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Letter to the Editor

Outcome status in children with sustained polyarticular and systemic juvenile idiopathic arthritis

Sir, Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease of childhood and an important cause of disability [1]. The reported outcome of JIA varies substantially [2–4]. Traditionally, measurement of outcome has focused predominantly on measurements of disease activity such as erythrocyte sedimentation rate (ESR) and an active joint count. Recent investigations have highlighted the limitations of such measures [5]. Additional functional outcome scales were introduced, such as the Childhood Health Assessment Questionnaire (CHAQ), the Juvenile Arthritis Functional Assessment Scale (JAFAS) and the Juvenile Arthritis Functional Assessment Report (JAFAR). At the same time, a preliminary investigation of outcome variables for clinical trials in childhood arthritis has been undertaken [6]. The core set consists of: (i) physician’s global assessment; (ii) parent/patient assessment of overall well-being; (iii) functional ability; (iv) active joint count; (v) number of joints with limited range of motion; and (vi) ESR. Giannini, Ruperto and colleagues [7, 8] proposed a 30% improvement from baseline of three out of six variables, with worsening of more than 30% on more than one of the remaining variables as a justified claim of improvement of the disease. We studied the application of the Paediatric Rheumatology International Trial Organization (PRINTO) outcome variables for sensitivity to change over time in a small selected group of patients with JIA. The recently introduced functional outcome tests are time-consuming and are in general applicable only to the more severely affected JIA patients. Therefore, this retrospective study presents data on a limited number of patients. Patients were selected on the basis of: (i) disease onset before January 1994; (ii) JIA with regular flares despite treatment with at least one disease-modifying anti-rheumatic drug (DMARD) in addition to non-steroidal anti-inflammatory drugs; and (iii) regular follow-up with at least three complete evaluations. This resulted in 25 patients, 16 females and nine males, 13 with polyarticular and 12 with systemic JIA.

To evaluate outcome, we used tests that are commonly used in our clinic that best reflected the proposed core set of outcome variables. The following tests were selected: the global assessment of arthritis domain of the CHAQ [9], the disability domain of the CHAQ, the Fuch Swelling Index (FSI) [10] and the paediatric Escola Paulista de Medicina Range of Motion Scale (pEPM-ROM) [11]. These tests all have high reliability and validity coefficients [9–11]. The physician’s global assessment, using a semiquantitative Likert scale (non-existing, mild, moderate and severe), was not suitable for analysis in this small group of patients, which was selected for severity. The ESR was extended by other inflammatory parameters: haemoglobin, C-reactive protein, white blood cells and platelets.

We aimed at assessment of a complete set of functional and laboratory parameters for each patient at 6-month intervals (January 1996 to January 1998). Data were collected around January and July to reduce seasonal influences. Differences between the first and fourth measurements were calculated (paired-samples t-test). To analyse longitudinal differences in outcome profiles over time or cross-sectional differences between subgroups, we used linear regression.

All our patients with polyarticular or systemic JIA indicated functional loss as well as discomfort caused by their disease. This is reflected by moderate to severe scores of overall mean CHAQ disability (range 1.0–1.9 on a scale from 0.0 to 3.0) and CHAQ severity (range 0.4–0.9). Laboratory parameters did not show a clear uniform trend over time (Table 1). CHAQ severity,

<table>
<thead>
<tr>
<th>Total population</th>
<th>Systemic JIA</th>
<th>Polyarticular JIA</th>
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<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>Mean 4</strong></td>
<td><strong>Change</strong>&lt;sup&gt;a, b&lt;/sup&gt;</td>
</tr>
<tr>
<td>CHAQ severity</td>
<td>1.39</td>
<td>0.99</td>
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<tr>
<td>CHAQ disability</td>
<td>1.85</td>
<td>1.00</td>
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<tr>
<td>FSI</td>
<td>1.90</td>
<td>1.32</td>
</tr>
<tr>
<td>pEPM-ROM</td>
<td>1.63</td>
<td>1.58</td>
</tr>
<tr>
<td>ESR</td>
<td>11.00</td>
<td>16.15</td>
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</table>

<sup>a</sup>P < 0.05; <sup>**</sup>P < 0.01.

<sup>a</sup>A patient can be considered as improved, according to PRINTO, if he or she shows at least 30% improvement from baseline in three of any six variables in the core set, with no more than one of the remaining variables worsening by more than 30%. Taking PRINTO’s definition strictly, only the polyarticular patients showed significant improvement.

<sup>a</sup>+ = improvement; − = deterioration.
CHAQ disability and the FSI showed statistically significant improvement over time ($P < 0.05$, $P < 0.05$ and $P < 0.01$ respectively) (Table 1). Differences between the polyarticular and systemic patients, longitudinally and cross-sectionally, were not statistically significant.

During the study period, DMARDs were tapered in seven out of 25 patients. The activity of the disease was recorded by the physician at the end of the study period. Eleven patients still had active clinical disease, 13 were clinically in remission with medication and one patient was in remission without medication.

Using PRINTO’s definition of clinical improvement (Table 1), two parameters improved by at least 30%, one by 29% and one worsened by more than 30%, although the clinical relevance of this change in ESR is questionable. When analysed separately, the polyarticular patients just met the criteria of improvement. The polyarticular subgroup showed marked deterioration in joint function, whereas the systemic patients improved slightly.

This study showed that all PRINTO variables available for analysis changed over time. Despite our general impression of improvement of disease activity, the criteria of clinically relevant improvement (of more than 30%) were not met by the group as a whole. If a cut-off value of 20% was used, our group would be described as improved. A change in ESR from 11 to 16 mm/h, although more than 30%, is obviously of no significance clinically. As our patients were selected for disease severity, the observed improvement could be explained by a concept of regression towards the mean.

The retrospective nature of the study does not permit full implementation of the definition of improvement by PRINTO. Future prospective research should confirm this study and could then be a uniform method to describe the response of JIA to treatment.

Analysis of the subgroups showed that the patients with polyarticular disease met the majority of the criteria for improvement of PRINTO. This study showed a more severe functional loss at the start and the end of the study period in the polyarticular patients. The outcome profile of our study is of particular relevance, as joint function is assumed to correlate well with the ability to lead an independent, productive life.

In interpreting improvement over time, it is important to realize that the individual characteristics of outcome parameters, e.g. ESR, can show rapid changes, whereas CHAQ disability is more stable. It seems important to develop outcome parameters that show equal stability over time. We conclude that, under the present treatment, most of the selected patients with sustained JIA showed stabilization or improvement of their disease.

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