Efficacy of Incentive Spirometer Exercise on Pulmonary Functions of Patients with Ankylosing Spondylitis Stabilized by Tumor Necrosis Factor Inhibitor Therapy

MIN WOOK SO, HYUN MI HEO, BON SAN KOO, YONG-GIL KIM, CHANG-KEUN LEE, and BIN YOO

ABSTRACT. ***Objective.*** To evaluate the effect of combining incentive spirometer exercise (ISE) with a conventional exercise (CE) on patients with ankylosing spondylitis (AS) stabilized by tumor necrosis factor (TNF) inhibitor therapy by comparing a combination group with a CE-alone group.

Methods. Forty-six patients (44 men, 2 women) were randomized to the combination group (ISE plus CE; n = 23) or the CE group (n = 23). The CE regimen of both groups consisted of 20 exercises performed for 30 min once a day. The ISE was performed once a day for 30 min. The trial duration was 16 weeks. Patients were assessed before and at the end of treatment by measuring the Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Functional Index (BASFI), chest expansion, finger to floor distance, pulmonary function measures, and 6-min walk distance.

Results. Both groups improved significantly in terms of chest expansion ($p < 0.01$), finger to floor distance ($p < 0.01$), and BASFI ($p < 0.05$) after completing the exercise program. However, only the combination group showed significant improvements in the forced vital capacity ($p < 0.05$), total lung capacity ($p < 0.01$), and vital capacity ($p < 0.05$). Although this did not achieve statistical significance, the combination group was mildly superior to the CE-alone group in functional disability and pulmonary function measures.

Conclusion. Combining ISE with a CE can provide positive results in patients whose AS has been clinically stabilized by TNF inhibitor therapy. (First Release Aug 1 2012; J Rheumatol 2012;39: 1854–8; doi:10.3899/jrheum.120137)

Key Indexing Terms:
ANKYLOSING SPONDYLITIS SPIROMETER PULMONARY FUNCTION TEST EXERCISE

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that primarily affects the sacroiliac joints and spine (although it may also involve entheses, peripheral joints, and extraarticular organs) and results in functional impairment, disability, and a poor quality of life[1]. The Assessment in AS (ASAS)/European League Against Rheumatism (EULAR) guidelines recommend that patients with AS should be managed by a combination of pharmacological and nonpharmacological therapy. The nonpharmacological arm encompasses education, exercise, and physiotherapy and is recommended for all phases of the disease[2,3]. In particular, exercise seems to play an important role in the management of AS, especially when done in a supervised outpatient group setting or intensively with inpatients[4,5,6]. Combining aerobic exercises such as swimming and walking with conventional exercises (CE) increases the functional capacities of patients with AS[7].

Pulmonary involvement is the most frequent extraarticular involvement in patients with AS, as has been demonstrated by plain radiographs in 0–30% of these cases or by high-resolution computed tomography in 40%–80% of these cases. Rigidity of the thorax occurs in AS cases with bony ankylosis of the thoracic vertebrae, and with costovertebral, costotransverse, sternoclavicular, and sternomandibular joints. Pulmonary function tests in AS cases have revealed a high prevalence of restrictive defects, characterized by a low forced vital capacity (FVC) frequently associated with a low thoracic expansibility that may disrupt functionality and affect quality of life[8,9].

An incentive spirometer is a device that is designed to achieve and sustain maximal inspiration. It is commonly used after major abdominal, thoracic, or cardiac surgery to prevent postoperative pulmonary complications. It seeks to achieve the early reexpansion of collapsed alveoli and prevent further atelectasis, to avoid subsequent infections[10,11].

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Breathing exercises using an incentive spirometer improve the maximum inspiratory pressure, arterial blood gases, pulmonary function measures, dyspnea, and health-related quality of life (HRQOL) in patients with chronic obstructive pulmonary disease (COPD)[12,13,14].

We hypothesized that combining incentive spirometer exercise (ISE) with CE may improve the efficacy of a rehabilitation program, resulting in better functional capacity and pulmonary function. In our study, the effects of combination treatment (ISE and CE) were compared to those of CE alone in patients whose AS had been stabilized by tumor necrosis factor (TNF) inhibitor therapy.

MATERIALS AND METHODS

Study design. This was a 16-week randomized open-label case-control single-center study (registration number KCT0000051). After a screening period of up to 6 weeks to ensure their eligibility to enter the study, patients were randomized to the combination treatment (ISE and CE) group or the CE-alone group. Patients were evaluated at screening, baseline, and at Week 16. The study protocol was approved by the Institutional Review Board of the University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea. Written informed consent was obtained from the patients.

Patients. The study protocol involved a recruitment period from October 1, 2010, to March 31, 2011. During this period, 50 patients with AS (47 men, 3 women), classified according to the modified New York criteria[15] and treated with TNF inhibitors, were enrolled into the study consecutively. The patients were outpatients in our hospital rheumatology department. Patients were eligible to participate in the trial if (1) they had been treated with the standard dose of infliximab (5 mg/kg every 6 weeks), etanercept (25 mg twice/week), or adalimumab (40 mg every 2 weeks) for at least 6 months and they did not require continuous intake of nonsteroidal antiinflammatory drugs; (2) they presented with low disease activity, i.e., their Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores in the previous 3 months were < 4/10 units; (3) they were aged between 18 and 60 years; and (4) they did not present with severe disability that seriously affected their independence in daily living activities (e.g., dressing, walking, moving, etc.). The exclusion criteria included (1) a medical condition that impaired functional capacity or pulmonary function even more than the AS, such as coexistent cardiac disease, respiratory disease, or severe arthritis; (2) abnormal chest radiograph; and (3) participation in rehabilitation treatment or routine exercise activities in the previous 6 months. Four eligible patients (3 men, 1 woman) declined to participate in the trial. Thus, 46 patients (44 men, 2 women) were randomly allocated to the combination treatment group (n = 23) or the CE-alone group (n = 23; Figure 1). Casual randomization using a statistical program was performed by a rheumatologist who was not involved in the study evaluation or intervention.

Exercise program. Prior to starting the program, educational sessions about AS and individual counseling were performed by a rheumatologist. All patients were taught how to perform the exercises correctly by a physiotherapist. For each of the exercises, participants were provided with simple, step-by-step written instructions with illustrations. The CE regimen consisted of 20 exercises for 30 min once a day. The exercises were motion and flexibility exercises of the cervical, thoracic, and lumbar spine; stretching of the erector spine muscle, hamstring muscles, and shoulder muscles; chest expansion exercises; and control abdominal and diaphragm breathing exercises[5]. The combination group was also instructed how to use the incentive spirometer, as follows: (1) hold the device straight up in front; (2) breathe out; (3) close lips tightly around the mouthpiece; (4) inhale slowly and deeply through the mouth until the 3 balls in the incentive spirometer rise; (5) when the patient feels he or she cannot breathe in any longer, take the mouthpiece out of the mouth; (6) hold the breath for 3–5 seconds, then breathe out slowly. This was repeated for 30 min once a day. The patients had to keep an exercise diary that was checked at each visit to the outpatient clinic. Good compliance was defined as exercising for ≥ 80% of the total days.

Clinical assessments. The patients were assessed before and at the end of the treatment to determine their functional capacity, disease activity, chest expansion, finger to floor distance, and pulmonary function measures. Functional capacity was assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI), which consists of 10 questions about the functional capacity of the patient with AS to perform daily activities. All items are valued with a 10-cm horizontal visual analog scale (VAS). The BASFI score is the sum of all values. Higher BASFI scores indicate greater functional limitation[16]. Disease activity was determined by measuring the BASDAI. The BASDAI consists of 6 questions about the 5 major symptoms (fatigue, pain in the spine and hips, pain or swelling of the peripheral joints,

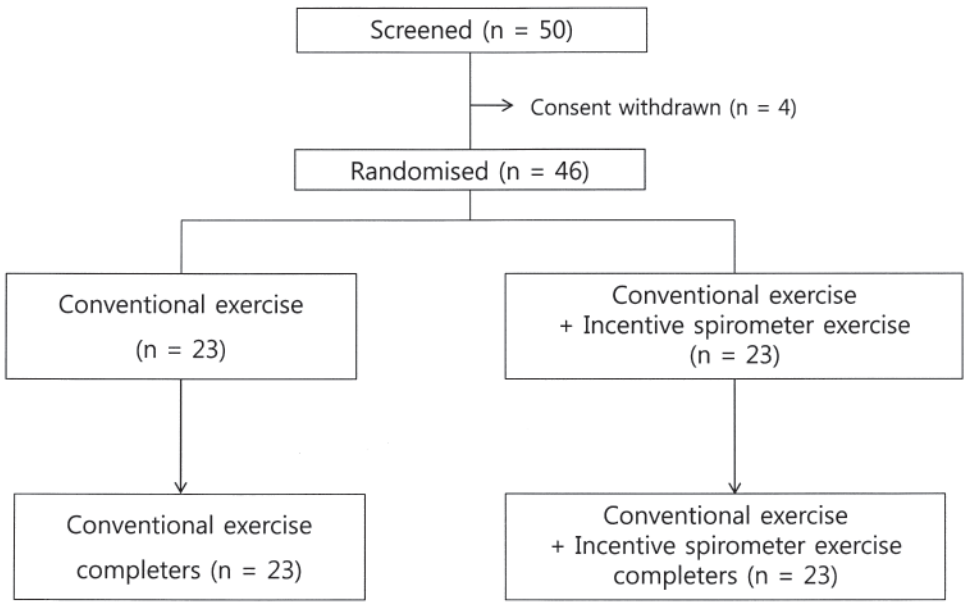

Figure 1. Progress of patients through the trial.

enthesitis, severity and duration of morning stiffness). The questions are answered on a 10-cm VAS. Higher BASDAI scores indicate higher disease activity[17]. Pulmonary function measures were assessed by spirometry (Vmax22; Sensormedics, Yorba Linda, CA, USA) and lung volume plethysmography (6200 Plethysmograph; Sensormedics). The FVC, forced expiratory volume in 1 s (FEV1), FEV1/FVC, vital capacity (VC), total lung capacity (TLC), and residual volume (RV) were recorded for each patient. The 6-min walk distance (6MWD) test was used to objectively assess functional performance and endurance. The 6MWD test was performed according to modified American Thoracic Society guidelines[18].

Statistical analysis. The baseline characteristics of the 2 groups were compared using Student's t-test for continuous variables and the chi-square test for categorical variables. Differences before and after treatment were tested by paired t-test or Wilcoxon signed-rank test. Student's t-test or Mann-Whitney U test was used to compare groups after treatment. The results were reported as means ± SD, and p values < 0.05 were considered significant. All statistical calculations were performed using SPSS version 12 (SPSS Inc., Chicago, IL, USA).

RESULTS

In total, 46 patients completed the study with a good level of compliance. The demographic and baseline characteristics of the study population are shown in Table 1. The 2 groups did not differ significantly with regard to any of these measures.

Functional disability testing revealed that after completing the 16-week exercise program, both groups improved significantly in chest expansion, finger to floor distance, and BASFI score (Table 2). However, pulmonary function testing revealed that only the combination group improved significantly in FVC, TLC, VC, and FEV1/FVC. Lastly, although the BASDAI and 6MWD test scores of both groups improved, these changes were not statistically significant (Table 2).

A comparison of the 2 groups showed that the combination group was mildly superior to the CE-alone group in improvement in functional disability and pulmonary function measures. However, this was not statistically significant (Table 2). No complications were observed in either group during the exercises.

Table 1. Demographic and baseline characteristics of the conventional exercise (CE) group and the CE plus incentive spirometer exercise (ISE) group.

Characteristics	CE Group, n = 23	CE + ISE Group, n = 23
Age, yrs	38.0 ± 9.1	34.6 ± 5.9
Men, n (%)	22 (95.7)	22 (95.7)
Body mass index, kg/m^2	24.8 ± 3.3	23.8 ± 2.5
Current smoker*, n (%)	14 (60.9)	15 (65.2)
Smoking amount, pack-yrs	15.0 ± 11.7	10.4 ± 6.0
Total symptom duration, yrs	12.9 ± 7.3	12.2 ± 6.4
Duration of TNF inhibitor therapy, mo	36.9 ± 18.1	37.3 ± 15.5
Erythrocyte sedimentation rate, mm/h	11.6 ± 8.8	8.2 ± 6.8
C-reactive protein, mg/dl	0.27 ± 0.34	0.14 ± 0.08
Chest expansion, cm	2.87 ± 1.42	3.41 ± 1.56
Finger to floor distance, cm	16.8 ± 14.3	11.1 ± 11.5
BASDAI (0–10)	2.75 ± 1.15	2.37 ± 1.09
BASFI (0–10)	1.72 ± 1.73	0.98 ± 1.23
Pulmonary function test		
FVC, liters	4.22 ± 0.62	4.27 ± 0.84
FEV1, liters	3.42 ± 0.61	3.45 ± 0.77
FEV1/FVC, %	80.9 ± 7.9	82.6 ± 5.5
TLC, liters	5.64 ± 0.70	5.66 ± 0.94
VC, liters	4.25 ± 0.63	4.30 ± 0.84
RV, liters	1.38 ± 0.42	1.34 ± 0.40
Patients with restrictive pattern, n (%)	6 (26.1)	5 (21.7)
6-min walk distance test, meters	509.2 ± 59.7	510.6 ± 57.1

* Current smoker was defined as still smoking prior to study enrollment. TNF: tumor necrosis factor; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; TLC: total lung capacity; VC: vital capacity; RV: residual volume.

DISCUSSION

Our randomized controlled study was performed with patients whose AS had been stabilized by TNF inhibitor therapy. The influence of ISE on functional disability and pulmonary functions combined with CE was assessed. Both combination therapy and CE alone significantly improved the functional disability measures, i.e., chest expansion, finger to floor distance, and BASFI scores. The patients given a combination treatment also improved significantly in pulmonary functions (FVC, TLC, and VC), whereas the CE-alone group patients did not. ISE and CE can further alleviate any functional disability and improve pulmonary functions in patients whose AS has been stabilized by TNF inhibitor therapy.

There is moderate evidence supporting the observation that in patients with AS, home-based or supervised exercise is better than no exercise, group exercise is better than home exercise, and the addition of spa-based exercises to weekly group exercises is better than weekly group exercises alone[4]. Karapolat, *et al* showed that patients with AS who join swimming and walking groups improved significantly more in pulmonary and exercise tolerance outcome measures than did control patients with AS[7]. However, the studies examining these issues had some limitations. First, only a few previous studies have evaluated the effects of exercise on pulmonary function measures. Ince, *et al* found significant improvements in VC after 3 months of a multimodal exercise program (involving aerobic, stretching, and pulmonary exercises) in patients with AS[19]. In another prospective cohort study, patients with AS were taught breathing exercises and upper extremity exercises that were performed daily at home for a 6-week period. The results showed significant improvement in a number of respiratory outcomes including maximal inspiratory pressure and maximal expiratory pressure values[20]. Pulmonary function was also examined by Durmus, *et al* who compared global posture reeducation (GPR) exercise, CE, and no exercise. Their analysis found that both exercise groups showed significant improvement in pulmonary function measures, with the

Table 2. Changes in functional and pulmonary measures at Week 16 relative to baseline, and comparison of the conventional exercise (CE) and CE plus incentive spirometer exercise (ISE) groups.

	CE Group		CE + ISE Group		Both Groups
	Baseline	After 16 Weeks	Baseline	After 16 Weeks	Between-groups p
Chest expansion, cm	2.87 ± 1.42	3.33 ± 1.61**	3.41 ± 1.56	4.17 ± 1.84**	NS
Finger to floor distance, cm	16.8 ± 14.3	13.4 ± 12.6**	11.1 ± 11.5	8.4 ± 9.9**	NS
BASDAI (0–10)	2.75 ± 1.15	2.58 ± 1.65	2.37 ± 1.09	1.97 ± 1.54	NS
BASFI (0–10)	1.72 ± 1.73	1.26 ± 1.56*	0.98 ± 1.23	0.75 ± 1.17*	NS
Pulmonary function test					
FVC, liters	4.22 ± 0.62	4.29 ± 0.61	4.27 ± 0.84	4.40 ± 0.84*	NS
FEV1, liters	3.42 ± 0.61	3.39 ± 0.57	3.45 ± 0.77	3.35 ± 0.72	NS
FEV1/FVC, %	80.9 ± 7.9	79.2 ± 8.2	82.6 ± 5.5	80.2 ± 6.6**	NS
TLC, liters	5.64 ± 0.70	5.72 ± 0.72	5.66 ± 0.94	5.80 ± 0.87**	NS
VC, liters	4.25 ± 0.63	4.33 ± 0.62	4.30 ± 0.84	4.45 ± 0.83*	NS
RV, liters	1.38 ± 0.42	1.39 ± 0.30	1.34 ± 0.40	1.35 ± 0.34	NS
6MWD test, meters	509.2 ± 59.7	522.2 ± 60.9	510.6 ± 57.1	511.9 ± 56.8	NS

* $p < 0.05$ and ** $p < 0.01$, baseline versus after 16 weeks. NS: not significant; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; FVC: forced vital capacity; FEV1: forced expiratory volume in 1 s; TLC: total lung capacity; VC: vital capacity; RV: residual volume; 6MWD: 6-min walk distance.

GPR exercise resulting in greater improvements in FVC, FEV1, and peak expiratory flow[21]. In our study, we tried to evaluate the effects of ISE on pulmonary function measures and showed that combining ISE with CE improved the pulmonary functions of study patients.

The second limitation of previous studies was that most did not include patients who were receiving TNF inhibitor therapy. Indeed, how physiotherapy and various exercises affect the outcomes of TNF inhibitor-treated patients with AS has rarely been studied. Lubrano, *et al* showed that etanercept and intensive inpatient rehabilitation had a synergistic effect on the outcome of active AS[22]. Spadaro, *et al* reported that combining occupational treatment with TNF inhibitor treatment produced positive benefits in pain, function, and disability[23]. Masiero, *et al* showed that combining intensive group exercise with an educational-behavioral program can provide positive results in patients whose AS has been clinically stabilized by TNF inhibitor therapy[24]. Our study included patients who were receiving TNF inhibitor therapy. To exclude the effects of TNF inhibitor therapy itself, all patients presented with low disease activity, i.e., their BASDAI scores in the previous 3 months were < 4/10 units.

Lastly, the studies failed to account for the difficulty that some patients with AS have in following specific nonpharmacological therapy recommendations (e.g., supervised exercise, group exercise, spa-based exercise, and swimming) apart from a home exercise program because of a lack of time, economic issues, and social status (e.g., access to swimming facilities). Therefore, nonpharmacological therapies that are inexpensive, convenient, and easy to use are needed. The incentive spirometer is designed to mimic natural sighing or yawning by encouraging the patient to take long, slow, deep breaths. It can also be used for inspiratory muscle training. The use of an incentive spirometer increases transpulmonary pressure, inspiratory volumes, and inspiratory muscle performance[25]. It is commonly used after major abdominal, thoracic, or cardiac surgery to prevent postoperative pulmonary complications. Scherer, *et al* reported that breathing exercises with the incentive spirometer improved the maximum inspiratory pressure and reduced dyspnea in patients with COPD[12]. Basoglu, *et al* showed that the incentive spirometer appeared to improve the arterial blood gases and HRQOL in patients with COPD exacerbations[13]. Igarashi, *et al* assessed the effects of incentive spirometer on pulmonary function and arterial blood gases in healthy adults of advanced age and in patients with COPD. They reported a significant decrease in alveolar-arterial oxygen gradient and increases in pulmonary function measures and arterial oxygenation[14]. The incentive spirometer has several advantages: it is inexpensive and simple to use, patients do not require supervision once trained in its use, and there are no known side effects. The achievement of the visual target encourages patients to try their best and thereby promotes patient compliance.

In our study, the subjects in both groups performed the same CE and complied with the program, which may explain the improvements in functional disability in both groups. Although both groups also showed mild improvements in BASDAI and 6MWD test scores, these differences relative to baseline did not achieve statistical significance. This may reflect that the patients in the study were stable and had low disease activity at baseline, which makes it difficult to observe a major improvement in BASDAI and 6MWD test scores. Although the combination treatment group showed mildly superior improvements in functional disability and pulmonary function over the CE-alone group, these differences did not achieve statistical significance.

This may reflect the relatively short duration and small sample size of our study.

To our knowledge, the effect of ISE on patients with AS has not yet been reported. Our study is the first to show that ISE and CE improved the functional disability and pulmonary functions of patients whose AS was stabilized with TNF inhibitor therapy. However, before these results can be generalized, additional studies should be performed with longer treatment durations and patients in various stages of the disease.

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