

Treatment of KNEE OSTEOARTHRITIS in Spa Health resorts: where do we stand?

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Abstract

Osteoarthritis (OA) includes degenerative joint disorders that affect articular cartilage in the first instance, followed by changes of all components of the joint. The disease is detected in a proportion of 33% by X-ray in patients aged over 60 years. Knee OA (KOA) ranks first among chronic diseases from the point of view of patient disability.

This article is a review of guidelines and articles regarding arthrosis, balneotherapy, and balneotherapy in KOA treatment. These were accessed on the Pubmed site in the period March-April 2015.

The components of balneo-therapy to which the selected articles refer include mud packs, mineral waters, climate change. These are evaluated in association or in comparison with other methods used in the rehabilitation specialty area for the treatment of KOA: kinesitherapy, intra-articular infiltrations, hydrothermotherapy.

The changes induced by these therapies on clinical evolution (pain relief, tenderness, functionality, quality of life, depression symptoms) or certain serum parameters (biomarkers of oxidative stress, inflammation and cartilage destruction, vitamin D and other serum metabolites) were recorded.

The results of our review are consistent with the studies focused on spa modalities in all types of OA. All these data helped defining the role of balneotherapy as part of the rehabilitation program for the treatment of KOA, through the benefits specific to it.

Conclusion: Balneotherapy has beneficial effects on patients with KOA, both clinically and serologic improvements. Further studies are needed to quantify these effects using KOA specific markers, to establish a hierarchy of balneotherapy methods based on their effects on KOA, as well as to refine indications depending on the stage of the disease.

Introduction

Balneology represents the branch that uses natural physical factors characteristic for spas, such as mineral waters, therapeutic muds (peloids)¹. Balneotherapy has been defined recently as the use of natural mineral waters, natural peloids and mud, and natural sources of different gases (CO₂, H₂S, and Rn) for medical purposes such as prevention, treatment, and rehabilitation².

Osteoarthritis (OA) is the most frequent rheumatological degenerative disease. Within this pathology, the knee is the

main affected joint in all populations throughout the world³.

Osteoarthritis includes degenerative joint disorders that affect articular cartilage in the first instance, followed by changes of all components of the joint. The disease is detected in a proportion of 33% by X-ray in patient saged over 60 years. Knee osteoarthritis ranks first among chronic diseases in terms of patient disability.

There are numerous studies on balneotherapy for knee OA in the literature, but they are on a small scale⁴. Therefore in this field there is a lack of high quality scientific evidence of the efficacy for knee OA. In a recent Cochrane systematic review, even those studies that met the selection criteria were found to be flawed.

It is worth to be mentioned that balneotherapy is disregarded by most clinical guidelines from other specialties: for exemple it

was not included in the 2013 EULAR recommendations⁵.

This article tries to answer the following questions: “does balneotherapy have good effects on KOA?”, “is it used worldwide?”, “is it worth to highlight its potential benefits through large clinical trials?”.

Materials and methods

Our objective was to make a review of the current guidelines and articles regarding clinical and para-clinical effects of balneotherapy in kneeosteoarthritis. These were accessed on the Pubmed site in the period March-April 2015.

Data extraction

This review covers the use of thermal mineral waters, mud pack within balneo-therapy means used in KOA. Other rehabilitation intervention which were either associated with balneo-therapy or used as a term of comparison are: aerobic, muscle strengthening and water-based exercise, intra-articular injections with Hyalgan. We searched the above-mentioned literature published between 2010 and 2014, using the following terms of search on Pubmed database: *balneo-therapy, spa therapy, thermal water, mineral water, peloid, mud pack, hydrotherapy*.

Regarding the inclusion criteria for reviewed articles, we included all clinical trials in the systematic review that assessed the effects of different balneotherapy procedures on clinical outcome, quality of life. Studies meeting the following criteria were selected for diagnose of KOA.

The randomized controlled trials comparing balneo-therapy with any intervention were also included.

Results

We found relevant 3 reviews and meta-analyses regarding the effect evaluation in spa modalities applied for KOA. 11 studies regard: the effects of mineral water and/ or mud pack therapy on clinical status and biological markers. And 1 study compares mud pack with intra-articular hyaluronic acid.

Treatment effectiveness evaluation

To evaluate the clinical status and the effects of balneo-therapy, the studies considered Visual Analogue Scale for spontaneous pain or WOMAC pain scale, WOMAC functional capacity, Psychosocial status, Depression, WOMAC osteoarthritis index, Hospital for Special Surgery (HSS) score, Knee Society clinical rating system (knee and function scores), Lequesne Index, WOMAC Index, SF-36, Arthritis Impact Measurement Scale (AIMS), Nottingham Health Profile (NHP) symptomatic drugs consumption. Some studies focused on plasmatic cartilage destruction markers, inflammatory mediators and other serum metabolites.

Meta-analysis with balneo-therapy in KOA patients

Françon A, Forestier R 2009⁴, Espejo-Antúnez L 2012⁶, Hua Liu 2013⁷, as a result of the meta-analysis, consider the balneo-therapy effective on KOA, because of persistent reducing pain, improvement of functional capacity, improvement in quality of life, reducing analgesic and non-steroidal antiinflammatory drug consumption⁴. Mud pack therapy is consider an effective therapy, reducing pain, improving function and quality of life^{6,7}.

Table 1. Meta-analysis balneo-therapy in KOA patients

<p>Françon A, Forestier R 2009⁴: Clinical practice guidelines published by the French National Authority for Health (HAS) and the European League Against Rheumatism (EULAR) and on the results of randomized clinical trials (RCT):</p> <p>Sixteen studies indicated a persistent improvement (at least twelve weeks) in pain, analgesic and non-steroidal antiinflammatory drug consumption, functional capacity and/or quality of life, in the following indications: chronic lower back pain, knee osteoarthritis, hand osteoarthritis, fibromyalgia, ankylosing spondylitis, rheumatoid arthritis (PR).</p>
<p>Espejo-Antúnez L, 2012⁶: randomized clinical trials, systematic reviews or meta-analyses whose objective was to analyse the effect of mud pack therapy on perceived pain, function and quality of life, with a sample size of ≥ 20 subjects, published since 2000 and showing conclusive results: mud pack therapy is considered an alternative and effective therapy in the clinical management of knee OA.</p>
<p>Hua Liu, 2013⁷: A quantitative meta-analysis of seven studies- randomized controlled trials and prospective comparative studies published before 9 March 2013 that compared mud therapy with control group treatments in patients with knee OA (410 patients). There was a significant difference between the groups in the visual analogue scale pain score and Western Ontario and McMaster Universities Osteoarthritis Index pain score, with differences in favour of mud therapy.</p>

Clinical studies evaluating the effects of mineral waters and mud pack on pain and function in KOA patients

We consider separately mineral water and mud pack studies in Table nr. 2 and Table nr. 3, whereas in Table nr. 4 we present a study that applied these procedures simultaneously.

Thermal mineral water baths resulted in significant improvement of the clinical status, reducing pain [measured with a visual analogue scale (VAS) or tenderness score (TS)], function [rated with the Western Ontario and McMaster Universities (WOMAC) scale, 50-ft walking duration, quadriceps muscle strength (QMS), active flexion degree (AFD), Nottingham Health Profile (NHP), Lequesne index of osteoarthritis severity] and quality of life [SF-36 quality of health questionnaire] after balneo-therapy; as seen in studies listed in Table nr. 2.

All 4 studies concluded that the hydrothermal treatment modalities, using spa water or tap water were found to be effective in the management of the clinical symptoms and quality of life in KOA patients. However, pain

and tenderness improved statistically better with balneo-therapy. There were no significant differences between the groups for the other variables, like walking duration, quadriceps muscle strength, active flexion degree. Intermittent balneo-therapy appears to be effective for patients with knee osteoarthritis^{8,9}. Positive effect on gait and improvement of clinical parameters have been obtained with balneo-therapy in short-term evaluations (2 weeks)¹⁰. Also, we found one clinical study¹¹ demonstrating that the beneficial effects of balneo-therapy in patients with knee OA last over time (12 weeks), with positive effects on the painful symptomatology, a significant improvement on functional capacities and quality of life; the conclusion was that balneo-therapy can represent a useful backup to pharmacological treatment of knee OA or a valid alternative for patients who do not tolerate pharmacological treatments¹¹.

The above mentioned studies have been conducted in countries such as Italy, Israel, Turkey.

Table 2. Clinical studies evaluating the effects of mineral waters on pain and function in KOA patients

Study	Treatment	Outcome measures	Follow-up period	Results
Yurtkuran M al, 2006 ⁸	52 patients with KOA home-based standardized exercise program and: group I (n = 27) spa water at 37 degrees C, 20 min day, 5 days a week, 2 weeks. group II (n = 25), TW heated to 37 degrees C, the same protocol .	pain (pVAS), tenderness score (TS), 50-ft walking duration, quadriceps muscle strength (QMS), active flexion degree (AFD), WOMAC OA index, Nottingham Health Profile (NHI	2nd and 12 week	Pain and tenderness improved better with balneo-therapy. Hydrotherapy improves clinical symptoms and quality of life.
Sherman 2009 ⁹	44 KOA patients: a treatment group (n=24), treated twice weekly for 6 consecutive weeks in sulfur pool heated to 35-36 degrees C; control group (n=20) treated in a Jacuzzi filled with tap water heated to 35-36 degrees C.	Lequesne index of osteoarthritis severity, WOMAC index, SF-36 quality of health questionnaire, VAS scales for pain (completed by patients and physicians), physical examination.	6 months	Intermittent balneo-therapy appears to be effective for patients with knee osteoarthritis
Kılıçoğlu O et al, 2009 ¹⁰	30 KOA patients: two daily thermomineral water baths for 2 weeks.	Gait analysis and clinical scores: Lequesne knee osteoarthritis index, VAS, investigator's global assessment, WOMAC score	2 weeks	Positive effects on gait properties and clinical health quality parameters.
Fioravanti 2012 ¹¹	60 outpatients with primary bilateral KOA: group I (30 patients) daily sulphate-bicarbonate-calcium mineral water bath; group II (30 patients), the control group, continued their regular outpatient care routine.	Visual Analogue Score(VAS) for spontaneous pain, Lequesne Index, Womac Index, SF-36, Arthritis Impact Measurement Scale (AIMS) symptomatic drugs consumption	15 days 12 weeks	Positive effects on the pain a significant improvement on functional capacities and QoL

Mud pack is a favorable option compared with hot pack for pain relief and for the improvement of functional conditions in treating patients with knee osteoarthritis¹². The mud-bath therapy performed at Chianciano Spa with

Sillene Spring water remarkably improved the clinical conditions of patients with knee arthritis and significantly reduces the frequency and severity of symptoms and the disability they cause¹³.

The tolerability is very good, no adverse effects were observed¹³.

Table 3. Clinical studies evaluating the effects of mud pack on pain and function in KOA patients

Study	Treatment	Outcome measures	Follow-up period	Results
Fraioli et al, 2010, Italy ¹³	61 KOA patients: group A underwent three cycles of mud-based sp therapy over a year's time, whereas group B did not	Clinical conditions, Visual Analogue Scale pain ratings, Lequesne indexes	1 year	No adverse effects observed in any of the patients group A. Improvement clinical conditions. Increase the frequency and severity of symptoms and the disability.
Sarsan et al, 2012 ¹²	27 patients with clinical and radiologic evidence of knee osteoarthritis, 2 groups: mature mud packs (n 15) or hot pack (n=12).	VAS, WOMAC, 6 min walking distance, Short Form-36 (SF-36), serum levels of tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), insulin-like growth factor 1 (IGF-1)	post-treatment and 3 and 6~months after treatment	Mud pack is a favorable option compared with hot pack for pain relief and for the improvement of functional conditions in treating patients with knee osteoarthritis.

Combination of mineral waters and mudpack in treatment of KOA patient determined improvements on pain, range of motion, psychological status and quality of life¹⁴.

Table 4. Clinical study evaluating the effects of both mineral waters and mud pack on pain, function, psychological status in KOA patients

Study	Treatment	Outcome measures	Follow-up period	Results
M Constantini et al, 2011 ¹⁴	44 KOA patients: mud packs and bicarbonate sulphurous mineral bath water from Term of TelespA (Benevento-Italy)	Pain (VAS scale) Degree of knee flexion (using goniometer) Level of anxiety and depression (SDS Zung Test and SAS Zung test) Quality of life (algofunction Lequesne indice).	Baseline End of treatment	Reduction of the pain, increase of the knee flexion, quality of life improvement

Mud pack therapy compared with intra-articular hyaluronic acid injections in KOA patients

Bostan et al, 2010¹⁵ compared the effectiveness of mud therapy with intra-articular hyaluronic acid injections in two clinical and radiological similar KOA patients. The conclusion is that treatment of knee osteoarthritis

with intra-articular hyaluronic acid injections or mud-pack therapy yielded similar results in the short-term in terms of functional improvement and pain relief; that means to consider mud-pack therapy as a noninvasive, complication-free, and cost-effective alternative modality for the conservative treatment of knee osteoarthritis.

Table 5. Mud pack therapy compared with intra-articular hyaluronic acid injections in KOA patients

Study	Treatment	Outcome measures	Follow-up period	Results
Bostan al, 2010 ¹⁵	23 KOA patients stage 2 or 3 (Kellgren-Lawrence criteria): 12 patients received mud therapy bilaterally (45 degrees C applied on both knees for 30 minutes daily for a total of 12 weekdays); 11 patients received a total of three bilateral intra-articular hyaluronic acid injections, each interspersed by weekly intervals.	WOMAC osteoarthritis index Hospital for Special Surgery (HSS) score, Knee Society clinical rating system (knee and function scores)	range 4 to 8 months after mud-pack therapy, range 5 to 7 months after intra-articular hyaluronic acid injections.	Similar results in the short-term in terms of functional improvement and pain relief.

Balneo-therapy at the Dead Sea improves clinical status (pain, function, ADL) in KOA and the effect is sustained at least three months¹⁶.

Balneo-therapy's effects on para-clinic parameters

Regarding cartilage destruction, spa therapy can modify plasma levels of the adipocytokines, leptin and adiponectin, important mediators of cartilage metabolism¹⁷. Adipo-cytokine, including leptin and adiponectin, may play an important role in the pathophysiology of osteoarthritis. In skeletal joints, adiponectin may act as a pro-inflammatory agent and may be involved in matrix degradation. Leptin modulates the immune response, affecting the bone and cartilage metabolism. Spa therapy decreases adiponectin levels, which means that balneotherapy may play a protective role in OA.

Serum levels of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), insulin-like growth factor-1 (IGF-1) B are known to increase in OA, as they are inflammatory mediators. Other serology metabolites cited in the reviewed literature are: YKL-40 level in mud pack therapy, which seems to slow down the progression of

knee OA C or Vitamin D¹⁸ significant changes after climate-therapy at the Dead Sea. Another study revealed reduction in oxidation, inflammation and cartilage degradation parameters¹⁹ in patients undergoing sulfur-based spa therapies for OA, including KOA.

On a study from 2012, Gungen et al²⁰ demonstrated that mud pack and hot pack therapy were both effective in symptomatic treatment of knee OA until the end of the 2-week treatment period, whereas only mud pack therapy was shown to be effective in functional status over time (3 months). On the other hand, at baseline serum mean YKL-40 and hsCRP levels of the patients were higher compared to healthy control group. No significant change was observed in hsCRP levels in both groups during the whole follow-up periods. Maintenance of YKL-40 level in mud pack therapy seems to slow down the progression of knee OA.

Fioravanti et al, 2009¹⁷ published a randomized single-blind controlled clinical trial, with 30 patients (Spa Centre, Rapolano Terme) with 12 applications in 2 weeks, daily, mud-packs applied on both knees for 20 min at an initial temperature of 45C and bicarbonate-sulphate mineral bath water at 38C for 15 min.

The authors found a slight, but not significant, increase in plasma leptin after 2 weeks of spa therapy, with no evident correlation with parameters of clinical efficacy (VAS, Lequesne Index). The decrease in adiponectin after spa therapy was found; this may play a protective role in OA. Spa therapy can modify plasma levels of the adipocytokines leptin and adiponectin. The authors consider that further studies on larger numbers of cases are needed to evaluate the effects of spa therapy on adipocytokines and the mechanisms with which said therapy may modify production thereof, as well as whether such modifications may have repercussions on cardiovascular risk factors.

Clinical practice guidelines

2013 EULAR recommendations⁽⁴⁾ for the non-pharmacological core management of hip and knee osteoarthritis consist of eleven evidence-based recommendations for the non-pharmacological core management of hip and knee OA, concerning the following topics: assessment, general approach, patient information and education, lifestyle changes, exercise, weight loss, assistive technology and adaptations, footwear and work. 2013 EULAR recommendations don't include balneo-therapy, though Spa was listed among the treatment modalities identified by the EULAR for the management of knee OA in 2003²¹.

We mention the response of Dr. Romain J Forestier and F Begümto 2013 EULAR recommendations, given by, in which they sustain that balneo-therapy should be among the means of therapy studied by EULAR. Their arguments are the following: "We think that creno-balneo-therapy is a non-pharmacological treatment.", "We suggest that, since creno-balneo-therapy is a well evaluated treatment, these non-pharmacological treatment guidelines should also analyse this and some other trials published in this field."²².

OARSI 2008 (OA Research Society International) Recommendations²³ for the management of hip and knee osteoarthritis cover

the use of 12 non-pharmacological modalities: education and self-management, regular telephone contact, referral to a physical therapist, aerobic, muscle strengthening and water-based exercises, weight reduction, walking aids, knee braces, footwear and insoles, thermal modalities, transcutaneous electrical nerve stimulation and acupuncture.

OARSI 2014 Recommendations²⁴ consider balneo-therapy as appropriate only for the sub-phenotype with multiple-joint OA and co-morbidities, the last ones restricting the alternatives of treatment due to intrinsic contraindications. The authors conclude that additional large and well-designed RCTs are needed in this field, as it would be uncertain for individuals without relevant co-morbidities and individuals with knee-only OA. However, no significant safety issues were reported within balneo-therapy.

Although it recommends an holistic approach of OA, the NICE clinical guidelines from 2014²⁵ do not mention spa procedures among the therapeutic interventions. Furthermore it doesn't give any aspecific indications for the OA localized in the knee.

AAOS (American Academy of Orthopaedic Surgeons) Recommendations for KOA ("Treatment of Osteoarthritis of the knee")²⁶ are strong for self-management programs, strengthening and low-impact exercises, neuromuscular education, engagement in physical activity and NSAIDs (oral or topical) or Tramadol for symptomatic patients. There is also a moderate recommendation for weight loss. Other therapies, worldwide used in KOA, such as physical agents including electrotherapy, acupuncture, manual therapy, a medial compartment unloader, lateral wedge insoles, glucosamine and chondroitin, acetaminophen, opioids or pain patches, intra-articular corticosteroids of hyaluronic acid, growth factor injections and/or platelet rich plasma, needle lavage have the strength of recommendation ranging from moderate to inconclusive, or even not recommended (acupuncture, glucosamine,

chondroitin and Hyaluronic acid injections). However, no references are made regarding spa modalities, whether or not they are indicated for KOA.

Discussions

Overall, the components of balneo-therapy to which the selected articles refer include mudpacks, mineral waters (bicarbonate–sulphate mineral bath water, Sulphur pool). These are compared or associated with other methods used in the rehabilitation specialty area for the treatment of kneeosteoarthritis: kinesitherapy, pharmacological therapy, biomechanical interventions, hydro / thermo – therapy.

The psychological improvement (evaluated through the SDS Zung Test and SAS Zung Test for anxiety and depression level) was obtained by M. Constantino et al, 2011¹⁴ study, in which the authors report reduction of the pain, increase of the knee flexion and quality of life improvement in patients with KOA that underwent both mud packing as well as mineral waters. These data are consistent with spa-modalities studies focused on generalised OA or affecting other joints, such as hip or spine. Ali Nasermoaddeli and Sadanobu Kagamimori mention a RCT conducted in Vichy (France) for a period of 3 weeks, which compares spa therapy with usual therapy performed at home. The group of patients had either hip, knee or lumbar spine OA. M. Constantino et al, 2011²⁷ searched the effect of sulfurous mud and general bath in axial spondyloarthritis (99 patients), 36% patients having KOA as an associated diagnose.

Kinetherapy, which means aerobic, muscle strengthening and water-based exercises²³ in KOA therapy, has improvements in certain patients' parameters when associated to spa therapy. Thus the cited studies have proved a difference in clinical symptoms and quality of life in the groups that followed both procedures (kinetherapy and spa therapy). Pharmacological therapy, like intra-articular injections with hyaluronates, compared to mud packs showed that the latter ones are a

noninvasive, complication-free, and cost-effective alternative modality¹⁵. Hidro-therapy with tap water is less effective, showing that mineral water improved better the pain (pVAS), tenderness score (TS)⁸.

Therefore, compared with other means of Physical Medicine, Spa therapy seems to have certain advantages. This is due to enhancement of good effects of regular in-patient and out-patient therapy routine. But the most important aspect are its specific characteristics such as: non-invasiveness, free of complications, cost-effective.

Both EULAR 2003 and OARSI 2008 (OA Research Society International) list balneo-therapy as means of treatment for KOA, under the terms of “SPA”, respectively “Thermal modalities”.

OARSI 2014 recommend balneo-therapy/spa therapy as appropriate for individuals with multiple-joint OA and relevant co-morbidities, more than that, it states that no significant safety events were found to be determined by balneo-therapy. The above mentioned sub-phenotype of population would have an indication for balneo-therapy due to paucity of treatment alternatives for that group.

Still, the presence of spa therapy is scarce in the guidelines issued for KOA therapy. 2013 EULAR recommendations, “2014 Nice clinical guidelines”, AAOS (American Academy of Orthopaedic Surgeons) Recommendations for KOA (“Treatment of Osteoarthritis of the knee”) don't include balneo-therapy in the management of KOA /OA, but focus on education, lifestyle changes, weight loss. Since it is known that a small to moderate proportion of people with knee OA met physical activity guidelines and recommended daily steps²⁸, balneologic resorts could be a friendly and relaxing environment, where patients could be educated, and closely guided in lifestyle changes. Thus helping in achieving the goals of all above mentioned guidelines.

Despite numerous small scale studies, there is a lack of high quality scientific evidence

for the efficacy of spa therapy for knee osteoarthritis. Perhaps for this reason, spa therapy does not appear in the recommended treatments of the European League Against Rheumatism nor in the AAOS clinical practice guideline (“Treatment of Osteoarthritis of the knee”).

Conclusions

In conclusion, balneo-therapy is effective on clinical status in KOA patients, in terms of pain, function, quality of life, reducing analgetics and NSAIDs consumption, diminution of depression & anxiety symptoms.

It is well known the good tolerability of spa therapy, and the hereby reviewed articles do not report any major adverse events associated with it. However, evidence-based and expert consensus guidelines need more evidence-based data to consider balneo-therapy among the means of KOA therapy. For this reason, properly designed, controlled, clinical trials are required in the field of spa/balneology modalities in KOA.

Our questions “does balneo-therapy have good effects on KOA?”, “is it used worldwide?”, “is it worth to highlight its potential benefits through large clinical trials?” have a indubitable answer: YES, but it is important to demonstrate these through larger studies.

Future challenges could be studies that quantify good effects using KOA specific markers, to establish a hierarchy of spa methods, as well as to refine indications depending on the stage of the disease.

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