with severe knee OA. We observed a significant superiority of spa therapy over drug therapy with NSAIDs and acetaminophen, although the number of patients in both groups is limited. The results might be seen as an indicator that that study is enough powered to the detect differences between the investigated therapies.

Secondly, we did not look for any biomarkers of osteoarthritis that spa therapy may influence, suggesting a disease modifying effect. In the literature, there is limited and conflicting evidence on the biologic effects of spa therapy and balneotherapy in patients with osteoarthritis [57–61]. A study reported a decrease of TNF-α levels [57], while the other an increase [58]. Again, here, these results are not comparable, as these studies evaluated different types of spa therapy modalities and spa waters such as balneotherapy plus mud pack therapy [57, 59, 60], low mineralised thermal water [58] and radon water [61]. On the other hand, the observed beneficial effects of spa therapy on pain and functional status may be seen without any effects on disease progression of knee osteoarthritis [62, 63]. This assumption could be substantiated with the fact that symptomatic relief obtained with most of the therapeutic options of knee OA is not necessarily accompanied with any structural effects such as slowing the progression of radiographic changes of OA [63, 64].

Thirdly, spa therapy is very popular with patients (less so with healthcare providers and healthy taxpayers) in Turkey. Patients who randomised to spa therapy group were happy with this allocation, but this was not the case for the drug therapy group who stayed at home and missed the "chance" to undertake a spa therapy course combining daily twice thermal baths with respite care and rest in a relaxing marine environment. Considering the high rate of placebo response in the osteoarthritis studies when patients' expectations are high [65], improvements seen in pain and functional indexes in spa group and not seen in pharmacotherapy group may be due to a strong placebo effect [66, 67]. But again, the long-term benefit of spa journey cannot be easily explained by this way [68].

In conclusion, the results of this pilot study indicate that a 10-day traditional spa therapy may have a role in the management of severe knee OA and might be an effective alternative to drug therapy in countries, like Turkey, where it is affordable and widely used by patients and is partly reimbursed by health insurance systems as well. However, further steps must be taken to reproduce these results by conducting a full randomised controlled study having sufficient statistical power with an estimated number of patients which is required to evaluate the comparative efficacy of spa and drug therapy in the treatment of severe knee OA.

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