

See discussions, stats, and author profiles for this publication at: <http://www.researchgate.net/publication/50990589>

Balneotherapy in fibromyalgia: A single blind randomized controlled clinical study

ARTICLE *in* RHEUMATOLOGY INTERNATIONAL · APRIL 2011

Impact Factor: 1.63 · DOI: 10.1007/s00296-011-1888-9 · Source: PubMed

CITATIONS

10

DOWNLOADS

48

VIEWS

281

6 AUTHORS, INCLUDING:



Arif Dönmez

Istanbul University

10 PUBLICATIONS 123 CITATIONS

SEE PROFILE



Mufit Zeki Karagulle

Istanbul University

27 PUBLICATIONS 356 CITATIONS

SEE PROFILE



Mustafa Turan

Gulhane Military Medical Academy

46 PUBLICATIONS 612 CITATIONS

SEE PROFILE



Nergis Erdogan

Istanbul University

13 PUBLICATIONS 54 CITATIONS

SEE PROFILE

Balneotherapy in fibromyalgia: a single blind randomized controlled clinical study

Seçil Özkurt · Arif Dönmez · M. Zeki Karagülle ·
Emel Uzunoglu · Mustafa Turan · Nergis Erdoğan

Received: 2 September 2010 / Accepted: 13 March 2011 / Published online: 2 April 2011
© Springer-Verlag 2011

Abstract We aimed to evaluate the effectiveness of balneotherapy in fibromyalgia management. Fifty women with fibromyalgia under pharmacological treatment were randomly assigned to either the balneotherapy (25) or the control (25) group. Four patients from the balneotherapy group and one patient from the control group left the study after randomization. The patients in the balneotherapy group (21) had 2 thermomineral water baths daily for 2 weeks in Tuzla Spa Center. The patients in the control group (24) continued to have their medical treatment and routine daily life. An investigator who was blinded to the study arms assessed the patients. All patients were assessed four times; at the beginning of the study, at the end of the 2nd week, the 1st month, and the 3rd month after balneotherapy. Outcome measures of the study were pain intensity, Fibromyalgia Impact Questionnaire (FIQ), Beck Depression Inventory (BDI), patient's global assessment, investigator's global assessment, SF-36 scores, and tender point count. Balneotherapy was found to be superior at the end of the cure period in terms of pain intensity, FIQ, Beck Depression Inventory, patient's global assessment, investigator's global assessment scores, and tender point count

as compared to the control group. The superiority of balneotherapy lasted up to the end of the 3rd month, except for the Beck Depression Inventory score and the investigator's global assessment score. Significant improvements were observed in PF, GH, and MH subscales of SF-36 during the study period in the balneotherapy group; however, no such improvement was observed in the control group. Balneotherapy was superior only in VT subscale at the end of therapy and at the end of the third month after the therapy as compared to the controls. It was concluded that balneotherapy provides beneficial effects in patients with fibromyalgia.

Keywords Balneotherapy · Spa · Hydrotherapy · Fibromyalgia · Chronic pain · SF 36 · Quality of life

Introduction

Fibromyalgia (FM) is characterized by chronic widespread pain, fatigue, and sleep disturbances. American Collage of Rheumatology 1990 Fibromyalgia Classification Criteria is based on a history of chronic widespread musculoskeletal pain for at least 3 months and more than 11 painful tender points with palpation [1]. Fibromyalgia is frequently accompanied by psychological disorders, chronic headache, irritable bowel syndrome, and urinary symptoms. Yunus suggested that all these disorders and syndromes should be collected under the name of central sensitization syndromes [2].

The etiology of fibromyalgia is unknown and its pathogenesis is not clearly understood. It is a more common entity among women. The prevalence of fibromyalgia among the woman population is 3.5% in the USA and 3.6% in Turkey [3, 4].

A. Dönmez (✉) · M. Zeki Karagülle · E. Uzunoglu ·
N. Erdoğan
Department of Medical Ecology and Hydroclimatology,
İstanbul Medical Faculty, İstanbul University, İstanbul, Turkey
e-mail: donmeza@istanbul.edu.tr

S. Özkurt
İlkevin Special Education and Rehabilitation Centre,
İstanbul, Turkey

M. Turan
Department of Medical Ecology and Hydroclimatology, Gulhane
Military School of Medicine, Etlik, Ankara 06018, Turkey

Fibromyalgia management requires a combination of pharmacologic and nonpharmacologic treatment modalities. Antidepressants and antiseizure medications are the main pharmacologic treatment agents. Several guidelines indicated that balneotherapy is one of the nonpharmacologic treatment modalities proved to be effective in the treatment of fibromyalgia [5–7].

It is evident that immersion once a day into the thermomineral baths is beneficial in fibromyalgia [8–13]. A traditional Turkish balneotherapy cure is shorter than classical thermal cures commonly applied in Europe [14]. It consists of two thermomineral bath applications in-a-day for 7–10 days; accordingly, it can be claimed that such application may result in more intensive stress in the organism. We aimed to assess the effectiveness of a two-week intensive balneotherapy course in patients with FM.

Patients and methods

The study was conducted at the Medical Ecology and Hydroclimatology Department of Istanbul University Medical Faculty and Tuzla Spa Center.

Patients

The patients with fibromyalgia were recruited from the Musculoskeletal Disorders Outpatient Clinic of the Department of Medical Ecology and Hydroclimatology, Istanbul Medical Faculty. The diagnosis was made according to the American Collage of Rheumatology 1990 criteria [1]. Ages of the patients varied between 20 and 60 years. All of the patients were evaluated using systemic clinical examination and laboratory tests. None of the patients had any other medical condition that might affect the study results. Laboratory tests were complete blood count, erythrocyte sedimentation rate, C-reactive protein level, glucose, hepatic and renal function tests, thyroid stimulant hormone levels, and X-rays. None of the patients had balneotherapy within the previous year, and their pharmacological therapy did not alter within the last 2 months. Fifty women with fibromyalgia were enrolled in the study and gave their written informed consent. The patients were randomized using a computer-generated random number list by an independent investigator and allocated to either the balneotherapy or the control arm of the study (25/25). Four patients from the balneotherapy group and one patient from the control group left the study after randomization. Declared reasons of the patients in the study group to leave the study were as follows: Two patients declared that they changed their mind and did not like to stay in Tuzla, one patient declared that she had urinary infection and had to stay in Istanbul during the

study period, and one patient declared that she just did not want to attend the study. The patient in the control group declared that she gave her consent thinking that she would be in the spa treatment group and did not want to be treated as control. The patients in the control group (24) continued to have their medical treatment at home and the patients in the balneotherapy group travelled to stay in Tuzla. Tuzla Spa Center is located near the patients' living area (maximum 50 km).

The patients allocated to the control group were ensured that they would have a balneotherapy course in the following year. The study design was approved by the Institute of Health Sciences of Istanbul University.

Interventions

All of the patients continued to take the medical therapy they were already on including analgesic and antidepressant drugs in addition to receiving patient education and exercise programmes. The patients in the balneotherapy group (21 patients) had two thermal baths every day except Sundays for 2 weeks in Tuzla Spa Center. Thermomineral water used in the study is classified as salt water and contains mainly sodium, chloride, and calcium with a total mineralization of 3,367 mg/L. The temperature of the mineral water was $36 \pm 1^\circ\text{C}$, and the duration of each bath was 20 min. The patients in the control group (24) continued to have their medical care. None of the patient had any additional medication during the study.

Assessments

One of the authors, blinded to the study arms, assessed all patients. Patients were assessed at the beginning of the study, at the end of the 2nd week, at the end of the 6th and the 14th weeks (one and 3 months after balneotherapy).

Measurements

Fibromyalgia impact questionnaire (FIQ), Beck Depression Inventory (BDI), Short Form 36 (SF-36), pain intensity, Patient's and Investigator's Global Assessment (PGA and IGA), and tender point count were the outcome measures of the study.

FIQ is a well-documented measure in fibromyalgia therapy studies. FIQ is a 10-item questionnaire assessing physical functioning, work status, depression, anxiety, sleep, pain, stiffness, fatigue, and well-being. Higher scores indicate greater impairment [15]. Its Turkish translation is validated [16].

BDI consists of 21 items (range 0–63) where higher scores indicate greater depression [17].

SF-36 is a 36-item questionnaire providing a generic indicator for health status. SF-36 generates scores for 8 dimensions; namely, physical functioning, role limitations due to physical health problems, bodily pain, social functioning, general mental health and well-being, role limitations due to emotional health problems, vitality, and general health perceptions. Higher scores indicate better health status [18]. Turkish translations of SF 36 were validated previously [19].

Pain is the main symptom of FM, and a reduction in pain intensity is expected as a result of balneotherapy. Pain intensity was assessed with FIQ using an 11-point ordinal pain scale. In this scale, 0 indicates no pain and 10 is the worst.

Both Patient's and Investigator's Global Assessment scores were also assessed using 100-mm Visual Analog Scale. Scale 0 indicates no symptom whereas 100 is the worst.

Point tenderness was assessed using dolorimeter (Pain, Diagnostic and Thermograph, Inc., Great Neck, NY), from eighteen points indicated in the ACR 1990 classification criteria.

Statistical analysis

Data related to age and symptom duration were given as mean and standard deviation whereas the other study data were presented as median (minimum and maximum) since the data distribution was not normal. Regarding the distribution characteristics, the data were evaluated using nonparametric statistical methods. Comparison of several paired groups (baseline and follow-up measurements) was made using Friedman's test. Independent groups were compared using Mann–Whitney *U* test. All statistical calculations were made using microprocessor and commercially available statistical software packages. Alpha value was set to 0.05 in all calculations, and calculated *P* value less than 0.05 was accepted as statistically significant.

Results

The demographic characteristics of the patients in treatment and control groups are summarized in Table 1. Demographic characteristics of both groups were similar.

Study variables are indicated in Table 2. Both groups were similar at the beginning of the study in terms of these variables.

In the balneotherapy group, significant improvements were observed in FIQ, BDI, pain, IGA, PGA, and TPC at the end of the treatment and follow-up as compared to the baseline (Table 3). However, such improvements were not observed in the control group in any of these variables (Table 4).

Accordingly, the balneotherapy arm was found to be superior to controls except for the third-month IGA and the first-month BDI scores (Table 4).

Regarding SF-36-measured health status of the patients, significant improvements were observed in PF, GH, VT, and MH dimensions of SF-36 during the study period in the balneotherapy group. No such significant changes were observed in the control group regarding SF-36 subscales. Comparing the groups at different time periods of the study in terms of SF-36 subscales, no significant differences were observed except for VT at the end of therapy and at the end of the third month after the therapy measurements.

Discussion

Our study data indicate that intensive balneotherapy has several beneficial effects in patients with fibromyalgia. In the balneotherapy group, significant improvements were observed in FIQ, BDI, pain, IGA, PGA, and TPC at the end of the treatment and follow-up as compared to the baseline (Table 3). However, such improvements were not observed in the control group in any of these variables (Table 4). Accordingly, the balneotherapy arm was found

Table 1 Demographic characteristics of the patients

	Group I (<i>n</i> = 21)	Group II (<i>n</i> = 24)
Sex	21 Women	24 Women
Age (years) (mean ± SD)	50.8 ± 6	46.87 ± 8.8
Height (cm) (mean ± SD)	160.76 ± 4.3	159.87 ± 6
Weight (kg) (mean ± SD)	70.3 ± 10.7	69.06 ± 9.4
Durations of symptoms (years) (mean ± SD)	12.9 ± 7	11.29 ± 6.2
Education duration (years) (mean ± SD)	9.8 ± 3.9	10.1 ± 3.9
Married	16	21
Divorced or Single	5	3
Occupational status	21 Housewife	24 Housewife
Number of patients under antidepressant therapy	5	6

Table 2 Study variables at the baseline in both groups

	Group	Mean	SD	Median	(min–max)	Significance
Pain (VAS)	Balneotherapy	71.19	19.58	72	(28–98)	0.11 ^a
	Control	61.96	18.95	60	(29–95)	
Investigator's Global Assessment (VAS)	Balneotherapy	76.38	11.83	75	(49–93)	0.41*
	Control	78.04	13.41	80	(41–95)	
Patient's Global Assessment (VAS)	Balneotherapy	66.14	22.72	69	(24–98)	0.65 ^a
	Control	63.33	18.74	62	(30–97)	
FIQ	Balneotherapy	55.17	18.84	60	(18–92)	0.38 ^a
	Control	50.61	15.83	50	(10–86)	
BDI	Balneotherapy	14.48	6.06	14	(5–26)	0.82 ^a
	Control	14	8.09	11	(3–30)	
Tender point count	Balneotherapy	16.81	2.23	18	(11–18)	0.64*
	Control	17.33	1.61	18	(11–18)	
SF-36 subdimensions						
<i>Physical functioning (PF)</i>	Balneotherapy	39.52	17.17	45	5–70	0.18*
	Control	48.96	18.71	47	15–80	
<i>Physical role (RP)</i>	Balneotherapy	26.19	33.05	23	0–100	0.16*
	Control	40.62	36.72	50	0–100	
<i>Social functioning (SF)</i>	Balneotherapy	57.74	19.56	62	12–100	0.53*
	Control	60.94	20.29	62	0–100	
<i>Emotional role (RE)</i>	Balneotherapy	38.09	41.21	33	0–100	0.41*
	Control	50	43.96	67	0–100	
<i>Bodily pain (BP)</i>	Balneotherapy	42.62	18.31	41	12–84	0.85*
	Control	41.5	19.05	41	0–100	
<i>General health (GH)</i>	Balneotherapy	45.43	18.37	45	5–82	0.50*
	Control	41–58	20.41	40	0–82	
<i>Vitality (VT)</i>	Balneotherapy	48.57	13.98	45	15–80	0.91*
	Control	48.96	16.01	50	15–85	
<i>Mental health (MH)</i>	Balneotherapy	59.24	13.83	56	32–84	0.40*
	Control	55.50	14.36	56	20–76	

^a Students *t* test, * Mann–Whitney *U* test

to be superior to the controls except for the third-month IGA and the first-month BDI scores (Table 4).

These findings support those of other studies published previously. Balneotherapy application provided a significant pain relief in patients with FM in our study group. Similar findings were obtained in other studies in which balneotherapy was combined with relaxation exercises, or with massage [8, 13]. Improvements in FIQ, BDI, PGA, and tender point count scores are the other benefits in our study group. Such changes were also reported in several studies [9–11, 13] and reviews [20–22].

Although the present study is primarily designed to depict the overall efficacy of spa therapy in patients with fibromyalgia, it also provides clues to explain the underlying mechanisms that may produce the intended outcomes of balneotherapy.

Heat and buoyancy in a thermal pool help to reduce muscle spasm. Decrease in muscle tonus may increase the

pain threshold at nerve endings. Pain-relieving effect of balneotherapy may be explained by the gate-control theory. The body surface of the individual is stimulated by temperature and hydrostatic pressure of water during immersion, and according to the theory, such stimuli decrease sensation of pain. Contribution of beta-endorphins on pain-relieving effect of balneotherapy is controversial. It has been reported that β -endorphin levels increase during a thermomineral bath [23]; however, it was also reported that a 3-week balneotherapy course did not affect plasma β -endorphin levels in osteoarthritis patients [24]. The effectiveness of balneotherapy with sodium chloride waters was shown in osteoarthritis in randomized controlled studies [25–27].

Contribution of environmental changes to the effect of balneotherapy was frequently discussed in the related literature. It is speculated that a change in the usual environment of patients with fibromyalgia would result in a

Table 3 Comparison of the evaluation results before, after completion, after 1 month, and after 3 months of intervention in balneotherapy group (* Friedman test)

	Before treatment [median (min max)]	After treatment [median (min max)]	At the end of 1st month [median (min max)]	At the end of 3 months [median (min max)]	* χ^2	<i>P</i>
Pain (mm.)	72 (28–98)	45 (4–87)	38 (6–83)	36 (7–95)	24.88	0.000
IGASc	75 (49–93)	53 (19–80)	60 (14–76)	60 (8–91)	26.88	0.000
PGASc	69 (24–98)	37 (8–69)	40 (12–85)	34 (12–91)	19.04	0.000
FIQ	57.6 (23–92.1)	41.9 (11.4–77.2)	46.9 (22.3–79.2)	42.6 (7–71)	19	0.000
BDI	14 (5–26)	10 (0–32)	10 (3–33)	10 (0–20)	19.4	0.000
TPC	18 (11–18)	14 (4–18)	15 (7–18)	17 (9–18)	15.8	0.001
PF	45 (5–70)	55 (10–80)	45 (0–80)	55 (10–85)	19.23	0.000
RP	23 (0–100)	25 (0–100)	25 (0–100)	50 (0–100)	50.01	0.171
SF	62 (12–100)	62 (25–100)	75 (25–100)	62 (25–100)	4.97	0.174
RE	33 (0–100)	33 (0–100)	66 (0–100)	33 (0–100)	2.28	0.516
BP	41 (12–84)	42 (32–74)	51 (22–72)	51 (0–84)	5.16	0.160
GH	45 (5–82)	65 (15–95)	55 (15–82)	52 (20–97)	10.55	0.014
VT	45 (15–80)	65 (30–95)	60 (20–80)	60 (20–90)	14.57	0.002
MH	56 (20–76)	68 (44–92)	64 (32–84)	68 (28–92)	9.97	0.019

IGASc Investigator's Global Assessment Score, PGASc Patient's Global Assessment Score, FIQ Fibromyalgia Impact Questionnaire, BDI Beck's Depression Inventory, TPC Tender Point Count

Table 4 Comparison of the evaluation results before, after completion, after 1 month, and after 3 months of intervention in control group (* Friedman test)

	Before treatment [median (min max)]	After treatment [median (min max)]	At the end of 1st month [median (min max)]	At the end of 3 months [median (min max)]	* χ^2	<i>P</i>
Pain (mm.)	60 (29–95)	62 (10–87)	60.5 (9–92)	65.5 (10–97)	1.72	0.63
IGASc	80 (41–95)	78.5 (26–95)	75 (40–93)	72 (20–90)	7.31	0.62
PGASc	62.5 (30–97)	62.5 (10–90)	63.5 (12–88)	68.5 (10–95)	1.038	0.79
FIQ	52.5 (10.3–86.1)	49.5 (19.7–87)	55 (15–77.8)	52.8 (12.1–80)	0.85	0.83
BDI	11.5 (3–30)	11.5 (2–31)	13 (4–30)	14.5 (0–24)	2.432	0.48
TPC	18 (11–18)	18 (12–18)	18 (11–18)	18 (11–18)	3.257	0.35
PF	47 (15–80)	47 (5–85)	47(5–85)	40 (5–85)	5.52	0.137
RP	50 (0–100)	50 (0–100)	25 (0–100)	25 (0–100)	3.50	0.320
SF	62 (0–100)	62 (12–100)	62 (25–100)	62 (12–100)	3.85	0.278
RE	66 (0–100)	50 (0–100)	33 (0–100)	33 (0–100)	0.48	0.924
BP	41 (0–100)	41 (0–100)	41 (10–100)	32 (20–100)	3.90	0.272
GH	40 (0–80)	53 (10–92)	51 (15–85)	51 (5–87)	5.76	0.124
VT	50 (15–85)	50 (5–70)	45 (20–90)	47 (20–90)	0.58	0.90
MH	56 (20–76)	58 (12–76)	56 (24–100)	56 (24–100)	0.72	0.869

greater sense of well-being [28]. Tubergen suggested that certain nonspecific variables of the spa environment such as environmental change, pleasant scenery, being in a noncompetitive atmosphere with fellow patients, and the absence of work duties may be beneficial for patients with fibromyalgia [29]. Nonspecific variables of the spa environment may have contributed to the achievement of clinical improvements in our study as well; however, such contribution should be limited because of the fact that environmental conditions of Tuzla Spa Center are very

similar to the patients' daily living environment. Findings of several other studies in the literature also imply that the role of environmental changes in providing beneficial effects in patients with FM is limited [8–11, 13]. In these studies, balneotherapy applications themselves rather than environmental changes contribute to the beneficial effects.

The present study has several limitations. The main limitation is the small number of patients included in the study; our budget hindered us from including more patients. Limiting the follow-up period to 3 months may be

perceived as another limitation of the study. The third limitation is letting the control group to go on with their daily life and not to change their living environment. Although their daily living environment conditions were very similar to those at the Spa Center, it would be possible to reveal the effect of nonspecific variables of the spa environment more clearly if the control group patients would stay in the same Spa Center without taking balneotherapy.

In conclusion, balneotherapy is found to be effective in treating patients with fibromyalgia. Beneficial effects are observed both in short and long terms. There is a need for further randomized controlled studies to verify these results and to identify whether balneotherapy is cost-effective in fibromyalgia treatment.

References

- Wolfe F, Smyte HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, Tugwell P, Campbell SM, Abeles M, Clark P et al (1990) The American Collage of Rheumatology 1990 criteria for classification of fibromyalgia: report of the multicentre criteria committee. *Arthritis Rheum* 33:160–172
- Yunus MB (2007) Fibromyalgia and Overlapping Disorders: The Unifying Concept of Central Sensitivity Syndromes. *Semin Arthritis Rheum* 36:339–356
- Wolfe F, Ross K, Anderson J, Russell IJ, Hebert L (1995) The prevalence and characteristics of fibromyalgia in the general population. *Arthritis Rheum* 38:19–28
- Topbaş M, Çakırbay H, Güleç H (2005) The prevalence of fibromyalgia in women aged 20–64 in Turkey. *Scand J Rheumatol* 34(2):140–144
- Buckhardt CS, Goldenberg D, Crofford L et al (2005) Guideline for the management of fibromyalgia syndrome pain in adults and children. *American Pain Society (APS), Glenview*
- Carville SF, Arendt-Nielsen S, Bliddal H et al (2008) EULAR evidence based recommendations for the management of fibromyalgia syndrome. *Ann Rheum Dis* 67:536–541
- Häuser Winfried, Kati Thieme B, Dennis C, Turk C (2010) Guidelines on the management of fibromyalgia syndrome—A systematic review. *Eur J Pain* 14:5–10
- Yurtkuran M, Çeliktaş M (1996) A randomized, controlled trial of balneotherapy in the treatment of patients with primary fibromyalgia syndrome. *Phys Rehab Kur Med* 6(4):109–112
- Buskila D, Shakra MA, Neumann L, Odes L, Shneider E, Flusser D, Sukenik S (2001) Balneotherapy for fibromyalgia at Dead Sea. *Rheumatol Int* 20:105–108
- Evcik D, Kızılay B, Gökçen E (2002) The effects of balneotherapy on fibromyalgia patients. *Rheumatol Int* 22:56–59
- Altan L, Bingöl Ü, Aykaç M, Koç Z, Yurtkuran M (2004) Investigation of the pool based exercises on fibromyalgia syndrome. *Rheumatol Int* 24(5):272–277
- Zijlstra TR, van de Laar MA, Bernelot Moens HJ, Taal E, Zakraoui L, Rasker JJ (2005) Spa treatment for primary fibromyalgia syndrome: a combination of thalassotherapy, exercise and patient education improves symptoms and quality of life. *Rheumatology (Oxford)* 44(4):539–546
- Dönmez A, Karagülle MZ, Tercan N, Dinler M, İşsever H, Karagülle M, Turan M (2005) Spa therapy in fibromyalgia: a randomised controlled clinic study. *Rheumatol Int* 26(2):168–172
- Odabaşı E, Karagülle MZ, Karagülle M, Turan M, Karagülle O (2002) Comparison of two traditional spa therapy regimens in patients with knee osteoarthritis. *Physikalische Medizin, Rehabilitationsmedizin, Kurortmedizin* 12(6):337–347
- Burckhardt CS, Clark SR, Bennet RM (1991) The fibromyalgia Impact Questionnaire: development and validation. *J Rheumatol* 18:728–733
- Sarmer S, Ergin S, Yavuzer G (2000) The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. *Rheumatol Int* 20:9–12
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. *Arch Gen Psychiatry* 4:561–571
- Ware JE, The Sherbourne CD, OS M (1992) 36-item Short-Form Health Survey (SF-36) I. Conceptual framework and item selection. *Med Care* 30:473–483
- Demirsoy C (1990) The MOS-SF 36 health survey: a validation study with Turkish sample. Dissertation (unpublished), University of Bosphorus, Istanbul
- Falagas ME, Zarkadoulia E, Rafailidis PI (2009) The therapeutic effect of balneotherapy: evaluation of the evidence from randomised controlled trials. *Int J Clin Pract* 63(7):1068–1084
- Mc Veigh JG, Mc Gaughey H, Hall M, Kane P (2008) The effectiveness of hydrotherapy in the management of fibromyalgia syndrome: a systematic review. *Rheumatol Int* 29:119–130
- Langhorst J, Musial F, Klose P, Hauser W (2009) Efficacy of hydrotherapy in fibromyalgia syndrome—a meta-analysis of randomized controlled clinical trials. *Rheumatology* 48:1155–1159
- Kubota K, Kurabayashi H, Tamura K, Kawada E, Tamura J, Shirakura T (1992) A transient rise in plasma beta-endorphin after a traditional 47 degrees C hot-spring bath in Kusatsu-spa, Japan. *Life Sci* 51(24):1877–1880
- Yurtkuran M, Ulus H, Irdesel J (1993) The effect of balneotherapy on plasma endorphine level in patient with osteoarthritis. *Phys Rehab Kur Med* 3:130–132
- Karagülle M, Karagülle MZ, Karagülle O, Dönmez A, Turan M (2007) A 10-day course of SPA therapy is beneficial for people with severe knee osteoarthritis. A 24-week randomised, controlled pilot study. *Clin Rheumatol* 26:2063–2071
- Balint GP, Buchanan WW, Adam A et al (2007) The effect of the thermal mineral water of Nagybaracska on patient with knee jointosteoarthritis, a double blind study. *Clin Rheumatol* 26:890–894
- Wigler I, Elkayam O, Paran D, Yaron M (1995) Spa therapy for gonarthrosis: a prospective study. *Rheumatol Int* 15:65–68
- Neumann L, Sukenik S, Bolotin A, Abu-Shakra M, Amir M, Flusser MD, Buskila D (2001) The Effect of Balneotherapy at the Dead Sea on the Quality of Life of Patients with Fibromyalgia Syndrome. *Clin Rheumatol* 20:15–19
- van Tubergen A, Hidding A (2002) Spa and exercise treatment in ankylosing spondylitis: fact or fancy? *Best Pract Res Clin Rheumatol* 16(4):653–666