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REVIEW

Fibromyalgia Syndrome and Spa Therapy: Myth or Reality?

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Abstract: Fibromyalgia syndrome (FS) is a common musculoskeletal disorder characterized by otherwise unexplained chronic widespread pain, a lowered pain threshold, high tender point counts, sleep disturbances, fatigue, headache, irritable bowel syndrome, morning stiffness, paraesthesias in the extremities, often psychological distress and depressed mood. Consequently, FS has a negative impact on working capacity, family life, social functioning and quality of life. Because of unknown etiology and not clearly understood pathogenesis, there is no standard therapy regime for FS. A variety of medical treatments, including antidepressants, opioids, analgesic or non-steroidal anti-inflammatory drugs, sedatives, muscle relaxants and antiepileptics, have been used to treat FS. Currently, no pharmacological treatment for FS is consistently successful. According to recent guidelines, the optimal treatment of FS requires a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities. Spa therapy is a popular treatment for FS in many European countries, as well as in Japan and Israel. 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. The objective of this review is to summarize the currently available information on clinical effects and mechanism of action of spa therapy in FS. We also provide some suggestions for further development in this area.

Keywords: spa therapy, fibromyalgia syndrome, balneotherapy, mud-packs, randomized clinical trial

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Introduction

Fibromyalgia syndrome (FS) is a chronic musculoskeletal pain disorder characterized by widespread pain and tenderness at marked sites of the body defined as tender points. It often is accompanied by other characteristic symptoms as sleep disturbances, fatigue, headache, irritable bowel syndrome, morning stiffness, paraesthesia of the extremities, frequent psychological distress, and depressed mood.[1] The prevalence of FS in the general population is estimated as 1%–2%, and it affects mainly women, six times more common than men.[2–5] As in other disabling conditions, FS influences working capacity, family life, social functioning, and quality of life (QoL).[6] Furthermore, it has been demonstrated that the QoL of relatives of FS patients also is impaired.[7] The pathophysiologic mechanisms underlying FS are still poorly understood but most probably include complex and interrelated disturbances of the neurobiological stress system (ie, the hypothalamic-pituitary-adrenal [HPA] axis, sympathetic nervous system, and different brain neurotransmitters).[8,9] These include reduced levels of biogenic amines, increased concentrations of excitatory neurotransmitters, including substance P and dysregulation of the HPA axis. A unifying hypothesis is that FS results from sensitization of the central nervous system.[1]

Because of unknown etiology and unclear pathogenesis, there are no standard therapy regime for FS. In recent years, at least three sets of guidelines have been developed by different medical organizations in an attempt to standardize the treatment of this condition (American Pain Society, European League Against Rheumatism, Association of the Medical Society of Germany).[10–12] Optimal management of FS includes a multidisciplinary approach with a combination of non-pharmacological and pharmacological treatment modalities tailored according to pain intensity, function, and associated features such as depression, fatigue, and sleep disturbance, decided through discussion with the patient.[10–12] A variety of medical treatments, including antidepressants (ie, amitriptyline, duloxetine, fluoxetine, and moclobemide), analgesics (ie, paracetamol and weak opioids like tramadol), non-steroidal anti-inflammatory drugs (NSAIDs), sedatives, muscle relaxants, and antiepileptics have been used to treat FS.[10–12] Given the complexity and chronicity of FS and the relatively poor response to pharmacological treatments, it is not surprising that patients often resort to complementary or alternative therapies.[13] Non-pharmaceutical treatment modalities, including exercise, physical therapy, massage, acupuncture, homeopathy, dietary, osteopathic manipulation, patient education, cognitive behavioral therapy and spa therapy were proposed from various authors.[10–17] There is strong evidence that cognitive behavioral therapy (CBT) and exercises are effective in FS.[10] Spa therapy comprises a broad spectrum of therapeutic modalities including hydrotherapy, balneotherapy, physiotherapy, mud-pack therapy, and exercise.[18–20] This therapeutic approach has been successfully used in many European countries, as well as in Japan and Israel for various illnesses. Nowadays, it still represents a popular treatment for many rheumatic diseases, such as FS, 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.[20]

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.[21] We summarize the currently available information on clinical effects and mechanism of action of spa therapy in FS.

Randomized Clinical Trials (RCTs) on Spa Therapy in FS

We conducted a search of the literature in May 2011. In an attempt to standardize the patient sample included, the search was conducted from 1990 (the date of publication of the ACR classification criteria for FS) to May 2011.[5] Medline was searched using the term "randomized clinical trial", "spa therapy", "mud" and "balneotherapy" in combination with FS. RCTs written in languages other than English were excluded from the search. We identified eight articles that met our inclusion criteria reporting seven RCTs on spa therapy in FS, including a total number of patients of 314 (Table 1). More than 90% of the participants in the studies were women. All studies were single blind with an "assessor" blind to the type of treatment. In five studies, mineral baths were used: in one study bathing was combined with exercise treatment, one

Table 1. Main characteristics of studies with spa therapy.

Authors	Sample size	Intervention	Outcome measures	Follow-up	Results
Yurtkuran[22]	A: 20 B: 20	A: Bal. (20 min × 5 days/ week for 2 weeks at 37 °C) + relaxations exercises B:Exercises only	VAS, PAS	6 weeks	Significant changes on VAS and PAS for group A at the end of treatment and at 6 weeks
Buskila[23]	A: 24 B: 24	A: Bal. (20 min daily for 10 days at 37 °C) B: No treatment	VAS (Pain and other minor symptoms), FIQ, TPC, Dolorimeter, FDI	3 months	Significant between group improvement in pain and TPC in favour of A, still seen after 3 months
Neumann[24]	A: 24 B: 24	A: Bal. (20 min daily × 10 days at 37 °C) B: No treatment	SF36, AIMS, VAS (Pain and other minor symptoms)	3 months	Significant improvement in most subscales of the SF36 for both groups. The improvement in physical components of the QoL index lasted 3 months, whereas improvement in measures of psychological well-being was of shorter duration. Subjects in group A reported greater and longerlasting improvement than subjects in the group B
Evcik[25]	A: 22 B: 20	A: Bal. (20 min × 5 days/week for 3 weeks at 36 °C) B: No treatment	VAS, FIQ, TPC, BDI	6 months	The group A showed statistically significant improvement in TPC, VAS, FIQ and BDI at the end of the therapy and this improvement persisted at 6 months except for BDI
Dönmez[26]	A: 16 B: 14	A: Spa therapy (thermal pool baths 20 min × 6 days/week for 2 weeks at 36 ± 1 °C, pressurizzed shower at 37 °C or classical massage for 15 min each on altermate days) B: No treatment	VAS (Pain and other minor symptoms), FIQ, TPC, BDI	9 months	Significant improvement in pain, TPC and FIQ for group A. The pain and TPC results persisted for up to one month and the FIQ results for up to 6 months
Ardiç[27]	A: 12 B: 12	A: Bal. (20 min × 5 days/week for 3 weeks at 37 °C) B: No treatment	VAS, TPC, FIQ, BDI	3 weeks	Statistically significant improvement in VAS, BDI, TPC and FIQ was only found in group A at the end of the treatment cycle
Fioravanti[28]	A: 40 B: 40	A: Mud-packs (15 min daily for 2 weeks at 45 °C) and baths (10 min daily for 2 weeks at 37 °C–38 °C) B: No treatment	FIQ, TPC, VAS (Pain and other minor symptoms), AIMS, HAQ	16 weeks	In group A, a significant improvement in all parameters was recorded after mud-pack therapy and after 16 weeks
Özkurt[29]	A: 25 B: 25	A: Bal. (20 min twice/day for 2 weeks at 36 °C ± 1 °C) B: No treatment	VAS, FIQ, BDI, PGA, IGA, SF-36, TPC	3 months	Statistically significant improvement was recorded in group A for all outcome parameters at the end of the treatment cycle and after 3 months, except for BDI and IGA

Abbreviations: Bal, Balneotherapy; VAS, Visual Analogue Scale; PAS, Pressure Algometric Scores; FIQ, Fibromyalgia Impact Questionnaire; TPC, Tender Point Count; FDI, Functional Disability Index; SF36, Short Form-36; AIMS, Arthritis Impact Measurement Scales; BDI, Beck Depression Inventory; HAQ, Health Assessment Questionnaire; PGA, Patient global assessment; IGA, Investigator's Global Assessment.

study evaluated the effect of spa therapy and one studied the effect of mud-pack treatment.

Yurtkuran et al[22] investigated the effect of the addition of balneotherapy to relaxation exercises in 40 patients with FS. The study was conducted in a daily living environment and the treatment duration was 2 weeks. Patients taking part in the balneotherapy program bathed at 37 °C for 20 min a day, 5 days per week followed by relaxation exercises. Patients in the control group received only relaxation exercises. Pain relief, as scored by Visual Analogue Scale (VAS), was achieved in both groups at the end of therapy and persisted for 6 weeks; however, significant improvements in mean Pressure Algometric Scores (PAS) during follow-up were only observed in the balneotherapy group.

Buskila et al[23] and Neumann et al[24] reported in two different papers the beneficial effect of Dead Sea balneotherapy on FS-related symptoms and QoL index in patients with FS. The authors enrolled 48 patients with FS, who were randomly assigned to treatment and control groups of 24 subjects each. The patients in the treatment group bathed for 20 min per day in a sulfur pool at 37 °C for 10 days, whereas the control group did not receive this treatment. All participants stayed in the Dead Sea area for 10 days and continued their regular medications for FS. Physical functioning, assessed by the Fibromyalgia Impact Questionnaire (FIQ), and FS-related symptoms, assessed by VAS, Functional Disability Index (FDI), Health Assessment Questionnaire (HAQ), tenderness measurements (Tender Point Count [TPC] and dolorimetry), and QoL index (Short Form-36 [SF36] and Arthritis Impact Measurement Scales [AIMS]) were recorded at baseline, at the end of treatment, and 1 month and 3 months later. Physical functioning and tenderness improved moderately in both groups. With the exception of tenderness threshold, the improvement was especially evident in the treatment group and even persisted beyond 3 months. Relief in the severity of FS-related symptoms (pain, fatigue, and stiffness) and reduced frequency of symptoms (headache, sleep disturbances and subjective joint swelling) were reported in both groups, but lasted longer in the treatment group. Significant improvement in most subscales of the SF36 was reported for both groups. Interestingly, the improvement in physical components of the QoL index usually lasted 3 months, whereas improvement in measures of psychological well-being was of shorter duration. Improvements in the control group were explained by temporary changes in lifestyle combined with the relaxed atmosphere of the Dead Sea resort. In conclusion, the authors demonstrated that staying in a Dead Sea spa, especially while receiving balneotherapy, improves FS-related symptoms and ameliorates some aspects of QoL, at least for 3 months.

Evcik et al[25] also reported significant improvements lasting up to 6 months in patients treated with balneotherapy. In this study, 42 patients (with ages ranged between 30 and 55 years and without cardiovascular comorbidities) with FS were randomly assigned to two groups. One group (22 patients) bathed for 20 min at 36 °C once a day, five times per week for 3 consecutive weeks (total 15 sessions), and the other group (20 patients) continued their regular medications without balneotherapy. Patients were evaluated using TPC, VAS for pain, Beck's Depression Index (BDI), and FIQ at basal time, after therapy and 6 months later. The balneotherapy group showed statistically significant improvements in TPC, VAS score, FIQ, and BDI values at the end of therapy; at 6 months, the improvement in all parameters except BDI persisted.

A study by Donmez et al[26] compared the effects of a stay at a spa center plus balneotherapy and the effects of regular care (control), recording significant improvements in major outcome measures, such as pain, TPC, and FIQ with respect to control. The pain and TPC results persisted for up to one month and the FIQ results for up to 6 months. However, they also could be attributed to the effects of the spa stay (not offered to controls, who continued their habitual medical treatment and/or daily exercises).

Ardiç et al[27] investigated the clinical effects of balneotherapy in the treatment of FS, considering serum levels of certain inflammatory markers, such as interleukin-1 (IL-1), prostaglandin E_2 (PGE_2) and leukotriene B_4 (LTB_4). One group of patients (n = 22) bathed 20 min per day for five days per week for three consecutive weeks, and the other group (n = 22) (control) continued with pharmacological treatment. A statistically significant improvement in algometric score, VAS, BDI, TPC, and FIQ and a significant decrease of the mentioned inflammatory markers were only found in the balneotherapy group at the end of the treatment cycle.

In a multicentric single-blind RCT study, Fioravanti et al[28] assessed the effects of a combination of mud packs and thermal baths (with two types of mineral water) on patients with primary FS who responded poorly to pharmacological therapy. They also analyzed tolerance to mud packs because no trial using this thermal treatment has been performed in FS. Eighty patients with primary FS were randomly allocated to two groups: 40 underwent a cycle of 12 mud packs and thermal baths over a period of 2 weeks, and 40 were enrolled as controls and continued their regular outpatient care routine. Because many other non-specific factors also may contribute to the effects observed after spa therapy, including changes in the environment, pleasant scenery, and the absence of work duties, to temper these factors, all patients lived near the spa, continued working, and did not modify their lifestyles. Another aspect that often amplifies the effects of spa therapy is its frequent association with physio-kinesiotherapy. These treatments were excluded from the protocol if they had not yet begun and were not already established. The following parameters were evaluated at baseline, after thermal treatment, and after 16 weeks: FIQ, TPC, VAS for "minor" symptoms, AIMS1, and HAQ. Controls were assessed at the same intervals. A significant improvement in all parameters was recorded after mud-pack therapy and after 16 weeks. The results were similar for the two types of mineral water. Regarding tolerance mud packs, no patient reported any exacerbation of symptoms, and the hot applications were well tolerated by all. No drop-outs occurred during spa therapy, and all patients completed the study.

Özkurt et al[29] investigated the efficacy of balneotherapy in 50 women with FS randomly assigned to either the balneotherapy (25) or the control (25) group. The patients in the balneotherapy group had 2 thermomineral water baths daily for 2 weeks in the Tuzla Spa Center. The patients in the control group continued to have their medical treatment and routine daily life. Outcome measures of the study were pain intensity (VAS score), FIQ, BDI, Patient's and Investigator's Global Assessment (PGA and IGA) scores, and SF36. Balneotherapy was found to be superior at the end of the cure period in terms of pain intensity, FIQ, BDI, PGA and IGA scores, and TPC as compared with the control group. The superiority of balneotherapy lasted up to the end of the 3rd month, except for the BDI score and the IGA scores.

Mechanism of Action of Spa Therapy in FS

The mechanisms by which immersion in mineral or thermal water or the application of mud alleviates chronic pain and the symptoms of FS are not completely known. The net benefit is probably the result of a combination of factors, among which, mechanical, thermal, and chemical effects are most prominent.[18–20] A distinction can be made between the non-specific (hydrotherapeutic in a broad sense) mechanisms of simple bathing in hot tap water, and the specific (hydromineral and crenotherapeutic) mechanisms, which depend on the chemical and physical properties of the water used. Whereas the former are well known, the latter are difficult to identify and assess. Buoyancy, immersion, resistance, and temperature all play important roles. Hot stimuli produces 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.[30]

Spa therapy provokes a series of endocrine reactions, particularly in the release of adrenocorticotropic hormone (ACTH), cortisol, prolactin and growth hormone (GH), although it does not alter the circadian rhythm of these hormones.[31] A dysregulation of the HPA axis, marked by mild hypocortisolemia and glucocorticoid feedback resistance, has been demonstrated in FS patients.[32,33] These findings can explain the beneficial clinical effects of spa therapy in FS.

Furthermore, various spa therapy techniques have been demonstrated to increase plasma levels of beta-endorphin.[34,35] Interestingly, it has been found that application of mature thermal mud in healthy individuals brings about a rapid increase in plasma beta-endorphin, which returns to pretreatment levels within the period of the so-called thermal reaction.[36] This increase in beta-endorphin explains the analgesic and anti-spastic effect of spa therapy, which is particularly important in patients with FS and is one of the key factors in the mechanism of individual tolerance to thermal mud baths.

A recent study has shown a reduction in circulating levels of IL-1, PGE_2 and LTB_4, important mediators of inflammation and pain, in FS patients undergoing a cycle of balneotherapy.[27] It has been suggested that inflammatory process mediated by cytokines, proteases, and inflammatory mediators located in the soft body tissue may play a role in the pathogenesis of FS, in up to one third of FS patients.[37] This inflammatory process would stimulate subcutaneous nociceptors, resulting in a sensation of pain. The detection of IL-1, IL-6, and tumor necrosis factor-α (TNF-α) in the skin of one-third of FS patients, and elevated plasma PGE_2 levels in FS support this hypothesis.[38] In another study of the same authors, it was demonstrated that reduction in masseter PGE_2 level after intramuscular glucocorticoid administration was associated with a decrease in resting pain.[39] The inhibitory effect of balneotherapy on the production and/or release of IL-1, PGE_2 and LTB_4 could explain the mechanism of clinical benefits of spa therapy in this disorder. Mineral water also may influence the oxidant-antioxidant system, which could be beneficial, because oxidative stress disorders have been described in FS.[40,41] In fact, in patients with FS, Bagis et al[42] demonstrated an increase of serum malondialdehyde (MAD) and a decrease of serum superoxide dismutase (SOD), which support the hypothesis that FS is related to an imbalance of oxidant/antioxidant system.

Finally, other factors may contribute positively to the beneficial effects of spa therapy in FS, such as change of environment, the "spa-scenery", the absence of (house) work duties, physical and mental relaxation, the non-competitive atmosphere with similarly suffering companions, and physical therapy.[18–20] As such, spa benefits could perhaps be attributed also to the effects of factors unrelated to the "water" therapy *per se.* These spa benefits are especially important in studies evaluating the effects of balneotherapy compared with no treatment or another treatment.

Discussion

The aim of this review was to summarize the currently available information on clinical effects and mechanism of action of spa therapy in the management of FS. We also provide some suggestions for further development in this area. The results of the RCTs on spa therapy for FS suggest a positive effect on pain, other FS-related symptoms, and QoL.[2,43] The studies assessed the medium-to-long-term effect and found that the clinical efficacy of spa therapy lasted for 4–6 months. Despite low tolerance of physical treatments by FS patients, spa therapy seems to be well tolerated and have a lower percentage of side effects, which also are less severe, than those associated with pharmacological treatments.

Some aspects of the studies on spa therapy for FS are disputable and could be a source of bias, for example, the lack of double-blind experimental design because of the difficulty of creating a placebo with the same characteristics as the treatment. Because of the lack of double-blinded studies, the placebo effect cannot be excluded and may contribute to confound results. The methodological quality of the RCTs analyzed was limited for the following reasons: (1) only two studies had a sample size of at least 25 per group, the number recognized as appropriate for detecting clinically significant differences between two active treatments;[44] (2) no studies distinguished between different FS subgroups, such as patients with predominant pain symptoms or patients with psychological involvement;[45] (3) no study included intention-to-treat analysis, but analyzed the completers, possibly favoring the results of spa therapy, even if the dropout rates were low; (4) most studies did not report the method of randomization used; and (5) the trials did not ensure that treatment allocation was concealed.[2,43]

Comparison of the studies was difficult as the baseline characteristics of the patients were heterogeneous, the interventions differed in type, intensity, and duration: the methods used for assessment of efficacy varied, and the patients were assessed at different times after the spa therapy. In particular, the heterogeneity of "spa therapy" makes it difficult to determine which form of spa therapy is most effective, and no study was designed to compare different types of spa care procedures.

Although the consistency of the results suggests that spa therapy has a therapeutic effect on FS, the methodological limitations of the studies preclude any definitive conclusions.

Furthermore, the mechanisms of action of spa therapy are not fully understood and one of the critical points is the controversial problem of the absorption of the minerals dissolved in thermal waters that is the demonstration of specific effects other than those linked to the simple action of heat.

Conclusions

In conclusion, spa therapy seems to be effective and useful in FS, reducing pain, improving function, and ameliorating QoL. The improvement reported in some clinical studies lasts over time. Nevertheless, the methodological limitations of available clinical studies, such as the lack of placebo double-blinded trials, preclude definitive conclusions. It cannot substitute conventional therapy but can complement to it. Actually, spa therapy can represent a useful backup to pharmacologic treatment of FS or a valid alternative for patients who do not tolerate pharmacologic treatments. Future studies to clarify the mechanisms of action and the effects derived from the application of thermal treatments, are imperative. Studies conducted according to rigorous methodological criteria in larger numbers of patients are needed to determine the potential of spa therapy for FS.

Author Contributions

Conceived and designed the experiments: Guidelli GM, Fioravanti A. Analysed the data: De Nobili E. Wrote the first draft of the manuscript: Guidelli GM, Tenti S. Contributed to the writing of the manuscript: Guidelli GM, Tenti S, Fioravanti A. Agree with manuscript results and conclusions: De Nobili E, Fioravanti A. Jointly developed the structure and arguments for the paper: Fioravanti A. Made critical revisions and approved final version: Guidelli GM, Fioravanti A. All authors reviewed and approved of the final manuscript.

Disclosures and Ethics

As a requirement of publication author(s) have provided to the publisher signed confirmation of compliance with legal and ethical obligations including but not limited to the following: authorship and contributorship, conflicts of interest, privacy and confidentiality and (where applicable) protection of human and animal research subjects. The authors have read and confirmed their agreement with the ICMJE authorship and conflict of interest criteria. The authors have also confirmed that this article is unique and not under consideration or published in any other publication, and that they have permission from rights holders to reproduce any copyrighted material. Any disclosures are made in this section. The external blind peer reviewers report no conflicts of interest.

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