Available online at www.sciencedirect.com
SCIENCE DIRECT®
Joint Bone Spine 72 (2005) 303–308
JOINT BONE SPINE
http://france.elsevier.com/direct/BONSOI/

Original article

Improvement of the clinical outcome in Ankylosing Spondylitis by balneotherapy

Merih Yurtkuran [a], Alev Ay [a,*], Yüksel Karakoç [b]

[a] *Department of Physical Therapy and Rehabilitation, Uludag University Atatürk Balneotherapy and Rehabilitation Center, Bursa, Turkey*
[b] *Department of Internal Medicine, Hospital of Social Insurances, Bursa, Turkey*

Received 5 January 2004; accepted 19 June 2004

Available online 15 September 2004

Abstract

Aims. **–** This study is designed to show the efficacy of balneotherapy and balneotherapy (BT) + nonsteroid antiinflammatory drug (NSAID) use in Ankylosing spondylitis (AS) patients.

Methods. **–** In this prospective study, BT, BT+ NSAID and NSAID therapy in 61 patients with AS were evaluated by ASAS core set. BT group (21 patients) was treated only with BT for 20 min, once a day, 5 days a week, over a period of 3 weeks. BT+NSAID group (20 patients) was treated with 1000 mg naproxen as well as BT. NSAID group (20 patients) was treated with 1000 mg naproxen. All of the participants did respiratory and postural exercises for 20 min a day and for the whole study period. Each patient was evaluated on admission (before treatment), at the end of the therapy and 6 months after the treatment.

Results. **–** At the end of the study, statistically significant improvement was observed in all the clinical parameters of the patients in BT (G1), BT+NSAID (G2) and NSAID (G3) groups. This significant symptomatic and clinical improvement was maintained even 6 months after the treatment. The changes from baseline to follow up were similar in G1 and G2 except duration of morning stiffness (DMS) and chest expansion (CE). Improvements in CE and DMS were better in G1 and G2, respectively. Improvements observed in G1 and G2 were superior to the improvements observed in G3 for the variables of morning pain, nocturnal pain, DMS, global well being of the patient, occiput-wall distance, CE, finger to floor distance and functional index. In Schober test, improvement observed in G1 was statistically superior to G3.

Conclusion. **–** We concluded that BT can be suggested as an effective symptomatic treatment modality in patients with AS. Furthermore, sufficient improvement in clinical parameters can be obtained by BT alone.

Keywords: Ankylosing spondylitis; Balneotherapy; NSAID

1. Introduction

Ankylosing spondylitis (AS) is defined as a chronic, systemic, inflammatory disorder that mainly affects the axial skeleton. Typical presentation is low back pain of insidious onset and morning stiffness that is improved with exercise. The main pathologic lesion is enthesitis mostly accompanied by paraarticular bone sclerosis (osteitis) and discitis. The inflammatory process erodes the skeletal fibrocartilage, hyalin cartilage, ligaments and paraarticular bone and leads to chondroosseous and fibrous ankylosis. The disease almost always involves the sacroiliac joints. Peripheric joints like hip and shoulders are involved as synovitis with a lesser ratio [1].

Nocturnal and morning pain and stiffness are the most prominent clinical features in AS accompanied by functional deterioration later on [1]. The therapeutic management of AS is based on the use of nonsteroidal antiinflammatory drugs (NSAIDs) and disease modifying drugs like sulphasalazine. Besides, symptomatic relief can be obtained by physical therapy regimens. NSAIDs are used to lessen the pain and the related symptoms. But they may cause some serious side effects [2]. Morris et al. [3] showed that NSAIDs can be as toxic as disease modifying drugs.

Balneotherapy (BT) has been used traditionally in the management of various rheumatic diseases since ancient

* Corresponding author. UÜTF Atatürk Rehabilitasyon Merkezi Kükürtlü Kaplicalari P.K. 16080, Kükürtlü, Bursa, Türkiye.
Tel.: +90-224-234-76-87; Fax: +90-224-234-76-90.
E-mail address: ay-alev@hotmail.com (A. Ay).

1297-319X/$ - see front matter © 2004 Published by Elsevier SAS.
doi:10.1016/j.jbspin.2004.06.006

Table 1
Thermal water analysis in Atatürk Balneotherapy and Rehabilitation Center

Filed analysis					
T (°C)	LF(uS)	pH	0_2 (mg/l)	m (mol/l)	p (mmol/l)
80.7	1460	6.34	0.6	8.8	4.7
Laboratory analysis					
Anions			mg/l		mval/l
HCO_3^{-2}			528.8		0.67
Cl^-			12.2		0.35
F^-			5.46		0.29
SO_4^{-2}			277.0		5.77
Total			823.6		13.0
Cations			mg/l		mval/l
Ca^{+2}			91.9		4.59
Mg^{+2}			7.41		0.61
Na^+			222.5		9.68
K^+			23.00		0.59
Li^{+2}			0.68		0.10
Total			345.5		15.5

times [4]. There are a few randomised controlled studies about this therapy regimen [5–10]. Goldby and Scott [5] pointed out that most of the studies were carried out retrospectively and they involved some methodological errors.

Because balneotherapy (spring water) has been used frequently in Turkey because of its availability, we intended to evaluate the efficacy of balneotherapy on the patients with AS. We planned to make a randomised controlled study to investigate the clinical effects of balneotherapy on the patients with AS and to compare it with NSAIDs.

2. Methods

2.1. Design

This prospective study was carried out as single blinded and the evaluation was done before (a), after (b) and 2 months after (c) the treatment by three physicians. Two of them who did the physical examination and pain evaluation were blind to the study.

2.2. Participants

Sixty-one Ankylosing spondylitis patients (14 females, 47 males) selected from the outpatients of Atatürk Balneotherapy and Rehabilitation Center were enrolled in the present study. The diagnosis of AS was made according to the New York diagnostic criteria [1]. None of the patients had active peripheric arthritis or other systemic involvements. Before inclusion, the patients taking NSAIDs were told to stop taking them for the last 1 week. Then the patients were randomly allocated into three treatment groups. Twenty-one patients of the balneotherapy group (six females, 15 males) were instructed to have baths for 20 min a day, 5 days a week and for a 3 weeks duration. Balneotherapy was applied in a therapeutic pool with a water temperature of 37 °C (80 °C spring water was waited to cool and become 37 °C). Table 1 shows the characteristics of the spring water used in the present study. Twenty patients in the BT+NSAID group (four females, 16 males) took 1000 mg naproxen and 400 mcg misoprostole (as a gastroprotective agent) a day in addition to BT; for 20 min a day, 5 days a week and for 3 weeks duration. Twenty patients in the NSAID group (three females, 17 males) took 1000 mg naproxen and 400 mcg misoprostole a day. All of the patients in BT, BT+NSAID and NSAID groups were instructed to do respiratory and postural correction exercises for the 6 month duration and for 20 min a day [2]. After the 3 weeks treatment, the patients were not given any medication (NSAID) unless clinical activation occurred, till the 6th month. The patients were followed clinically by phone and home visits. After the therapy (between the 2nd month and 6th month) it was determined that five of them had peripheric arthritis and clinical activation (two from BT group, one from BT+NSAID group and three from NSAID group) and they were given medication. So they were extracted from the study.

2.3. Methods and outcome

Variables used in the study were taken from ASAS core set [11] including morning pain and nocturnal pain measured with Visual Analogue Scale (1–100), morning stiffness (minutes), erytrocyte sedimentation rate, global well being of the patient, occiput-wall distance (cm) and chest expansion (cm), finger to floor distance (cm), lumbar flexibility measured with Schober test [12,13] and functional index [14].

2.4. Statistical analysis

Demographic and baseline characteristics of patients in BT, BT+NSAID and NSAID groups were compared by One way ANOVA (for age, duration of illness, occiput-wall distance (OWD), duration of morning stiffness (DMS), erytro-

Table 2
Demographic and baseline clinical characteristics of the patients in BT (balneotherapy), BT+NSAID (balneotherapy+nonsteroidal antiinflammatory drug) and NSAID (nonsteroidal antiinflammatory drug) groups

	BT Group 1(n = 21)	BT+NSAID Group 2 (n = 20)	NSAID Group 3 (n = 21)
Age	46 ± 5	51 ± 7	50 ± 11
Sex (F/M)	6/15	4/16	3/17
Duration of the illness (year)	10 ± 3	12 ± 5	9 ± 6
Bilateral grade II–III sacroiliitis	15	12	11
Grade III–IV sacroiliitis	9	8	6
Morning pain (VAS)	46.0 ± 28.8	39.0 ± 25.4	38.1 ± 21.7
Nocturnal pain (VAS)	38.8 ± 29.6	45.2 ± 30.4	43.0 ± 31.3
Duration of morning stiffness (minutes)	23.8 ± 31.2	40.3 ± 51.4	24.9 ± 45.3
ESR	31 ± 19	29 ± 23	36 ± 14
Occiput-wall distance (cm)	2.6 ± 3.7	2.8 ± 5.6	3.3 ± 4.6
Chest expansion (cm)	3.1 ± 1.8	4.1 ± 2.3	3.6 ± 2.0
Finger to floor distance (cm)	3.6 ± 5.0	3.7 ± 5.0	4.4 ± 4.9
Schober test (cm)	2.7 ± 1.6	2.7 ± 1.3	3.7 ± 0.9 [a]
Functional index	25 ± 18	29 ± 13	23 ± 17
Global well being (0–10)	4 ± 6	4 ± 5	5 ± 4

ESR, erytrocyte sedimentation rate; VAS, Visual Analogue Scale.
[a] $P < 0.05$.

cyte sedimentation rate (ESR), global well being of the patient (GWB), chest expansion (CE), finger to floor distance (FFD), Schober test and functional index (FI)), chi-square test (for sex parameter) and Kruskal–Wallis test (for morning and nocturnal pain) as independent samples (Table 2). Freidman nonparametric repeated measures ANOVA test and Dunn's multiple comparisons test was used to compare the change scores and to find the differences among groups a, b and c for morning and nocturnal pain (Tables 3–5). Repeated measures ANOVA test and post hoc test is used to compare the change scores/percent changes and to determine the differences among groups a, b and c for ESR, DMS, GWB, OWD, CE, FFD, Schober test and FI (Tables 3–5). Kruskal–Wallis and Dunn's multiple comparisons test are used to compare and to determine the differences among BT, BT+NSAID and NSAID groups for the sixth month changes

Table 3
Statistical analysis for periodical change scores in BT (balneotherapy) group. Values are mean ± SD

	a	b	c	a–b	a–c
Morning pain (VAS)	46.00 ± 28.86	22.60 ± 19.95	19.80 ± 21.72	***	***
Nocturnal pain (VAS)	38.80 ± 29.62	17.40 ± 21.36	10.80 ± 16.75	**	***
Duration of morning stiffness (minutes)	23.80 ± 31.23	12.72 ± 24.35	8.28 ± 11.20	***	***
ESR	31 ± 19	29 ± 21	27 ± 15	ns	ns
Global well being (0–10)	4 ± 6	7 ± 3	6 ± 4	*	*
Occiput-wall distance (cm)	2.60 ± 3.70	1.68 ± 2.94	1.66 ± 3.08	**	**
Chest expansion (cm)	3.17 ± 1.84	4.40 ±1.95	4.40 ± 1.83	**	**
Finger to floor distance (cm)	3.78 ± 5.06	2.22 ± 3.51	2.88 ± 4.35	*	ns
Schober test (cm)	2.74 ± 1.68	3.08 ± 1.66	3.17 ± 1.54	**	**
Functional index	25 ± 18	15 ± 7	19 ± 11	**	*

ESR, erytrocyte sedimentation rate; VAS, Visual Analogue Scale; a, before treatment; b, after treatment; c, 6 months after treatment; SD, Standard deviation; ns, $P > 0.05$, *, $P < 0.05$, **, $P < 0.01$, ***, $P < 0.001$.

Table 4
Statistical analysis for periodical change scores in BT+NSAID group. Values are mean ± SD

	a	b	c	a–b	a–c
Morning pain (VAS)	39.0 ± 25.4	17.9 ± 16.2	14.5 ± 14.4	***	***
Nocturnal pain (VAS)	45.2 ± 30.4	22.1 ± 20.2	17.1 ± 18.8	***	***
Duration of morning stiffness (minutes)	40.3 ± 51.4	13.0 ± 20.5	10.2 ± 15.4	****	****
ESR	29±23	27±19	22±26	ns	ns
Global Well Being (0-10)	4±5	6±2	6±5	*	*
Occiput-wall distance (cm)	2.8 ± 5.6	1.9 ± 4.0	1.9 ± 4.3	**	**
Chest expansion (cm)	4.1 ± 2.3	4.6 ± 1.9	4.9 ± 2.2	*	**
Finger to floor distance (cm)	3.6 ± 5.0	1.7 ± 3.0	2.6 ± 3.9	**	ns
Schober test (cm)	2.7 ± 1.3	3.0 ± 1.2	2.9 ± 1.4	**	*
Functional index	29 ± 13	15 ± 20	21 ± 17	**	*

ESR, erytrocyte sedimentation rate; VAS, Visual Analogue Scale; a, before treatment; b, after treatment; c, 6 months after treatment; ns, $P > 0.05$, *, $P < 0.05$, **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$.

Table 5
Statistical analysis for periodical change scores in NSAID (nonsteroidal antiinflammatory drug) group

	a	b	c	a–b	a–c
Morning pain (VAS)	38.1 ± 21.7	25.5 ± 19.7	23.8 ± 19.7	**	**
Nocturnal pain (VAS)	43.0 ± 31.3	28.0 ± 20.7	22.1 ± 13.2	**	**
Duration of morning stiffness (minutes)	24.9 ± 45.3	16.8 ± 22.7	16.0 ± 25.2	**	**
ESR	36 ± 14	35 ± 22	34 ± 25	ns	ns
Global well being (0–10)	5 ± 9	7 ± 3	6 ± 4	ns	ns
Occiput-wall distance (cm)	3.3 ± 4.6	2.1 ± 4.6	2.0 ± 5.0	**	**
Chest expansion (cm)	3.6 ± 2.0	4.0 ± 1.9	4.0 ± 2.7	*	*
Finger to floor distance (cm)	4.4 ± 4.9	3.9 ± 5.0	3.9 ± 5.0	*	ns
Schober test (cm)	3.7 ± 0.9	3.9 ± 1.6	3.9 ± 2.3	*	ns
Functional index	23 ± 17	22 ± 11	24 ± 19	ns	ns

ESR, erytrocyte sedimentation rate; VAS, Visual Analogue Scale, a, before treatment; b, after treatment; c, 6 months after treatment; SD, Standard deviation; ns, $P > 0.05$, *, $P < 0.05$, **, $P < 0.01$.

in morning and nocturnal pain (Table 4). One way ANOVA and post hoc test are used to compare and determine the differences among BT, BT+NSAID and NSAID groups for the sixth month changes in DMS, GWB, ESR, OWD, CE, FFD, Schober test and FI (Table 4). The nature of distribution for the percent changes in nocturnal pain, DMS, OWD, CE, Schober test and FFD in BT, BT+NSAID and NSAID groups are demonstrated on Fig. 1.

3. Results

The groups were homogenous for demographic and clinical characteristics of the patients which were sex, age, duration of illness, severity of sacroiliitis, pain, duration of morning stiffness, ESR, global well being of the patient, occiput-wall distance, chest expansion, finger to floor distance and functional index. Lumbar flexibility measured by Schober test was better in NSAID group when compared with the other groups (Table 1). There was statistically significant improvement in all of the variables of BT (G1), BT+NSAID (G2) and NSAID (G3) groups at the end of the treatment as well as 6 months after the treatment except ESR, finger to floor distance and Schober test (Tables 3–5). The sixth month changes in ESR and finger to floor distance were not significant in any of the three groups (Tables 3–5). In G1 and G2, the sixth month changes in Schober test ($P < 0.01$, $P < 0.05$, respectively) and GWB ($P < 0.05$, $P < 0.05$) were statistically significant (Tables 3,4). In G3, there was not a statistical change in Schober test ($P > 0.05$) (Table 5). Comparison and demonstration of the 6th month changes in G1 and G2 were almost similar for all the parameters. G2 was superior to G1 for the 6th month improvements observed in DMS ($P < 0.05$). G1 was superior to G2 for the 6th month improvements observed in CE ($P < 0.05$). Improvements in all the variables observed in G1 and G2 were superior to G3 except Schober test and ESR. Only G1 was better than G3 for the improvement observed in Schober test ($P < 0.05$) (Table 6, Fig. 1).

All of the patients completed the study. Moderate gastrointestinal side effects (dispepsy, nausea, abdominal pain) were observed in four patients of G2 and six patients of G3.

4. Discussion

It is well known that physiotherapy including postural exercises is the most effective therapy regimen in the treat-

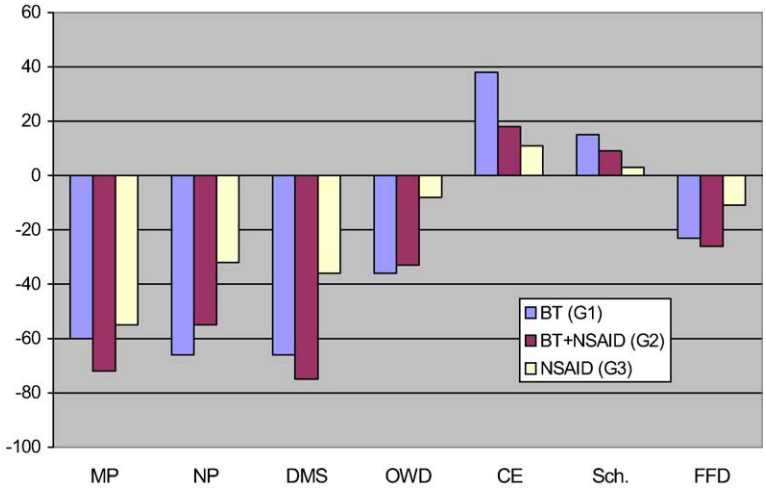

Fig. 1. Demonstration of group 1 (G1), group 2 (G2) and group 3 (G3) for the sixth month percent of changes.

Table 6
The comparison of group 1 (G1), group 2 (G3) and group 3 (G3) for the sixth month change scores after the end of the therapy. Values are mean ± SD

	BT (G1)	BT+NSAID (G2)	NSAID (G3)	G1–G2	G1–G3	G2–G3
Morning pain (VAS)	–28.0 ± 18.9	–28.0 ± 21.2	–20.8 ± 19.5	ns	*	*
Nocturnal pain (VAS)	–26.2 ± 24.6	–24.5 ± 22.7	–14.3 ± 25.7	ns	*	*
Duration of morning stiffness (minutes)	–15.5 ± 11.5	–30.1 ± 17.4	–08.8 ± 15.4	*	*	**
ESR	–0.1 ± 1.3	–0.2 ± 1.6	–0.05 ± 2.11	ns	ns	ns
Global well being (0–10)	0.5 ± 0.12	0.5 ± 2.34	0.1 ± 1.8	ns	*	*
Occiput-wall distance (cm)	–0.9 ± 3.9	–0.9 ± 2.4	–1.2 ± 5.0	ns	*	*
Chest expansion (cm)	1.2 ± 0.9	0.7 ± 1.7	0.3 ± 1.6	*	*	*
Finger to floor distance (cm)	–0.9 ± 3.8	–0.9 ± 5.0	–0.5 ± 4.3	ns	*	*
Schober test (cm)	0.4 ± 1.6	0.2 ± 0.9	0.1 ± 1.5	ns	*	ns
Functional index	–0.2 ± 1.2	–0.2 ± 1.8	0.0 ± 2.6	ns	**	**

ESR, erytrocyte sedimentation rate; VAS, Visual Analogue Scale; ns, not significant; *, $P < 0.05$; **, $P < 0.01$.

ment of AS patients to prevent functional deterioration [2]. On the other hand, NSAIDs are used to control the pain and the morning stiffness as a therapeutic adjuvant to physiotherapy. As a matter of fact, the main difficulty in using NSAIDs are the serious gastrointestinal side effects including bleeding and perforation of an existing peptic ulcus [3].

Goldby and Scott [5] emphasized that very few prospective studies have been conducted on BT. The beneficial effect of balneotherapy (hot mineral water and mud packs) was reported in a study of 2 weeks duration in Tiberias Hot Springs of İsrael including 14 patients with clinically active AS. There was significant improvement in morning stiffness, finger to floor distance and global assessments of disease severity at the end of the first week, after the treatment and 3 months later. However, no change was noted in the Schober test, chest expansion or laboratory parameters. In addition, a significant reduction of the use of analgesics and NSAIDs was noted in most of the patients [15].

Sukenik et al. [7] reported that clinical activation of the patients with RA might improve with BT. Guillemin et al. [8] showed the symptomatic relief in patients with chronic low back pain at the end of a treatment with balneotherapy and later on (for 9 months duration).

In the recent prospective controlled studies made in Atatürk Balneotherapy and Rehabilitation Center it was concluded that balneotherapy might improve the symptoms of the patients with fibromyalgia and mechanic low back pain [9,10].

In respect to the recent studies we intended to compare BT with BT+NSAID and NSAID for alleviating the symptoms of AS. Three of the therapy regimens were accompanied by postural correction exercises specific for this type of patients [2]. We observed a similar and clear improvement of symptoms and mobility in AS patients through BT and BT+NSAID. Pain, morning stiffness, occiput-wall distance, chest expansion, finger to floor distance and lumbar flexibility measured by Schober test changed significantly in both of the groups at the end of the therapy. This improvement continued to exist even 6 months after the treatment except in 'finger to floor distance' and 'Schober test' (Tables 3,4). Similarly, in the study of Van Tubergen et al. [16], it was shown that in patients with AS, a 3-week course of combined spa-exercise therapy, in addition to drug treatment and weekly group physical therapy alone, provided beneficial effects and these beneficial effects lasted for 40 weeks. It was explained that the beneficial effects of spa therapy were attributable to a combination of specific and nonspecific effects including change of environment, thermal (38–40 °C) and radon effect.

BT and BT+NSAID groups were superior to NSAID group for the improvement observed 6 months after the treatment in morning and nocturnal pain, morning stiffness, chest expansion and finger to floor distance (Table 6, Fig. 1). There were no gastointestinal side effects in BT group unless the other two groups. Therefore, the question arises if BT alone is enough to maintain the improvements mentioned above.

An increase in blood flow is a well known physiological response to heat application induced by BT. Application of heat to the inflamed tissue brings in fresh blood supply to remove the nociceptive elements. Repair of the inflamed tissue is enhanced by fresh oxygen brought in after removal of the free oxygen radicals [17]. Thermal stimuli may also effect the pain sensation as a counter-irritant or by the gate control theory of Melzack and Wall [17]. Antalgic effect could also be explained by the action of peripheral beta-endorphines though in a recent study made in ARMKK it was found that BT changed the pain scores significantly while there was no significant increase in the peripheral beta endorphine levels [18]. Furthermore adhering collagen fibers caused by immobilization tend to unlink with increasing temperature during treatment. Capsular and tendinous flexibility is thus regained [19].

Therefore, BT can decrease the anoxia and inflammation by inducing vasodilatation, reducing muscle spasms and lessening pain secondary to the pathology underlying AS. The vicious cycle of spasm-pain-spasm can be broken by relieving muscle spasms. Davis and Harrison [19] claimed that the relief of pain maintained by the inhibition of the sensory cutaneous nerve endings activity was brought out temporarily by the thermal stimuli. He also explained that the pain soon returned after the treatment. The continuity of the antalgic effect was due to muscle relaxation. He added that

the heat effect and bouyancy of the spring water could also induce sedation and increase mobility.

Because the acrotothermal water used in this study has not got a known pure antalgic or therapeutic effect on the soft tissue, the study was not designed to offer an explanation for the mineral effect of our water. But it is clear that muscle tone and pain intensity are influenced by the hydromechanical and thermal stimuli mentioned above. On the other hand, bouyancy provided an excellent environment in which arms and legs could move freely without burdening the skeleton so, exercises could be done more easily. Soft tissue and lumbar flexibility increased by the effects of the thermomineral water [19,20]. These findings support the improvements which we had observed.

All the patients were treated on an outpatient basis. Because there is only a little difference between G1 and G2 in therapeutic response, the costs also should be taken into consideration in terms of evaluation. Daily cost of BT, BT+NSAID and NSAID alone were 1.17$, 2.6$ and 1.5$, respectively. Therefore, the most cost-effective treatment modality seems to be BT. Similarly, in an another study of Van Tubergen et al. [21], combined spa-exercise therapy besides standard treatment with NSAIDs and weekly group physical therapy was found more effective and showed favorable cost-effectiveness and cost-utility ratios compared with standard treatment alone in patients with AS.

In conclusion, symptoms and soft tissue disturbances of AS can be improved by balneotherapy alone and it can be suggested as a cost-effective treatment modality. Future balneotherapy interventions with longer follow up periods may be helpful to put forth the therapeutic efficacy in AS patients.

References

[1] Arnett F. Ankylosing spondylitis. In: Koopman W, editor. Arrthritis and allied conditions: a textbook of rheumatology. Baltimore: William & Wilkins; 1997. p. 1197–208.

[2] Pelster B. Ankylosing spondylitis and its management. In: Pelster B, editor. Rheumatic diseases and their management. Wiesbaden: Medical Tribune-Verlagsgesellschaft mbH. 1999. p. 22–4.

[3] Morris A, Madhol R, Sturrach R, Capell H, Mackenzie J. Enteroscopic diagnosis of small bowel ulceration in patients receiving nonsteroidal antiinflammatory drugs. Lancet 1991;337:520.

[4] Behrend T. The balneotherapy of rheumatoid arthritis. Rheumatol Rehabil 1979(8):86–7.

[5] Goldby L, Scott D. The way forward for hydrotherapy. Br J Rheum 1994;32:771–3.

[6] Nguyen M, Revel M, Dougados M. Prolonged effects of 3 week theraphy in a SPA resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial. Br J Rheum 1997;36:77–81.

[7] Sukenik S, Buskila D, Neumann L, Kleiner-Baumgarten A, Zimlichman S, Horowitz J. Sulphur bath and mud pack treatment for rheumatoid arthritis at the Dead Sea area. Ann Rheum Dis 1990;49:99–102.

[8] Guillemin F, Constanat F, Collin J, Boulange M. Short and long-term effects of spa therapy in chronic low back pain. Br J Rheumatol 1994;33:148–51.

[9] Yurtkuran M, Çeliktas M. A randomized, controlled trial of balneotherapy in the treatment of patients with primary fibromyalgia syndrome. Phys Rehab Kur Med 1996;6:109–12.

[10] Yurtkuran M, Kahraman Z, Sivrioglu K, Afsin Y, Dogan M. Balneotherapy in low back pain. Eur J Phys Med Rehabil 1997;4:120–3.

[11] Van der Heijde D, Calin A, Dougados M, Khan M, Van der Linden S, Bellamy N. Selection of instruments in the Core Set for DC-ART, SMARD, physical therapy and clinical record keeping in Ankylosing spondylitis. Progress Report of The ASAS Working Group. J Rheumatol 1999;26:951–4.

[12] Huskisson E. Measurement of pain. Lancet 1974;2:1127–31.

[13] Macrae I, Wright V. Measurement of back movement. Ann Rheum Dis 1969;28:584.

[14] Dougados M, Gueguen A, Nakache J, Nguyen M, Mery C, Amor B. Evaluation of a functional index and an articular index in Ankylosing spondylitis. J Rheumatol 1988;15:302–7.

[15] Sukenik S, Flusser D, Abu-Shakra M. The role of spa therapy in various rheumatic diseases. Rheum Dis Clin North Am 1999;25:883–97.

[16] Van Tubergen A, Lanewe R, Van Der Heijde D, Hidding A, Wolter N, Asscher M, et al. Combined spa-exercise therapy is effective patients with Ankylosing spondylitis:a randomized controlled trial. Arthritis Rheum 2001;45:430–8.

[17] Lehmann J, Lateur B. Ultrasound, shortwave, microwave, laser, superficial heat and cold in the treatment of pain. In: Wall P, Melzack R, editors. Textbook of pain. London: Churchill Livingstone; 1994. p. 1237–46.

[18] Yurtkuran M, Ulus I, Irdesel F. The effect of balneotherapy on the plasma beta-endorphine (BE) level in patients with osteoarthritis. Phys Kur Med 1993;3:130–2.

[19] Davis B, Harrison R. Treatment of specific conditions. In: Davis B, Harrison R, editors. Hydrotherapy in practise. Singapore: Churchill Livingstone; 1988. p. 137–70.

[20] Kondrad K, Tatrai T, Hunka A, Vereckei E, Korondi I. Controlled trial of balneotherapy in treatment of low back pain. Ann Rheum Dis 1992;51:820–2.

[21] Van Tubergen A, Boonen A, Landewe R, Rutten-Van Molken M, Van Der Heijde D, et al. Cost effectiveness of combined spa-exercise therapy in Ankylosing spondylitis: a randomized controlled trial. Arthritis Rheum 2002;47(5):459–67.