THE EFFECTS OF KOLOP PELOID ON KNEE OSTEOARTHRITIS IN DAY HOSPITAL CARE: A RANDOMIZED, CONTROLLED, SINGLE-BLIND, FOLLOW-UP PILOT STUDY

Remény Horváth 1, Magdolna Domoki 1, Éva Tóth 2, Tamás Bender 3, Ildikó Katalin Tefner 4

Abstract

Introduction
We investigated the effects of Kolop peloid on the clinical parameters and quality of life of patients with knee osteoarthritis in day hospital care.

Material and Method
We studied 60 patients randomized into two groups. Both groups received standardized combined physiotherapy and balneotherapy for the painful knee joint for three weeks, five days a week, including the following treatments: pool bath in 31°C mineral water for 30 minutes; aquatic exercise in 31°C mineral water pool bath for 20 minutes; and magnetotherapy applied on the knee joint. In addition, the peloid-treated group received Kolop peloid packs on the painful knee joint for 30 minutes at each session; the temperature of the pack was 42°C. The control group received standardized combined therapy on the knee joint without peloid packs. The disease-specific Western Ontario and McMaster Universities Arthritis Index (WOMAC), the EuroQol-5D quality of life questionnaire, the need for analgesics and NSAIDs, and the grade of periarticular tenderness were recorded before treatment, right after treatment (at Week 3), and 3 months after treatment (at Week 15).

Results
In patients treated with Kolop peloid, the clinical parameters (WOMAC pain, joint stiffness and function) improved more significantly from baseline to the end of treatment and to the end of the follow-up period than in the control group. Quality of life improved more in the Kolop peloid-treated group, and significant difference was seen between the two groups at the end of the follow-up period.
Introduction

The medical use of peloid is a popular therapeutic option in balneotherapy, in particular for musculoskeletal disorders [1]. A recently published review analyzed studies evaluating the effects of peloid therapy on knee osteoarthritis. Of the 20 studies reviewed, pain decreased in 17 studies, function improved in 12 studies, and quality of life improved in 5 studies. The authors concluded that peloid therapy is an effective therapeutic modality in the treatment of knee osteoarthritis, though studies with a better methodological quality are needed [2].

In some of the studies reviewed, peloid treatment was used as monotherapy among others in order to optimally evaluate its effect [3-10]. In everyday practice, peloid therapy is widely used as part of combined physiotherapy [11-15]. Combined physiotherapy is a therapeutic method with cumulative effects when a physiotherapy plan is made taking into account the patient’s condition, disease activity, and the aims to be achieved. In Hungary, combined spa treatment or as its former and internationally accepted name, day hospital care for musculoskeletal disorders is of great importance from the professional standpoint. In day hospital care patients stay in the hospital only during daytime but go home for the night. The day hospital combines the advantages of complex hospital therapy among others with the lower costs [16-17].

One of the basic profiles of the day care hospitals in Budapest is peloid therapy. The day care hospitals in Budapest use Kolop peloid for this purpose. In peloid therapy, the thermophysical properties of Kolop peloid predominate, and when the peloid is used mixed with the thermal mineral waters of Budapest, it is considered as “complete” [18].

To date, no studies have been published in the English literature evaluating the effects of peloid therapy as part of combined physio- and balneotherapy treatment, evaluating the effect of peloid pack therapy plus standardized, combined physiotherapy and balneotherapy treatment versus combined physiotherapy and balneotherapy treatment without peloid pack therapy.

The primary objective of our study was to evaluate the beneficial effect of Kolop peloid on the clinical parameters of patients with knee osteoarthritis in the day hospital care setting, and how strong this effect is compared to the control group. Our secondary objective was to find out the effect of clinical improvement on quality of life compared to baseline and to the control group.

| the follow-up period. Periarticular tenderness decreased more in the peloid group compared to the control group, although this difference was not significant. |

| Conclusion |

The use of Kolop peloid in day hospital care is a possible therapeutic option in the treatment of patients with knee osteoarthritis.

Key words : peloid, mud-pack therapy, knee osteoarthritis, Kolop, balneotherapy, physiotherapy, randomized, controlled, single-blind trial
Protocol and study parameters

Design
In this randomized, controlled, follow-up study, we evaluated the effects of Kolop peloid on knee osteoarthritis in patients randomized (1:1) into two groups. The study was performed in the day care hospitals of the Széchenyi and St. Lukács Thermal Baths of the Budapest Bath cPlc.

Participants
Inclusion criteria: patients suffering from chronic knee pain treated in the day care hospitals of the Széchenyi and St. Lukács Thermal Baths of the Budapest Baths cPlc.; diagnosis of knee osteoarthritis based on the ACR criteria [19]; complaints present for at least 3 months; radiologic stage: Kellgren-Lawrence 1-3.

Exclusion criteria were: medical history of surgery on the affected knee joint (arthroscopy is allowed); arthroscopy of the affected knee joint within 6 months prior to treatment; hip joint or spinal surgery within 6 months prior to treatment; current knee pain is caused by obvious trauma; systemic or local steroid therapy or balneotherapy within 2 months prior to treatment; intra-articular hyaluronic acid therapy within 12 months prior to treatment; starting new oral SYSADOA (Symptomatic Slow Acting Drugs in Osteoarthritis) therapy within 3 months prior to treatment; lumbar radiculitis; palpable and significantly tender Baker’s cyst; synovitis; inflammatory joint disorder; flexion contracture (greater than 10 degrees); general contraindications of balneotherapy; Transcutaneous electrical nerve stimulation (TENS) therapy is allowed up to two weeks prior to treatment; exercise is allowed.

Study participants were recruited from the day care hospitals of the Széchenyi and St. Lukács Thermal Baths of the Budapest Baths cPlc. by the rheumatologists working in these institutions. The study took place between September 2012 and January 2013. Study participants received written information and signed an informed consent form before the study. The study was approved by the regional ethics committee (approval number: 20822-1/2012).

Intervention
Both groups received standardized, combined physiotherapy and balneotherapy on the painful knee joint for 3 weeks, five days a week, including the following treatments: pool bath in 31°C mineral water for 30 minutes, aquatic exercise in 31°C mineral water for 20 minutes, and magnetotherapy for 15 minutes. In addition, the peloid-treated group received Kolop peloid packs on the painful knee joint for 30 minutes at each session; the temperature of the pack was 42°C. The control group received standardized combined physiotherapy and balneotherapy on the knee joint without peloid packs.

We used Kolop peloid in our study. Kolop is located in Jász-Nagykun-Szolnok country (Hungary) under the municipality of Tiszasüly. It used to be a health resort (Kolop Bath). Kolop peloid has been used in the spas of Budapest since 1920 [20]. Kolop peloid is a river mud mainly consisting of inorganic substances [21].
Outcomes
Assessments including a detailed past medical history, verification of inclusion and exclusion criteria, and recording of possible side effects was performed before the first treatment (Week 0), after the 3-week treatment (Week 3), and three months after treatment (Week 15). Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) patient-specific questionnaire [22] and EuroQol-5D quality of life questionnaires were administered. Tenderness along the medial and lateral joint spaces of the knee and along the insertion of the pes anserinus was graded using the following scale: no tenderness: 1 point, mild tenderness: 2 points, moderate tenderness: 3 points, severe tenderness: 4 points.

Randomization, and blinding
The person randomizing the patients used a computer program for randomization. After randomization, an independent person assigned the patients into the appropriate group. Three independent assessors blinded to the treatment examined the patients in a previously standardized manner before treatment, at the end of treatment, and at the follow-up visit. The independent physician supervising the treatment was available during the treatments and he/she was the one to detect side effects. Statistical analysis was performed by an independent person.

Statistical analysis
Statistical analysis was performed by using IBM SPSS Statistics 20. Distribution was assessed by the Kolmogorov-Smirnov test. Data obtained from WOMAC and EQ-5D questionnaires were analyzed by independent samples t-test and paired samples t-test. Data regarding tenderness were compared by Mann-Whitney test and Wilcoxon test. Significance value was 0.05. At multiple comparisons (paired samples t-test, Wilcoxon test), p-value was 0.017 regarding WOMAC and EuroQol-5D questionnaires and p-value was 0.0125 regarding tenderness with Bonferroni correction. The WOMAC Likert indices were normalized on 0-100 scales. The results were evaluated by intention-to-treat analysis.

Results
Results obtained from 60 patients were evaluated: 30 patients were treated in the Kolop peloid group and 30 patients in the control group. No side effects were noted. Patient compliance was adequate, all patients attended all visits. The two groups were comparable in gender (7 men and 23 women participated in the peloid-treated group, and 9 men and 21 women participated in the control group), age, and need for analgesics and NSAIDs (8 patients in the peloid-treated group and 9 patients in the control group received medication for knee pain).

WOMAC
The WOMAC pain, stiffness, function, and total scores significantly improved from baseline to the end of treatment in both groups, and further improvement was observed during the follow-up period (Table 1).
<table>
<thead>
<tr>
<th></th>
<th>Visit 1 (baseline)</th>
<th></th>
<th>Visit 2 (week 3)</th>
<th></th>
<th>Visit 3 (week 15)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=30</td>
<td>n=30</td>
<td>mean (SD)</td>
<td>mean (SD)</td>
<td>n=30</td>
<td>n=30</td>
</tr>
<tr>
<td>Peloid hot pack control</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>between-group difference</td>
<td></td>
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<tr>
<td>WOMAC pain score</td>
<td>47.11 (15.049)</td>
<td>29.47 (14.17)</td>
<td><em>p</em>&lt;0.001</td>
<td></td>
<td>34.94 (14.042)</td>
<td>23.53 (13.265)</td>
</tr>
<tr>
<td>WOMAC stiffness score</td>
<td>54.45 (19.847)</td>
<td>42.57 (22.525)</td>
<td>NS</td>
<td></td>
<td>39.45 (18.853)</td>
<td>33.9 (19.446)</td>
</tr>
<tr>
<td>WOMAC function score</td>
<td>53.55 (14.93)</td>
<td>39.9 (15.507)</td>
<td><em>p</em>&lt;0.001</td>
<td></td>
<td>41.69 (14.672)</td>
<td>33.82 (15.925)</td>
</tr>
<tr>
<td>WOMAC total score</td>
<td>155.11 (44.645)</td>
<td>111.94 (48.61)</td>
<td><em>p</em>&lt;0.001</td>
<td></td>
<td>116.08 (43.224)</td>
<td>91.24 (45.372)</td>
</tr>
<tr>
<td>EQ-5D index</td>
<td>0.61 (0.144)</td>
<td>0.57 (0.184)</td>
<td>NS</td>
<td></td>
<td>0.67 (0.171)</td>
<td>0.63 (0.194)</td>
</tr>
<tr>
<td>VAS score of general health status</td>
<td>52.53 (11.611)</td>
<td>56 (13.386)</td>
<td>NS</td>
<td></td>
<td>63.9 (13.725)</td>
<td>61.07 (12.616)</td>
</tr>
<tr>
<td>Medial joint tenderness</td>
<td>2.9 (0.759)</td>
<td>2.9 (0.759)</td>
<td>NS</td>
<td></td>
<td>2.13 (0.571)</td>
<td>2.2 (0.664)</td>
</tr>
<tr>
<td>Lateral joint tenderness</td>
<td>2.63 (0.999)</td>
<td>2.67 (0.802)</td>
<td>NS</td>
<td></td>
<td>2.07 (0.583)</td>
<td>2.1 (0.712)</td>
</tr>
<tr>
<td>Pes anserinus insertion tenderness</td>
<td>1.97 (1.033)</td>
<td>1.97 (0.964)</td>
<td>NS</td>
<td></td>
<td>1.6 (0.675)</td>
<td>1.7 (0.837)</td>
</tr>
</tbody>
</table>

Table 1 Study parameters and their changes in comparison with baseline in the two groups and the between-group differences
The initial parameters (Week 0) suggested a more severe disease in the peloid-treated group compared to the control group (a significant difference was seen in the WOMAC pain, function, and total scores between the two groups). However, improvement from baseline to the end of treatment (Week 3) and to the end of the follow-up period (Week 12) was more significant in the Kolop peloid-treated group compared to the control group (Table 2).

<table>
<thead>
<tr>
<th>Change between visit 2 and visit 1</th>
<th>Change between visit 3 and visit 1</th>
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</thead>
<tbody>
<tr>
<td>Peloid hot pack</td>
<td>Control</td>
</tr>
<tr>
<td>n=30</td>
<td>n=30</td>
</tr>
<tr>
<td>mean (SD)</td>
<td>mean (SD)</td>
</tr>
<tr>
<td>WOMAC pain score</td>
<td>WOMAC stiffness score</td>
</tr>
<tr>
<td>12.17 (6.52)</td>
<td>15 (7.69)</td>
</tr>
<tr>
<td>p=0.001</td>
<td>p=0.08</td>
</tr>
<tr>
<td>WOMAC function score</td>
<td>WOMAC total score</td>
</tr>
<tr>
<td>11.85 (5.23)</td>
<td>39.03 (17.26)</td>
</tr>
<tr>
<td>p=0.00</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Peloid hot pack</td>
<td>Control</td>
</tr>
<tr>
<td>n=30</td>
<td>n=30</td>
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<tr>
<td>mean (SD)</td>
<td>mean (SD)</td>
</tr>
<tr>
<td>WOMAC pain score</td>
<td>WOMAC stiffness score</td>
</tr>
<tr>
<td>17.93 (12.12)</td>
<td>22.87 (11.43)</td>
</tr>
<tr>
<td>p=0.001</td>
<td>p=0.001</td>
</tr>
<tr>
<td>WOMAC function score</td>
<td>WOMAC total score</td>
</tr>
<tr>
<td>18.057 (80.08)</td>
<td>58.85 (26.88)</td>
</tr>
<tr>
<td>p=0.01</td>
<td>p=0.001</td>
</tr>
</tbody>
</table>

Table 2: The improvement of WOMAC pain, stiffness, function and total score between the post-treatment visits and the baseline, and the between-group differences

Quality of life (EuroQol-5D)
The EuroQol-5D quality of life index improved from baseline to the end of treatment in both groups, but this improvement was significant in the control group only; however, at Week 3, there was no significant difference between the two groups. By the end of the follow-up period (Week 12), both groups improved significantly compared to baseline. At the end of the follow-up period (Week 12), the EuroQol-5D quality of life index was significantly better in the Kolop peloid-treated group compared to the control group (Table 1).

The VAS score indicating the current general health status of the patients significantly improved from baseline to the end of treatment in both groups, and further improvement was observed during the follow-up period. At the end of the follow-up period (Week 12), general health status was significantly better in the Kolop peloid-treated group compared to the control group (Table 1).

Tenderness
Tenderness along the medial and lateral joint spaces and along the insertion of the pes anserinus significantly decreased in both groups by the end of treatment, and further
improvement was observed during the follow-up period. Although the Kolop peloid-treated group showed a greater improvement compared to the control group, there was no significant difference between the two groups (Table 1).

**Discussion**

Our study showed the beneficial effects of Kolop peloid on knee osteoarthritis in the short and long term. According to the results of our study, peloid therapy combined with mineral water bathing, aquatic exercise and magnetotherapy provided significantly better results regarding pain, function and quality of life than mineral water bathing, aquatic exercise and magnetotherapy without peloid therapy.

In our opinion, the reason why patients in the Kolop peloid-treated group had more severe disease at baseline according to the WOMAC score was that several patients with severe disease refused to participate in the study after randomization and before filling the questionnaires if they did not have the opportunity to receive peloid treatment. These patients were excluded from the study. This difference was indicated less sensitively by the EuroQol-5D questionnaire.

Our study is the first evaluating the additive beneficial effects of mud therapy as part of combined treatment. In a randomized, multicenter trial involving 382 patients with knee osteoarthritis, Forestier et al. evaluated the effects of peloid therapy as part of combined physiotherapy and balneotherapy. The control group received standard care only (pharmacotherapy, counsel, physiotherapy). Combined physiotherapy and balneotherapy (manual massage, hydrojet, hot peloid therapy and aquatic exercise in thermal mineral water) for 18 days applied together with standard care resulted in greater improvement in pain and function (WOMAC) in the long term (6 months) compared to the control group not receiving combined physiotherapy and balneotherapy [15].

According to controlled clinical studies evaluating the effects of peloid used as monotherapy, peloid therapy has an analgesic effect and causes improvement of joint function in patients with knee osteoarthritis [3-10].

Many authors described this favorable effect when peloid therapy was combined with thermal mineral water bathing [11-14]. Peloid therapy alone [10-11] or in combination with other treatments [15] has been shown to have a favorable effect on the quality of life in patients with knee osteoarthritis.

The improvement observed in the control group is not surprising. Several tap water-controlled, double-blind studies have shown the analgesic and function-improving effect of mineral water bathing in patients with knee osteoarthritis, which effect was more pronounced compared to the control group [23-27].

It has been shown that land based exercise reduces pain and improves function in patients with osteoarthritis of the knee compared to the group of patients who do not exercise [28]. A Japanese review published in 2010 evaluating meta-analyses performed between 1990 and August of 2008 on hydrotherapy concluded that aquatic exercise has
similar effects to that of land based exercise [29]. According to some recently published, randomized, controlled studies aquatic exercise has a more pronounced analgesic effect in hip and knee osteoarthritis compared to land based exercise [30,31]. Although magnetotheraphy is widely used in practice, its effect has not yet been proven [32]. Many authors have studied the role and the mechanism of heat therapy in decreasing pain and inflammation [33-35]. In response to heat, elasticity of collagen-rich tissues increases, muscle spasm decreases, which presumably reduce pain, and joint function improves [34]. Inferring from other studies, mud therapy decreased the level of inflammatory mediators and had a positive effect on the markers of antioxidant status and cartilage degradation [36-39]. Only few data exists about the absorption and chemical effects of mud components [40-41].

The first day care hospital for musculoskeletal disorders, the Rheuma Rehabilitation Centre was founded in Amsterdam, the Netherlands in 1967, providing complex care at a hospital level. Based on the Dutch experiences, the first day care hospital department of Budapest was founded in the Lukács Thermal Bath in 1967, followed by the Széchenyi Bath in 1982 and the Gellért and Rudas Baths in 1997.

In Hungary, patients with musculoskeletal disorders receive personalized, 15- and 20-day treatment in day care hospitals. This treatment is supported by social security. The goal of the treatment is to provide specialized spa treatment to patients with musculoskeletal disorders who are able to walk but require combined physiotherapy. One of the big advantages of day hospital care is that the patient is not separated from his/her normal family environment during the treatment. Depending on the local conditions, admitted patients receive 4-hours daily treatments in one or two shifts. Independently from the nature of the disease, each patient can participate in 2 treatment courses per calendar year (including other spa treatments) [15,16].

According to the data of the authors of this study, the number of nursing days in the day care hospitals of the three “historic spas” of Budapest (St. Gellért, St. Lukács and Széchenyi) was 78,812 in 2011; and 5,255 patients received combined therapy. Since January of 2003, costs of combined therapy are only partially covered by social security support, and patients make co-payments [42].

The advantages of day care hospital include: its setup in spas requires less investment similarly to the lower costs of the outpatient clinics and combines the advantages of hospital therapy. No night shifts, fewer personnel are needed, patients do not receive meals, and the same time the patients are not separated from their family environment.

**Limitation of the study**

Lack of group homogeneity regarding the baseline WOMAC scores. Single-blind method.

**Conclusions**

This controlled, follow-up study showed that Kolop peloid has favorable effect on knee osteoarthritis both in the short and long term. Peloid therapy combined with mineral
water bathing, aquatic exercise and magnetotherapy provided significantly better results regarding pain, function and quality of life than mineral water bathing, aquatic exercise and magnetotherapy without peloid therapy. In patients treated with Kolop peloid, clinical parameters (WOMAC pain, joint stiffness, and function) improved significantly more compared to the control group. At the end of the follow-up period, quality of life was significantly better in the peloid-treated group compared to the control group. Periarticular tenderness improved more in the peloid-treated group compared to the control group, however this difference was not significant. According to our opinion the more significant improvement observed in the peloid-treated group was caused by the favorable effect of the peloid. We can conclude that Kolop peloid is a possible therapeutic option in the treatment of patients with knee osteoarthritis.

Acknowledgments
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Conflicting interests
Regarding material costs, this study was sponsored by Budapest Baths cPlc.

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