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Original article

High intraindividual week-to-week variability in BASDAI and BASFI values: Are several evaluations needed before starting or stopping TNFα antagonist therapy for spondyloarthropathies?

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Abstract

Objective: To evaluate intraindividual variability of the BASDAI, BASFI, and HAQ in patients with spondyloarthropathies.
Methods: The three variables were collected prospectively in 24 patients, once a week for 30 weeks. They were also collected retrospectively in 31 patients on stable infliximab regimens with a mean of 11.5 ± 4 injections, starting at the fourth infusion.
Results: The BASDAI and BASFI showed high intraindividual variability from week to week; SDs greater than 1 were found for the BASDAI in 14/24 patients and for the BASFI in 10/24 patients, and ranges greater than 4/10 occurred for the BASDAI in 13/24 patients and for the BASFI in 10/24 patients. Although the mean BASDAI was greater than 4 in only 6/24 patients, values greater than 4 occurred on one or more occasions in 19 (79%) patients. The retrospective study of infliximab-treated patients from the fourth infusion onward also showed high variability of BASDAI and BASFI values, with SDs greater than 1 in 18/31 patients and ranges greater than 4 in 14/31 patients and greater than 2 in 22/31 patients.
Conclusion: Repeated determination of the BASDAI and BASFI by the patients (using paper forms or personal digital assessments) may help to identify candidates for treatment intensification, to optimize infliximab injection regimens in good responders, and to avoid unnecessary switching from one TNFα antagonist to another.

Keywords: BASDAI; BASFI; Fluctuation; Variation; Monitoring; Anti-TNF; Spondyloarthropathy; Spondylarthritis; Ankylosing spondylitis

1. Introduction

The metrological validity and the usefulness of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI) in cohort studies of patients with spondyloarthropathies are firmly established. Both indices contribute markedly to efficacy evaluations in cohort studies, as they exhibit good sensitivity to change, reproducibility, internal validity, and correlational validity [1]; it should be noted, however, that the correlational validity of the original English-language versions has not been evaluated [2]. The BASDAI and BASFI are simple to determine and, in contrast to the Assessment in Ankylosing Spondylitis (ASAS) score, enable comparisons of patient-perceived disease severity along a linear 0–100 scale. The BASDAI is among the list of criteria recommended for deciding whether to intensify TNFα antagonist therapy in the individual patient. Suboptimal disease control has been defined as a BASDAI score of 4/10 or greater by international [3] and national [4] panels of experts. A survey among patients showed that the 4/10 cutoff discriminated effectively between the groups of patients who perceived their disease as well controlled or poorly controlled [5].

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The performance of the BASDAI and BASFI in the individual patient remained to be evaluated. In particular, the relevance of the 4/10 cutoff in a given patient needed to be established. Both indices rely on subjective variables, and patients who want to receive newer drugs may manipulate their results to artificially worsen their scores, although awareness of the indices among patients remains limited, at least in France [6]. Furthermore, the BASDAI and BASFI are not specific, and their values are similarly high in fibromyalgia and in spondyloarthropathies [7], two entities that can be extremely difficult to differentiate [8,9]. Finally, the considerable sensitivity to change of the BASDAI and BASFI may be a disadvantage, as score increases may lead to TNFα antagonist initiation in a patient who is merely experiencing a short-lived flare or to TNFα antagonist discontinuation in a patient who is exhibiting a transient rebound in disease activity.

These considerations may explain why experts used a higher mean BASDAI cutoff of 5.5/10 in a survey of rheumatologist practices regarding TNFα antagonist initiation [10]. Furthermore, infliximab is often continued, at least for some time, despite marked increases in the BASDAI and BASFI scores. These increases are frequently ascribed to pharmacokinetic factors (end-of-dose effect and/or efficacy fluctuations across treatment courses). They may be related, however, to transient discontinuation of concomitant medications (such as nonsteroidal antiinflammatory drugs [NSAIDs]) and to variations in disease activity that go undetected in studies of large cohorts, in which spontaneous improvements and spontaneous deteriorations cancel each other out.

To investigate the meaning of score changes over time in individual patients, we prospectively collected the BASDAI, BASFI, and Health Assessment Questionnaire (HAQ) scores once a week for 30 consecutive weeks in 24 patients who were members of a support group for patients with spondyloarthropathies. In addition, we retrospectively collected the BASDAI, BASFI, and HAQ values after the third course of infliximab therapy in 31 spondyloarthropathy patients, each of whom received five or more courses. The infliximab dosage was stable in each patient, and the injections were given at 8-week intervals.

2. Methods

The BASDAI, BASFI, and HAQ questionnaires were completed once a week (on Sundays) for 30 consecutive weeks by 24 patients with spondyloarthropathies. Of the 2160 expected scores, 46 were missing, leaving 2114 scores for the study. The patients were 13 women and 11 men belonging to a support group for patients with spondyloarthropathies. Their age range was 27–68 years (mean, 49 ± 14 years) and disease duration was 2–35 years (mean, 15 ± 9 years). The 30-week data collection period fell in the same period of the year in all 24 patients. The patients were asked to complete the score questionnaires based on their diary notes for the last week, without looking at the values for the previous weeks. Dosages of NSAIDs and analgesics were to remain unchanged if possible, and any treatment changes were to be recorded every week. Of the 24 patients, 2 were on TNFα antagonist therapy at study initiation; 1 was taking infliximab and the other etanercept. In 2 additional patients, etanercept was started 13 weeks (case #6) and 16 weeks (case #8) into the study, respectively. These two patients were kept in the study despite the major change in their treatment, for two reasons: substantial intra-individual variability in BASDAI and BASFI scores occurred in the infliximab-treated patients (see below); and the BASDAI score changes were greatest before etanercept initiation (15–72 in case #6 and 8–82 in case #8), so that including the 17 and 14 remaining weeks, respectively, produced little change in the BASDAI SD (the SD increased slightly in case #6, from 29.9 ± 3.9 for the 13 weeks before etanercept to 16.3 ± 17.8 for the full 30-week period; it decreased slightly in case #8, from 43.07 ± 23.7 for the 16 weeks before etanercept to 35.56 ± 21.3 for the full 30-week period). The 20 remaining patients received stable treatment with NSAIDs ($n = 19$) and/or glucocorticoids ($n = 3$), and/or disease-modifying antirheumatic drugs ($n = 8$; sulfasalazine in 5 patients, methotrexate in 2 and azathioprine in 1).

The diagnosis of spondyloarthropathy was confirmed by the physicians who were providing follow-up to the patients. However, 1 patient (case #18) had a diagnosis of spondyloarthropathy with secondary fibromyalgia. This patient was kept in the study because the variability of her BASDAI scores was not increased compared to the other patients (Fig. 1, column 18) and her BASFI scores showed less variability, albeit with higher absolute values (Fig. 2, column 18).

In the retrospective part of the study, we reviewed the charts of 34 patients who received at least three infliximab infusions to treat spondyloarthropathies and who completed

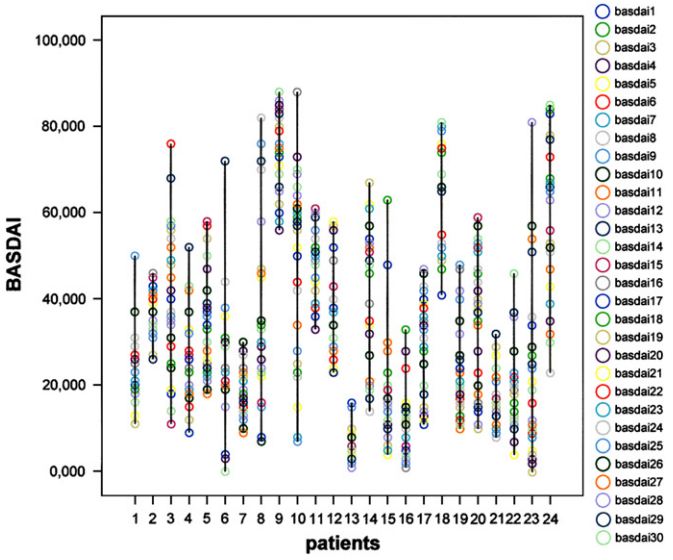

Fig. 1. BASDAI score variations over the 30-week study in each of 24 patients with spondyloarthropathy. Scores varied from 0 to 80 or more in individual patients (see for instance case #23). Scores greater than 4 occurred at least once in 19 (79%) patients. (For interpretation of the references to color in this figure, the reader is referred to the web version of this article.)