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Joint inflammation score – a simple tool for assessment of arthritis activity

Abstract

Objective: To assess validity and elaborate mode of practical application of joint inflammation score (JIS), a new tool for arthritis activity assessment.

Methods: 414 patients with rheumatoid arthritis (RA) followed up during two open trials of leflunomide safety and efficacy was included in the study. Arthritis activity was assessed at baseline and then every 4 weeks. Following parameters were evaluated: tender joint count (TJC), swollen joint count (SJC), patient's global health assessment (GHA), joint pain, morning stiffness duration and erythrocyte sedimentation rate (ESR). DAS 28 was used as a primary outcome measure. Joint inflammation score (JIS) was constructed by integration of three DAS 28 initial parameters – SJC calculated from the results of 28 joints examination, GHA and ESR. JIS is the sum of these three measures. GHA and ESR are not transformed before summation but SJC should be multiplied by 10.

Results: Significant improvement was achieved already after 4 weeks of treatment. Outcome measures continued to improve during 6 months of follow up. There was a significant correlation between DAS 28 and JIS (Pearson correlation 0.87, $p<0.01$). Presence of such correlation allowed us to compare them in pairs to reveal JIS ranges equivalent to high, moderate and low RA activity in DAS 28 assessment so as JIS changes values defining different degrees of improvement.

Conclusion: Scales of JIS values and changes defined in this study allow using this tool in wide clinical practice for assessment of RA activity and treatment efficacy.

Keywords: rheumatoid arthritis, activity, inflammation

Research Article

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Introduction

Rheumatoid arthritis (RA) is a chronic disease that usually causes progressive joint destruction, functional decline and disability. Aggressive and prolonged disease modifying treatment provides the only possibility to reduce RA progression and preserve joint function. But in most cases antirheumatic drugs do not completely stop inflammation and some residual changes usually remain in spite of more or less prominent improvement. Besides the course is quite variable and effect of therapy is often changeable. So a reliable method of monitoring disease activity is urgently needed to assess treatment efficacy and make necessary correction of therapy according to achieved results and severity of inflammation.

But now we have not got a method of RA activity assessment suitable for everyday clinical practice. Chronic inflammation of joints produces different manifestations that to some extent reflect arthritis activity but no single feature can be used as a sufficient index of patient state. Common way of RA activity assessment is based on concurrent evaluation of several parameters. Most significant of them were included in the core set of disease activity measures suggested by the American College of Rheumatology (ACR).[1] It consists of a tender joint count (TJC), swollen joint count (SJC), patient's assessment of pain, patient's and physician's assessment of global disease activity, patient's assessment of physical function and laboratory evaluation of one acute phase reactant.

Different combinations of these parameters for comprehensive assessment of disease activity can be constructed with core data set. Measures included in such combined scores can be analyzed together or as separate parameters. The last principle is utilized in ACR definition of improvement in RA which describes the minimal significant improvement as at least 20% decrease of TJC, SJC and 3 of the 5 remaining ACR core set measures.[3] ACR definition is a common tool for assessment of treatment efficacy but it can not be used for evaluation of degree of disease activity.

Disease activity score (DAS) is a more universal instrument that includes several activity measures and allows to assess as the result of the treatment as current state of the patient. There are several modifications of DAS. The most popular of them is DAS 28 which requires examination of only 28 most representative joints including shoulders, elbows, wrists, metacarpophalangeal joints, proximal interphalangeal joints and the knees.[3] TJC, SJC and patient's general health assessment (GHA) are estimated during examination. One of the acute phase reactants - erythrocyte sedimentation rate (ESR) or C-reactive protein is also included. Values of these measures are summarized after a special transformation.

DAS 28 has been widely used in clinical trials and is considered as a quite reliable index. But its calculation is a rather complex procedure. So it is not suitable for everyday clinical practice and rheumatologists assess RA activity at their own choosing depending mainly on

individual experience. Absence of an appropriate method of arthritis activity assessment does not allow performing reliable monitoring of its changes and significantly hamper choosing of appropriate treatment. We have therefore constructed joint inflammation score (JIS) – a new simple instrument for assessment of arthritis activity. The objective of the present study was to assess validity and elaborate mode of practical application of this tool.

Material and methods

Patients and treatment

The study consisted of two main stages. The first was conducted between November 2001 and November 2002 when in 4 medical centers of Moscow efficacy and safety of leflunomide (LF) was evaluated during 16 weeks of treatment. The drug was provided by the manufacturer and prescribed 100 mg/day during the first 3 days and 20 mg/day thereafter. 75 rheumatologists working in different regions of Russian Federation participated in the second stage of the study that was performed between February 2003 and April 2004. The manufacturer provided LF for the first month of the treatment and later the patients bought it. The drug was administered as during the first stage.

Laboratory evaluation

Patients were evaluated at baseline and then every 4 weeks. Routine laboratory tests such as complete blood count, ESR, liver function tests and urine analysis were performed.

Assessment of RA activity

Arthritis activity was assessed at baseline and then every 4 weeks. Following parameters were evaluated: TJC, SJC, GHA, joint pain on visual analog scale (VAS) and morning stiffness duration. DAS 28 was used as a primary outcome measure.

JIS was constructed on the base of DAS 28. 3 parameters were integrated in it – SJC calculated from the results of examination of 28 joints, GHA and ESR. JIS is the sum of these three measures. GHA and ESR are not transformed before summation but SJC should be multiplied by 10. Such manipulation provides equivalence between value of this parameter and its real clinical significance in comparison to other two measures. So JIS is calculated according to the following formula

$$JIS=10^{*}\,SJC + GHA + ESR$$

Statistical analysis

Association between DAS 28 and JIS was analyzed with Pearson correlation coefficient. Statistical significance of differences was assessed by Student's t test.

Results

During the first stage of the study 200 patients attending 4 Moscow medical centers were included. 196 from them received LF for at least 4 weeks, 192 – 8, 188 – 12, 175 – 16 weeks. At the time of the second stage 214 patients were followed up. 208 from them received the drug for at least 4, 202 – 8, 195 – 12, 188 – 16, 182 – 20 and 174 – 24 weeks. Thus total 414 patients were included (380 female and 34 male aged 16 – 75 years, mean 7,4±7,3 years). 330 of them were positive for rheumatoid factor. Mean duration of treatment with LF was 18,4±5,7 weeks. All patients received non-steroidal anti-inflammatory drugs, 121 were treated with corticosteroids 2,5-20 mg/day equivalent to prednisolone (mean 2,9-4,7 mg/day). During the study LF was withdrawn in 52 patients because of side effects and in 18 due to lack of efficacy.

Significant improvement was achieved already after 4 weeks of treatment. Outcome measures continued to improve during 6 months of follow up (Table 1). DAS 28 significant decrease in comparison with previous value was achieved after 4, 8, 12, 16 and 24 weeks. DAS 28 decrease between 16 and 20 weeks was not statistically significant. TJC showed equivalent changes. JIS significantly decreased after 4, 8, 12, and 16 weeks. So did SJC. Changes of other measures of disease activity were not so evidently associated with mode of decrease of integrated indices. Thus significant improvement of GHA was achieved after 4, 8, 12, 16 and 20 weeks. ESR substantially decreased only after 4 weeks. Later improvement of this parameter was maintained but additional decrease was not achieved. Joint pain significantly improved every 4 weeks and morning stiffness after 4 and 8 weeks of follow up.

Table 1 Changes of activity measures and integrated scores of RA activity during treatment (M±σ)

	Pain (mm on VAS)	Morning stiffness (min.)	TJC	SJC	GHA (mm on VAS)	ESR (mm/hour)	DAS 28	JIS
baseline	59.8 ±22.4	151±193	13.7±6.2	11.1±5.6	58.4±20.1	31.0±14.3	6.08±1.08	203.0±72.5
4 weeks	44.4±22.1*	84±139*	9.9±6.4*	7.5±5.4*	44.6±19.0*	27.1±13.6*	5.04±12.8*	141.6±68.6*
8 weeks	38.5±20.1*	66±130*	7.9±6.1*	5.8±5.0*	39.2±19.1*	27.4±13.6	4.67±1.25*	120.5±64.2*
12 weeks	34.9±21.5*	52±99	6.6±5.6*	4.6±4.7*	36.4±19.7*	26.1±13.0	4.34±1.27*	105.9±60.9*
16 weeks	31.6±20.4*	44±103	5.6±5.3*	4.1±4.3*	32.3±19.2*	25.0±12.5	4.10±1.21*	95.5±56.7*
20 weeks	29.9±19.9*	52±102	5.4±5.2	2.4±3.5	33.1±20.0*	23.8±12.6	3.97±1.25	81.0±52.0
24 weeks	29.1±21.1*	40±97	5.3±4.7*	3.8±4.3	31.7±21.0	24.0±13.2	3.79±1.17*	77.3±54.3

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There was a significant correlation between DAS 28 and JIS (Pearson correlation 0,87, p<0,01). Presence of such correlation allowed us to compare them in pairs to reveal JIS ranges equivalent to high, moderate and low RA activity in DAS 28 assessment. In patients with high RA activity which was defined as DAS 28>5,1 JIS values varied from 69 to 407. In 80% of cases they were higher than 142. In moderate activity characterized by DAS 28 between 3,2 and 5,1 JIS ranged from 17 to 282. 70% of these values were between 61 and 142. In patients with low RA activity (DAS 28<3,2) JIS varied from 7 to 133. In 80% of cases it was lower than 62. This coincidence provides the possibility to define JIS values more than 140 as evidence of high RA activity, JIS between 60 and 140 as moderate and JIS less than 60 as low activity of disease.

The same principle was applied for comparative analysis of both scores changes. According to DAS 28 efficacy assessment three degrees of index decrease are defined which allow to classify clinical improvement considering the corresponding end value of DAS 28: <0,6, 0,6-1,2, >1,2. When DAS 28 decrease in our patients exceeded 1,2 corresponding JIS change varied from increase on 2 to decrease on 337. In 70% of these cases JIS decrease exceeded 99. When DAS 28 diminishment ranged from 0,6 to 1,2 JIS changes varied from increase on 52 to decrease on 172. 70% of these values were between 18 and 97. When DAS 28 improvement was less than 0,6 JIS changes ranged from increase on 161 to decrease on 123. In 70% of cases these values were less than 20. Such results allow us to define three degrees of JIS diminishment: >100, 100-20,<20. Method of treatment efficacy assessment with JIS considering index changes and final degree of disease activity is presented in Table 2.

Table 2 Assessment of treatment efficacy depending on decrease and final value of JIS

JIS final value	JIS decrease		
	>100	20-100	<20
<60	good response	moderate response	no response
60-140	moderate response	moderate response	no response
>140	moderate response	no response	no response

Discussion

At present DAS 28 is the most popular but not the only integrated index suggested to assess activity of RA. ACR core set of disease activity measures was used as the base for construction of several indices developed as alternative to DAS 28. Authors who constructed them tried to make an instrument sufficiently simple and reliable for everyday clinical work. Two main ways were applied in such studies. The first consists of calculation method simplification requiring increase of initial parameters number to provide sufficient reliability.[4] The second supposes rather difficult calculation method but less number of initial measures.[5] As a result tools developed in these works remained too complex to be widely applied in clinical practice.

Developing JIS from DAS 28 we managed significantly simplified as calculation method as initial parameters evaluation. We excluded TJC from the initial data set because its counting is too laborious to be routinely performed and is not usually carried out in everyday work. Yet SJC and state of health assessment so as ESR estimation are common measures of RA activity evaluation in clinical rheumatology. Constructing an integrated score we took into account that values of GHA on VAS and ESR fluctuate in comparable limits while SJC magnitude does not correspond its real clinical significance. Multiplying this parameter by 10 provides conformity of its value with its real significance against the other two measures. Joint inflammation intensity is the deciding factor considered when defining RA activity in practical work and joint swelling is the main sign of active arthritis. So developing JIS we strengthened SJC contribution to the resulting value.

Such construction principle remarkably distinguishes JIS from DAS 28 that largely depends on measures defining by the patients (joint tenderness and GHA). To some extent TJC and GHA provide redundant information so exclusion of one of them may be quite justified. Such a possibility is permitted by the authors of DAS considering GHA as an optional parameter. JIS and DAS 28 are not equivalent to each other because different principles were applied for their development. Nevertheless they show strong correlation in RA activity evaluation on sufficiently large groups of patients. Such concordance allowed us to use DAS 28 for defining JIS ranges corresponding to different degrees of disease activity and different variants of treatment efficacy. Scales of JIS values and changes defined in this study allow using this tool in wide clinical practice for assessment of RA activity and treatment efficacy.

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Conflict of interest

Authors declare there is no conflict of interest in publishing the article.

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