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ORIGINAL ARTICLE

Home-based exercise therapy in ankylosing spondylitis: short-term prospective study in patients receiving tumor necrosis factor alpha inhibitors

Semra Yigit · Zerrin Sahin · Saliha Eroglu Demir · Deniz Hatun Aytac

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Abstract The importance of exercise and regular physiotherapy in patients with ankylosing spondylitis (AS) under treatment with tumor necrosis factor alpha inhibitors (TNFα inhibitors) was reported in some studies, but the literature on this topic is still scarce. The aim of this study was to assess the effects of home-based exercise therapy on functional capacity, disease activity, spinal mobility, quality of life, emotional state and fatigue in patients with AS receiving TNFα inhibitors. Forty-two AS patients were trained on the disease, and home-based exercise program was demonstrated to all the patients. At baseline and at the end of 10 week, we evaluated Bath AS Disease Activity Index, Bath AS Functional Index, Bath AS Metrology Index, Multidimensional Assessment of Fatigue Scale, Beck Depression Inventory and Short-Form 36. Patients following home-based exercise program five times a week at least 30 min per session (exercise group) were compared with those exercising less than five times a week (control group). At baseline, exercise and control group had similar demographic features. After 10 weeks, all outcome parameters showed statistically significant improvements in exercise group. There were significant differences in all the parameters except social functioning subscale of Short-Form 36 between groups in favor of exercise group at 10th week ($P < 0.05$). Home-based exercise program is an effective therapy in increasing functional capacity and joint mobility, decreasing disease activity, improving emotional state, fatigue and quality of life for AS patient receiving TNFα inhibitors. We need to find out new ways to provide continuity of AS patients with it.

Keywords Ankylosing spondylitis · Home-based exercise · TNF alpha · Disease activity · Functional capacity · Quality of life

S. Yigit
Ministry of Health, Gebze Fatih State Hospital, Physical Medicine and Rehabilitation Clinic, Izmit, Turkey

Z. Sahin · D. H. Aytac
Ministry of Health, Haydarpasa Research and Training Hospital, Physical Medicine and Rehabilitation Clinic, Istanbul, Turkey

S. E. Demir (✉)
Physical Medicine and Rehabilitation Department, Bezmialem Vakif University, Istanbul, Turkey
e-mail: saliha45@yahoo.com

Introduction

Ankylosing spondylitis (AS) is a chronic progressive inflammatory disorder with unknown etiology, mainly affecting the sacroiliac joints and spine, with possible involvement of other joints, entheses, and extra-articular structures. The major symptoms in patients with AS are pain, stiffness and progressive loss of spine mobility which may result in physical limitations [1–3]. All of these symptoms affect negatively patients' functional status and health-related quality of life (QoL). As a consequence, AS is an important cause of work disability and generates a major socioeconomic burden [1, 4].

Treatments for AS should be aimed for improvement in pain and stiffness and preventing structural damage which results in progressive deformity [5]. A combination of non-pharmacological and pharmacological treatments was reported for optimal management. Non-pharmacological treatment should include patient education and regular exercise [5–7]. The primary aim of exercise treatment is to avoid stiffening in a flexed position and to maintain or improve functional capacity and QoL. The long-term goal

is to try to maintain a good posture [8]. Exercise treatment in AS including home-based exercise, supervised exercise, group exercise, or spa-based exercises is beneficial [9–11]. Home-based exercise therapy consists of a series of exercises which a patient performs unsupervised and independently at a prescribed duration and frequency [11]. It is reported to be an effective, low-priced and easy applicable therapy in patients with AS [12, 13].

Pharmacological management of AS is limited to the use of non-steroidal anti-inflammatory drugs (NSAID) and tumor necrosis factor alpha inhibitors (TNFα inhibitors) [5]. TNFα inhibitors are effective management agents in AS. Most recent studies evaluating the efficacy of exercise on AS did not include patients receiving TNFα inhibitorss. Some studies reported the importance of exercise and regular physiotherapy in patients with AS under treatment with TNFα inhibitors, but the literature on this topic is still scarce [14].

The primary aim of the present study was to clinically assess the effects of home-based exercise therapy on functional capacity, disease activity, and spinal mobility in AS patients receiving TNFα inhibitorss. The secondary aim was the evaluation of the effects of exercises on fatigue, emotional state and QoL during the study period.

Material and methods

Patients diagnosed with AS according to the Modified New York Criteria and aged 18–65 years were allocated into the study. They were recruited from our outpatient physical medicine and rehabilitation clinic. Subjects were eligible to participate in the program if they were receiving TNFα inhibitors at least 3 months and able to understand the content of questionnaire and the exercise program. All patients reached maximal therapeutic benefit from the beginning of TNFα inhibitors therapy. In addition to their demographic characteristics (age, gender, height, weight, body mass index (BMI) (kg/m^2), educational level), the patients were also questioned for the duration since diagnosis, smoking, and drug usage (NSAID, disease modifying anti-rheumatic drugs, TNFα inhibitors). Presence of peripheral arthritis and The Bath Ankylosing Spondylitis Radiology Index (BASRI) scores were recorded. Exclusion criteria included severe comorbidities affecting heart, lung, liver or kidneys, having mental retardation, the presence of severe arthritis or prosthetic device and exercising regularly for previous 6 months. All individuals gave informed consent in accordance with the Helsinki Declaration of 1975.

Forty-two patients were individually trained on pathogenesis, clinical manifestations, and course of the disease and preventive measures for the disease were explained. Information about physiotherapy was given. Home-based exercise program including muscle relaxation, flexibility exercises for cervical, thoracic and lumbar spine, range of motion exercises of coxofemoral joints, stretching exercises for the major muscle groups (erector spine, abdominal muscles, shoulder muscles, hip flexors, hamstring and quadriceps stretch), muscular strengthening, straight posture and respiratory exercises was practically demonstrated with a CD presentation. Moreover, a training and exercise manual booklet and CD were prepared and given to all of them. They were asked to follow this exercise program at home individually five times a week at least 30 min per session for 10 weeks [15]. They were allowed to take routine medical therapy and asked to come their routine control visit 10 weeks later. Their medical treatments were not modified during the study, and patients did not participate in other exercise program or rehabilitative intervention.

Evaluations were performed at baseline and repeated at the end of 10 week by the same clinician. Evaluation parameters were as follows:

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) The BASDAI is a self-administered questionnaire consisting of six questions relating to the five major symptoms (fatigue, spinal pain, joint pain or swelling, areas of localized tenderness, severity and duration of morning stiffness). The questions are answered on a 10-cm visual analog scale (VAS). The individual scores are averaged to form 0–10 scale, with lower scores indicating less active disease [16, 17].

The Bath Ankylosing Spondylitis Functional Index (BASFI) The BASFI consists of ten questions (eight questions on daily activities, two questions that assess the patients' ability to cope with everyday life). All items are valued with a 10-cm VAS. The mean of the ten scales gives the BASFI score (0–10), with higher scores indicating more severe impairment [18, 19].

The Bath Ankylosing Spondylitis Metrology Index (BASMI) BASMI is composed of five measurements: cervical rotation, tragus-to-wall distance, lateral flexion, modified Schober's distance and intermalleolar distance. Each measurement indicates either 0 (mild disease involvement), 1 (moderate disease involvement), or 2 (severe disease involvement) points, resulting in a total BASMI score of 0–10 [20].

Multidimensional Assessment of Fatigue Scale (MAF) MAF scale contains five dimensions of fatigue: degree, severity, distress, impact on activities of daily living, and timing. Each of them is answered on a 10-cm VAS. Scores ranged from 0 (no fatigue) to 50 (severe fatigue) [21].

Beck Depression Inventory (BDI) BDI is a 21-item test presented in multiple-choice format, which purports to measure presence and degree of depression. Responses

are made on a four-point scale, ranging from 0 to 3, with 3 representing the most severe symptoms. Total score ranges from 0 to 63 [22].

Short Form-36 (SF-36) SF-36 is a widely applied generic instrument for measuring health status and consists of eight dimensions: physical functioning, social functioning, physical role, emotional role, mental health, vitality (fatigue and energy level), and bodily pain. The scale's score may vary from 0—worst possible health status or QoL—to 100—best possible health status or QoL [23].

Of 42 subjects, two subjects were excluded from the study because they did not come to control visit. All the patients were questioned for the adherence of home-based exercise program as how many days per week they exercised and how long each exercise session lasted. Because half of them did not follow the exercise program, patients were grouped as exercise and control group. Patients following home-based exercise program five times a week at least 30 min per session on a regular basis (exercise group) were compared with those exercising less than five times a week (control group) according to the study of Uhrin et al. [15].

Statistical analysis

Statistical analyses were performed with NCSS 2007 for Windows. Descriptive data were presented as mean ± standard deviation (SD). Demographic and clinical characteristics were compared using the Chi-squared test. Within-group and between-group differences were investigated. Mann–Whitney *U*-test was used for the comparison of the two groups. Wilcoxon's signed rank test was used for within-group change. A P value <0.05 was considered as statistically significant.

Results

Forty patients completed the study. Twenty patients following home-based exercise program five times a week at least 30 min per session (exercise group) were compared with patients who did not follow the exercise program regularly (control group). Patients in control group ($n = 20$) were not doing the exercises at least one time a week on a regular basis from the beginning of the study. At baseline, the main demographic and clinical features of the groups were similar (Table 1). All the included patients were receiving TNFα inhibitors at least 6 months. The duration of TNFα inhibitors treatment did not differ between groups ($P > 0.05$). The patients in control group stated that the main reason for the incompliance with the exercises was lack of time.

No statistically significant difference was found in terms of BASDAI, BASFI, BASMI, BDI, MAF, and SF-36 scores between groups at baseline ($P > 0.05$) (Tables 2, 3). BASDAI, BASFI, BASMI, BDI, MAF, and SF-36 scores showed statistically significant improvements after 10 weeks in exercise group ($P < 0.05$). All of these values remained unchanged in control group at 10th week compared to baseline ($P > 0.05$). The intergroup comparison of the improvement showed a significant difference in BASDAI, BASFI, BASMI, BDI, MAF scores and subscales of SF-36 except social functioning subscale between groups in favor of Group 1 ($P < 0.05$) (Table 4).

Discussion

This study was performed to investigate the efficacy of home-based exercise therapy in AS patients receiving TNFα inhibitors. The results of the present study showed significant improvements in all the clinical and functional parameters in patients performing home-based exercises on a regular basis.

AS is associated with significant pain, functional disability, and diminished QoL [24]. Physical activity and exercise are increasingly considered as an important part of the treatment program for AS, together with appropriate medication. Home-based exercise program was reported to be an efficient therapy in improving pain, the functional capacity, and joint mobility [7, 11, 13]. Some studies also reported positive effects on QoL [2, 12, 13, 25, 26], reduction in fatigue [25], and depression [2, 12, 26]. However; currently available data do not adequately address what role physical therapy may have on patients with AS receiving TNFα inhibitors [5]. There are a few studies evaluating the effects of exercises in patients with AS receiving TNFα inhibitors [9, 27–29]. In one of these studies evaluating the effects of inpatient rehabilitation program (an intensive standardized supervised exercise program, twice daily) and etanercept treatment, Lubrano et al. [29] compared different interventions to the same sample of patients at different period of time. They reported a significant difference for BASFI, anthropometric measurements, and acute phase reactants in favor of combination treatment (rehabilitation and etanercept) when they compared the 3-week combination treatment to 3-week etanercept treatment alone. No differences were reported for disability and QoL for this comparison. Spadaro et al. [28] investigated the effect of occupational therapy in 27 AS patients receiving TNFα inhibitors at least 12 weeks. The occupational therapy group was given a range of movement spine exercise home program besides occupational therapy. They reported more significant improvement in BASFI, pain, SF-36 mental component summary, and BASDAI in the occupational therapy group and no significant improvement in BASMI, CRP and ESH

Table 1 Demographic and clinical features of the patients

	Exercise group ($n = 20$)	Control group ($n = 20$)	P
Age (years) (mean ± SD)	40.30 ± 8.05	36.45 ± 7.19	>0.05
Gender (M/F) (*n*)	15/5	17/3	>0.05
The duration since diagnosis (years)	9.55 ± 5.19	7.95 ± 4.59	>0.05
BASRI (mean ± SD)	8.15 ± 2.48	7.90 ± 2.25	>0.05
TNFαi (*n*)			
Adalimumab	2	3	>0.05
Etanercept	10	7	
Infliximab	8	10	
The duration of TNFα inhibitors medication (months) (mean ± SD min–max)	19.80 ± 12.33 (6–48)	17.00 ± 15.63 (6–60)	>0.05
Education (years) (*n*)			
5	10	9	>0.05
5–8	3	1	
8–12	7	6	
>12	0	4	

n number of cases; *SD* standard deviation; *BASRI* the Bath Ankylosing Spondylitis Radiology Index; *TNF* tumor necrosis factor

Table 2 Baseline and 10th week results of BASDAI, BASFI, BASMI, BDI, and MAF scales of the patients

	Exercise group			Control group		
	Baseline	At 10th week	P	Baseline	At 10th week	P
BASDAI	3.85 ± 2.45	2.61 ± 1.83	<0.001	3.81 ± 2.38	3.77 ± 2.33	>0.05
BASFI	3.22 ± 2.96	2.27 ± 2.10	<0.01	3.86 ± 2.36	4.00 ± 2.41	>0.05
BASMI	5.05 ± 2.74	4.15 ± 2.62	<0.01	5.55 ± 2.50	5.70 ± 2.52	>0.05
BDI	8.30 ± 7.27	5.75 ± 6.03	<0.01	11.15 ± 10.45	10.7 ± 10.33	>0.05
MAF	21.48 ± 12.62	15.95 ± 11.52	<0.01	24.85 ± 13.60	24.42 ± 13.38	>0.05

Data are expressed as means ± SD. *BASDAI* the Bath Ankylosing Spondylitis Disease Activity Index; *BASFI* the Bath Ankylosing Spondylitis Functional Index; *BASMI* the Bath Ankylosing Spondylitis Metrology Index; *BDI* Beck Depression Inventory; *MAF* Multidimensional Assessment of Fatigue Scale

Table 3 Baseline and 10th week results of SF-36 subscales of the patients

SF-36 subscales	Exercise group			Control group		
	Baseline	At 10th week	P	Baseline	At 10th week	P
General health	54.88 ± 22.18	71.45 ± 15.93	<0.01	50.55 ± 24.33	52.80 ± 23.36	>0.05
Physical functioning	62.75 ± 22.51	73.50 ± 18.93	<0.01	60.25 ± 27.22	59.50 ± 25.95	>0.05
Role physical	58.75 ± 42.36	85.00 ± 32.85	<0.07	61.25 ± 37.59	61.15 ± 39.30	>0.05
Role emotional	63.31 ± 35.71	84.99 ± 27.53	<0.05	65.48 ± 32.33	68.81 ± 30.41	>0.05
Social functioning	81.25 ± 29.10	90.00 ± 22.43	<0.05	61.25 ± 36.25	65.58 ± 31.71	>0.05
Bodily pain	57.12 ± 23.05	73.35 ± 17.21	<0.01	57.20 ± 24.74	54.30 ± 27.49	>0.05
Mental health	76.40 ± 15.02	83.00 ± 12.03	<0.01	68.2 ± 19.01	68.2 ± 19.05	>0.05
Vitality	58.25 ± 18.08	70.00 ± 16.86	<0.01	52.00 ± 21.61	54.25 ± 21.11	>0.05

Data are expressed as means ± SD. *SF-36* Short Form 36

values after 16 weeks. A recent randomized controlled study compared the effects of combined TNFα inhibitors and rehabilitation treatment with TNFα inhibitors alone at 2 and 6 months in patients with AS. They reported significant improvements in BASDAI, BASMI and chest expansion values in rehabilitation group (an educational-behavioral intervention and exercise training) compared to educational group and control group and in BASFI values

Table 4 Intergroup comparison of the improvement (pre-post scores) of BASDAI, BASFI, BASMI, BDI, MAF and SF-36 scores of two groups

	Pre-post scores		*P*
	Exercise group ($n = 20$)	Control group ($n = 20$)	
BASDAI	1.24 ± 1.00	0.04 ± 0.29	<0.001
BASFI	0.96 ± 1.06	−0.14 ± 1.07	<0.001
BASMI	0.9 ± 1.07	−0.15 ± 0.37	<0.001
BDI	2.55 ± 3.38	0.45 ± 1.82	<0.01
MAF	5.53 ± 7.08	0.43 ± 2.84	<0.01
SF-36 subscales			
General health	−16.58 ± 19.17	−2.25 ± 6.17	<0.01
Physical functioning	−10.75 ± 12.28	0.75 ± 5.91	<0.001
Role physical	−26.25 ± 35.79	−0 ± 8.11	<0.01
Role emotional	−21.68 ± 24.85	−3.33 ± 14.89	<0.01
Social functioning	−8.75 ± 19.91	−4.33 ± 17.35	>0.05
Bodily pain	−16.23 ± 18.99	2.90 ± 10	<0.001
Mental health	−6.60 ± 8.73	−0 ± 7.57	<0.05
Vitality	−11.75 ± 15.5	−2.25 ± 8.03	<0.05

Data are expressed as means ± SD. *BASDAI* the Bath Ankylosing Spondylitis Disease Activity Index; *BASFI* the Bath Ankylosing Spondylitis Functional Index; *BASMI* the Bath Ankylosing Spondylitis Metrology Index; *BDI* Beck Depression Inventory; *MAF* Multidimensional Assessment of Fatigue Scale; *SF-36* Short Form 36

in both rehabilitation group and educational group compared to control group. That study included patients with AS who had started TNFα inhibitors at least 9 months previously [27]. A survey study in patients with AS on treatment with TNFα inhibitors reported that patients perceived mild to moderate benefit from physical therapy in term of fitness, function, and maintenance of posture, stiffness, and long-term outcome [9].

The present study included patients were receiving TNFα inhibitors at least 6 months. There was no statistically significant difference in terms of disease activity with BASDAI, functional capacity with BASFI, and joint mobility with BASMI between groups at baseline. The changes from baseline of BASDAI, BASFI and BASMI scores improved more significantly in patients following home-based exercise program than in the control group. These improvements point to positive effects of exercises.

Fatigue is a major symptom in most patients with AS and seems to be associated with more severe disease. In a recent study, it was observed that half of the patients with AS had severe fatigue [30]. It has an impact on QoL and should be considered in the management of AS [31]. Fatigue is assessed by BASDAI-question 1. However, it has been reported that assessment of fatigue by a comprehensive questionnaire might have been more informative since it is a multifactorial and multidimensional symptom [32]. Fatigue and depression frequently occur together. Exercise has positive effects for reducing psycological distress and fatigue. The effects of exercise programs on physical health rather than the psycological health have been studied in many recent studies [25]. As psychological symptoms of patients with AS can affect QoL, this factor should be included in the assessment stages of the treatment success [2]. In the present study, evaluation of emotional state with BDI, fatigue with MAF scale and QoL with SF-36 may be counted as a strong aspect. All of these evaluation parameters showed significant improvements after 10 weeks between groups in favor of exercise group.

Home-based exercise programs are easily performed and conveniently available to patients without cost [5]. However, most of the AS patients do not exercise regularly [2]. Falkenbach [33] reported that only 29% of Austrian or German patients with AS exercised daily. Bodur et al. [32] similarly reported that only 22.7% of the patients with AS in Turkey had regular exercise habits. In the present study, home-based exercise program was demonstrated to all the patients. At the end of 10 weeks, half of the patients were doing exercises on irregular basis, for example, three times a week and none next 2 weeks. We observed that these patients were not exercising at least one time a week on a regular basis. It was reported that unsupervised recreational exercise and back exercises were effective interventions in patients with AS, but benefits were seen only in periods with more than 30 min per day of exercise or periods in which back exercises were performed at least 5 days per week [13, 25]. Staying consistent in an exercise plan rather than quantity of the exercise program was reported to be crucial for its effectiveness in AS patients [13, 34]. Taking into account these reports, we grouped the patients as exercise group and control group.

Adherence to long-term treatment regimes was reported to be lower than adherence to medication, and the attrition rate from exercise programs was reported 50% within the first 6 months [35]. Various factors of compliance and adherence to regular exercises such as higher disability level [33], feeling bad [35], lack of time, fatigue and aggravation of symptoms with exercise [36] were reported

in AS patients. Different ways were used to check whether they were doing the exercises. One of them was to telephone to patients on a daily [12], weekly [25, 37, 38], or monthly basis [27]. Compliance with home exercises was reported optimal in these studies. Sweeney et al. [39] reported that intervention package including an exercise/information video, exercise progress chart, patient education booklet, and AS exercise reminder stickers in patients with AS significantly improves self-efficacy for exercise and self-reported levels of exercise. In the current study, all the patients were trained on the importance of the exercise program and given visual education materials. Patients had never been communicated along 10 weeks. Ten weeks later, half of the patients failed to comply with the exercise program. When we looked for the possible affecting factors of adherence, we could not find any statistically significant difference in terms of demographic properties (such as age, the duration since diagnosis, duration of TNFα inhibitors medication and educational level), joint mobility, functional capacity, disease activity, and QoL at baseline between patients who were exercising or not. The values of fatigue and BDI were higher in control group than in exercise group at baseline. However, these differences were not at the level of significance ($P > 0.05$). Lack of time was pointed out as the main reason for the incompliance with the exercises in control group.

There are several limitations of the study such as a small sample number and lack of randomized control group. Patients were grouped according to their compliance with the exercises. In spite of these limitations, it is noteworthy that patients' education about the disease and the role of the exercise therapy in addition to visual education material in the current study was not enough to provide the compliance and adherence of AS patients to regular home-based exercises. Because home-based exercises are low-priced and easy applicable therapy for every patient, we need to find out new ways to provide the continuity of AS patients with it.

As a conclusion, the present study showed that home-based exercise program is an effective therapy in increasing functional capacity and joint mobility, decreasing disease activity, improving emotional state, fatigue and QoL for patient with AS receiving TNFα inhibitors. New ways to motivate patients to do regular exercise should be investigated.

Conflict of interest None.

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