

Intensive management reduced disease activity in rheumatoid arthritis

Grigor C, Capell H, Stirling A, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. *Lancet*. 2004;364:263-9.

QUESTION

In patients with rheumatoid arthritis (RA), is intensive management (IM) more effective than routine care (RC) for reducing disease activity?

METHODS

Design: Randomized controlled trial.

Allocation: Concealed.*

Blinding: Blinded (outcome assessors).*

Follow-up period: 18 months.

Setting: 2 National Health Service teaching hospitals in Glasgow, Scotland, UK.

Patients: 111 patients who were 18 to 75 years of age (mean age 53 y, 70% women) and had RA < 5 years with a disease activity score > 2.4 (1.6 = low disease activity, 2.4 = moderate, and 3.6 = high). Exclusion criteria were previous combination disease-modifying antirheumatic drug (DMARD) treatment or relevant liver, renal, or hematologic disorders.

Intervention: IM ($n = 55$) or RC ($n = 55$). Patients in the IM group began treatment with a new DMARD and were seen monthly by the same rheumatologist for injection of up to 3 swollen joints with triamcinolone acetonide up to 120 mg per visit. After 3 months and at any assessment thereafter, patients with a disease activity score > 2.4 received an escalation of oral therapy according to a protocol for tight control of disease activity. This usually comprised a progression from monotherapy to triple therapy and thereafter to protocols that included cyclo-

sporine or leflunomide. RC-group patients were reviewed every 3 months with no composite measure of disease activity used in clinical decision making. Patients with active synovitis received a DMARD. Corticosteroid intraarticular injections were given as for patients in the IM group.

Outcomes: Decrease in disease activity score and proportion of patients with a good response (European League Against Rheumatism [EULAR] definition: disease activity score < 2.4 and a decrease from baseline of > 1.2). Secondary outcomes were remission rates (EULAR definition: disease activity scores < 1.6), American College of Rheumatology (ACR) response rates, visual analogue pain score, assessor's global assessment of disease activity, Sharp radiologic score, and patient function.

Patient follow-up: 1 patient withdrew after randomization; of 110 patients, 103 (94%)

completed the trial. 110 patients were included in the intention-to-treat analysis.

MAIN RESULTS

IM-group patients had a greater decrease in disease activity score than did RC-group patients (Table). More IM-group patients had a good EULAR response, remission, and an ACR 70 response (Table). IM-group patients also had greater improvements in other measures of disease activity and functional outcome.

CONCLUSION

In patients with rheumatoid arthritis, intensive management reduced disease activity and slowed radiographic progression more than routine care.

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*See Glossary.

Intensive management vs routine care for rheumatoid arthritis at 18 months†

Outcomes	Change from baseline		Difference (95% CI)	
	Intensive management	Routine care	RBI (CI)	NNT (CI)
Disease activity score	-3.5	-1.9	1.6 (1.1 to 2.1)	
	Event rates		RBI (CI)	NNT (CI)
EULAR good response	82%	44%	88% (38 to 166)	3 (2 to 5)
EULAR remission	65%	16%	300% (122 to 658)	3 (2 to 4)
ACR 70 response	71%	18%	290% (126 to 611)	2 (2 to 3)

†EULAR = European League Against Rheumatism; ACR = American College of Rheumatology. Other abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

COMMENTARY

The study by Grigor and colleagues underlines the need for early and aggressive treatment of RA with disease-controlling antirheumatic drugs. It also emphasizes the need to measure treatment effects and to change management as necessary. While rheumatologists are well aware of the need for early treatment, the assumption exists that patients are referred to rheumatologists at an early stage in their disease progression. This, of course, does not always occur.

A new goal in the treatment of RA is achievement of remission, which has been shown to be possible in a large percentage of patients and is confirmed by this study. However, treatment effects are not generally measured and if the goal (remission) is not reached, treatment is often not adjusted according to response.

Routine clinical practice usually implies scheduled 3-monthly visits. In this study, the combination of monthly visits and assessment of disease activity as a guide for modifying treatment led to better outcomes than usual care. However, while a total management concept was tested, it

cannot be determined which of the various interventions prompted the difference (more frequent visits, assessing disease activity, adjusting treatment if remission was not reached, or the formal treatment plan).

Regardless, the total management system is feasible and can be implemented as a whole. It would be interesting to test the addition of intra-articular steroid injections to the protocol, since this intervention is not used by all rheumatologists. Can the same result be achieved by intramuscular/oral steroids or by intensifying the treatment schedule?

The high percentage of patients in remission was reassuring and underscores the efficacy of conventional antirheumatic drugs if offered in a tight management protocol. Slowing of radiographic progression was less striking, but because insufficient detail hindered determining how radiographic assessment was done and what the results were, it is difficult to fully appreciate the meaning of this component of the data set.

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