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REVIEW

May spa therapy be a valid opportunity to treat hand osteoarthritis? A review of clinical trials and mechanisms of action

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Abstract Osteoarthritis (OA) is the most common form of arthritis and its current treatment includes non-pharmacological and pharmacological modalities. Spa therapy represents a popular treatment for many rheumatic diseases. The aim of this review was to summarize the currently available information on clinical effects and mechanisms of action of spa therapy in OA of the hand. We conducted a search of the literature to extract articles describing randomized clinical trials (RCTs) in hand OA published in the period 1952–2015. We identified three assessable articles reporting RCTs on spa therapy in hand OA. Data from these clinical trials support a beneficial effect of spa therapy on pain, function and quality of life in hand OA. Spa therapy seems to have a role in the treatment of hand OA. However, additional RCTs are necessary to clarify the mechanisms of action and the effects of the application of thermal treatments.

Keywords Spa therapy · Balneotherapy · Mud-pack therapy · Hand osteoarthritis · Randomized controlled trials

Introduction

Osteoarthritis (OA) is the most common form of arthritis and a major contributor of functional impairment and disability in older people (Zhang and Jordan 2010). The most frequently affected peripheral joints are knees, hips and hands (Oliveria et al. 1995; Zhang et al. 2002). Hand OA is often underestimated as a cause of disability, although it may have a considerable impact on quality of life (QoL) by limiting performance of daily activities, such as dressing and feeding (Dahaghin et al. 2005). Furthermore, OA of the hand is frequently associated with obesity, hypercholesterolaemia and cardiovascular diseases (Yusuf et al. 2010; Massengale et al. 2012). Despite its high prevalence, its impact on QoL and associated pathology, the therapeutic options in hand OA are still limited (Addimanda et al. 2012; Mahendira and Towheed 2009). Current treatment of OA of the hand includes non-pharmacological and pharmacological modalities (Zhang et al. 2007).

Spa therapy is one of the most commonly used non-pharmacological approaches for OA in many European and Middle Eastern countries (Gutenbrunner et al. 2010). Spa therapy comprises a broad spectrum of therapeutic modalities including hydrotherapy, balneotherapy, physiotherapy, mud-pack therapy and exercise (Bender et al. 2005). Nowadays, it still represents a popular treatment for many rheumatic diseases, because of their chronic nature, problems related to the use of drugs that often have significant side effects, and the occasional lack of valid therapeutic strategies. Thousands of years of history and the abundance of spa resorts in many European countries have undoubtedly contributed to the popularity of these therapies. However, despite their long history and popularity, spa treatments are still the subject of debate, and their role in modern medicine is still not clear (Verhagen et al. 2000). Furthermore, it is important to explain the difference between the terms "spa therapy" and "spa", because the lack of international accepted language in this field could generate some misunderstandings. Spa therapy includes all medical activities based on scientific evidence that are employed

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in health resorts and are aimed at health promotion, prevention, therapy and rehabilitation. The term spa refers, instead, to wellness concepts. Most of these concepts lack a systematic medical approach and are aimed simply at short-term well-being (and of course economic profit) (Gutenbrunner et al. 2010).

There have been several publications about the use of spa therapy in OA; however, the majority of these trials concerned OA of the knee (Forestier et al. 2010; Fioravanti et al. 2011a, b, c, 2014a, b; Kulisch et al. 2014; Tenti et al. 2014). However, very few studies evaluated the effectiveness of this treatment in patients with primary OA of the hand.

The aim of this review was to summarize the currently available information on clinical effects and mechanisms of action of spa therapy in OA of the hand.

Methods

We conducted a search of the literature (Cochrane Library, PubMed, MEDLINE, EMBASE, Web of Science, Scopus, PED-ro, Web of Knowledge databases) in June 2015 using the terms "randomized clinical trial", "spa therapy", "mud", "mud-pack" and "balneotherapy" in combination with "osteoarthritis", "arthrosis" and "hand osteoarthritis". We applied no date restrictions, so the period examined was 1952 (year of the first publication in this field) to June 2015 (date of our search). We used no language limits, but articles written in languages other than English were excluded. We also searched the ClinicalTrials.gov for ongoing and recently completed trials. Studies were eligible if they were randomized clinical trials (RCTs). Participants had hand OA according to American College of Rheumatology (ACR) criteria (Altman 2010). Balneotherapy and mud-pack therapy had to be the intervention under study and had to be compared with another intervention or with routinary medical care. Outcomes that we considered are pain, stiffness, improvement, disability, tender joints, swollen joints, withdrawals due to adverse events and serious adverse events. Initially, two review authors (F.A., T.S.) independently selected trials by inspecting titles, keywords and abstracts to determine whether studies met the inclusion criteria regarding design, participants and interventions. We retrieved for final assessment full publications of studies which met the inclusion criteria. Two review authors (S.G., C.S.) independently extracted data on trial methods, participants, interventions, types of outcome measures, duration of follow-up, loss to follow-up and results.

We stratified the analysis in different sections:

- Trials comparing balneotherapy versus controls
- Trials comparing mud-bath therapy versus routinary medical care
- Clinical and preclinical studies discussing the mechanism of action of spa therapy

Results

A search conducted for this update resulted in 327 references. Of these, three studies were found to be eligible on the basis of full paper assessment and were included in this review (Horváth et al. 2012; Kovács et al. 2012; Fioravanti et al. 2014a, b); see study flow chart in Fig. 1.

A total of 168 participants were enrolled, and the number of participants in the intervention groups ranged from 21 to 30. The percentage of males was between 6.66 and 19.04 % and that of females was 80.95 and 93.33 %. The mean age ranged from 58 to 72.4 years. One study had three treatment arms, and the other two studies had two treatment arms. Two studies were single blind with an "assessor" blind to the type of treatment; one study was double blind. In two studies, mineral baths were used; in one study, bathing was combined with local mud-pack application. The temperature of baths were different in the three studies and ranged between 36 and 38 °C.

All studies used several outcome measures including pain and function. From the total search, 173 studies were excluded because of their language of publication; 15 studies were not assessed because they appeared not to be RCTs, but review articles; 63 studies were not considered because the patients involved were not affected by hand OA but diagnosed with knee and/or hip and/or spine OA; 73 studies were excluded because they did not concern the efficacy of spa therapy in OA.

Studies that analyse the effects of balneotherapy in hand OA

Horváth et al. (2012) in a RCT single-blind study investigated the effectiveness of thermal mineral water compared with magnetotherapy without balneotherapy as control, in the treatment of hand OA. Sixty-three patients between 50 and 70 years of age were randomly assigned into three groups of 21 patients each. The subjects in the first two groups bathed in thermal mineral water of two different temperatures (36 and 38 °C) for 3 weeks five times a week for 20 min a day and received magnetotherapy to their hands three times weekly. The third group received only magnetotherapy. Each patient was assessed at baseline, immediately after treatment and after 13 weeks. Assessment included visual analogue scale (VAS) scores, handgrip strength, pinchgrip strength, the number of swollen and tender joints of the hand, the duration of morning joint stiffness (MJS), Health Assessment Questionnaire (HAQ), (Fries et al. 1980) and Short Form-36

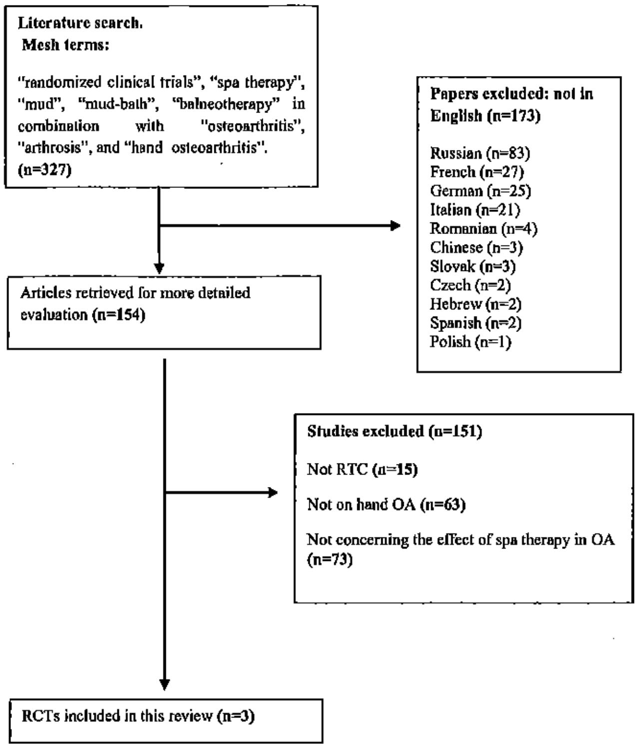

Fig. 1 Study flow diagram

(SF-36) questionnaire (Ware and Sherbourne 1992). Statistically significant improvement was observed in several studied parameters after the treatment and during the follow-up study in the thermal water groups versus the control group. The 38 °C thermal water treatment significantly improved the pinch strength of the right hand (0.6 (95 % confidence interval (CI) 0.2 to 1.1) vs. 0.03 (95 % CI −0.3 to 0.4), $P<0.05$) and the HAQ parameters (−0.4 (95 % CI −0.6 to −0.2) vs. −0.1 (95 % CI −0.2 to 0.1), $P<0.01$) even in the long term.

Subsequently, the efficacy of sulphurous water was investigated by Kovács et al. (2012). Forty-seven patients with OA of the hand satisfying the ACR (Altman 2010) criteria were enrolled into the double-blind, randomized, controlled study. One group of the patients ($n=24$) received balneotherapy, bathing in sulphurous thermal water for 20 min per occasion, 15 times in all during a period of 3 weeks. The control group ($n=21$) had a bath exclusively in warm tap water. Assessments were carried out in both groups on four occasions: at the beginning and at the end of the treatment, and 3 and 6 months after the beginning of the treatment. The parameters studied were the following: pain in the hand, MJS, grip strength of both hands, HAQ, Australian/Canadian Hand Osteoarthritis Index (AUSCAN), EuroQol (EQ5D/EQVAS) and quality of life questionnaire (Bellamy et al. 2002; EuroQol Group 1990). At the end of treatment, the improvement was more pronounced in the patient group treated with the sulphurous water. After 3 months, significant improvement could be detected in all parameters, except the MJS and EQ5D. After 6 months, the values of pain, HAQ and AUSCAN continued to be significantly better in comparison with the baseline values. The improvement in quality of life was significant only at the end of the treatment, 6 months later not any longer. The control group showed significant improvement in evach parameter, except pain, HAQ and EuroQol, at the end of the treatment; however, this improvement was less expressed than in the balneotherapy group. After 3 and 6 months, no improvement could be detected in any parameter in the group that had bath in the tap water. The difference between the two groups was significant after the bath in point of pain (VAS) and 3 months later both in point of pain (VAS) and of health state (EQVAS), but it was not significant in the point of MJS, grip strength, HAQ, AUSC AN and EQ5D. In conclusion, the two RCTs (one single blind and one double blind) showed that balneotherapy is beneficial for patients with hand OA, in both the short and the long term. This was confirmed by the improvement of subjective and objective parameters (grip strength, pinch strength, HAQ score, MJS, swollen joint count, tender joint count, the SF-36, AUSCAN and EQ5D scores), without adverse events (Table 1).

Studies that analyse the effects of mud-bath therapy in hand OA

Despite the common use, there is only one article that evaluates the effect of mud-pack therapy alone in patients with hand OA. More recently, the short- and long-term efficacy (1 year) of mud-bath therapy in hand OA was demonstrated by Fioravanti et al. (2014a, b). This was a prospective randomized, single-blind controlled trial. Sixty outpatients with primary bilateral hand OA who fulfilled the ACR criteria (Altman 2010) were included in the study (Table 1). Patients were recruited by the general practitioners in the rural area within a 30-km radius of the "Fonteverde Spa" (Siena, Italy) and resided in the area near the spa, allowing them to continue to live at home and carry out their daily routines during the study period. Patients who fulfilled the screening criteria were randomized to 1:1 and allocated to one of two groups. One group ($n=30$) was treated with 12 daily local mud-packs and generalized thermal baths with a sulphate-calcium-magnesium-fluorides mineral water added to usual treatment. The control group ($n=30$) continued regular outpatient care routine. Each patient was examined at baseline time, after 2 weeks, and after 3, 6, 9 and 12 months. Primary outcome measures were the global spontaneous hand pain on a VAS scale and the Functional Index for Hand Osteoarthritis (FIHOA) score (Dreiser et al. 2000; Gandini et al. 2012). Secondary outcomes were HAQ, MJS, SF-36 and symptomatic drug consumption.

Table 1 RCTs on spa therapy in hand OA

Authors	Trial design	Simple size	Interventions	Frequency	Outcome measures	Time of assessment	Follow-up	Results
Horváth et al. (2012)	SB 3 parallel groups	Total: 63 A: 21 B: 21 C: 21	A: Balneotherapy (36 °C)+magnetotherapy B: Balneotherapy (38 °C)+magnetotherpay C: Magnetotherapy	A and B: 20 min daily for 5 days a week for 3 weeks	VAS, handgrip strength, pinchgrip strength, the number of swollen and tender joints, the duration of morning joint stiffness, HAQ and SF-36	Baseline, week 3 and 13	13 weeks	Statistically significant improvement was observed in several studied parameters after the treatment and during the follow-up in groups A and B versus C. In the group B a significant improvement of the pinch strength and of HAQ was also observed in the long term
Kovács et al. (2012)	DB 2 parallel groups	Total: 45 A: 24 B: 21	A: Balneotherapy B: Tap water baths	20 min per occasion, 15 times in all during a period of 3 weeks	VAS, MJS, grip strength, HAQ, AUSCAN and EuroQol	Baseline, at the end of the treatment, week 12 and 24	24 weeks	At the end of treatment, the improvement of the evaluated parameters was more pronounced in the group A. At week 12, this improvement persisted, except for the MJS and EQ5D, while at week 24 was maintained only for VAS, HAQ and AUSCAN continued
Fioravanti et al. (2014a, b)	SB 2 parallel groups	Total: 60 A: 30 B: 30	A: Local mud-packs and generalized thermal baths B: Routinary medical care	20 min for mud-pack and 15 min for balneotherapy for a total of 12 applications carried out over a period of 2 weeks	VAS, FIHOA, HAQ, MJS, SF-36 and symptomatic drug consumption	Baseline, week 2, 12, 24, 36 and 48	48 weeks	All parameters resulted significantly improved in group A at the end of therapy and at week 12. FIHOA, HAQ and the drugs consumption continued to be significantly better at week 24

SB single blind, *VAS* visual analogue scale, *HAQ* Health Assessment Questionnaire, *SF-36* Short Form-36, *DB* double blind, *MJS* morning joint stiffness, *AUSCAN* Australian/Canadian Hand Osteoarthritis Index, *EQ5D+EQVAS* EuroQol, *FIHOA* Functional Index for Hand Osteoarthritis

The authors demonstrated that the efficacy of mud-bath therapy was significant in all the assessed parameters, both at the end of therapy and after 3 months. Furthermore, in patients treated with mud-bath therapy, the values of FIHOA score, HAQ and symptomatic drug consumption continued to be significantly better after 6 months of the follow-up in comparison with basal values. This finding is unexpected, since FIHOA score was previously reported to be less sensitive to change than the global hand pain assessment (Dreiser et al. 2000; Gandini et al. 2012). However, other investigators have found a more pronounced effect of symptomatic pharmacological therapy on hand function than on hand pain (Altman et al. 2009; Gabay et al. 2011), and it is plausible that mud-bath treatment may have a greater effect on hand function and for a longer period of time than on pain control (see the "Mechanisms of action of spa therapy in OA" section). On the contrary, there were no significant modifications of the parameters throughout the follow-up in the control group. The differences between the two groups were significant for all parameters at the 15th day and at 3 months follow-up; regarding FIHOA, HAQ and symptomatic drug consumption, the difference between the two groups persisted significant at 6-month follow-up. The reduction in the consumption of symptomatic drugs [acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs)] induced by mud-bath is particularly important, above all for the elderly, considering the toxicity of NSAIDs, (Bresalier et al. 2005; Kearney et al. 2006) as well as their cost, given that their use is often coupled with gastro-protective therapies. These data are in agreement with a previous study on cost/efficacy of spa therapy in OA which demonstrated a significant decrease in recourse to additional treatments (hospital admissions, physical and pharmacological therapies) and absence from work for OA after a cycle of spa therapy (Fioravanti et al. 2003). Finally, tolerability of mud-bath therapy seemed to be good; 5 % of patients presented side effects due to treatment, but these were of light intensity and did not interrupt the therapy. In control group, 9 % of patients presented prevalently gastrointestinal side effects, probably correlated to the higher recourse to symptomatic drugs compared to patients in the spa group; in particular, 6 % presented epigastralgia, and 3 % complained of gastric pyrosis.

In conclusion, these results demonstrated that a cycle of local mud-packs and balneotherapy added to conventional treatment provides a positive effect on the painful symptomatology and on functional capacities that lasts over time.

Mechanisms of action of spa therapy in OA

Actually, the mechanisms by which immersion in mineral or thermal water or the application of mud alleviate the main symptoms of OA and of other rheumatic diseases are not fully understood.

The efficacy seems to be the result of a combination of factors, among which mechanical, thermal and chemical effects are most prominent (Sukenik et al. 1999; Fioravanti et al. 2011a, b, c). A distinction can be made between the non-specific and the specific mechanisms of action. The former (hydrotherapeutic in a broad sense) consisting in simple bathing in hot tap water are well known, while the latter (hydromineral and crenotherapeutic), depending on the chemical and physical properties of the water used, are difficult to identify and assess. Buoyancy, immersion, resistance and temperature all play important roles. Hot stimuli produce analgesia on nerve endings by increasing the pain threshold. It causes relief of muscle spasms through the gamma fibers of muscle spindles and activates the descending pain inhibitory system. According to the "gate theory", pain relief may be due to the temperature and hydrostatic pressure of water on the skin (Melzack and Wall 1965; Guidelli et al. 2012). The effect of heat was also pointed out by the EULAR's task force's recommendation for hand OA that presented local application of heat (for example, paraffin wax, hot pack) as a beneficial treatment, but level of evidence is low (Zhang et al. 2007). Spa therapy provokes a series of neuroendocrine reactions and, in particular, induces the release of adrenocorticotropic hormone (ACTH), cortisol, prolactin and growth hormone (GH), although it does not alter the circadian rhythm of these hormones. The effect of thermal stress on the hypothalamus-pituitary-adrenal axis seems to be particularly important for the anti-edemigenous and anti-inflammatory effects of corticosteroids (Kuczera and Kokot 1996). Furthermore, various spa therapy techniques have been demonstrated to increase plasma levels of beta-endorphin (Kubota et al. 1992). This increase in beta-endorphin is probably the key factor in the mechanism of individual tolerance to thermal mud-baths.

Mud-bath therapy reduces the circulating levels of prostaglandin E2 (PGE2) and leukotriene B4 (LTB4), important mediators of inflammation and pain, in patients with knee OA or fibromyalgia syndrome (Bellometti and Galzigna 1998; Ardiç et al. 2007). Crenotherapy also affects the synthesis of various cytokines involved in the ongoing chondrolysis and inflammation in OA, such as interleukin (IL)-1β and tumor necrosis factor (TNF)-α (Cecchettin et al. 1995; Bellometti et al. 2002). Spa therapy has also been shown to exert positive effects on the oxidant/anti-oxidant system, resulting in a reduced release of reactive oxygen species (ROS) and nitrogen (RNS) (Braga et al. 2008; Bender et al. 2007). In two recent studies, Fioravanti et al. (Fioravanti et al. 2011a, b, c, 2015) assessed the possible modifications of some adipokines (leptin, adiponectin, resistin and visfatin) in patients with knee OA after a cycle of mud-bath therapy. At the end of the therapy, serum leptin levels showed a slight but not significant increase while serum adiponectin and resistin levels showed a significant decrease; no significant modifications of visfatin were found. These adipocytokines play an important role in the pathophysiology of OA. In particular, adiponectin is detected in both synovial fluid and in serum of OA patients (Presle et al. 2006) and has been reported to increase the production of metalloproteinases (MMPs), cytokines and PGE2 by chondrocytes and synovial fibroblasts (Koskinen et al. 2011). Resistin, a novel adipocyte-secreted hormone, has received attention for its involvement in insulin resistance in obesity and diabetes mellitus (Francin et al. 2014). Recent research shows that human resistin is expressed in immune cells and possesses many characteristics of a proinflammatory cytokine (Steppan et al. 2001; Senolt et al. 2007; Koskinen et al. 2014). Although the study regarding the role of resistin in OA is sparse, some studies showed its direct effect on cartilage matrix and cytokine production.

The anti-inflammatory and chondroprotective effects of mud-bath were confirmed by experimental studies in animal models of arthritis (Cozzi et al. 2004; Britschka et al. 2007). In particular, Britschka et al. (2007) performed a study in zymosan-induced arthritis in rats; after 21 days of the application of mud, the animals were killed and a histological analysis on synovial tissues and cartilage was carried out. Examination of the synovial tissue in particular revealed reduced hyperplasia of the lining, reduced vascularization and cellular infiltration in the group of rats treated with mud applications, in contrast to the group of rats treated with simple heated tap water and the untreated (control) group of rats. At cartilage level, there was a macroscopically visible reduction of the erosive lesions, as well as an increase in chondrocyte density and collagen and proteoglycan content only in the mud-treated animals.

A possible chondroprotective role of mineral water or mineral components was demonstrated by some pilot studies in chondrocyte cultures. Burguera et al. (2014) studied the possible activity of hydrogen sulphide (H_2S) in human OA chondrocytes stimulated with IL-1β. They analysed the effects of different concentrations of a fast natrium hydrogen sulphide (NaHS) or a slow morpholin-4-ium-4-methoxyphenyl[morpholino] phosphinodithioate (GYY4137) release H_2S donor on three key aspects of the inflammatory and degenerative process in OA. After incubation with H_2S donors, the authors demonstrated a significant reduction of nitric oxide (NO), PGE2, IL-6 and MMP-13 released by the cells in culture medium. This was achieved by downregulation of relevant genes involved in the synthesis routes of these molecules, namely inducible NO synthase (iNOS), cyclooxigenase-2 (COX2), prostaglandin E synthase (PTGES), IL-6 and MMP-13. Nuclear factor (NF)-kB nuclear translocation was also reduced. NaSH and GYY4137 show anti-inflammatory and anti-catabolic properties when added to IL-1β activated OA chondrocytes. Supplementation with exogenous H_2S sources can regulate the expression of relevant genes in OA pathogenesis and progression, counteracting IL-1β pro-inflammatory signals that lead to cartilage destruction in part by reducing NF-kB activation.

These data were confirmed by Li et al. (2013) in normal human chondrocytes stimulated by lipopolysaccharide (LPS). GYY4137 decreased LPS-induced production of NO, PGE2, TNF-α and IL-6 and reduced the levels and catalytic activity of NOS and of COX-2 and NF-kB activation. Furthermore, GYY4137, in a previous study, showed a potent inhibition on oxidative-stress-induced cell death (Fox et al. 2012). The incubation of human chondrocyte cell line C-28/I2 with another H_2S donor, NaHS, provided proof that constitutive as well as IL-1β-induced IL-6 and IL-8 expression was partially and transiently blocked by the NaHS (Kloesch et al. 2012).

Fioravanti et al. (2013) studied the possible chondroprotective role of highly mineralized water, strongly acidic sulphate, rich in calcium, magnesium and iron [Vetriolo's thermal water (VW)] in human OA chondrocytes cultivated with or without IL-1β. For this purpose, OA chondrocytes were cultivated in deionized water (DW) (DW-DMEM, controls), or in one of three different VW-DMEM media, in which DW had been totally (100 %) or in part (50 or 25 %) substituted with VW. The results showed that VW alone at 25 or 50 % concentration did not affect the viability of cultured OA chondrocytes and determined a significant survival recovery rate in cultures stimulated with IL-1β. NO levels were low both in DW-DMEM cultures and in those reconstituted with 25 or 50 % of VW and were significantly increased by IL-1β. VW at 25 or 50 % concentration significantly ($P<0.001$) reduced the NO production induced by IL-1β. The data of the NO levels were confirmed by the immunocytochemistry assay for iNOS. Furthermore, the authors confirmed the pro-apoptotic effect of IL-1β and demonstrated a protective effect of VW at 25 or 50 % concentration. The results concerning biochemical data were further confirmed by the morphological findings obtained by a transmission electron microscope. OA chondrocytes cultivated in presence of IL-1β displayed an altered ultrastructure with numerous vacuoles in the cytoplasm where rough endoplasmic reticulum, Golgi bodies and mitochondria were strongly reduced; in the cultures reconstituted with VW 20 and 50 %, the ultrastructural features of chondrocytes were similar to those observed in control cells. In conclusion, this study demonstrated that VW alone at 25 or 50 % inhibits the negative effects of IL-1β in chondrocyte cultures.

Finally, other elements need to be taken into consideration concerning the mechanisms of action of mud applications and balneotherapy in rheumatic diseases, such as the particular climatic and environmental conditions of spas and the fact that people rest more and are far from daily stress during stays at spa resorts (Fioravanti et al. 2011a, b, c).

Conclusion

The aim of this review was to summarize the currently available information on clinical effects and mechanisms of action of spa therapy in the management of hand OA. Unfortunately, only three RCTs were performed in OA of the hand. Two studies evaluated the efficacy of balneotherapy and one study the efficacy of a combination of mud-packs applied on both hands followed by generalized bath. The results showed that balneotherapy and mud-bath therapy improved pain and function as well as the QoL; furthermore, the clinical efficacy lasts over time, after the treatment. Spa therapy resulted to be well tolerated and has a lower percentage of side effects, which also are less severe, than those associated with pharmacological treatments. However, the number of patients included in these RCTs is very small, and the comparison between the various studies is difficult as the baseline characteristics of the patients are heterogeneous, the interventions differ in type intensity and in length, and in certain studies the treatment protocol consists in a combination of more modalities (for example, balneotherapy and magnetotherapy). Patients have been assessed at different time points after treatment and the outcome measures used for the assessment of efficacy were different.

In conclusion, spa therapy seems to have a role in the treatment of hand OA, considering that the therapeutic options for this condition are still limited. It cannot substitute for conventional therapy but can complement to it. The improvement reported in some clinical studies lasts over time. Additional RCTs with high methodological quality concerning the effectiveness of spa therapy in hand OA are necessary in order to obtain strong evidence on the effects of spa therapy. Future researches to clarify the mechanisms of action and the effects deriving from the application of thermal treatments are imperative.

Conflict of interest The authors declare that they have no conflict of interest.

Authors' contribution All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

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