outcome. Clinical features, in particular uncontrolled hypertension, heavy proteinuria (>1 g/24 h), and recurrent urinary tract infections have an independent and cumulative negative effect on the outcome of pregnancy. Women with moderate to severe disease (stages 3-5) are at highest risk of complications during pregnancy and of an accelerated decline in renal function. Successful management of women with chronic kidney disease during pregnancy requires team work between primary care clinicians, midwives, specialists, and the patient. Frequent monitoring of simple clinical and biochemical features will guide timely expert intervention to achieve optimal pregnancy outcome and conservation of maternal renal function.

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CHANGE PAGE

Patients with suspected rheumatoid arthritis should be referred early to rheumatology

Kimme L Hyrich

ARC Epidemiology Unit, University of Manchester, Manchester M13 9PT
kimme.hyrich@manchester.ac.uk

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Change Page aims to alert clinicians to the immediate need for a change in practice to make it consistent with current evidence. The change must be implementable and must offer therapeutic or diagnostic advantage for a reasonably common clinical problem. Compelling and robust evidence must underpin the proposal for change.

The clinical problem

Rheumatoid arthritis affects 1% of adults and is associated with progressive joint damage and disability and increased mortality. Treatment with disease modifying anti-rheumatic drugs (DMARDs), such as methotrexate, has been shown to reduce the progression of radiologically evident joint damage and improve long term disability. A shift towards starting DMARD treatment as early as possible has therefore occurred. Guidelines recommend that patients should be referred early, ideally within six weeks of the onset of symptoms,[1] and that DMARDs should be started within 12 weeks of onset.[2] However, a recent survey found that only 50% of patients were assessed by a rheumatologist within this time.[3] I propose that patients with suspected rheumatoid arthritis should be referred to rheumatology as soon after first presentation as possible.

Evidence for change

Benefits of early treatment:

A recent meta-analysis of 12 studies (six open label extensions of randomised controlled trials and six observational cohort studies) examined the association between delay to DMARD treatment and radiological progression in patients with early rheumatoid arthritis (<2 years at presentation).[4] The average time between early and delayed treatment was nine months. After a median of three years of observation, patients who received early treatment had 33% less progression than delayed patients.

A second meta-analysis of 14 randomised controlled trials of DMARD treatment in rheumatoid arthritis found that the strongest predictor of improvements in disease activity (according to the American College of Rheumatology definition[5]) was shorter disease duration at start of treatment. The best response was in patients treated within a year of symptom onset.[6]

The very recent PROMPT trial compared methotrexate and placebo in 110 patients with undifferentiated polyarthritis (not yet fulfilling criteria for established rheumatoid arthritis).[7,8] The median disease duration was nine months. The trial concluded that treatment with methotrexate delayed the onset of

Methods

I searched Medline (1950 to May 2007) with the following MeSH headings: "rheumatoid arthritis", "antirheumatic agents", and "treatment outcome", as well as the key words "early" and "delay". In addition, I reviewed bibliographies of identified papers and recent treatment guidelines.

KEY POINTS

Early treatment of rheumatoid arthritis results in better long term outcomes

Patients with suspected rheumatoid arthritis should start treatment with disease modifying anti-rheumatic drugs (DMARDs) as soon as possible, ideally within three months of onset

Most patients with rheumatoid arthritis do not receive DMARD treatment within three months of onset

Delay is probably due to a combination of patient related and physician related factors

rheumatoid arthritis and slowed joint damage in patients with undifferentiated polyarthritis. The results were most pronounced in patients positive for anti-cyclic citrullinated peptide antibodies, a highly specific antibody for rheumatoid arthritis.

How early is early?

Evidence is accumulating that very early rheumatoid arthritis (within the first 12 weeks) may be an immunopathologically distinct phase of disease.[9 10] Thus, a "window of opportunity" may exist within the first 12 weeks of disease, during which introducing DMARDs may have different effects than treatment at a later date, including prevention of erosions and possibly complete switching off of the disease.

Few studies have tested this very early window of opportunity, and these have had methodological limitations. Clinical and radiological outcomes (including higher remission rates) were significantly better at three years among a small observational cohort of 20 patients who started DMARD treatment three months after disease onset (very early) than in the 20 with a median 12 months' disease at start of treatment (early).[11] These findings are very promising, although a larger randomised controlled trial is ideally needed to confirm the observations.

Barriers to change

Only half of all patients with rheumatoid arthritis are first seen by a rheumatologist within three months. A large proportion of this delay undoubtedly occurs before the patient even seeks primary care. However, once contact is made, the challenge for all doctors is recognising early rheumatoid arthritis, for which no specific diagnostic criteria exist. Many patients with inflammatory arthritis will have spontaneous remission. Others may have a partial beneficial response to non-steroidal anti-inflammatory drugs despite ongoing inflammation, which may mask the underlying diagnosis. Rheumatoid arthritis is a clinical diagnosis and is often difficult to diagnose in the early phases. However, improved diagnostic and imaging methods and newer immunological tests, such as for anti-cyclic citrullinated peptide antibodies, may identify patients who will progress to rheumatoid arthritis before more classic findings, such as radiographic erosions and rheumatoid factor, are clinically evident. The benefits of treating most patients with suspected early rheumatoid arthritis would outweigh the risks of drug toxicity for the few who do not have rheumatoid arthritis.

How should we change our practice?

In patients with a suspected inflammatory arthritis (persistent joint swelling in more than one joint, early morning stiffness ≥30 minutes, or involvement of metacarpophalangeal or metatarsophalangeal joints[1]), urgent referral (ideally within six weeks of symptom onset) to rheumatology should be made with a clear indication that inflammatory arthritis (or rheumatoid arthritis) is suspected. This should be done without waiting for the results of tests such as rheumatoid factor and plain radiographs, which are often normal in the early phase of disease. All rheumatologists should make it a priority to see patients with suspected inflammatory arthritis on an urgent basis.

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