



Evaluation of the effect of Lake Hévíz thermal mineral water in patients with osteoarthritis of the knee: a randomized, controlled, single-blind, follow-up study

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Background. Osteoarthritis is the most frequent joint disease and is a leading cause of pain and locomotor disability in elderly people. The treatment of osteoarthritis includes non-pharmacological, pharmacological, and surgical therapies. Silver level evidence has been found concerning balneotherapy in osteoarthritis.

Aim of the study. The aim of this study was to evaluate how Lake Hévíz thermal mineral water therapy influences pain, knee function, and quality of life in patients with knee osteoarthritis, compared to the control group.

Study design. randomized, controlled, single-blind, follow-up study.

Setting. Spa Hévíz and St. Andrew Hospital for Rheumatic Diseases

Population. This study included 77 outpatients between 45 and 75 years of age with mild to moderate osteoarthritis of the knee meeting the American College of Rheumatology classification criteria.

Methods. Patients were randomized into two groups. In group I (n=38), subjects bathed in Lake Hévíz and in group II (N.=39), patients were treated in a pool full of tap water. Water temperature was 34°C for both groups. Participants underwent 30-minute therapy sessions, five times a week for three weeks. Outcome measures were pain visual analogue scale scores, active flexion degree, knee circumference, stair-climb time, Western Ontario and McMaster Universities osteoarthritis index (WOMAC), and EuroQoL Group 5-Dimension Self-Report Questionnaire score (EQ-5D). Study parameters were recorded at baseline, immediately after treatment, and after 15 weeks.

Results. Comparison of the two groups revealed a statistically significant difference in pain visual analogue

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scale scores (P<0.01), active flexion degree (P<0.01), physical function components of WOMAC (P<0.05), and EQ-5D scores (P<0.05) even after 15 weeks.

Conclusions. Balneotherapy improved pain, function as well as the quality of life in patients with knee osteoarthritis.

Clinical Rehabilitation Impact. Balneotherapy is a potentially useful treatment modality for patients with knee osteoarthritis.

KEY WORDS: Balneology - Osteoarthritis, knee - Mineral waters.

Balneotherapy uses the beneficial effects of naturally occurring mineral waters, gases, and peloids. Thermal mineral waters are mostly used for bath therapy. We call immersion when the body is dipped into water up to substernal height in a vertical position. The effects of balneotherapy are partially attributable to the aquatic environment and its basic physical characteristics (density, specific gravity, hydrostatic pressure, buoyancy, viscosity, and temperature of the water) as well as the effects of substances dissolved in the water.¹ In addition

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to the inorganic components solved in the water, organic fractions are also present, and analysis of the organic substances has also started.² The exact mechanism of action of this type of treatment is not known.³

Balneotherapy is used for medical purposes predominantly in countries rich in thermal mineral water.⁴ In the past decades, several clinical studies, reviews, and meta-analyses have evaluated the efficacy of balneotherapy mainly in the treatment of musculoskeletal disorders.⁵⁻¹¹

Osteoarthritis is the most common musculoskeletal disorder, a slowly progressing, degenerative process leading to gradual destruction of the articular cartilage. It predominantly develops in weight-bearing joints. It can affect every aspect of a person's daily life and overall quality of life. The evidence-based therapeutic recommendations for knee osteoarthritis emphasize the importance of reducing joint pain and stiffness, preserving joint mobility, and improving physical disability and quality of life. The guidelines recommend the combination of non-pharmacological and pharmacological treatments in individually tailored therapy.¹²⁻¹⁴

A Cochrane review published by Verhagen *et al.* in 2008 was based on the analysis of 7 randomized, controlled trials. Silver level evidence was found concerning balneotherapy in osteoarthritis. Because of the poor methodological quality and the absence of an adequate statistical analysis and data presentation, the scientific evidence is weak. The authors emphasize the need for further additional, confirmatory studies.¹⁵

Studies involving patients with knee osteoarthritis and systematic reviews confirmed the analgesic and knee function improving effect of balneotherapy as well as its positive influence on quality of life. However, in most of the studies, bath therapy was combined with other therapies (exercise program, massage, showers, mud therapy).¹⁶⁻¹⁹ Furthermore, only a limited number of previous studies covered the assessment of quality of life.

Therefore, the primary endpoint of the study was the evaluation and documenting of the pain-reducing effect of Lake Hévíz thermal mineral water on knee pain at rest or on exertion in patients with mild to moderate knee osteoarthritis as well as the assessment of the therapeutic effect compared to the control group treated with warmed tap water. The secondary endpoints included the evaluation of the

effect of Lake Hévíz thermal mineral water on knee function and quality of life.

Materials and methods

This was a randomized, single-blind, controlled, parallel-group, follow-up study. The study was conducted in accordance with the Declaration of Helsinki, International Conference on Harmonization/Good Clinical Practice standards and was approved by the Regional Research Ethics Committee (Approval No. 18/2011).

Participants

This study included male and female patients between 45 and 75 years of age with mild to moderate, bilateral primary osteoarthritis of the knee (meeting the American College of Rheumatology knee osteoarthritis classification criteria²⁰) diagnosed and documented with imaging techniques (comparative knee radiograph not older than 2 years). Patients had been suffering from knee pain characteristic for osteoarthritis for at least 3 months.

After verbal agreement, the physician of the Rheumatology Outpatient Clinic of Keszthely City Hospital and the rheumatologists of our Institute invited the patients to join the study, bearing in mind the inclusion and exclusion criteria. The enrolled patients received the treatment in an outpatient setting and they were able to continue their daily activities and work. The specialists of our Institute and the members of the Lake Hévíz Emergency Medicine Team were constantly available during the treatment for the management of side effects and problems emerging during treatment. Before enrollment, study participants were informed verbally and in writing about the purpose of the study and the study procedures. Prior to enrollment, patients read the Patient Information Sheet and signed the Informed Consent Form.

Exclusion criteria were conditions and diseases excluding warm water bath treatment (patients suffering from any severe internal, rheumatic, urogenital, or skin disorders or mental illnesses, which contraindicates bath treatment). Intra-articular corticosteroid injection within 1 month prior to the start of treatment, intra-articular hyaluronic acid therapy within 6 months prior to the initiation of treatment.

Physiotherapy within 3 months prior to the start of treatment. Any change in nonsteroidal anti-inflammatory therapy or chondroprotective therapy within 1 month prior to treatment. Patients suffering from inflammatory rheumatic diseases (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, crystal arthropathies, etc.), patients with palpable fluid in the knee. Knee surgery within 6 months prior to the study; presence of metal implant in the knee joint. Patients with any previous fractures in the knee area, and/or knee injury within 6 months prior to the study. Patients with hip or spinal surgery within a year preceding the study. Patients with radiculopathy.

Study procedures

The study took place at Spa Hévíz and St. Andrew Hospital for Rheumatic Diseases (H-8380 Hévíz, Dr. Schulhof Vilmos sétány 1, Hungary), from May 2012 to August 2012.

Lake Hévíz is a biologically active, natural thermal lake is located in West Hungary. The spring of the 4.4 hectare lake, comes from a 38 m deep cave. Water-output of the lake is 410 L/sec and with this the total water volume of the lake is replaced in about every three and a half days. Its temperature never decreases under 24° centigrade in winter, in summer it can reach even 37 degrees centigrade. The bed of the lake is covered with a 6 to 8 m thick mud layer. Resulting from the eventful earth history and geological characteristics, the lake forms a hydrogeological unit together with the surrounding moorland and marshland, which has a unique, special fauna characteristic for a hot spring.²¹

Patients were randomized into one of the two treatment groups. One group was treated in a covered area of Lake Hévíz and the control group was treated in a (1.2 to 1.4 m deep) pool bath filled with tap water of the same temperature as that of the thermal water. During the study, the temperature of the lake bath (34 °C) was the same as that of the pool bath. Patients received Lake Hévíz or pool bath treatment for 30 minutes 5 days a week, a total of 15 times. Patients were asked not to swim during bathing.

In order to follow up the patients, they were constantly under supervision during the treatment. Patients were considered as having completed the study if they participated in more than 80% of the

treatment sessions. Patients did not receive any other physiotherapy in addition to the bath therapy. Further balneo/physiotherapy treatment, intra-articular corticosteroid or hyaluronic acid therapy, arthroscopic surgery, any change in nonsteroidal anti-inflammatory therapy or chondroprotective therapy was not allowed during the study and follow-up. Participants were evaluated just before treatment (Week 0), after the end of treatment (Week 3), and during the follow-up visit (Week 15). Patients were examined by seven rheumatologists. Before the study, the study personnel standardized and practiced joint assessment two times on patients not participating in the study. Patients randomized into the control group were given the opportunity to bath in the lake for free 15 times after the follow-up visit.

Randomization and blinding

Patients were randomly assigned into two groups following simple randomization with a computer-generated sequence. The randomizer was not involved in the conduction of the study. The randomizer received the information about the patients in e-mail. The person performing the statistical analysis did not participate in the randomization process. After randomization an independent person assigned the participants to the appropriate groups.

Baseline and post-therapy assessments were performed by rheumatologists. The same patient was examined by the same physician every time. The examiners were blinded regarding the received therapy. Patients were told not to inform the study doctor about whether they received balneotherapy in Lake Hévíz or in the pool.

Evaluations

— Visual analogue scale (VAS): characteristics of knee pain and condition were assessed on a 0-100 mm scale as follows:

- VAS I: knee pain at rest, as rated by the patient;
- VAS II: knee pain on exertion, as rated by the patient;
- VAS III: condition of the knee, as rated by the patient;
- VAS IV: condition of the knee, as rated by the investigator;

— WOMAC (Western Ontario and McMaster Uni-

versities Arthritis) index: a self-report questionnaire was used to characterize knee joint pain, joint stiffness, and physical function. The VAS version of the index was used, with the patient assessing each question on a 0-100 mm VAS;²²

- Angle of knee flexion on the left and right side measured by a goniometer (angle);
- Knee circumference (cm);
- Stair-climb time in seconds to walk up 22 stairs in the pool bath building of the hospital;
- EQ-5D a self-report questionnaire for the measurement of general health-related quality of life.²³

Thermal water composition

The thermal mineral water of Lake Hévíz is rich in dissolved and gas components, thereby it combines the favorable characteristics of carbonate, sulfur, calcium, magnesium, hydrogen carbonate and very light radon-containing waters.

The characteristics and composition of Lake Hévíz water are shown in Table I.

Statistical analysis

Sample size calculation was based on power analysis ($\alpha=0.05$, $\beta=0.80$, effect size=0.65). Results were processed and evaluated in Microsoft Excel. For the statistical comparison of the samples, self-controlled and group-controlled methods: one-sample (paired) and two-sample t-tests were used. The analysis of the results was conducted by intention to treat. In order to avoid over-estimation of the therapeutic effect, data from dropped-out patients were replaced by data of the last measurement. The level of significance was set at $P<0.05$.

Results

Of the 77 patients included in the study, 75 completed more than 80% of the therapy sessions. Demographic and baseline clinical characteristics of patients are shown in Table II. Treatment groups were similar with regard to demographic data and baseline clinical characteristics. Two patients discontinued the treatment (1 patient in the thermal group and 1 patient in the control group). Two patients in the control group did not attend the Visit 3. Disposition of patients is presented in Figure 1.

Examination of the knee revealed an improvement in the pain parameters measured by VAS scale in both study groups. After the 3-week treatment, patients receiving thermal water therapy showed a significant therapeutic response compared to the control group, with a decrease in VAS I, VAS II, VAS III, and VAS IV scores ($P<0.01$). During the follow-up period, long-term significant improvement was seen in all of the VAS scales ($P<0.01$). All three dimensions of the WOMAC index (pain, joint stiffness, function) showed major improvement after the treatment and during the follow-up period, than in the control group. Comparing the changes in the study groups after the treatment, all parameters of the WOMAC index showed significantly better improvement in the thermal water-treated group (pain $P<0.05$, stiffness $P<0.01$, function $P<0.01$), during the follow-up only in function score ($P<0.05$). Knee function and movement were characterized by changes in flexion angles. Knee flexion improved in both knee in both groups. Improvement of joint function was significantly better in the thermal water-treated group than in the control group after the treatment (right

TABLE I.—*Characteristics and composition of Lake Hévíz water.*

Total hardness of water	198 CaO mg/L		
pH	7.14		
Water temperature	in summer: 32-35 °C in winter: 24-26 °C		
Sodium	21.7 mg/L	Chlorine	25.0 mg/L
Potassium	6.45 mg/L	Iodine	0.02 mg/L
Magnesium	36.1 mg/L	Fluoride	1.18 mg/L
Calcium	82.1 mg/L	Hydrogen carbonate	384 mg/L
Iron	0.24 mg/L	Sulphate	63.0 mg/L
Ammonium	0.22 mg/L	H ₂ S	0.10 mg/L
Free CO ₂	20.9 mg/L	Filtered sulfur	23.3 mg/L
Dissolved O ₂	2.85 mg/L	Unfiltered sulfur	23.5 mg/L
Others	mud, radon, meta borid acid, meta silica acid, organic acid, special ecosystem		

TABLE II.—Demographic data and other baseline clinical characteristics of the patients by treatment group.

	Thermal water	Control
Enrolled	N.=38	N.=39
Male/female	8/30	9/30
Age	65.6 (6.4)	65.5 (7.7)
VAS I at rest	33.6 (23.4)	33.2 (21.8)
VAS II on exertion	55.2 (20.2)	58.0 (20.9)
VAS III patient's assessment	52.1 (20.1)	53.5 (16.0)
VAS IV physician's assessment	46.2 (15.0)	51.2 (16.1)
WOMAC		
Pain	38.5 (23.5)	46.6 (19.9)
Stiffness	49.4 (26.9)	51.2 (20.6)
Function	43.4 (21.7)	44.5 (17.8)
Knee		
Flexion, right side	109.1 (15.5)	111.3 (18.5)
Flexion, left side	112.6 (12.5)	113.3 (17.4)
Circumference, right side	40.4 (3.7)	40.9 (4.3)
Circumference, left side	40.3 (3.8)	40.7 (4.5)
Stair-climb time	20.3 (3.6)	21.9 (5.1)
EQ-5D	0.6281 (0.2406)	0.6005 (0.2035)
EQ-5D VAS	59.1 (16.6)	54.7 (15.9)

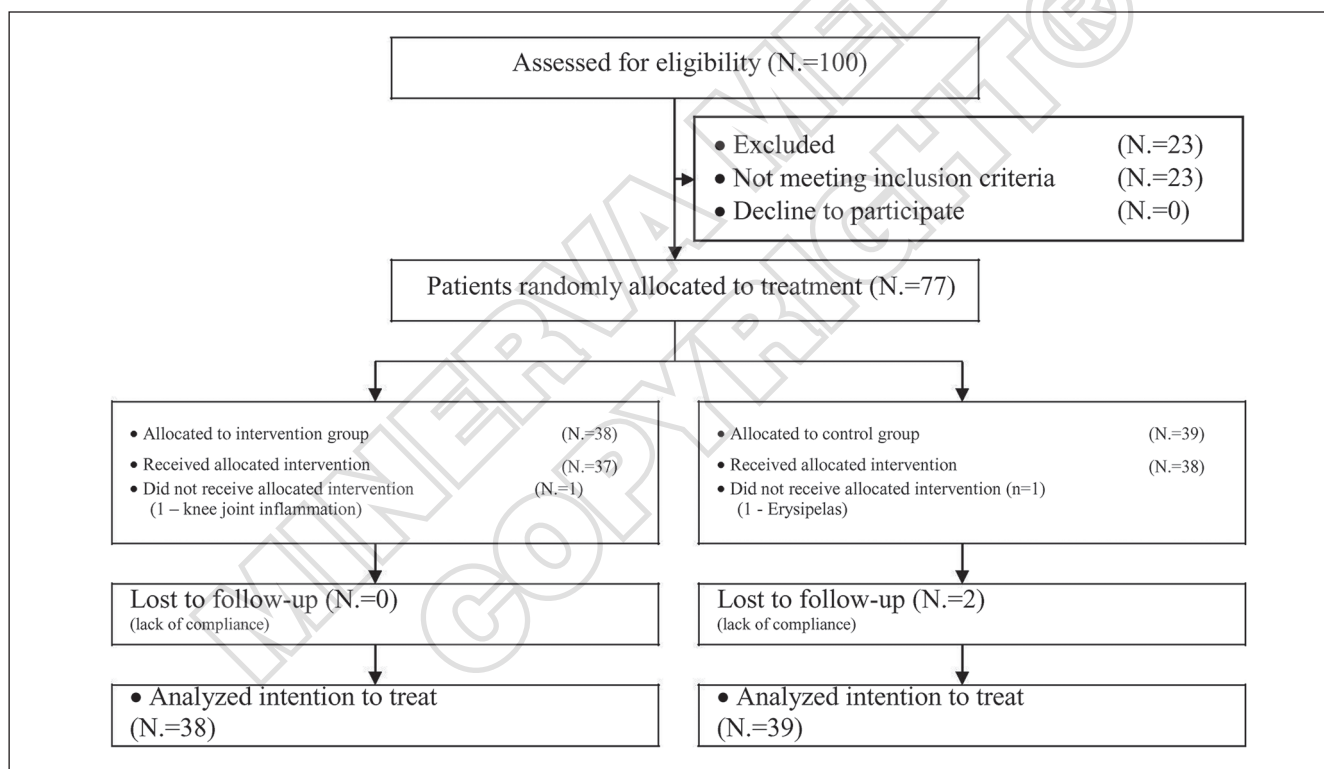


Figure 1.—Disposition of the patients.

side $P < 0.01$, left side $P < 0.05$). Similar results were obtained during the follow-up period (both sides $P < 0.01$). As a response to treatment, stair-climb time decreased in both groups; patients completed the

unit distance in a shorter period of time. Stair-climb time was slightly more decreased in the thermal water-treated group than in the control group when compared to baseline. The difference between the

two groups was not significant. The utility index of the EQ-5D questionnaire showed permanent and significant improvement of general health-related quality of life in the thermal water-treated group compared to the control group after the treatment, and during the follow-up period ($P<0.05$). The responders' self-rated health measured on the EQ-5D VAS scale slightly improved, but the changes were not statistically significant between the two groups. The measured values, the changes compared to baseline, and statistical data are presented in Table III.

Discussion

In this randomized, controlled, single-blind, follow-up study we evaluated the effectiveness of

thermal mineral water on pain, function and quality of life in patients with knee osteoarthritis. The primary endpoint parameters indicating pain at rest and on exertion measured on a visual analogue scale and the secondary endpoint parameters such as the physical function parameter of the WOMAC index, angle of knee flexion, and index values of the EQ-5D global health-associated quality of life questionnaire showed greater improvement and were statistically significant and more durable in the thermal water-treated group compared to the control group. The difference in the above mentioned parameters were significant between the two groups at the end of treatment and during the follow-up period. No adverse reactions were observed during treatment sessions or during the whole study period.

The results of our study demonstrated explicitly

TABLE III.—Measured values, changes from baseline, and statistical data of groups at various time points of the study.

	Assessment 2 (3 weeks later)			Assessment 3 (15 weeks later)			
	Changes from baseline		Group comparison	Changes from baseline		Group comparison	
	Thermal water Mean 95% CI	Control Mean 95% CI		Thermal water – Control	Thermal water Mean 95% CI		Control Mean 95% CI
VAS I	-21.1 -27.7 to -14.6	-3.7 -9.6 to 2.2	$P<0.01$	-18.8 -26.0 to -11.5	-2.8 -10.5 to 5.0	$P<0.01$	
VAS II	-22.8 -27.1 to -18.5	-6.8 -12.0 to -1.7	$P<0.01$	-19.0 -25.6 to -12.4	-2.4 -8.8 to 4.0	$P<0.01$	
VAS III	-21.7 -27.1 to -16.3	-8.5 -13.1 to -3.9	$P<0.01$	-19.9 -27.1 to -12.8	-6.2 -11.0 to -1.3	$P<0.01$	
VAS IV	-15.1 -18.6 to -11.5	-8.0 -11.7 to -4.3	$P<0.01$	-16.5 -21.3 to -11.7	-5.6 -9.8 to -1.3	$P<0.01$	
WOMAC	Pain	-11.9 -16.7 to -7.1	-5.5 -9.5 to -1.6	$P<0.05$	-9.2 -15.2 to -3.2	-6.8 -10.4 to -3.1	NS
	Stiffness	-18.2 -24.7 to -11.7	-3.6 -7.8 to 0.7	$P<0.01$	-14.0 -21.9 to -6.2	-7.1 -12.4 to -1.8	NS
	Function	-15.5 -20.0 to -11.0	-2.7 -5.7 to 0.3	$P<0.01$	-12.0 -18.6 to -5.4	-3.9 -7.9 to 0.1	$P<0.05$
Knee	Flexion right side	15.4 11.7 to 19.1	6.1 1.8 to 10.5	$P<0.01$	14.9 11.9 to 17.9	5.9 2.4 to 9.5	$P<0.01$
	Flexion left side	11.9 4.7 to 19.2	3.3 0.7 to 6.0	$P<0.05$	14.7 11.4 to 18.1	2.8 -0.9 to 6.6	$P<0.01$
	Circumference right side	-0.3 -0.7 to 0.1	-0.1 -0.3 to 0.1	NS	-0.4 -0.8 to 0.0	-0.2 -0.7 to 0.4	NS
	Circumference left side	-0.4 -0.8 to -0.1	-0.1 -0.4 to 0.2	NS	-0.6 -1.1 to -0.1	0.2 -0.4 to 0.7	NS
Stair-climb time	-3.2 -4.3 to -2.2	-1.6 -3.0 to -0.3	NS	-1.5 -3.1 to 0.1	-1.4 -2.3 to -0.4	NS	
EQ-5D	0.1606 0.0975 to 0.2237	0.0634 0.0 to 0.1268	$P<0.05$	0.1062 0.0328 to 0.1797	-0.0263 -0.1073 to 0.0547	$P<0.05$	
EQ-5D VAS	6.1 -1.5 to 13.6	2.5 -2.5 to 7.4	NS	5.1 -2.1 to 12.3	-4.4 -10.7 to 2.0	NS	

the effects of thermal mineral water, in the short and long term, compared to the control group who were treated with the tap water. The decrease in pain was not only statistically but also clinically significant. In our own study the VAS scales for the reduction in pain showed a more informative response. The vast majority of studies compared the thermal mineral water treatment for outpatient care with a group not receiving such treatment.^{18, 24, 25}

Many Hungarian, Turkish, Israeli author study compares the treatment of thermal mineral water with tap water treatment. Studies were carried out on treatment with waters of different mineral content. Similar to our results in previous studies comparing the efficacy of balneotherapy applied as a 15 to 18 day course to tap water control in patients with knee osteoarthritis,^{26, 27} a significant decrease in pain was observed. Some patients in the group treated with tap water also showed improvements which confirms the well-known analgesic effect of hot water, but the effect of short-term thermal mineral water proved to be significantly better.²⁸ This has ratified a systematic review and meta-analysis published by Bender and associates in 2013 which analyzed the pain-reducing effect of balneotherapy. Based on their results, regardless of the composition of the mineral water, balneotherapy significantly decreased joint pain in patients with chronic low back pain and knee and hand osteoarthritis.²⁹

After the treatment, the WOMAC index parameters of pain, stiffness, physical function and even long-term physical function showed significant clinical improvements.

Reduction in pain and improvement in WOMAC scores were most prominent after the treatment course; and at Week 15 this effect already showed a decreasing trend.

These results differ from the results of Fioravanti and associates published in 2012, who compared the effects of balneotherapy with routine regular outpatient care and found further reduction in pain, parameters of WOMAC and Lequesne indexes at the 3-month follow-up visit.²⁴

In contrast, if the thermal mineral water treatment was applied intermittently twice a week for 6 weeks, no significant difference was observed between the treatment group and the tap water-treated control group in pain decrease, improvement in the Lequesne and WOMAC indexes, and improvement in the parameters of the SF-36 questionnaire.³⁰

Few previous studies have focused on the assessment of changes in the physical state. Our results of knee flexion, showed significant improvement after treatment compared to the control group and during follow-up as well. The stair climb speed improved in both groups, although the change in the thermal mineral water treated group was greater, but no significant difference was observed when comparing the groups.

In contrast to our results in a study by Kovacs and Bender it was showed that the stair-climb time improved significantly following 3 week balneotherapy.²⁷

Only a limited number of studies evaluated the effect of balneotherapy on quality of life.

In our study, EQ-5D a self-report questionnaire was evaluated, after the treatment and during the 3-month follow-up period, significant improvement was noted.

In other studies, using the SF-36 questionnaire³⁰ and the Arthritis Impact Measurement Scales,²⁴ a significant improvement in quality of life was seen at the end of the treatment course and during the 3-month follow-up period.^{24, 31}

In studies where balneotherapy was combined with exercise and other treatments,^{18, 19} even in case of severe knee osteoarthritis,²⁵ pain decrease as well as improvement in muscle strength, walking distance, physical function, and quality of life was found to be more significant and longer term. These results were supported by a multicentre study involving a large number of patients.³²

With regard to the common side effects of continuous pharmacological, NSAID therapy, a balneotherapy course can be a useful therapeutic tool or adjunctive therapy in the treatment of knee osteoarthritis.

Our study has some limitations. First, those patients, who bathed in the covered part of the lake, were not allowed to swim, due to the deepness of the water, they had a better opportunity to move around. This might have influenced the improvement in function.

Further studies should include larger sample, maybe as a multicenter study. A larger number of patients would have increased the power of the study.

Furthermore, patients were not blinded to the received therapy. Bathing in the lake did not make the application of the double-blind method possible. In

the future the double-blind method should be used with the tap water control group to ratify the effectiveness of the thermal water treatment.

On the other hand patients randomized into the control group were given the opportunity to bathe in the lake for free 15 times after the follow-up visit. This could have led to the results being influenced, however, this contradicts the documented improvement of the control group also.

Finally, in a future study it would be useful to design longer follow-up periods and to associate it with a study into its cost-effectiveness.

Conclusions

This randomized, tap water-controlled, single-blind study supported the efficacy of balneotherapy in the treatment of patients with mild to moderate osteoarthritis of the knee. Our results showed significant improvement in knee pain reduction, knee function, and quality of life and these changes were measurable even 12 weeks after the treatment.

This modality is another proven adjunct to the therapeutic armamentarium comprising, among others, drug treatment and physiotherapy.

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