Rheumatology 2005;44:539–546 doi:10.1093/rheumatology/keh537
Advance Access publication 3 February 2005

Spa treatment for primary fibromyalgia syndrome: a combination of thalassotherapy, exercise and patient education improves symptoms and quality of life

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***Objectives*. To study the effect of a combination of thalassotherapy, exercise and patient education in people with fibromyalgia.**
***Methods*. Patients with fibromyalgia, selected from a rheumatology out-patient department and from members of the Dutch fibromyalgia patient association, were pre-randomized to receive either 2½ weeks of treatment in a Tunisian spa resort, including thalassotherapy, supervised exercise and group education (active treatment) or treatment as usual (control treatment). Primary outcome measure was health-related quality of life, measured with the RAND-36 questionnaire. Secondary measures included the Fibromyalgia Impact Questionnaire, the McGill Pain Questionnaire, the Beck Depression Inventory, tender point score and a 6-min treadmill walk test.**
***Results*. Fifty-eight participants receiving the active treatment reported significant improvement on RAND-36 physical and mental component summary scales. For physical health, differences from the 76 controls were statistically significant after 3 months, but not after 6 and 12 months. A similar pattern of temporary improvement was seen in the self-reported secondary measures. Tender point scores and treadmill walk tests improved more after active treatment, but did not reach significant between-group differences, except for walk tests after 12 months.**
***Conclusions*. A combination of thalassotherapy, exercise and patient education may temporarily improve fibromyalgia symptoms and health-related quality of life.**

KEY WORDS: Fibromyalgia, Thalassotherapy, Exercise, Health-related quality of life.

Introduction

Fibromyalgia (FM) is a syndrome characterized by chronic widespread musculoskeletal pain and increased tenderness to palpation. Apart from these core symptoms, several additional symptoms such as fatigue, stiffness, disturbed sleep, subjective joint swelling, psychological distress and impaired cognitive function are considered part of the syndrome [1]. No factor has been identified as the single cause of FM; a multifactorial model is used to describe how various biological and psychosocial factors can contribute to the onset and persistence of chronic pain [2]. Although the concept of FM and its validity as a clinical entity remain the subject of debate [3], it has been recognized that FM has a major impact on health status, quality of life, functional and employment status, use of health-care resources and costs [4–7]. These findings highlight the need for an effective therapy, but at present no curative treatment for FM is available.

Many studies have focused on self-management strategies, such as patient education, coping skills training and physical exercise [8]. Although these strategies often prove to be superior to placebo treatment, the relevance of their effects remains unclear. Nevertheless, there is a growing tendency to offer multidisciplinary treatment programmes for FM, based on the assumption that combining different types of non-pharmacological therapy will increase and prolong their positive effects [9–13].

In a prospective study on pain and pain relief in FM, Canadian patients reported that exercise, relaxation, baths and massage were the interventions most commonly preferred [14]. These four interventions are also the basic ingredients of treatment courses in spa resorts. Although spa therapy—bathing in thermal water—has a long history in the treatment of various rheumatic diseases, its effects have not been studied properly [15]. In FM, minor improvements in pain intensity have been reported after balneotherapy, using thermal water [16], plain water with or without herbal oils [17] or hydrogalvanic baths [18]. However, small patient numbers and methodological shortcomings limit the validity of these data. In a randomized controlled trial, 24 FM patients receiving balneotherapy at the Dead Sea showed significant improvement in quality of life for at least 3 months. However, 24 controls who stayed in the same area without receiving balneotherapy also improved, albeit to a lesser extent [19].

Individual FM patients have reported beneficial effects from thalassotherapy, a form of spa treatment in which sea water, algae and the seaside climate are applied as therapeutic ingredients [20, 21]. Though not supported by scientific evidence, thalassotherapy

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Submitted 27 January 2004; revised version accepted 7 December 2004.

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is practised in many Mediterranean countries, especially France, where it is applied in the treatment of various conditions.

The aim of the present study was to assess the effects of a group programme of thalassotherapy, exercise and self-management education in patients with FM, both in terms of FM-related symptoms and of health-related quality of life.

Patients and methods

Subjects

People with primary fibromyalgia syndrome (FMS) were included if they fulfilled the following criteria: a diagnosis of primary FMS made by a rheumatologist, according to the ACR 1990 classification criteria [22]; age between 18 and 65 yr; willingness to undergo an in-patient treatment of some weeks. Exclusion criteria were: secondary FMS (i.e. presence of another underlying disease that causes chronic widespread pain); co-morbidity interfering with spa treatment; other serious co-morbidity; dependency on a wheelchair or help from other people; current involvement in a law procedure concerning disability or employment; recent spa treatment for musculoskeletal disorders; difficulty understanding Dutch.

Study design

The study was designed as a pre-randomized controlled trial. Obviously, patients could not be blinded for the intervention. Knowledge of being either in the spa treatment group or in the control group might considerably influence the results. In order to reduce this patient-related bias, patients were not informed of the comparison between groups. A modified pre-randomized study design according to Zelen [23] was applied, in which the consent-before-randomization sequence was reversed. Patients eligible for inclusion were randomly allocated to the treatment or control group using a computer-generated randomization list and closed numbered envelopes. Patients allocated to the spa treatment group (SPA) were then fully informed about the spa treatment and the corresponding study protocol. Patients allocated to the control group (CTL) received only information about their part of the study protocol which was described as a study of the social consequences of FM. They were not told that they formed a control group for an intervention study. Moreover, to maintain this patient blinding, patients in the SPA group were specifically asked not to talk to other patients about the study. They were instructed to inform only their spouses, close relatives and (if necessary) their employer.

The pre-randomized study design carries the risk of selection bias. In our study, for instance, employed patients or patients with small children may find it more difficult to leave their job or their family for 2½ weeks. Therefore patients in the SPA group are more likely to refuse participation than CTL patients. To prevent this type of selection bias, the following question was included in the screening questionnaire: 'If a few weeks' admission to a rehabilitation centre would be useful for treating your fibromyalgia, would you be prepared to do so?' If the answer was 'no', the person was excluded. After discussing the specific ethical issues raised by the pre-randomized design, the study was approved by the Medical Ethical Committee of Medisch Spectrum Twente Hospital, Enschede, The Netherlands. All participants gave written informed consent.

Patient selection

Two comparable methods of patient selection were applied. First, from our Diagnosis Registry we selected all patients aged between 18 and 65, who had visited one of our regional rheumatology clinics in 1997 or 1998 and in whom a clinical diagnosis of FMS had been made. Eligible cases were sent a letter asking the patient to 'participate in a study on the social consequences of FM'. Second, through an advertisement in the Dutch FM patient association (FES) magazine (with 10 000 members at that time), patients were asked to 'participate in a study on the social consequences of FM'. All patients interested in the study were asked to answer a screening questionnaire and return it by mail. If their answers to this questionnaire revealed no apparent reasons for exclusion, they were seen by the investigator (TRZ), who after an interview and physical examination decided if patients were eligible for inclusion.

Intervention

Treatment groups consisted of 17–21 patients. They were accompanied by three people: the principal investigator (TRZ, a rheumatologist), a sports instructor and a FM patient familiar with thalassotherapy. Some weeks before the journey a group meeting was arranged to make each other's acquaintance and to give information about the journey, the spa treatment and the follow-up. Participants were required to contribute €227 (or less if they could not afford this), covering a small part of the total cost of travel and accommodation. The spa treatment was given on Jerba, a peninsula off the coast of southern Tunisia with a temperate Mediterranean climate. The first group went in March–April 1999, the second and third groups in May and June 2000. On day 1 patients travelled to Jerba by air. They stayed in a luxurious tourist hotel on a full-board basis, sharing rooms with a fellow patient. Spouses or relatives were not allowed to join them. On day 19 the group returned home. The treatment programme consisted of four elements: thalassotherapy, exercise, patient education and recreational activities.

Thalassotherapy was provided in a thalassocentre, a well-equipped institute located within the hotel complex. Its Tunisian staff are well-trained and maintain high standards of hygiene and service. On day 2, before starting thalassotherapy, patients were seen by the spa doctor, who composed a therapy programme according to their individual demands. The programme consisted of seven or eight sessions divided over 15 days. Each session included four out of the following modalities: *hamam* (Turkish bath), *algotherapy* (hot packs with algae), *douche à affusion* (massage while lying under a shower), whirlpool, underwater jetstream massage, pool exercise and massage. The different treatment modalities alternated with resting periods; a complete thalassotherapy session took approximately 3 hours. If patients experienced adverse effects or other problems related to thalassotherapy, their programme was adjusted in consultation with the spa doctor.

A series of seven 1-hour sessions of supervised group exercise was scheduled on days when no thalassotherapy was given. Exercise groups consisted of four or five persons. The exercise programme included warming-up, gentle stretching and various forms of low-impact aerobic exercise, e.g. treadmill walking, cycling and swimming. Patients were instructed to exercise within their own abilities, trying to reach 70% of the predicted maximum heart rate for their age (beats per minute = 220 − age). Apart from the supervised exercise sessions, participants were encouraged to start each day with 20–30 min of swimming and to take some form of light exercise (e.g. walking on the beach or recreational swimming) on mornings or afternoons with no formally scheduled thalassotherapy or exercise sessions.

The patient education programme consisted of seven sessions of 1–1½ hours, directed by the rheumatologist (TRZ). The first and seventh sessions were plenary sessions, the other sessions were in smaller groups of approximately 10 persons. The programme was a mixture of lectures by the rheumatologist, plenary discussions and discussions in small groups, and small assignments to be prepared before the next session. The following issues were

included: general information on FM; importance of physical fitness and exercise; the role of emotions in FM; finding a balance between workload and capacity; stress handling; coping with reactions from others; sense and nonsense about drugs, diets, complementary and alternative medicine. Patients were encouraged to share their experiences, but mere complaining was gradually restricted, whereas positive coping styles and practical problem-solving were emphasized. Elements of self-management programmes were applied [24], based on the self-efficacy theory of Bandura [25].

Recreational facilities were available according to the standards for luxurious tourist hotels. They included indoor and outdoor swimming pools, a sandy beach, day trips and a range of other day- and night-time entertainment.

Although recreational and tourist activities were part of the programme, instructions for participants emphasized that they should join in the treatment programme, and not just treat it as a holiday. They were strongly advised to take adequate rest after lunchtime and at night.

Control condition

Control (CTL) subjects were told they were participating in an observational study to assess the impact of FM on several aspects of health and social functioning. They continued treatment as usual, provided by their own physicians.

Assessments

At baseline (1 week before travelling to Jerba) the SPA subjects answered a set of several self-administered questionnaires (see below). At the beginning and the end of their stay in the spa resort, a tender point examination and a physical fitness test were performed. In the second week after their return patients answered the same set of questionnaires. At 3, 6 and 12 months, tender point examination and physical fitness testing as well as questionnaires were repeated. CTL subjects were assessed with the same instruments at baseline and after 3, 6 and 12 months. They were not assessed after 1 month, since this might have appeared rather irrational to them.

General health status, measured with the RAND 36-item health survey (RAND-36), was chosen as the primary outcome measure. The RAND-36 bas been translated and validated for use in Dutch patients [26]. It is almost identical to the SF-36, which is universally applied in studies of various chronic disorders. The SF-36 had sufficient sensitivity to change in a study of cognitive behavioural therapy and in a study of balneotherapy for FMS [19, 27]. Two summary components were computed, aggregating scores from eight subscales of the RAND-36 into two summary scores: Physical Component Summary (PCS or physical health) and Mental Component Summary (MCS or mental health) [28]. Raw scale scores of the RAND-36 were transformed into Z scores, using Dutch means and standard deviations [29], which were multiplied with the US factor score coefficients and summed over all eight subscales (US factor scores were used to facilitate international comparisons). Finally, t-scores were calculated by multiplying the obtained PCS and MCS sums by 10 and adding 50 to the product to obtain transformed summary scores that are normally distributed with a mean of 50 and a standard deviation of 10 [28]. General health was also measured with a 100-mm visual analogue scale (VAS) for general health during the past week.

Disease specific health status was measured with a Dutch translation of the Fibromyalgia Impact Questionnaire (FIQ). The FIQ is a validated self-report inventory which has been recommended as a primary endpoint in FM clinical trials [30, 31]. Respondents are requested to rate their status within the past week. Questions 1–10, rated on a four-point adverbial rating scale, are summed to form one subscore for physical impairment. Item 11 asks for the number of days on which one felt good, item 12 asks how many days of work were missed because of fibromyalgia. Items 13–19, dealing with job difficulty, pain, daytime fatigue, morning tiredness, stiffness, anxiety and depression, are rated on a 100-mm VAS. Results for each item are normalized to yield a score between 0 and 10, with higher scores indicating greater impairment. FIQ total score is computed by summing all except the two job-related items, thus ranging from 0 to 80.

The FIQ has been translated into various languages [32–36], but our Dutch translation has not been formally validated yet. Therefore a number of other validated, frequently used outcome measures were included to study individual domains of the FIQ. Depression was measured using a Dutch translation of the 1979 version of Beck's Depression Inventory (BDI) [37, 38]. Pain was assessed using the McGill Pain Questionnaire—Dutch Language Version (MPQ-DLV) [39]. Fatigue was measured with the subscales 'subjective fatigue' and 'physical activity' of the Checklist Individual Strength (CIS) [40]. This instrument asks respondents to judge a set of statements concerning their fatigue on a seven-point adjectival rating scale from 1 (=correct) to 7 (=incorrect). The CIS has been validated as a measure of fatigue in different patient populations. Sleep problems are frequently mentioned as part of FMS, but are not included as an item in the FIQ. To assess sleep quality, a separate 100-mm VAS for sleep over the past week was added to the questionnaire.

Tender points were examined by applying a pressure of approximately 4 kg with the tip of the thumb or index finger on the 18 points defined in ACR classification criteria [22]. From this assessment the total number of painful tender points (tender point score, TPS; range 0–18) and a graded tender point score (GTPS) were recorded. For GTPS each point was scored by the assessor on a scale from 0 to 3 (0, no pain; 1, mild pain, no grimace; 2, spontaneous verbal reaction to pain and grimace; 3, severe pain with withdrawal) and the sum of 18 points was recorded [41, 42]. Patients and controls were all assessed by the same observer (TRZ).

Physical fitness was measured with a modified 6-min walk test. Patients walked on a computerized treadmill system (Technogym^{TM} Runrace HC-1200) with automatic heart rate monitoring (Polar^{TM}) for 8 min. They were constantly supervised and received instructions on how to walk without leaning on the handlebars and how to maintain a normal walking pace. During the first 2 min the treadmill system automatically adjusted its speed and slope, until the patient reached the target heart rate of $0.70 \times (220 - \text{age})$/min. The treadmill speed did not exceed normal walking pace, thus allowing all patients to perform at their own level without actually having to run. From speed, slope and the patient's weight the system computed the amount of labour performed. Labour during the last 6 min was recorded as a measure of physical fitness. Using this procedure, the test result was independent of patient motivation or perceived exertion.

Statistical analysis

Demographic characteristics of SPA and CTL groups were compared with the χ^2 test (binary data), Mann–Whitney test (ordinal data) or two-tailed independent t-test (continuous data). Results of SPA subjects after 1 month were compared to baseline using the paired-samples t-test or Wilcoxon signed ranks test. Since control patients were not assessed after 1 month, between-group comparison at that time was not performed. For the primary outcome measure (RAND-36) results at 3, 6 and 12 months were analysed by univariate analysis of covariance (ANCOVA) with baseline values as covariate. Before applying ANCOVA the assumptions for performing ANCOVA (homogeneity of variance

and parallelism of regression) were checked. For FIQ total score and all other outcomes, results at 3, 6 and 12 months were analysed by comparing change scores between groups, using the two-tailed independent-sample *t*-test or the Mann–Whitney test (change score T_x = value T_x − value T_o).

Results

Results of patient selection and randomization are presented in Fig. 1. A total of 170 patients initially fulfilled inclusion criteria; 84 of them were randomized into the SPA and 86 into the CTL group. After randomization and information, more patients refused participation in the SPA group than in the CTL group. Reasons for refusal in the SPA group were: three job related, six family related, two financial, 12 unknown. In the CTL group these were: one marked improvement of FM symptoms, one disappointment with the study protocol, six unknown. Three SPA and two CTL subjects withdrew due to co-morbidity occurring in the period between inclusion and study start. Finally, 58 patients received spa treatment and 76 patients entered the control protocol. Baseline demographic characteristics for both groups are shown in Table 1. No statistically significant group differences were found.

During follow-up, the response rate by self-reported questionnaire was high: 95.3% for SPA and 95.6% for CTL. Only one SPA subject withdrew from follow-up after 6 months; several attempts were made to contact her, but she did not respond or return the remaining questionnaires. Although all CTL subjects continued to return their questionnaires (by mail if necessary), their overall rate of attendance at the follow-up visits was lower: 80.3% for CTL *vs* 89.1% for SPA. All but one of the CTL subjects remained unaware of the fact that they were controls for a spa treatment group.

Following treatment, SPA subjects reported significant improvement in mental and physical component summary scores (Table 2) and on all subscales of the RAND-36 (data not shown). After 3 months, the differences between SPA and CTL were statistically significant for physical but not for mental health. After 6 and 12 months, no statistically significant differences between SPA and CTL were found.

Results of FIQ subscales and total score are presented in Table 3. At baseline there were no statistically significant differences between SPA and CTL. At $T=1$ month the SPA group showed improvement on FIQ total score ($P \leq 0.01$ for the paired-sample *t*-test) and on all individual items, except 'days missed work'. After 3 months, improvements were less pronounced, but differences between FIQ total score of SPA and CTL were statistically significant. After 6 months, change scores in the SPA group still suggested improvement, but differences from CTL were not statistically significant. After 12 months, few differences in favour of the SPA group remained, whereas SPA subjects even scored somewhat higher on depression.

Results of other outcome measures are summarized in Table 4. BDI scores for depression improved in the SPA group shortly after treatment, but during follow-up no significant difference between SPA and CTL was seen. The same applies to outcomes of VAS sleep. The MPQ-DLV total pain rating index decreased by 35% after spa treatment; at $T=3$ months change scores in the SPA group were still significantly larger than in the CTL group. The CIS subscale 'subjective fatigue' improved by 26% after spa treatment; the difference between SPA and CTL remained statistically significant for 6 months. Improvement on the subscale 'activity' was less pronounced. VAS ratings of general health in the SPA group initially improved by 26%. This improvement had been halved after 3 months and disappeared after 6 months. Tender points significantly decreased after spa treatment, both in terms of number and severity. However, this also occurred in the CTL group, though more gradually. Therefore change scores only differed significantly between groups at $T=3$ months. Finally, SPA and CTL groups both performed better on the treadmill walk test during follow-up than at baseline. Differences between groups were statistically significant at the 12 month assessment only.

SPA subjects were overall very satisfied with thalassotherapy. Minor adverse events such as sunburn and mild self-limiting gastroenteritis occurred frequently, as might be expected in a Mediterranean environment, and caused some patients to

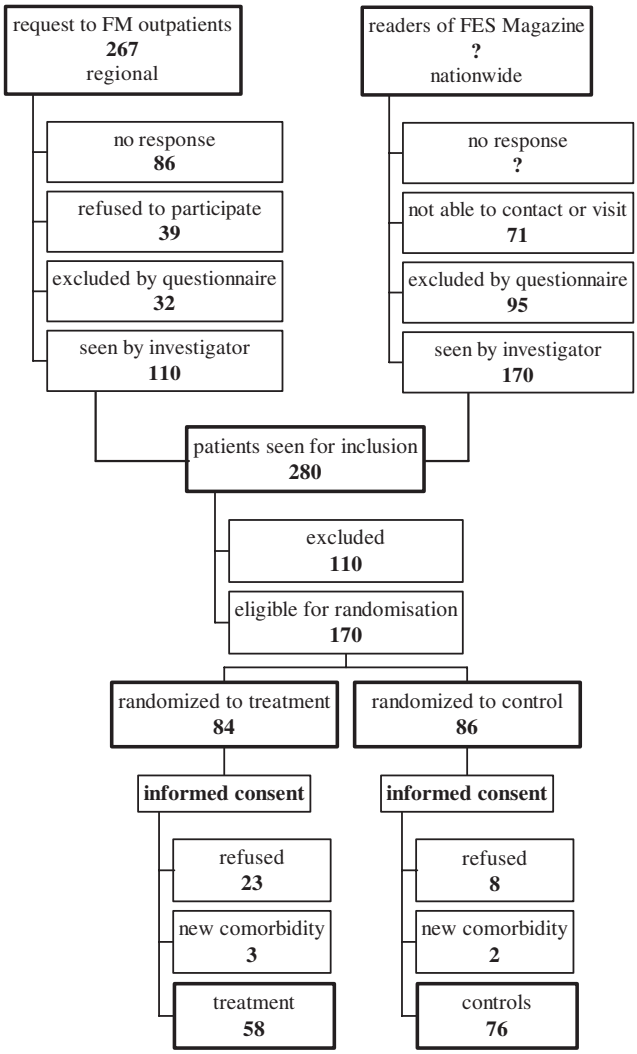

FIG. 1. Flow chart of patient selection and randomization.

TABLE 1. Baseline demographic data of spa treatment (SPA) and control (CTL) groups

	SPA	CTL
No. of patients (female:male)	58 (55:3)	76 (73:3)
Age (yr), median (range)	48 (22–64)	47 (24–64)
Married or living with a partner (%)	44 (76)	66 (87)
Years since continuous symptoms onset, median (range)	10 (2–35)	10 (1–42)
Educational level, median (range)[a]	3 (1–6)	3 (1–6)
Employment status		
Employed (%)	24 (41.4)	27 (35.5)
Health-related unemployment (%)	25 (43.1)	32 (42.1)
Other reasons for unemployment (%)	9 (15.5)	17 (22.4)

[a]Maximum possible range is 1 (elementary school)–6 (university).

Table 2. Results of RAND-36

RAND-36 components	Baseline value T_o	Change from baseline			
		$T=1$ month	$T=3$ months	$T=6$ months	$T=12$ months
Physical component					
Spa	28.6 (8.0)	6.3 (8.2)*	3.6 (8.8)**	1.3 (9.6)	2.6 (7.4)
Control	27.8 (7.4)	–	0.8 (6.7)	0.5 (5.8)	1.6 (7.8)
Mental component					
Spa	45.7 (11.5)	6.5 (10.2)*	0.8 (11.2)	0.2 (9.8)	−2.2 (11.1)
Control	46.5 (10.2)	–	1.2 (9.1)	0.1 (11.4)	0.5 (10.1)

Data are presented as mean scores (S.D.) at baseline and mean change from baseline (S.D.) at follow-up assessments. Maximum range for each item is 0–100. Positive change indicates improvement.
*$P<0.001$ for post-spa change from baseline (paired t-test).
**$P=0.02$ for spa *vs* control (ANCOVA).

Table 3. Results of Fibromyalgia Impact Questionnaire

FIQ subscales	Baseline value T_o	Change from baseline			
		$T=1$ month	$T=3$ months	$T=6$ months	$T=12$ months
Physical functioning					
Spa	4.5 (1.7)	−0.9 (1.6)	−0.6 (1.4)	−0.3 (1.6)	−0.1 (1.8)
Control	4.5 (1.6)		−0.0 (1.4)	−0.1 (1.5)	−0.2 (1.5)
Days not feeling good					
Spa	7.2 (2.4)	−3.0 (1.2)	−1.3 (3.1)	−0.4 (3.1)	−1.0 (2.6)
Control	6.6 (2.7)		0.1 (2.7)	0.1 (2.6)	−0.4 (3.2)
Days missed work					
Spa	0.9 (2.2)	−0.4 (1.2)	−0.8 (2.3)	0.5 (3.5)	1.1 (3.8)
Control	0.8 (2.6)		0.7 (1.9)	1.2 (3.4)	1.5 (3.1)
VAS job difficulty					
Spa	5.7 (2.2)	−1.5 (2.8)	−0.9 (2.6)	−0.2 (3.0)	−0.3 (2.1)
Control	5.7 (2.1)		−0.0 (2.0)	0.1 (2.1)	−0.0 (2.6)
VAS pain					
Spa	5.9 (1.8)	−1.6 (2.3)	−0.7 (1.9)	−0.1 (2.3)	−0.1 (1.7)
Control	5.8 (1.7)		0.0 (1.5)	0.1 (1.7)	−0.3 (1.9)
VAS fatigue					
Spa	6.5 (2.0)	−1.6 (2.8)	−1.0 (2.0)	−0.8 (2.5)	−0.3 (2.1)
Control	6.3 (1.9)		−0.1 (1.7)	0.1 (1.6)	−0.3 (2.0)
VAS morning tiredness					
Spa	6.6 (1.9)	−1.5 (2.6)	−0.9 (2.2)	−0.3 (2.5)	−0.1 (2.1)
Control	6.2 (2.3)		−0.0 (2.3)	0.3 (2.0)	−0.1 (2.7)
VAS stiffness					
Spa	6.3 (2.1)	−1.9 (2.7)	−0.8 (2.0)	−0.3 (2.3)	−0.5 (1.9)
Control	6.4 (2.0)		−0.4 (1.7)	−0.1 (1.7)	−0.5 (1.9)
VAS depression					
Spa	2.6 (2.4)	−0.7 (2.1)	−0.2 (2.4)	0.1 (2.4)	0.6 (2.8)
Control	2.8 (2.3)		−0.1 (2.1)	−0.1 (2.2)	−0.3 (2.4)
VAS anxiety					
Spa	3.7 (2.8)	−1.3 (2.7)	−0.6 (2.7)	−0.5 (2.7)	−0.2 (3.0)
Control	3.4 (2.4)		−0.2 (2.0)	0.1 (2.3)	−0.4 (2.0)
FIQ total score (range 0–80)					
Spa	43.2 (11.9)	12.8 (12.9)*	−6.3 (11.4)**	−2.6 (13.8)	−1.7 (10.8)
Control	42.3 (11.6)		−0.9 (10.2)	0.3 (9.2)	−2.5 (12.0)

Data are presented as mean scores (S.D.) at baseline and mean change from baseline (S.D.) at follow-up assessments. Raw data were transformed into normalized scores, all ranging from 0 to 10, with higher scores indicating a worse condition. Negative change indicates improvement.
*$P<0.01$ for SPA group between baseline and $T=1$ month.
**$P<0.01$ for difference between SPA and CTL group.

occasionally skip a thalassotherapy session. Two patients experienced more significant adverse events, although these were not strictly related to thalassotherapy. One of them sprained an ankle while visiting a nearby village. The other patient was examined in a local hospital after falling off a horse. She sustained only superficial injuries and could return to the hotel after tetanus vaccination. In the remaining week she followed an adjusted regimen of thalassotherapy and exercise.

Discussion

The results of this study confirm our hypothesis that a combination of thalassotherapy, exercise and patient education can significantly improve symptoms and health-related quality of life in FM. After 3–6 months, most outcome measures showed improvement. After 6 months, however, most differences between SPA and CTL group were no longer statistically significant, indicating that

TABLE 4. Results of other outcome measures

Instrument (range)	Baseline value T_o	Change from baseline			
		$T=1$ month	$T=3$ months	$T=6$ months	$T=12$ months
BDI total score (0–63)					
Spa	13.2 (6.8)	−2.9 (3.8)*	−1.7 (5.5)	−2.0 (4.5)	−0.3 (5.5)
Control	13.0 (6.7)		−1.2 (5.3)	−0.8 (5.4)	−0.8 (4.7)
MPQ-DLV pri-total (0–63)					
Spa	21.1 (8.4)	−7.3 (8.3)*	−4.0 (7.3)***	−2.8 (8.5)	−1.4 (6.9)
Control	21.0 (8.8)		−2.5 (8.6)	−2.0 (8.3)	−1.5 (7.9)
CIS subjective feeling (8–56)					
Spa	45.2 (8.7)	−11.6 (11.0)*	−5.5 (9.1)***	−3.6 (9.4)****	−2.8 (9.5)
Control	44.0 (8.2)		−1.4 (6.5)	−0.2 (7.4)	−1.3 (8.2)
CIS activity (3–21)					
Spa	12.0 (6.1)	−1.8 (5.3)**	−0.8 (3.8)****	−0.0 (4.5)	0.7 (5.5)
Control	10.9 (5.3)		1.1 (4.9)	1.6 (4.8)	0.7 (5.4)
VAS sleep (0–10)					
Spa	5.5 (2.1)	−1.5 (2.8)*	−0.1 (2.2)	0.1 (2.5)	0.4 (2.5)
Control	5.9 (2.2)		−0.3 (2.3)	−0.1 (2.3)	−0.4 (2.5)
VAS general health (0–10)					
Spa	6.1 (1.8)	−1.6 (2.6)*	−0.8 (2.2)****	−0.0 (2.3)	−0.1 (1.9)
Control	6.2 (1.6)		0.2 (1.7)	0.1 (1.7)	−0.5 (1.8)
No. of tender points (0–18)					
Spa	13.8 (2.5)	−2.2 (2.8)*	−2.0 (3.4)***	−1.2 (3.3)	−1.9 (3.8)
Control	13.6 (2.6)		−0.6 (2.2)	−1.0 (2.8)	−1.7 (3.1)
GTPS (0–54)					
Spa	20.0 (7.5)	−4.0 (6.0)*	−3.6 (6.2)***	−1.7 (6.9)	−2.6 (7.8)
Control	18.5 (5.3)		−0.2 (3.9)	−0.7 (4.7)	−1.5 (5.5)
Treadmill walk test (kCal)					
Spa	26.6 (9.0)	2.9 (7.3)*	5.9 (8.3)	5.7 (10.2)	5.1 (7.6)****
Control	28.0 (9.2)		3.3 (6.8)	4.4 (6.9)	1.7 (6.7)

Data are presented as mean scores (S.D.) at baseline and mean change from baseline (S.D.) at follow-up assessments. Negative change indicates improvement, except for treadmill walk test.

BDI, Beck Depression Inventory; MPQ-DLV, McGill Pain Questionnaire—Dutch Language Version; PRI, Pain Rating Index; CIS, Checklist Individual Strength; GTPS, Graded Tender Point Score.

*$P<0.01$ for SPA group between baseline and $T=1$ month.

**$0.01\leq P\leq 0.05$ for SPA group between baseline and $T=1$ month.

***$P<0.01$ for difference between SPA and CTL group.

****$0.01\leq P\leq 0.05$ for difference between SPA and CTL group.

our combined programme should be regarded as a palliative treatment with temporary effects.

A randomized controlled trial is generally considered the best way to study the effect of an intervention. Had we used a conventional RCT design in the present study, then patients allocated to the CTL group would probably have been very disappointed and hence would have withdrawn or be negatively influenced. To avoid this, a pre-randomized design was chosen, allowing us to keep CTL subjects unaware of the treatment condition. Obviously SPA subjects could not be blinded to the treatment, so results may have been influenced by suggestion or by a 'desire to please the observer'.

Our pre-randomized design carried a risk of selection bias, as would have been the case for a conventional randomized controlled trial. We tried to avoid this by excluding in advance those who objected to admission to a rehabilitation clinic for FM. The resemblance of patient characteristics in the SPA and CTL groups indicates that major selection bias did not occur. The 1-month assessment for SPA subjects was included to evaluate short-term effects. We chose not to assess CTL subjects after 1 month, therefore no direct comparison between SPA and CTL group for that interval could be made.

Our results suggest that the positive effects of spa treatment extend to several domains, including general health, pain, fatigue and physical functioning, which are all very relevant in FM. The same pattern of improvement occurs in various outcome measures, indicating that positive outcomes are not a result of multiple testing but reflect actual health improvement.

Improvement in mental health was less pronounced and of shorter duration than in physical health, suggesting that our treatment programme exerts predominantly physical effects. We would like to mention, however, that the rather low baseline levels of depression in our study sample left only limited room for improvement. In our study mean VAS depression was 27 mm and mean BDI 13.1, whereas other studies reported 42 to 66 mm for VAS depression [9, 10, 13] and 16 to 22 for BDI [10, 11, 43].

The results from the 6-min walk tests at 3- and 6-month intervals suggest improvement of physical fitness in both groups. Two and a half weeks of exercise training may generally be considered too short to improve physical fitness. However, most exercise studies in FM have applied exercise frequencies of two to three times 1 hour per week [44, 45–47], whereas our patients exercised on a daily basis. Additionally, the patient education programme may have encouraged them to continue exercising at home. Maybe this explains why, after 12 months, the SPA group performed significantly better on the walk test. However, these results must be interpreted with caution.

There was a significant difference in tender point scores between SPA and CTL subjects after 3 months. At longer follow-up, however, this difference diminished, mainly because tender point scores in the CTL group gradually decreased. This is in line with findings from Dunkl *et al.* [31], who showed that in patients reporting worse or unchanged symptoms over a 6-month period, the tender point count still decreased by 0.62 and 0.91 points respectively. A possible explanation for this finding might be that

once subjects become accustomed to tender point assessments, they tend to respond less.

Although there are no gold standards for improvement in FM, some of our results can be compared with data from other studies. First, in various chronic pain disorders, including FM, a two-point reduction or a 30% improvement on an 11-point numerical pain rating scale represents a clinically important difference (defined as a patient global impression of 'much improved' or 'very much improved') [48]. Assuming that the same applies to a 100-mm VAS pain, the 27% improvement observed after thalassotherapy indeed appears to be clinically relevant. Second, in a study on responsiveness of outcome measures for FM, 'general improvement' (as judged by patients after 6 months) corresponded to a mean reduction of FIQ total score by 15.8 points [31]. In our study the mean initial reduction after thalassotherapy was 12.8 points (30% from baseline), again indicating relevant improvement. Third, our results are better than those reported for other combined treatment programmes: 9% improvement of FIQ total score after six sessions of patient education and six sessions of exercise instructions [9], 25% after 6 months of weekly group therapy [10] and 14% after 6 months of hydrotherapy and six education meetings [49].

Despite the initial size of the treatment effect, its temporary nature raises questions about cost-effectiveness, which should be addressed before implementing this programme. Furthermore, one should ask what the additional effect of such a programme is, compared with conventional exercise and patient education. Our study does not provide definite answers to this question, but some remarks can be made. It seems plausible to suggest that a warm, dry and sunny climate may improve FM symptoms, since a majority of FM patients report that their symptoms are influenced by weather conditions [50, 51]. In contrast with these patient impressions, formal studies on the relationship between weather conditions and fibromyalgia found hardly any correlation [52–55]. However, these studies focused on weather changes within the same climate, whereas transition to a totally different climate may influence FM symptoms more strongly. Several additional factors might contribute to the overall beneficial effect, such as a relaxing environment, support from other patients and absence of work duties. The importance of such factors was mentioned by Neumann *et al*. [19], who reported that FM patients staying at the Dead Sea but not receiving balneotherapy still showed significant improvement. A similar comment was made by the authors of a recent study on spa-exercise therapy in ankylosing spondylitis [56]. On the other hand, both studies reported additional improvement in the spa or balneotherapy group compared with controls, indicating that apart from the non-specific 'holiday effect' there is also a specific treatment effect involved.

In conclusion, a combination of thalassotherapy, exercise and patient education can produce significant subjective improvement in patients with FM, lasting for 3–6 months.

Acknowledgements

This study was funded by the Dutch Arthritis Association, grant NR 97–1–303.

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