

Evidence-based hydro- and balneotherapy in Hungary—a systematic review and meta-analysis

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Abstract Balneotherapy is appreciated as a traditional treatment modality in medicine. Hungary is rich in thermal mineral waters. Balneotherapy has been in extensive use for centuries and its effects have been studied in detail. Here, we present a systematic review and meta-analysis of clinical trials conducted with Hungarian thermal mineral waters, the findings of which have been published by Hungarian authors in English. The 122 studies identified in different databases include 18 clinical trials. Five of these evaluated the effect of hydro- and balneotherapy on chronic low back pain, four on osteoarthritis of the knee, and two on osteoarthritis of the hand. One of the remaining seven trials

evaluated balneotherapy in chronic inflammatory pelvic diseases, while six studies explored its effect on various laboratory parameters. Out of the 18 studies, 9 met the predefined criteria for meta-analysis. The results confirmed the beneficial effect of balneotherapy on pain with weight bearing and at rest in patients with degenerative joint and spinal diseases. A similar effect has been found in chronic pelvic inflammatory disease. The review also revealed that balneotherapy has some beneficial effects on antioxidant status, and on metabolic and inflammatory parameters. Based on the results, we conclude that balneotherapy with Hungarian thermal-mineral waters is an effective remedy for lower back pain, as well as for knee and hand osteoarthritis.

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Introduction

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 rehabilitation (Gutenbrunner et al. 2010). It can be implemented as head-out immersion in mineral water; as the application of mud- or peloid-packs to body regions; as exposure to gases during bathing and by inhalation; or by drinking mineral water. Balneotherapy can be administered at spas with a special resort environment and atmosphere, or elsewhere (Bender et al. 2005). It is an ancient, traditional treatment modality used in Europe and in other parts of the world (Balint et al. 1993; Konrad 1994) for musculoskeletal (Kamioka et al. 2010), gynaecological (Zámbó et al. 2008), and dermatological (Brockow et al. 2007) conditions (psoriasis in particular), peripheral vascular disease (Pagourelis et al. 2011), and many other disorders (Dubois et al. 2010; Fabry

et al. 2009). Thermal mineral waters have been used empirically for the treatment of different diseases for centuries. During the last 30 years, a number of controlled trials have demonstrated the efficacy of balneotherapy in treating certain diseases. Although the mode of the action of balneotherapy is still unclear, its efficacy appears confirmed by recent reviews (Harzy et al. 2009; Falagas et al. 2009). Hungary abounds in thermal-mineral waters; in this regard, it is among the richest countries in the world. Approximately 1,300 springs have been registered, and 800 of these are used for medical purposes. Additional balneotherapy resources include five healing caves, five different types of peloid and mud, and post-volcanic discharges of radon and carbon dioxide gases (mofettes). The thermal lake of Hévíz (near Lake Balaton in western Hungary) is the largest of its kind in Europe; its bottom is covered by a special mud, which is also used for medical purposes.

Aims of the study

Balneology research in Hungary started in the nineteenth century; the Hungarian Balneological Society was founded in 1891. The first tap-water-controlled, double blind trial with balneotherapy treating rheumatoid arthritis (RA) patients was performed in Hungary (and published in Hungarian by Bathory et al. 1981). Another Hungarian trial of a similar design but on osteoarthritis(OA) patients was the first trial to be reported in English (Szucs et al. 1989); it has been followed by a series of controlled trials published by Hungarian authors in the international literature. Some of the Hungarian clinical trials are specialised in that their study populations were recruited from local, ambulatory patients, their design eliminated the placebo effect of the spa environment and atmosphere, and the control subjects were treated with heated tap water (Szucs et al. 1989; Kovacs and Bender 2002; Balogh et al. 2005; Bender et al. 2007; Balint et al. 2007; Zámbo et al. 2008; Kulisch et al. 2009; Olah et al. 2010; Kovacs et al. 2012; Tefner et al. 2012). Recently, Karagülle and Karagülle (2004), as well as Katz et al. (2012) reviewed Turkish and Israeli balneological trials, so to follow suit, we decided to undertake a systematic review of trials by Hungarian authors. Our aim was to provide an overview of Hungarian research into the field of balneotherapy, including both clinical trials and experimental work to study the mode of action of different Hungarian thermal mineral waters. Further, we intended to conduct a meta-analysis of the studies meeting predefined criteria. We chose the relief of pain as the primary outcome measure, whereas secondary outcome parameters included improvement of function, activity level, quality of life, changes in laboratory parameters, and the reduction of analgesic and non steroid anti-inflammatory drug (NSAID) requirements.

Materials and methods

Data sources

A review and meta-analysis of randomised controlled trials (RCTs) was conducted according to the Quality of Reporting of Meta-analyses (QUOROM) statement (Moher et al. 1999; Clarke 2000). Two authors independently screened the Cochrane Library, as well as the PubMed, Web of Science, Scopus, PED-ro, Web of Knowledge databases.

Data extraction

The review and meta-analysis was limited to studies of Hungarian thermal mineral waters, published by Hungarian authors in the English-language literature between 1989 and 2012. We searched the above-mentioned literature databases using the following search terms: balneotherapy, spa therapy, thermal water, mineral water, radon bath, radon cave, peloid, underwater traction therapy, hydrotherapy. Two reviewers (T.B. and I.T.) selected clinical trials and extracted their data (study characteristics and results) independently of each other, according to a standard set of criteria. Another investigator (Z.P.) performed the meta-analysis.

Study selection

We identified all articles discussing hydro- and balneotherapy in Hungary including reports of clinical, experimental, historical, or semantic studies, as well as letters on the effect of mineral water, radon baths, or cave and peloid treatment.

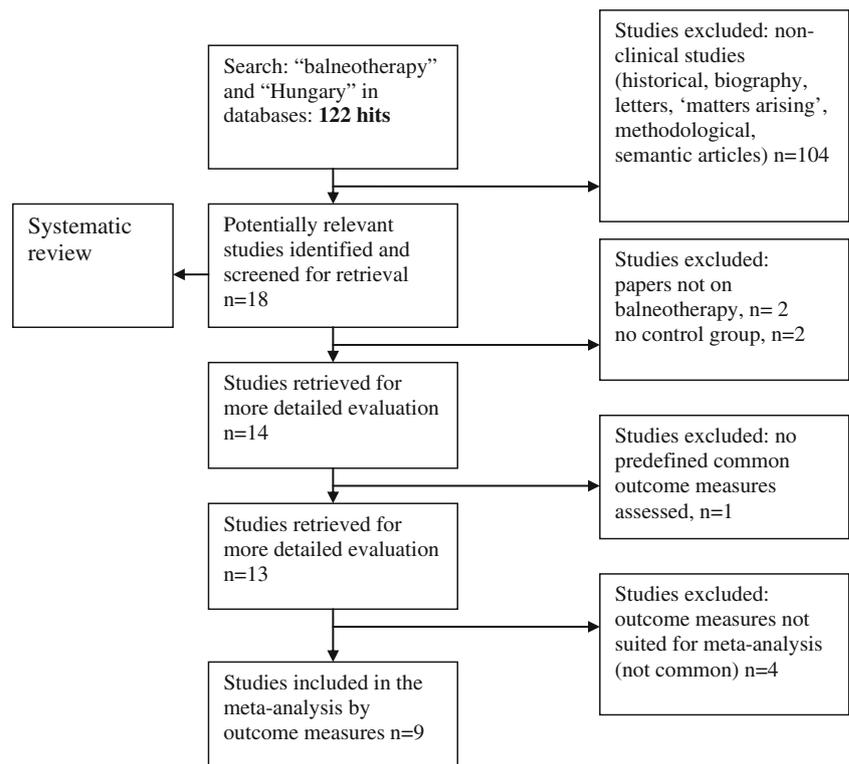
Inclusion criteria for review/meta-analysis

All clinical trials were included in the systematic review. Studies meeting the following criteria were selected for meta-analysis: any form of balneotherapy or hydrotherapy administered with or without any other treatment; randomised controlled trials comparing balneotherapy with any alternative intervention; full papers reporting Hungarian studies in English; trials carried out in Hungary; studies with at least one symptom-specific outcome measure, such as pain, activity, function, quality of life, or laboratory findings.

Assessment of methodological quality

The internal validity of the clinical studies was assessed using the 11-point van Tulder scale (van Tulder et al. 2003; Furlan et al. 2009). Each criterion was scored 1 (if met) or 0 (if unmet or unknown). Studies scoring lower than 50 % were considered 'low quality' (7 studies); those scoring between 50 and 75 % (7 studies) were rated as 'moderate quality', and those over 75 % 'high quality' (4 studies).

Fig. 1 Flowchart of the review and meta-analysis of randomised controlled trial (RCT) studies



Statistical methods

Mean values and standard deviations (SD), or test statistics were recorded for each of the nine studies, and effect sizes were computed using the standardised mean difference (SMD) technique. The SMD is a scale-free measure of the ratio of the difference in mean outcomes between the groups to the SD of the outcome in the study population. The intervention effect expressed in SMD units is a standardised value rather than the original unit of measure. Sample size and effect sizes were processed with the MedCalc software package (<http://www.medcalc.be>) with the purpose of generating forest plots as graphical displays of effect size for each study.

Missing data

Study authors were contacted and missing data obtained through personal communication (Fig. 1).

Results

Systematic review

The literature search identified 122 studies. Among these, we found 18 possibly relevant studies for data retrieval according to the initial inclusion criteria (clinical trials) (Szucs et al. 1989; Konrad et al. 1992; Kovacs and Bender 2002; Holló et al. 2004; Balogh et al. 2005;

Bender et al. 2007; Balint et al. 2007; Gaal et al. 2008; Olah et al. 2008; Zábó et al. 2008; Nagy et al. 2009a, b; Kulisch et al. 2009; Olah et al. 2010, 2011; Tefner et al. 2012; Horvath et al. 2012; Kovacs et al. 2012). Data from 1,199 subjects (patients and controls) of the 18 clinical studies were evaluated. Dropouts comprised 7.1 % ($n=85$) of all patients, and a single adverse event (an allergic reaction to sulphur) occurred in only one study. The main causes of discontinuation were poor compliance and intercurrent disease.

Knee osteoarthritis

Three randomised, double blind, tap-water-controlled studies were identified, including the first trial of this kind published in English (Szucs et al. 1989). Immersion in thermal mineral water resulted in significant improvement of the clinical indices, namely pain [measured with a visual analogue scale (VAS)] and function [rated with the Western Ontario and McMaster Universities (WOMAC) scale] after balneotherapy (Szucs et al. 1989; Kovacs and Bender 2002; Balint and Szebenyi 1997; Gaal et al. 2008) (Table 1).

Hand osteoarthritis

The two RCTs (one single blind and one double blind) showed that balneotherapy is beneficial for patients with hand osteoarthritis, in both the short and the long term. This

Table 1 Effect of balneotherapy on knee osteoarthritis. *WOMAC* Western Ontario and McMaster Universities index, *RCT* randomised controlled trial

Trial	Study design	Internal validity score	Treatment	<i>n</i>	Outcome measures	Follow-up period	Results
Balint et al. 2007	Double blind RCT	7	Group 1: immersion in mineral water (34 °C) for 30 mins, 5 days a week for 4 weeks, as a 20-session treatment course	27	WOMAC activity, joint stiffness, pain and total score	3 months	WOMAC activity, pain, and total scores improved significantly in the balneotherapy group and the difference remained significant at the end of the follow-up. The same parameters improved significantly also in the tap water group after balneotherapy, but this improvement was no longer detected at the end of the 3-month follow-up period
			Group 2: the same as in the treatment group, but using heated tap water	25			
Szucs et al. 1989	Double blind RCT	6	Group 1: daily 20-min treatments in 36 °C thermal mineral water on 18 occasions	30	Number of patients with pain at baseline, erythrocyte sedimentation rate, white blood cell count	3 weeks	Number of patients with pain at baseline, pain and tenderness decreased in the treatment group after treatment
			Group 2: the same as in the treatment group, but using tap water	32			
Kovacs and Bender 2002	Double blind RCT	7	Group 1: bathing the painful knee in thermal mineral water cooled to 36 °C for 30 mins daily, over 15 days	32	Tenderness on palpation, overall ambulation capability, patient's and physician's rating of therapeutic effect, pain intensity (using VAS), range of motion, stair-climbing time	15 weeks	All monitored parameters improved in both groups; however, the magnitude of the improvement was significantly greater in patients treated with thermal water
			Group 2: the same as in Group 1, but using a mixture of tap water and thermal mineral water (36 °C) of negligible mineral content?	25			
Gaal et al. 2008	Prospective study	3	15 balneotherapy sessions lasting 30 min each were administered daily, using 33-°C water	38	Changes in NSAID/analgesic consumption, VAS mean disease severity rated by the patients, doctor's global assessment VAS score, the VAS of pain intensity, WOMAC scores, mean cumulative SF-36 (quality of life) scores	10–14 weeks	All parameters improved significantly in both balneotherapy groups. The favourable effect was prolonged for 3 months after treatment

was confirmed by the improvement of subjective and objective parameters [grip strength, pinch strength, Health Assessment Questionnaire (HAQ) score, morning joint stiffness, swollen joint count, tender joint count, the Short Form-36 (SF-36), HAQ-DI, Australian/Canadian Hand Osteoarthritis Index (AUSCAN), and Euro QoL Group (EQ5D) scores], without adverse events (Kovacs et al. 2012; Horvath et al. 2012) (Table 2).

Chronic low back pain

One double blind and two single blind, tap water-controlled studies were published along with an RCT and a prospective study. The first three studies showed the beneficial effect of thermal mineral water compared

with tap water. Both the clinical indices and the quality of life parameters improved significantly in the active treatment groups. The use of tap water as control is a rarity in the literature on the evaluation of mineral waters for low back pain. In a study with 1-year follow-up, analgesic consumption recorded at the last visit was significantly lower in the balneotherapy group compared to the controls (Konrad et al. 1992; Balogh et al. 2005; Gaal et al. 2008; Kulisch et al. 2009; Tefner et al. 2012) (Table 3).

Underwater traction treatment

Underwater traction (also known as weight bath therapy) was introduced by the Hungarian physician, Károly Moll

Table 2 Effect of balneotherapy on hand osteoarthritis. *VAS* Visual analogue scale, *HAQ* Health Assessment Questionnaire, *SF-36* Short Form-36, *AUSCAN* Australian/Canadian Hand Osteoarthritis Index, *EQ5D* Euro Qol Group scores

Trial	Study design	Internal validity score	Treatment	<i>n</i>	Outcome measures	Follow-up period	Results
Horvath et al. 2012	Randomised, single blind, controlled trial	9	Group 1: head-out immersion in 38 °C thermal mineral water for 20 min, five times a week for 3 weeks and standard pulsed magnetic field therapy applied to the hands three times a week over 3 weeks	21	Pain in the joints of the hands at rest and upon exertion as rated by the patient, patient's and physician's global assessment, grip strength, pinch strength, HAQ, morning joint stiffness (min), swollen joint count, tender joint count, SF-36	13 weeks	Statistically significant improvement was observed in several studied parameters after treatment and during follow-up in the thermal water groups versus the control group
			Group 2: the same as in Group 1, but using 36 °C thermal-mineral water	21			
			Group 3: pulsed magnetic field therapy	21			
Kovacs et al. 2012	Randomised, double blind, controlled trial	8	Group 1: head-out immersion for 20 min per session in a bath-tub filled with thermal mineral water, on 15 occasions altogether, over a period of 3 weeks. The temperature of the water was 37 °C.	24	Pain VAS, morning joint stiffness (min), grip strength, HAQ-DI, AUSCAN (total, pain, stiffness, physical function), EQ5D, EQVAS (quality of life)	6 months	At the end of treatment, the improvement was more pronounced in the patient group treated with thermal mineral water. The difference between the groups was significant regarding pain VAS and EQVAS, both immediately and 3 months after treatment. The same was observed regarding AUSCAN after 3 months, as well as regarding HAQ after 3 and 6 months
			Group 2: the same as in the treatment group, but in tap water of the same temperature	21			

(Moll 1953) In a controlled study of patients suffering from cervical and lumbar degenerative disc disease, underwater traction reduced pain intensity (VAS), increased spinal mobility, and improved the quality of life (Olah et al. 2008) (Table 4).

Chronic pelvic inflammatory disease

A 3-week course of balneotherapy was beneficial as an add-on intervention in the management chronic pelvic inflammatory disease. The improvement of clinical parameters was significantly greater with thermal mineral water than with tap water (Zámbó et al. 2008) (Table 5).

Physiological effects

Effect of radon baths on the endocrine system In Hungary, some mineral waters contain small amounts of radon, which had no significant effect on endocrine parameters. According to another study, radon speleotherapy had a minor influence on the endocrine system in patients suffering from chronic lung disease (Nagy et al. 2009a, b) (Table 6).

Effects on inflammatory and metabolic indices Four studies investigated changes in inflammatory and metabolic indices. One controlled study found that mineral water had a more beneficial effect on antioxidant status than tap water. In hypertensive patients, the differences between baseline and post-treatment HbA_{1C} levels were more pronounced in the balneotherapy group than in the controls. The C-reactive protein levels in hypertensive patients decreased significantly after balneotherapy. In a study of patients with psoriasis, no change of beta-endorphin levels could be detected during balneo-phototherapy (Holló et al. 2004; Bender et al. 2007; Olah et al. 2010, 2011) (Table 7)

Meta-analysis

Of the 18 clinical trials, 9 were excluded; 2 studies lacked a proper control group (Gaal et al. 2008; Holló et al. 2004); 1 study measured the effect of underwater traction and not that of balneotherapy (Olah et al. 2008). One additional study evaluated radon cave therapy and not balneotherapy (Nagy et al. 2009a, b). Following a more detailed review of these provisionally selected articles, a further five papers were excluded for

Table 3 Effect of balneotherapy on chronic low back pain

Trial	Study design	Internal validity score	Treatment	<i>n</i>	Outcome measures	Follow-up period	Results
Tefner et al. 2012	RCT single blind	8	30-min-long balneotherapy sessions over 3 weeks, 5 days a week, using thermal-mineral water of 31 °C The same as in the treatment group, but using heated tap water	30 27	VAS for pain at rest and on exertion, range of motion for the lumbar spine, Oswestry index, EuroQoL-5D and SF-36 questionnaires	15 weeks	In the treatment group, the mobility of the lumbar spine, the Oswestry index, the VAS scores, the EuroQoL-5D index, and most of the SF-36 items improved significantly on the short and on the long term
Kulisch et al. 2009	RCT double blind	9	20-min-long balneotherapy sessions daily over 3 weeks, using thermal-mineral water of 34 °C, add-on electrotherapy 3 times per week The same as in the treatment group, but using heated tap water	36 35	VAS score of low back pain at rest and on exertion, VAS score by the investigator, Schober's sign, lateral flexion of the lumbar spine to the right (cm) and to the left (cm) (Domján sign), Oswestry's Index, SF-36	13 weeks	There was a significant improvement in all parameters in the thermal water group after treatment and at follow up. The improvement in the control group was less substantial compared with baseline values. Comparison of the two treatments revealed a statistically significant difference in some outcome measures (doctor's opinion, Schober's sign, Oswestry's Index after treatment, pain at rest, patients' opinion, lateral flexion to the left at follow up)
Balogh et al. 2005	RCT single blind	7	Daily 30-min baths in warm (36 °C) water on 15 consecutive days (except Sundays). The same as in the treatment group, but in heated tap water	26 30	VAS score of low back pain, patient's rating of efficacy, physician's rating of efficacy, ability to perform activities of daily living, lifting, walking, standing, muscle spasm, paravertebral tenderness, flexion and extension of the spine, Schober's sign, lateral flexion and rotation of the spine (measured with a goniometer), analgesic dose requirements	3 months	Bathing in mineral water resulted in a statistically significant improvement reflected by the VAS, and manifested by the mitigation of muscle spasm, the alleviation of local tenderness, enhanced flexion-extension and rotation of the spine, as well as by the improvement of the Schober's index after treatment. Hydrotherapy resulted only in temporary improvement of the VAS score
Konrad et al. 1992	RCT	5	Group A: immersion in thermal mineral water (37 °C) Group B: underwater traction bath in thermal mineral water (37 °C) Group C: underwater massage in thermal mineral water (37 °C) for 15 min, three times a week, over 4 weeks Control group: non-steroidal anti-inflammatory drugs only	35 44 26 53	Number of analgesic tablets taken, VAS score of low back pain, spinal mobility, and the straight-leg raising sign	12 months	Analgesic consumption and pain scores decreased significantly in all three treatment groups, with no differences between the groups. After 1 year, only analgesic consumption was significantly lower in the treated groups, compared with the control group
Gaal et al. 2008	Prospective study	3	15 balneotherapy sessions lasting 30 min each, administered daily, at neutral water temperature (33–34 °C)	38	Number of patients taking NSAID/analgesic drugs, VAS mean disease severity rated by the patient, the Oswestry scores (%), mean cumulative SF-36 scores	10–14 weeks	All monitored parameters were significantly improved by balneotherapy. The favourable effect was prolonged for 3 months after treatment

Table 4 Effect of underwater traction therapy on neck and lumbar pain

Trial	Study design	Internal validity score	Inclusion criteria	Treatment	n	Outcome measures	Follow-up period	Results
Olah et al. 2008	Controlled, non-randomised follow-up study	4	Subset A: lumbar pain caused by lumbar disc disease (demonstrated by MRI), radiating to the lower extremities Subset B: neck pain caused by cervical disc disease (demonstrated by MRI), radiating to the upper extremities	Group 1: McKenzie exercises for 20 min, electrotherapy with weight bath therapy Group 2: McKenzie exercises for 20 min and electrotherapy (as Group 1) but without weight bath therapy	18/18 18/18	Lumbar pain (VAS), floor-finger distance, lateral flexion (cm), Oswestry Index, SF-36 Cervical pain, lateral flexion, dorsal flexion, SF-36(quality of life)	3 months	Underwater cervical or lumbar traction resulted in significant improvement of all study parameters by the end of treatment, and it was still present 3 months later Among the controls, significant improvement of just a single parameter was seen in patients with lumbar, and of two parameters in those with cervical disc disease

the following reasons: one study lacked a relevant common endpoint (Szucs et al. 1989), and diverse outcome measures were assessed in at least four studies (Bender et al. 2007; Nagy et al. 2009a, b; Olah et al. 2010, 2011). Only studies with a symptom-specific outcome measure evaluated in at least four studies were selected. In the end, nine studies fulfilled the inclusion criteria for meta-analysis (Konrad et al. 1992; Kovacs and Bender 2002; Balogh et al. 2005; Balint et al. 2007; Zámbo et al. 2008; Kulisch et al. 2009; Horvath et al. 2012; Tefner et al. 2012; Kovacs et al. 2012). In view of the inclusion criteria, we selected “pain at rest” and “pain on loading” (both measured by VAS), because these were assessed in four and nine trials, respectively. If the paper did not specify what kind of pain was measured, we contacted the authors for clarification. We found that “pain on loading” improved significantly in seven out of the nine studies (Fig. 2). In this meta-analysis, the overall improvement of “pain on loading” was about 70–80 % (SMD 0.747, 95 % CI 0.931 to –0.563, fixed effect; SMD 0.783, 95 % CI 1.144 to 0.422, random effect). “Pain at rest” improved in three out of four studies (Fig. 3); overall improvement was about 70 % (SMD 0.715, 95 % CI 0.998–0.433, random effect, SMD 0.715, 95 % CI 0.998–0.433 fixed effect). Using summarised analysis, the aggregate improvement of “pain on loading” and of “pain at rest” was significant. The heterogeneity test was significant for “pain on loading”. In seven trials, “pain on loading” improved significantly relative to the control group treated with heated tap water (Konrad et al. 1992; Kovacs and Bender 2002; Balint et al. 2007; Zámbo et al. 2008; Horvath et al. 2012; Tefner et al. 2012; Kovacs et al. 2012). However, in the remaining two trials, the improvement of “pain on loading” was significant also in the tap water group (Balogh et al. 2005; Kulisch et al. 2009). This finding may be explained by the cumulative soothing effect of warm water and concomitant interventions (such as electrotherapy). In these two studies, additional parameters, namely muscle spasm (measured by a manual method) and quality of life improved significantly in patients treated with thermal mineral water, as compared with the controls.

Discussion

In Hungary, balneotherapy has long been used as a traditional treatment, for the country is rich in thermal mineral waters. The majority of the published papers focus on balneotherapy for musculoskeletal disorders, although an increasing number of publications report its application in other clinical fields. Additional applications include

Table 5 Effect of balneotherapy on chronic inflammatory pelvic disease

Trials	Study design	Internal validity score	Treatment	<i>n</i>	Outcome measures	Follow-up	Results
Zámbó et al. 2008	Randomised, double blind	6	Daily baths of 20 mins (38.8 °C) on ten occasions	20	Pain (VAS) elicited by palpating the uterus, the adnexes and the parametrium, parametrial and adnexal mass; psychic status (VAS); ultrasound Doppler index	3 weeks	In comparison with tap water, treatment with mineral water accomplished significantly greater improvement, as reflected by the relief of pain elicited by handling the uterus, and by the improvement of psychological status
			The same as in treatment group, but using heated tap water	20			

inhalation treatment for laryngeal diseases and oncology rehabilitation programs, whereas the drug sparing effect of balneotherapy can be utilized in psychiatry (Dubois et al. 2010). Furthermore, it is useful in cardiovascular rehabilitation, especially because of the positive haemorheological effects of natural carbonated mineral water (Pagourelis et al. 2011). In the international medical literature, Kamioka et al. (2010) reviewed hydro- and balneotherapy papers published between 1990 and 2008. The authors could not draw any conclusions regarding balneotherapy, because of the diversity of outcome measures, the lack of proper control groups, and poor study design. Falagas et al. (2009) reviewed balneotherapy studies excluding hydrotherapy trials. They selected 29 RCTs of 1,720 patients; 8 of these evaluated balneotherapy in osteoarthritis, 4 in fibromyalgia, 4 in ankylosing spondylitis, 4 in rheumatoid arthritis, 3 each in psoriatic arthritis and chronic low back pain, and 1 in Parkinson's disease. In 17 trials, pain decreased significantly compared to the control group, whereas in 8 trials there was no difference. The analgesic effect of balneotherapy lasted for 3 months in 9 studies of longer duration. In their meta-analysis of studies evaluating balneotherapy in osteoarthritis (including the study by Kovacs and Bender 2002), Verhagen et al. (2008) found only a few well-designed trials using appropriate statistical methods. The authors concluded that the effect of balneotherapy is "unproven" and called for additional well-designed studies. The systematic review by Forestier and Françon (2008) led to similar conclusions regarding balneotherapy trials of knee osteoarthritis. The small number of included patients and the poor methodology precluded any conclusions regarding the decrease of pain, improvement of function and quality of life following balneotherapy of patients with osteoarthritis of the knee. Harzy et al. (2009) reviewed 9 RCTs evaluating the balneotherapy of knee osteoarthritis. They found that pain measured by VAS decreased significantly for 8–12 weeks in six RCTs and for 20–24 weeks in two RCTs; articular function also improved significantly over the longer term. Recently, Forestier et al. (2010) published a multicenter

RCT (conducted at three study sites) of 382 patients with knee joint osteoarthritis. The active group was treated with baths in thermal mineral water for 18 days in addition to massage, underwater massage, and mud packing. The control group received drugs and exercised. Balneotherapy was significantly superior in improving pain and joint function as measured by WOMAC, even after 6 months of follow-up. Pittler et al. (2006) published their meta-analysis of 5 RCTs (of 580 patients) appraising the effect of balneotherapy in chronic back pain. Active treatment comprised complex balneotherapy in 5 RCTs, but only immersion in thermal mineral water in one RCT. The controls—patients on the waiting list for balneotherapy—received drugs and exercised. The author rated the results as "encouraging" regarding the decrease of pain, and emphasised the need for further research. Since 2005, three tap water-controlled RCTs, all by Hungarian authors, have evaluated the effect of balneotherapy on back pain (Tefner et al. 2012; Kulisch et al. 2009; Balogh et al. 2005). The physical effect of temperature, buoyancy, and hydrostatic pressure, etc. during balneo- and hydrotherapy are well-established (Sramek et al. 2000). The chemical effects of balneotherapy, such as the absorption of minerals through the skin, is scarcely documented (Shani et al. 1985). The mode of action of thermal-mineral water treatment has been discussed in several papers, of which the work of Fioravanti et al. (2011) provides the most comprehensive overview. Only two countries—Turkey and Israel—have reviewed domestic balneotherapy research. Karagülle and Karagülle (2004) analysed 15 papers on studies evaluating the treatment of various musculoskeletal diseases at eight Turkish spa resorts. One of these studies examined the effect of mud pack treatment, whereas the others appraised that of bathing in thermal mineral water. The analgesic effect was significant in all balneotherapy trials. Katz et al. (2012) reviewed the research focused on Dead Sea balneo- and climatotherapy. Bathing in Dead Sea water and the exposure to UV radiation has a beneficial effect on psoriasis. Dead Sea balneo- and climatotherapy decreases pain, improves joint function and quality of life in rheumatoid arthritis, in

Table 6 Effect on endocrine parameters of exposure to radon in a spa bath and in healing caves

Trials	Study design	Internal validity	Inclusion criteria	Treatment	n	Outcome measures	Follow-up	Results/response
Nagy et al. 2009a, b	Controlled, non-randomised, follow-up study	1	Any form of chronic respiratory disease, with the exception of acute exacerbations	Group 1: 4 h a day spent in the cave for 2 or 3 weeks (except weekends) during the summer period characterized by a high radon concentration Group 2: the same as in Group 1, but during the winter period characterized by a low radon concentration	46	Thyroid stimulating hormone, free thyroxine, cortisol, prolactin, dehydroepiandrosterone sulphate, adrenocorticotrop hormone, and beta endorphine levels	2 weeks	Significant decrease of cortisol levels, which was not directly correlated with radon concentration
Nagy et al. 2009a, b	Controlled, non-randomised study	5	Patients with degenerative lesions of the spine and joints Joint and spinal diseases	Group 1: Fifteen balneotherapy sessions of 30 min duration were administered at the same time of the day at low radon concentration. Water temperature was 31 °C Group 2: The same as in the treatment group, but at a negligible radon content. Water temperature was 32 °C	27	Thyroid stimulating hormone, cortisol, prolactin, dehydroepiandrosterone sulphate, adrenocorticotrop hormone	3 weeks	No significant differences between pre- and post-treatment values, or between the two patient groups

Table 7 Effect of balneotherapy on inflammatory and metabolic indices

Trial	Study design	Internal validity score	Inclusion criteria	Treatment	n	Outcome measures	Follow-up period	Results
Bender et al. 2007	Controlled trial	5	Subjects with chronic lumbar pain with a duration of at least 6 months; none had received balneotherapy in the preceding 3 months	Ten 30-min balneotherapy sessions over 2 weeks, 5 days a week, using thermal-mineral water of 34 °C Group 1 at Cserkeszőlő and Group 2 at Mórahalom Group 3: the same as in the treatment groups, but using heated tap water	10 10 10	Catalase, glutathione peroxidase, malondialdehyde, and superoxide dismutase serum levels	2 weeks	Balneotherapy with either of the two mineral waters significantly reduced the activity of all four enzymes studied compared to the controls
Holló et al. 2004	Prospective, non-randomised, controlled trial	2	Outpatients with extensive psoriatic skin involvement	Narrow-band UV B light therapy combined with simultaneous bathing in 10 % Dead Sea salt solution five times a week, up to a total of 35 sessions	12	Plasma β -endorphin level	7 weeks	There was no significant change in the plasma levels of beta-endorphin after the clinical clearance of psoriatic skin lesions
Olah et al. 2010	Double blind, controlled, follow-up study	7	Outpatients with degenerative musculoskeletal disorders treated with balneotherapy for any reason	Group 1: 30-min balneotherapy sessions on 15 occasions, five times per week using thermal-mineral water of 38 °C Group 2: the same as in the treatment group, but using tap water with initiated colour and the same temperature	21 21	HSP-60, TAS (total antioxidant status), CRP, cholesterol, LDL/HDL ratio, triglyceride, LDL, HDL	15 weeks	No significant difference between the groups
Olah et al. 2011	Randomised, controlled trial with follow-up	6	Subset 'A': 44 overweight and obese patients with a body mass index (BMI) of >25 kg/m ² Subset 'B': Non-overweight hypertensive patients	Group 1: Balneotherapy with 38 °C thermal water on 5 occasions per week, in 15 sessions of 30 min each Group 2: The subjects simply continued on their pre-existing drug therapy	22/22 22/20	Cholesterol, triglyceride, HDL-C, LDL-C, glucose, HbA1c, fructosamine, iron, transferrin, ferritin, CRP, TAS, coenzyme Q10, albumin, β_2 microglobulin, bilirubin, uric acid, NAG, cystatin C, NO2	15 weeks	In obese patients, haemoglobin A _{1c} level decreased in both groups, otherwise there was no difference between the groups In hypertensive patients, differences could be detected between baseline and post-treatment haemoglobin A _{1c} levels in both groups, the change of which was significantly greater in the balneotherapy group In hypertensive patients, CRP levels decreased significantly after balneotherapy

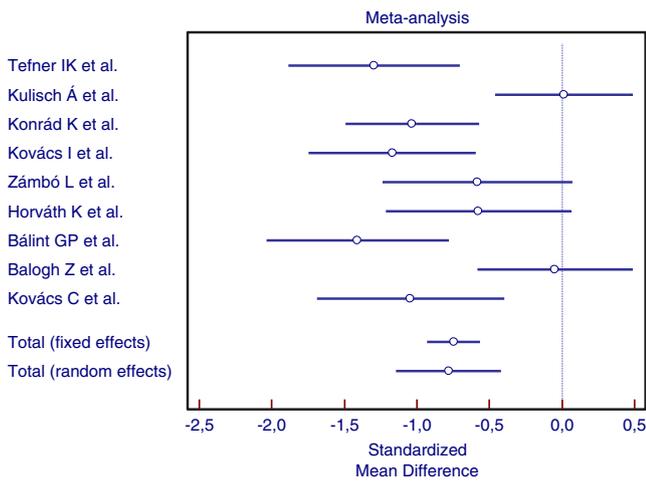


Fig. 2 Visual analogue scale (VAS) intensity of pain on loading

ankylosing spondylitis, as well as in psoriatic arthritis and in osteoarthritis. Dead Sea balneotherapy did not increase blood pressure, as shown by ambulatory blood pressure monitoring (ABPM). Although our selection criteria identified only 18 Hungarian studies, all the remaining Hungarian papers, letters, and methodology publications appeared in important international journals (Balint and Szebenyi 1997; Bender et al. 2001, 2002; Somlai et al. 2007; Gerencsér et al. 2010; Varga 2011; Kavasi et al. 2011a, b; Varga 2012; Szendi et al. 2012). The Hungarian study of underwater traction (“weight-bath”) confirmed earlier biomechanical findings (Kurutz and Bender 2010).

Based on the numerous Hungarian and non-Hungarian tap water-controlled studies, we can state that thermal mineral water alleviates pain caused by different musculoskeletal diseases regardless of the qualitative and quantitative composition of mineral water. This finding may suggest that the minerals might act on cutaneous nerve endings, and thereby achieve long-lasting gate control; experimental skin

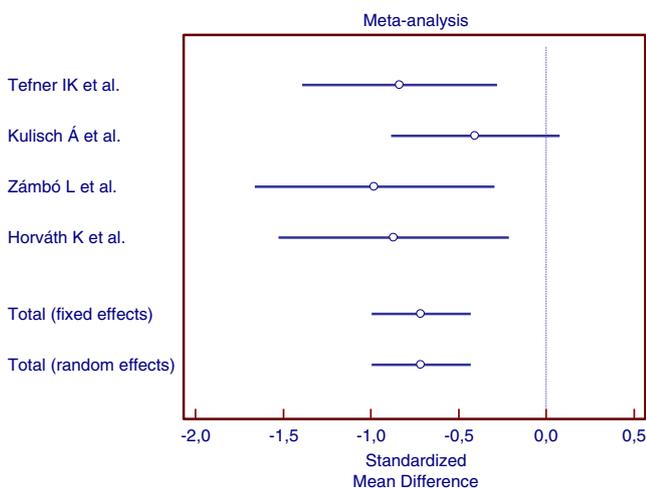


Fig. 3 VAS intensity of pain at rest

biopsy studies could answer this question. The first tap water-controlled trial studying the effect of balneotherapy in chronic inflammatory gynaecological diseases was published by Hungarian authors. There are additional Hungarian studies about the effect of balneotherapy on the antioxidant system, as well as on inflammatory and metabolic parameters, which have been shown to remain normal even in patients with hypertension and obesity. The effects of exposure to radon in caves and in mineral water on some endocrine parameters were also studied. The Hungarian study of vertical underwater traction (weight bath—a balneotherapy modality introduced in the 1950s) was the first in the literature to demonstrate the clinical efficacy of this treatment in cervical and lumbar disc disease under controlled study conditions. We are aware, however, that only well-designed and implemented trials can prove or refute the efficacy of balneotherapy. Hungarian authors were the first to use balneotherapy with heated tap water as placebo control in a double-blind controlled study. This was possible because most of the Hungarian thermal mineral waters do not have a characteristic smell, and their colour can be imitated when necessary. Hungarian authors have aspired to conduct trials under ordinary, non-spa conditions, in local, ambulatory patients, keeping them in their everyday environment. The abundance of thermal springs in Hungary made it possible to realise this ambition.

Limitations of the study

Several of the included studies had small patient populations, and their outcome measures were heterogeneous. The studies were diverse in terms of the type, intensity, and duration of treatments, as well as in regard of the methodology and timing of clinical assessments. The lack of sponsors is a serious problem even for well-designed trials. The selection of a suitable control group may be difficult, and the blinded use of tap water is often impossible. Accordingly, and as shown by van Tulder scores, studies performed 10–20 years ago were of poor quality. In the last 10 years, the design and implementation of RCTs conforms to consensus guidelines. The only common feature of the analysed studies was their primary outcome measure; between-study heterogeneity and methodological flaws prevented the analysis of their secondary endpoints. Occasionally, the type of pain (i.e. pain at rest, at loading or on weight bearing) was ascertained by personal communication with the authors, and not from the information presented in the results section of the papers.

Publication bias

Only studies published in English were included. Therefore, a number of reports in Hungarian—including that of the first

double-blind, tap water-controlled study of balneotherapy in rheumatoid arthritis—were disregarded.

Conclusion

Our review and the meta-analysis of nine articles appear to confirm that the studied Hungarian thermal mineral waters significantly reduce pain in degenerative joint and spinal disease, as well as osteoarthritis of the hand and knee, and that they also alleviate chronic low back pain.

Conflict of interest None.

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