Concise Report

Effectiveness of rehabilitation in active ankylosing spondylitis assessed by the ASAS response criteria

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Objective. To assess the effectiveness of rehabilitation in a group of patients with active ankylosing spondylitis (AS) by the Assessment in Ankylosing Spondylitis (ASAS) Working Group response criteria.

Methods. Fifty-two active AS patients consecutively admitted to a rehabilitation inpatient clinic were enrolled. Patients underwent a 3-week intensive rehabilitation programme and were then discharged with home exercises. The primary outcome measure was the proportion of patients achieving a response based on ASAS 20 at discharge, and at 6 and 12 weeks after. Secondary outcome measures included an improvement in the Revised Leeds Disability Questionnaire (RLDQ) and function expressed as anthropometric measures.

Results. The ASAS 20 was achieved in 46 patients (88.5%) at the end of the rehabilitation, in 31 (59.6%) and in 17 (32.7%) patients at 6 and 12 weeks follow-up, respectively. The percentage of ASAS 20 responders statistically declined over time measured from the end of rehabilitation compared with 6 (P < 0.001) and 12 weeks follow-up (P < 0.001).

Conclusion. The present study shows the effectiveness of rehabilitation as assessed by the ASAS 20, a validated instrument for treatment response, suggesting its usage in rehabilitation settings. Moreover, the results obtained show that the effectiveness of the intensive inpatient rehabilitation declined over time.

Key words: Ankylosing spondylitis, ASAS response criteria, Rehabilitation, Physical therapy, Disability.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory disease that can lead to severe damage of the spine with functional impairment, disability and poor quality of life [1].

AS requires a combined management (pharmacological and rehabilitation) and recently, the introduction of anti-TNF-α agents has positively changed the treatment scenario [2, 3].

Rehabilitation plays an important part of the management, particularly when carried out as a supervised outpatient group or as inpatient intensive showing short-term improvement [4, 5]. Doubts remain about sustained improvement for long periods of time [6, 7], and it seems that AS patients experienced progressive loss of movement independently to the disease duration and the reported frequency of unsupervised exercise [8]. Recently, some experimental exercise protocols showed promising short- and long-term results in outpatient physiotherapy settings [9, 10].

These contradictory results may depend on methodological differences such as patients’ selection, type of physiotherapy and outcome measures.

We showed a synergistic effect of anti-TNF-α agents and an intensive inpatient rehabilitation in the management of active AS, indicating that the combination treatment seemed to be more effective than a simple rehabilitation programme [11].

Non-pharmacological therapy (including education, exercise and physiotherapy) was included in the recommendations for the AS management by the Assessment in AS (ASAS) Working Group/EULAR [12]. The ASAS Working Group also proposed some response criteria to measure treatment effects in clinical trials to allow a standardized evaluation of therapies [13]. These response criteria have shown high specificity and moderate sensitivity and have been validated in studies with anti-TNF-α therapy [14]. The ASAS response criteria incorporate four domains including physical function, pain, patient global assessment and inflammation. An improvement of ≥20% and net improvement of ≥10 units on a scale of 0–100 in each of the three domains with no worsening in the fourth define the response criteria. The term ASAS 20 means an improvement of at least 20% of these core sets of criteria and allows the calculation of treatment response between the ‘responder’ and the ‘no responder’ patients.

At the time of the present study, no data on the effectiveness of rehabilitation using the ASAS response criteria have been reported since this composite index has never been taken into account in a rehabilitation setting.

The aim of the present study was to assess the effectiveness of an intensive inpatient rehabilitation programme in a group of patients with active AS by the ASAS response criteria. The response was calculated at the end of the intensive inpatient rehabilitation, at 6- and 12-week follow-up visits after the discharge.

Patients and methods

Study design

The study protocol considered a recruitment period from 1 January 2005 until 31 October 2005. During that period of time 73 AS patients, classified by the modified New York criteria [15], were consecutively seen at our outpatient rehabilitation clinic; out of them, 52 were considered active and eligible for the present study.

The exclusion criteria were: complete ankylosing of the spine; previous admission for inpatients physiotherapy within 12 months; previous usage of anti-TNF-α inhibitors; the usage of DMARDs (disease-modifying anti-rheumatic drugs) other than sulfasalazine or methotrexate within 4 weeks of enrolment; the usage of >10mg prednisolone daily; variation of dosage of NSAIDs or prednisolone within 2 weeks of enrolment. None of the 52 active AS patients showed any of the exclusion criteria. All patients treated with methotrexate or sulfasalazine were on stable dosage for at least 6 months.
All patients gave their written informed consent and the study protocol was approved by the local ethics committee.

Recruited AS patients, after an initial outcome assessment (Time 1), carried out a 3-week intensive inpatient rehabilitation. At discharge (Time 2), the patients, after a re-assessment of outcome measures, received a daily home exercise programme. Then, after the discharge they had another re-assessment at 6 weeks (Time 3) and at 12 weeks (Time 4). After the last follow-up visit they received, if necessary, some new pharmacological treatment.

**Disease activity assessment**

The disease was considered active if: (i) it was not controlled by NSAIDS; and (ii) at least three of the following conditions were present: (a) patient’s global assessment ≥ 40 mm on a visual analogue scale (VAS) rated from 0 (none) to 100 mm (most severe); (b) inflammatory pain (100 mm VAS) ≥ 40 mm; (c) Bath AS Functional Index (BASFI) value ≥ 40 mm; (d) erythrocyte sedimentation rate (ESR) > 28 mm 1st h or raised C-reactive protein (CRP).

Moreover, as a measure of the disease activity a value ≥ 4 (0–10) of the Bath Ankylosing Spondylitis Activity Index (BASDAI) was also taken into account.

**Interventions**

All participants carried out an intensive standardized exercise programme consisting of two daily sessions supervised by a senior physiotherapist with experience in AS and they were divided in groups including six to eight patients.

Each session of the exercise programme included: (i) warm-up, followed by 30 min of strengthening exercises with maximal isometric pain free and dynamic contractions against gravity; (ii) stretching exercises with neuro-motor facilitation for 15 min; (iii) endurance exercises for a progressive duration on the basis of the patient’s functional capacity and disease severity; (iv) respiratory exercises for 15 min. Patients tried to reach 60% of their predicted heart rate at maximal exercise for 5 days and this was progressively increased to a maximum of 80% of the predicted rate until the end of rehabilitation. After 3 weeks of rehabilitation all patients were discharged and they received a daily home exercise programme, consisting of six groups of exercises as previously described [6].

**Outcome assessment**

The primary outcome measure was the proportion of patients achieving a response based on ASAS 20 at the end of the rehabilitation and at 6 and 12 weeks after discharge.

ASAS 20 was calculated as composite index: ≥ 20% relative improvement and absolute improvement of ≥ 10 units in three or more of the following four domains, with no worsening in the fourth: inflammation (mean question 5 and 6 of the BASDAI), function (BASFI), patient perception of pain (patient pain VAS) and patient global assessment.

As secondary outcome measures we selected and performed: (i) the Italian version of the Revised Leeds Disability Questionnaire (RLDQ) [16]; (ii) the following anthropometric measures [17]: (a) tragus to wall distance; (b) chest expansion and (c) modified Schober’s test. The assessment of peripheral joints, eye and skin involvement, the detection of HLA B27 antigen and blood tests were also performed.

**Statistical analysis**

Statistical analysis was carried out using the SPSS package (version 13.0). McNemar test was used to assess any statistical differences between the proportion of ASAS 20 positive at the end of rehabilitation, at 6 and 12 weeks. Comparisons between baseline, after treatment and at 6 and 12 weeks were done using Wilcoxon signed-rank test for the secondary end-points. Descriptive data were expressed, if not otherwise specified, as mean ± S.D. Statistical significance was accepted at P < 0.05.

**Results**

**Descriptive data**

Of the 52 enrolled patients (39 M, 13 F; mean age 45.7 ± 10.0, disease duration was 7.8 ± 4.8 yrs, 42 (81%) were HLA B27-positive. Seventeen (33%) were on DMARDs and all patients were taking NSAIDS. All patients carried out the pharmacological treatment throughout the study without any modifications.

Six patients (12%) showed a clinical peripheral joint involvement. Psoriasis was seen in five patients (10%) and eye involvement in eight patients (15%).

None of the enrolled patients dropped out of the study.

**Changes in the outcome measures**

The ASAS 20 was achieved in 46 patients (88.5%) at the end of the rehabilitation; 31 patients (59.6%) still achieved the ASAS 20 at 6 weeks while at 12 weeks only 17 patients (32.7%) achieved it. The six patients who did not achieve the ASAS 20 at the end of rehabilitation did not differ for age, sex, disease duration and medical therapy.

A statistically significant difference was found between the percentage of ASAS 20 responder at the end of rehabilitation compared to that at 6-weeks follow-up (46/52 vs 31/52, P < 0.001) and between the percentage at the end of rehabilitation compared to that at 12 weeks (46/52 vs 17/52, P < 0.001).

ASAS 40 was reached only in two patients (3.8%) at the end of rehabilitation.

Data obtained from the four points assessment for main outcome measures are showed in the Figs 1 and 2.

All the secondary outcome measures showed a statistically significant differences at the end of rehabilitation and these differences were also noted at 6 weeks and 12 weeks of follow-up. In particular, RLDQ showed a statistical difference between the beginning and the end of rehabilitation and between the beginning and at 6 weeks follow-up as well as at 12 weeks (Fig. 2).

All anthropometric measures showed an improvement with a statistically significant difference: tragus to wall distance improved at the end of rehabilitation and this was also noted at 6 and 12 weeks. Chest expansion also showed an improvement and this lasted throughout the four-point observations: in particular, at the end of rehabilitation a statistically significant difference was recorded, as well as for the modified Schober test (Fig. 2).

**Discussion**

The optimal management of AS still remains unresolved. Recently we showed the synergistic effects of anti-TNF-α and intensive rehabilitation as possible combination treatment for AS patients [11]. At the time of the present study no data had been published on the effectiveness of intensive inpatient rehabilitation using the ASAS response criteria. Therefore, we designed a study aimed to assess the effectiveness of a standardized intensive inpatient rehabilitation programme in a group of active AS patients using validated response criteria. Our results showed that this intensive programme can determine an achievement of the ASAS 20 in >80% of the patients. The ASAS 20 was also reached in ~60% at 6 weeks follow-up and in more than 30% at 12 weeks after discharge. The achievement of the ASAS 20 lasted in 60% of the patients for 6 weeks indicating that rehabilitation can determine a short-term improvement, while its effectiveness declined over time. And these results are in keeping with the literature showing a good short-term
improvement with some doubts on a long term effect, even if more recently studies on new exercise programmes showed promising short- and long-term results [9, 10].

However, the present study has taken into account a validated instrument for treatment response based on a composite index and at present no data were available on its usage in rehabilitation. In fact, previous studies on the role of inpatient or outpatient rehabilitation have taken into account single endpoints as a measure of treatment response [4] and never a composite index. Therefore, we believe that using the ASAS response criteria it would be advisable to better measure the effectiveness of rehabilitation. Moreover, an improvement of the secondary outcome measures (RLDQ, anthropometric measures) were also seen during the intensive rehabilitation and at the follow-up visits, showing a good physical and functional amelioration, as already previously obtained using the same programme [11]. The results obtained are in favour of using the ASAS response criteria in the field of rehabilitation to better discriminate the effectiveness and to assess the duration of this intervention.

Finally, we did not consider a control group because the ideal control would be a ‘placebo’ group and since the patients were admitted in an inpatients setting that would not have been feasible. However, the aim of our study was to assess the effectiveness of an intensive inpatients programme already used in our previous studies, still deemed useful in active AS patients and covered by the NHS. Indeed, it would be interesting to assess the effectiveness of different types of rehabilitation in different settings such as outpatient using the ASAS response criteria. We still need to know more about the different types of rehabilitation to be used to treat AS and how frequent it should be carried out for the best improvement.

Disclosure statement: The authors have declared no conflicts of interest.

References
FIG. 2. Changes, at the four-point assessment of RLDQ and main anthropometric measures. The boxes extend from 25th percentile to 75th percentile with a line at the median (the 50th percentile). The whiskers show the highest and the lowest values of the series. The reported data showed mean ± s.d., and (*) indicates statistical significance compared with time 1.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Time 1</th>
<th>Time 2</th>
<th>Time 3</th>
<th>Time 4</th>
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<tbody>
<tr>
<td>RLDQ</td>
<td>1.8 ± 0.5</td>
<td>1.4 ± 0.4</td>
<td>1.4 ± 0.4</td>
<td>1.4 ± 0.4</td>
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<tr>
<td>Tragus to wall distance</td>
<td>21.5 ± 4.3</td>
<td>16.3 ± 3.8</td>
<td>16.6 ± 3.1</td>
<td>18.2 ± 5.1</td>
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<tr>
<td>Modified Schober test</td>
<td>1.9 ± 0.6</td>
<td>2.4 ± 0.7</td>
<td>2.3 ± 0.6</td>
<td>2.2 ± 0.6</td>
</tr>
</tbody>
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8 Lubrano E, Helliwell P. Deterioration in anthropometric measures over six years in patients with ankylosing spondylitis. An initial comparison with disease duration and reported exercise frequency. Physiotherapy 1999;85:138–43.