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SHORT REPORTS

Does Mud Pack Treatment Have Any Chemical Effect? A Randomized Controlled Clinical Study

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ABSTRACT

Objective: The aim of this study was to reveal the efficacy of mud pack treatment in patients with knee osteoarthritis and to find the contribution of chemical factors to the build up of these effects.

Methods: Sixty patients were randomly assigned to directly applied mud pack (study) group or to nylon-covered mud pack (control) group. Thirty patients in the study group had mud application 15 times to both knees: heated mud, up to 43°C, was applied to skin directly for 30 minutes. Thirty patients in the control group had the same treatment as the study group except heated mud was applied over an impermeable nylon pack. Primary outcome measures of the study were the Western Ontario and McMaster Universities (WOMAC) index, pain intensity on a visual analog scale (VAS), patient's assessment of disease severity index, physician's assessment of disease severity index, and analgesic consumption. The patients were evaluated before and after (end of 15th application) the intervention and followed up for 24 weeks at 4-week intervals. The results were assessed on an intent-to-treat basis.

Results: As compared to the baseline, significant decreases were observed in WOMAC, pain intensity, disease severity index scores, and analgesic consumption in both groups after the intervention. Observed improvements in the study group were found to be superior to the control during the whole postintervention follow-up, except for analgesic consumption in the third week. A significant number of patients in the study group showed minimal clinically important improvement as compared to the control group.

Conclusion: Mud pack treatment significantly improved the pain and functional status of patients with knee osteoarthritis, whether applied directly or coated with nylon. Direct application was found to be superior, which implies chemical properties of the mud contribute to the build up of therapeutic effect.

INTRODUCTION

Osteoarthritis (OA) is the most frequent musculoskeletal disorder and is becoming an important health concern considering the increase in the older population.[1] No curative therapy is available for the disease and many patients attempt alternative modes of treatment, including balneotherapy. Balneotherapy is one of the oldest forms of natural therapies for rheumatic diseases and other musculoskeletal conditions.[2] Recently, a statement of the American College of Rheumatology positioned balneotherapy as an essential complementary therapy for rheumatic diseases.[3] Additionally, balneotherapy is also one of the nonpharmacologic interventions to be assessed for its efficacy in OA by the European League Against Rheumatism (EULAR).[4] Muds are therapeutic substances used in balneotherapeutic treatments. They consist of various amounts of organic and inorganic materials and provide heat transfer by conduction.

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Muds are superior to the other balneotherapeutic mediums in terms of their long-term heat conduction capacity.[5] Their beneficial effects in terms of pain relief and functional status improvement has been reported in patients with osteoarthritis,[6–9] rheumatoid arthritis,[10,11] psoriatic arthritis,[12] and fibromyalgia syndrome.[13,14] The beneficial effect of mud pack treatment is often attributed to its thermal effects; however, several studies suggest that a specific mode of action should also be considered. Gallic, vanilic, humic, fulvic, and protocatechic acid derivates are commonly found in the chemical composition of muds[15] and it can be speculated that they may contribute to the effects of mud. The mechanism of such specific action is not obvious. Moreover, it is hard to attribute the observed effect to a specific chemical. It is certain that existing evidence is not enough to reveal the role of the chemical composition of mud in the beneficial effects of mud pack treatment. Therefore, the current study aimed to reveal the efficacy of mud pack treatment on clinical symptoms of patients with knee OA and to find the possible contribution of the chemical components of the mud.

MATERIALS AND METHODS

Patients

One hundred forty-one (141) patients with bilateral primary OA of the knee were enrolled in the study. Their diagnosis were made using American College of Rheumatology classification criteria for knee OA.[16] Patients included in the study had documented radiological alterations in their knee joint = grade 3 or more according to the Kellgren-Lawrence criteria[17] (grade 0, normal; grade 1, doubtful; grade 2, minimal; grade 3, moderate; grade 4, severe), and had an average pain intensity of 60 or more on a 100-mm visual analog scale (VAS) in the ten days before the baseline assessment. None of the patients had skin or systemic disease that could counterindicate the use of local heat. None of the patients had had intra-articular injection, electrotherapy, or balneotherapy within the previous 6 months. One hundred twenty-one (121) patients with symptomatic knee OA fulfilled the selection criteria. Twenty of these eligible patients refused to participate in the study, stating that having such treatment on an outpatient fashion would impede their daily life. Finally, 101 patients gave their informed consent according to the Helsinki Declaration and agreed to participate in the study. For this study, 60 patients were randomly selected using a computer-generated random number list and allocated to either the directly applied mud pack (study; $n = 30$) or nylon-covered mud pack (control; $n = 30$) arms of the study.

Treatment protocol

All patients had 15 mud pack treatments on an outpatient basis, daily for three weeks, except Saturdays and Sundays. In the study group, thermal mud at 43°C was applied directly to both knees for 30 minutes. In the control group, mud at 43°C was applied to both knees over a 0.5-mm impermeable nylon film for 30 minutes. Throughout the treatment and follow-up period, patients in both groups continued to receive their regular medications, including paracetamol (acetaminophen) or nonsteroidal anti-inflammatory drugs (NSAIDs) whenever they felt it necessary. The patients were asked to record their analgesic consumption daily and report it to their physician at follow-up visits.

Assessment

Each patient had 8 evaluations: before the first mud pack application (baseline-week 0), after the last mud pack application (week 3), and 6 times during the follow-up period at 4-week intervals (weeks 7, 11, 15, 19, 23, 27). Evaluations were carried out by the same physician (HE) who was blinded to the evaluation period and to the study arm. There were no dropouts until week 19. One patient each from the study and the control group left follow-up at week 19, and four patients from the control group left the study at week 23. The last observation data of the withdrawn patients were carried forward to week 27 so that all 60 patients were included in the analyses.

Outcome measures

The primary outcome measures were the Western Ontario and McMaster Universities osteoarthritis index (WOMAC) global index; pain intensity scored on a 100-millimeter visual analog scale (VAS); the patient's global assessment of disease status and response to therapy score; the physician's global assessment of disease status and response to therapy score; and analgesic consumption.

WOMAC is a multidimensional measure scored using a 5-point Likert scale. The sum of the scores used in the study was obtained by adding the subscale scores for pain, stiffness, and physical functional disability. Scores ranged from 0–96.

Pain intensity was defined using a VAS.

Both the patient's and physician's global assessments of disease status and response to therapy scores were defined using a scale from 0 (excellent) to 5 (unbearable). Analgesic consumption was reported at each visit by asking patients for their daily analgesic consumption records.

We defined minimal clinically important improvement (MCII) for relative changes as: –40.8% for pain; –39.0% for patient's and physician's global assessment; and –26.0% for WOMAC score.[18] A decrease of 40.8% or more in analgesic consumption was considered meaningful.

Mud

Regarding its physical, chemical, and geological properties, the mud used in this study has been classified as torf mud. It was obtained from the Denizli region of Turkey.

Table 1. Baseline Characteristics of Patients

Variable	*Study group* (n = *30*)	*Control group* (n = *30*)	P
Age (years)	69.2 ± 1.3	69.0 ± 1.5	0.908[a]
Gender (F/M)	28/2	27/3	
VAS	81.0 ± 9.8	82.0 ± 8.4	0.557[a]
WOMAC global index	72.8 ± 7.3	76.0 ± 10.8	0.119[a]
Kellgren-Lawrence score	III (n = 5)	III (n = 4)	0.718[b]
	IV (n = 25)	IV (n = 26)	

Data expressed as mean ± standard deviation.

VAS, visual analog scale; WOMAC, Western Ontario and McMaster Universities osteoarthritis index.

[a]Mann-Whitney U test.

[b]Chi-square test.

Statistical analysis

The analysis of outcomes was performed on an intent-to-treat basis with the use of the last observation carried forward for dropouts. Nonparametric methods were used in statistical calculations due to the distribution characteristics of the data. Comparison of several paired groups (baseline and follow-up measurements) was performed using Friedman's test. Study groups were compared using the Mann-Whitney U test. All statistical calculations were performed using SPPS for Windows v. 11.0 (SPPS, Chicago, IL). Alpha value was set to 0.05 in all calculations, and a p value less than 0.05 was accepted as statistically significant.

RESULTS

The clinical and demographic characteristics of the study population are given in Table 1. There were no significant differences in the characteristics of the study and control groups.

WOMAC, pain, and patient's and physician's global assessments of disease status and response to therapy scores

Significant clinical improvements were observed in both groups during the study and follow-up periods (Tables 2, 3). However, comparing the index scores in terms of percent change from baseline for the two groups indicated that applying mud directly provided better results (Table 4). Similarly, the number of patients who had minimal clinically important improvement was significantly higher in the study group at week 3 and remained significantly high through to the end of the follow-up period (Table 5).

Analgesic consumption

Analgesic consumption was significantly decreased in both groups. The percent change from baseline and the proportion of patients with >40.8% decrease in analgesic consumption was similar in both groups at week 3. However,

Table 2. Comparisons of Baseline (Week 0), Post-treatment (Week 3), and Follow-up Evaluations in Study Group

	WOMAC	*VAS*	*DSIp*	*DSIph*	*Analgesic consumption (tablets/month)*
Week 0	72.8 ± 7.3	81.0 ± 9.8	7.5 ± 1.5	7.3 ± 1.43	27.9 ± 16.1
Week 3	34.9 ± 9.2[a]	43.6 ± 10.6[a]	3.5 ± 1.0[a]	3.2 ± 1.0[a]	7.1 ± 3.8[a]
Week 7	33.8 ± 9.4[a]	42.0 ± 9.8[a]	3.1 ± 1.1[a]	2.9 ± 1.1[a]	3.1 ± 3.5[a]
Week 11	33.6 ± 8.8[a]	43.3 ± 10.3[a]	3.2 ± 0.9[a]	3.0 ± 1.1[a]	4.0 ± 5.4[a]
Week 15	35.7 ± 7.9[a]	44.5 ± 9.3[a]	3.2 ± 1.0[a]	3.1 ± 1.0[a]	3.8 ± 5.7[a]
Week 19	36.5 ± 6.9[a]	46.0 ± 10.8[a]	3.4 ± 1.1[a]	3.3 ± 1.0[a]	4.6 ± 6.2[a]
Week 23	39.2 ± 10.1[a]	48.3 ± 15.2[a]	3.7 ± 1.4[a]	3.6 ± 1.4[a]	6.9 ± 8.0[a]
Week 27	40.8 ± 11.4[a]	51.3 ± 17.4[a]	3.8 ± 1.4[a]	3.6 ± 1.4[a]	8.5 ± 8.1[a]
Chi square value[b]	95.009	108.507	120.344	128.104	108.390
P	0.0001	0.0001	0.0001	0.0001	0.0001

[a]$p < 0.001$, Mann-Whitney U test.

[b]Friedman's test.

Data are expressed as mean ± standard deviation.

WOMAC, Western Ontario and McMaster Universities osteoarthritis index; VAS, visual analog scale; DSIp, patient's global assessments of disease status; DSIph, physician's global assessments of disease status.

Table 3. Comparison of Baseline (Week 0), Post-treatment (Week 3), and Follow-up Evaluations in the Control Group

	WOMAC	*VAS*	*DSIp*	*DSIph*	*Analgesic consumption (tablets/month)*
Week 0	76.0 ± 10.8	82.0 ± 8.4	7.2 ± 2.0	6.3 ± 1.8	27.2 ± 13.4
Week 3	53.2 ± 12.7[a]	69.7 ± 12.1[a]	4.4 ± 1.9[a]	5.1 ± 2.0[a]	6.9 ± 3.3[a]
Week 7	65.4 ± 15.7[b]	74.8 ± 12.4[b]	5.9 ± 2.5[b]	5.6 ± 2.3[b]	19.5 ± 10.8[b]
Week 11	70.4 ± 14.9[b]	76.9 ± 13.3	6.7 ± 2.5[b]	5.9 ± 2.3[b]	25.2 ± 15.0
Week 15	73.7 ± 13.1	78.3 ± 13.8	6.8 ± 2.4[b]	5.9 ± 2.2[b]	25.2 ± 15.2
Week 19	74.6 ± 12.6	80.5 ± 14.3	6.9 ± 2.5	6.2 ± 1.9	25.7 ± 14.6
Week 23	75.9 ± 11.8	80.3 ± 11.5	7.0 ± 2.3	6.2 ± 2.0	25.7 ± 14.5
Week 27	75.8 ± 11.1	81.1 ± 10.5	7.1 ± 2.2	6.3 ± 1.9	26.3 ± 13.9
Chi square value[c]	64.761	42.070	57.857	41.830	104.948
p	0.0001	0.0001	0.0001	0.0001	0.0001

[a]$p < 0.001$, Mann-Whitney U test.
[b]$p < 0.01$, Mann-Whitney U test.
[c]Friedman's test.
Data are expressed as mean ± standard deviation.
WOMAC, Western Ontario and McMaster Universities osteoarthritis index; VAS, visual analog scale; DSIp, patient's global assessments of disease status; DSIph, physician's global assessments of disease status.

the study group was found to be superior in the subsequent evaluations.

Side-effects

No side effects were observed during the study period in either group.

DISCUSSION

The findings of this study indicate that mud pack treatment, especially direct application of mud, is effective on knee OA in terms of pain alleviation, functional capacity, and reduced analgesic consumption.

Although statistically significant improvements were observed in both groups at the end of treatment and during the follow-up period, the most important issue in such treatment efficacy studies is the clinical meaning of such changes. In other words, observed statistically meaningful changes may not translate to a clinical benefit. The most difficult issue is to decide whether observed difference is clinically important.[18] That is why the use of minimal clinically important improvement is necessary to interpret clinical study results.

Direct application of mud packs was found to be superior regarding the change from baseline and minimal clinically important improvement parameters. This implies that the chemical properties of the mud are also important in achieving the beneficial effects of mud pack treatment.

Efficacy of mud pack treatment in knee OA has been shown in several studies.[6–8,19] Our results are in accordance with the literature. However, to our knowledge, this is the first study in terms of studying equal thermal effects for both groups and using a longer (6 month) follow-up duration.

Table 4. Comparison of Study Group and Control Group in Terms of Percent Changes from the Baseline

	WOMAC	*VAS*	*DSIp*	*DSIph*	*Analgesic consumption (tablets/month)*
Weeks 0–3	0.0001	0.0001	0.019	0.0001	0.691[a]
Weeks 0–7	0.0001	0.0001	0.0001	0.0001	0.0001
Weeks 0–11	0.0001	0.0001	0.0001	0.0001	0.0001
Weeks 0–15	0.0001	0.0001	0.0001	0.0001	0.0001
Weeks 0–19	0.0001	0.0001	0.0001	0,0001	0.0001
Weeks 0–23	0.0001	0.0001	0.0001	0.0001	0.0001
Weeks 0–27	0.0001	0.0001	0.0001	0.0001	0.0001

[a]No significantly different change in favor of study group at 0.05 level.
WOMAC, Western Ontario and McMaster Universities osteoarthritis index; VAS, visual analog scale; DSIp, patient's global assessments of disease status; DSIph, physician's global assessments of disease status.
Mann-Whitney U test is used. Data expressed as *p*-value.

Table 5. Number of Patients Who had Minimal Clinically Important Improvement

		Study group n (%)	*Control group n (%)*	*P*[a]
WOMAC (≥26%)	Week 3	30 (100.0)	18 (60.0)	0.0001
	Week 7	30 (100.0)	6 (20.0)	0.0001
	Week 11	30 (100.0)	6 (20.0)	0.0001
	Week 15	30 (100.0)	2 (6.7)	0.0001
	Week 19	30 (100.0)	0 (0.0)	0.0001
	Week 23	27 (90.0)	0 (0.0)	0.0001
	Week 27	26 (86.7)	0 (0.0)	0.0001
VAS (≥40.8%)	Week 3	19 (63.3)	2 (6.7)	0.0001
	Week 7	22 (73.3)	2 (6.7)	0.0001
	Week 11	21 (70.0)	2 (6.7)	0.0001
	Week 15	20 (66.7)	2 (6.7)	0.0001
	Week 19	18 (60.0)	2 (6.7)	0.0001
	Week 23	17 (56.7)	0 (0.0)	0.0001
	Week 27	15 (50.0)	0 (0.0)	0.0001
DSIp (≥39%)	Week 3	28 (93.3)	17 (57.0)	0.0001
	Week 7	29 (96.6)	9 (30.0)	0.0001
	Week 11	28 (93.3)	5 (16.7)	0.0001
	Week 15	28 (93.3)	3 (10.0)	0.0001
	Week 19	27 (90.0)	3 (10.0)	0.0001
	Week 23	24 (80.0)	3 (10.0)	0.0001
	Week 27	24 (80.0)	2 (6.7)	0.0001
DSIph (≥39%)	Week 3	27 (90.0)	3 (10.0)	0.0001
	Week 7	26 (86.7)	5 (16.7)	0.0001
	Week 11	26 (86.7)	3 (10.0)	0.0001
	Week 15	26 (86.7)	3 (10.0)	0.0001
	Week 19	26 (86.7)	2 (6.7)	0.0001
	Week 23	23 (76.7)	2 (6.7)	0.0001
	Week 27	23 (76.7)	2 (6.7)	0.0001
Analgesic consumption[b] (≥40.8%)	Week 3	30 (100.0)	30 (100.0)	1.0
	Week 7	30 (100.0)	20 (66.7)	0.001
	Week 11	29 (96.6)	6 (20.0)	0.0001
	Week 15	29 (96.6)	5 (16.7)	0.0001
	Week 19	29 (96.6)	5 (16.7)	0.0001
	Week 23	27 (90.0)	5 (16.7)	0.0001
	Week 27	25 (83.3)	5 (16.7)	0.0001

[a]Chi square.
[b]Tablets per month.
WOMAC,Western Ontario and McMaster Universities osteoarthritis index; VAS, visual analog scale; DSIp, patient's global assessments of disease status; DSIph, physician's global assessments of disease status.

We assume that the method we used in this study (direct application versus nylon-covered mud pack) is an appropriate technique to provide a similar thermal effect in both groups. The other studies in the literature used mineral-depleted mud, hot mineral water, or hot packs as controls. Such controls aim to keep the thermal effect of the medium while preventing its chemical effects. However, such interventions are defective in terms of revealing isolated effects of the thermal component since the heat retention capacity of the mud is closely linked with its chemical properties. It has been shown that muds rich in organic substances are more effective in conducting heat than those poor in organic substances.[20] In other words, it is difficult to maintain an appropriate and consistent thermal effect when using organic-rich and organic-poor muds. It is strongly possible that the heat retention capacity of the mud is weakened by mineral depletion due to changes in its chemical properties. Hot packs and hot mineral water applications are afflicted with the same condition. For example, after 20 minutes, the site that had hot mineral water applied was 10°–20°C colder than the site that had mud applied.[20] Accordingly, both groups in our design were subjected to similar thermal conditions.

The mechanism of action of mud pack application is not revealed in detail. It is suggested that both thermal and chemical properties of mud may play roles in such effects.[21] The results of the current study suggest that the chemical effect, as well as the thermal effect, of the mud is important in the beneficial outcomes of mud application. This is further supported by the observation that analgesic consumption was less in the directly applied mud group.

Wigler et al.[7] compared the effects of (1) thermomineral water baths combined with mud packs and (2) rinsed mud

packs alone in knee OA patients and reported significant improvements in both groups in terms of index of severity, patient and physician assessment of disease severity, and analgesic consumption. Fluster et al.[8] reported significant improvement in Lequesne knee index scores that lasted three months after treatment with rinsed mud packs of OA patients.

Favorable effects reported in these studies may be attributable to the thermal effects of the application. It has been reported that thermal stimulation increases extensibility of collagen-rich tissues, which improves the range of motion of involved joints, diminishes pain, and relieves muscle spasms.[22] The analgesic effect of heat may be explained by increased concentrations of β-endorphin.[23] Although it is known that β-endorphin is normally produced in the central nervous system, it has been hypothesized that human skin can release significant amounts of opioid peptides, modifying the threshold of pain under different stimuli, such as heat or UV radiation.[24] Heat may also have an anti-inflammatory effect. Anti-inflammatory effects of heat may arise from the increased secretion of cortisol and catecholamines induced by thermal stress.[25,26]

While the thermal effects of mud pack application have been elucidated, the chemical effects have not been exposed properly. Additionally, there is no consensus on which substances are responsible for chemical effects.

An anti-inflammatory compound of mature mud, sulphoglycolipid, a product of colonized microorganisms during the maturation process, has been shown to contribute to the therapeutic activity of thermal mud.[27] Beer et al.[28] reported that fulvic and ulmic acids, water-soluble compounds of mud, were found to have a stimulatory effect on contractile activity of smooth muscle tissue. It is also assumed that gallic, vanilic, and protocatechic acid derivatives may have a role in the chemical effects of mud.[15] However, it is still not clear which elements or organic substrates are essential and what is the ideal concentration of these elements in order to attain an optimal response to treatment.

It has been hypothesized that mud pack treatment combined with thermomineral water baths may affect certain cytokines, but relevant information is weak. Decreases in plasma levels of interleukin-1 and tumor necrosis factor-α, and consequent reduction in cartilage inflammation and tissue destruction with mud pack treatment have been reported.[29–31] Additionally, it has been found that matrix metalloproteinase-3 plasma levels were significantly lower in OA patients treated with mud baths.[32] However, it is not clear whether these effects are due to mud packs or thermomineral water baths.

It is often stated that staying at a resort hotel provides a strong placebo effect in balneotherapeutic evaluation studies. This study was carried out in an outpatient setting and both groups were subjected to the same environment. Accordingly it can be claimed that our study is exempt from such an effect.

The absence of a control group that received application of a different mud, which might have allowed further evaluation of the chemical effect of the treatment, may be taken as a weakness of this study. Such a group was not included in the study because the effects of the chemical content of the mud has not been shown saliently and there is no consensus about the effect mechanism of mud therapy in terms of chemical components.

CONCLUSIONS

Patients suffering from knee OA benefited from mud application for a considerable amount of time. Study outcomes strongly imply that chemical components of the mud actively contribute to this effect. Mud treatment should be anticipated to be an effective complementary treatment modality that is effective in terms of reducing pain, analgesic consumption, and improving functional capacity.

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