Management of rheumatoid arthritis

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Abstract

The management of rheumatoid arthritis (RA) has changed substantially over recent years. The emphases are now on early recognition of persistent synovitis in primary care, rapid referral to specialist services and prompt use of disease-modifying anti-rheumatic drugs (DMARDs). For patients with newly diagnosed active RA, a combination of DMARDs should be offered as first-line treatment as soon as possible. Corticosteroids are often administered in early disease, but their use is not a good long-term strategy for most patients. A multidisciplinary approach is important, and patient education is essential. Tumour necrosis factor-α inhibitors and other biological drugs have had a big impact on the management of RA not responding to conventional DMARDs, but in the UK their use has been restricted by cost to patients with ongoing active disease who have failed to respond to two DMARDs. It is sometimes possible to reduce therapy in patients who are doing well, but whether DMARDs can be safely stopped in all patients in remission is contentious. In the future there will be improvements in early diagnosis and better prognostic markers, and health economic arguments will extend eligibility for biologic drugs so that pharmacological strategies will make remission the rule and not the exception.

Keywords Biologic drugs; diagnosis; disease-modifying anti-rheumatic drugs; management; prognosis; remission; rheumatoid arthritis

Over the past 20 years the management of rheumatoid arthritis (RA) has undergone dramatic changes, based upon an emerging understanding of the pathogenesis and natural history of the disease. Traditionally, RA was diagnosed late in the disease course, the symptoms were treated without addressing the underlying damaging nature of RA, referral to specialist teams was delayed, and drugs that might slow the disease process down (disease-modifying anti-rheumatic drugs [DMARDs]) were introduced after joints had radiologically eroded. These management approaches should now be of historical interest only. However, managing RA still involves many challenges (Table 1).

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What's new?

- Data have emerged to show that early recognition and aggressive intervention for RA make a long-term difference to prognosis
- Biologic therapies have revolutionized the lives of many patients who have failed on conventional DMARDs
- Remission used to be an unachievable aspiration for most patients, whereas nowadays it is a realistic goal

Making an early diagnosis

Much of the joint damage that results in disability begins early in the course of the disease.[1] There is increasing evidence for a 'window of opportunity' in which delays in diagnosis and access to DMARDs might have a profoundly deleterious effect on long-term outcomes.[1] To do nothing will lead inevitably to a painful, functional and structural decline in the great majority of patients. Merely to treat with non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics is inadequate, as these drugs do nothing to slow down the disease process. Although symptom-relieving medication is important, as pain control is the top priority for patients, this has to be combined with drugs that have the potential to prevent disease deterioration. Consequently, early diagnosis of RA is vital to facilitate access early appropriate management.

There is no single clinical, radiological, or serological test that enables a diagnosis of RA to be made with certainty. In patients who present with a dramatic crippling symmetrical peripheral polyarthritis with high levels of inflammation and rheumatoid factor and/or anti-citrullinated peptide/protein antibodies (ACPA) on investigation, there is rarely diagnostic doubt, and both patient and clinician will see aggressive intervention as a high priority. The greater challenge is in patients with an insidious onset of symptoms, with no dramatic evidence of synovitis, and investigations showing no abnormalities. The diagnosis of early RA is largely a clinical skill, with a suggestive history combined with evidence of early symmetrical small joint synovitis (e.g. metacarpophalangeal joints). All patients with early RA need to know they are in capable hands and to understand the rationale behind introducing powerful drugs promptly and in combination for active disease. A patient with normal investigations may still require urgent DMARDs on the basis of an expert history and examination.

The National Institute for Health and Care Excellence (NICE) has published its guidance on referral to specialist rheumatology services of any person with suspected persistent synovitis of undetermined cause.[2] This stated that in patients with particular manifestations of inflammatory arthritis (persistent joint swelling in more than one joint, or involvement of hand or feet joints, or a delay of 3 months or longer between onset of symptoms and seeking medical advice), urgent referral to rheumatology should be made. This should be done without waiting for the results of tests, such as rheumatoid factor and X-ray, which are often normal in the early phase of disease.

The challenges of managing RA

- Raising public awareness of inflammatory arthritis so that patients present early to their GP
- Educating GPs to refer appropriate patients early
- Making an early diagnosis
- Differentiating those patients who will do well from those who will do badly
- Regular and intense follow-up of early RA patients, with rapid and sustained suppression of disease activity
- Deciding on the best combination of symptom-treating and disease-modifying drugs
- Making best use of corticosteroids throughout the course of the disease
- Educating patients about their disease so that they are more in control
- Involving the multidisciplinary team early and throughout the course of the disease to assess the impact of RA on the person's life and intervene appropriately
- Monitoring the response to treatment
- Deciding on how to modify therapy in those patients who are not responding satisfactorily to therapy
- Determining the best time to introduce biological therapies
- Deciding on when to cut down or withdraw treatment in patients who are doing well
- Providing a structured annual review to assess formally the impact of the disease on the musculoskeletal system, other comorbidities, and all aspects of the patient's life

Table 1

Present and potential future ways of predicting poor prognosis disease

Clinical	Number of peripheral joints involved (particularly MCPs and MTPs)
	Symmetrical distribution of synovitis
	Insidious onset rather than explosive disease
	Female gender
	High level of disability at the onset
	Tobacco smoking
	Obesity
Blood tests	High ESR or CRP
	Normochromic normocytic anaemia
	High titres of rheumatoid factor
	High titres of ACPA
Radiology	Early erosive damage on X-rays
	Ultrasound and MRI scans showing cartilage and subchondral bone damage long before conventional X-rays[a]
Genetic tests	HLA-DRB1 typing to detect the presence of the 'shared epitope'[a]
	Other prognostic genetic tests[a]

ACPA, anti-citrullinated peptide antibodies; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MCP, metacarpophalangeal; MRI, magnetic resonance imaging; MTP, metatarsophalangeal.
[a] Potential future approaches.

Table 2

Deciding what therapeutic approach to use in each patient

The main objectives in management of early RA are to induce remission by commencing treatment early in the disease, and to treat intensively with regular monitoring of disease activity.[2] There is more evidence for how to treat active, rather than milder, forms of RA. Some patients may respond to a single DMARD,[3] while those with poor prognosis disease may need early aggressive combination drug strategies.[4–8] The NICE guidelines on RA management[2] recommend that for patients with newly diagnosed active RA, a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids) should be offered as first-line treatment as soon as possible, ideally within 3 months of the onset of persistent symptoms. The NICE guideline also states that for patients with newly diagnosed RA for whom combination DMARD therapy is not appropriate, DMARD monotherapy should be started, placing greater emphasis on fast escalation to a clinically effective dose rather than on the choice of DMARD. Clinical features and tests that help to determine prognosis are summarized in Table 2. The commonly used conventional drugs and their monitoring requirements are summarized in Table 3. A change in DMARD is warranted if toxicity occurs or no benefit accrues. Methotrexate is now the most commonly used DMARD with a high rate of sustained response[9,10] and the risk of toxicity is reduced by the coprescription of folic acid. Parenteral administration of methotrexate has been shown to be effective in over half of patients failing to respond to, or not tolerating, oral therapy.[9,10]

Using corticosteroids optimally in the course of the disease

Glucocorticoids may be used in the initial phase of the disease, as rescue therapy for disease flares, and occasionally in long-term management.[11] Unlike NSAIDs, there is good evidence to show that corticosteroids slow down the course of the disease.[11,12] Over the short term they exert a profound effect on the symptoms of RA, but as a single agent they have limitations, with diminishing returns on symptom control over time. The adverse consequences of long-term corticosteroids are also well documented, with even low-dose therapy often resulting in eventual osteoporosis and increased rates of infection.[13]

The following rules should be applied to using corticosteroids throughout the course of a patient's RA.

- In early disease, corticosteroids can suppress inflammation rapidly without having to wait for DMARDs to become efficacious.
- The most satisfactory method is to inject them straight into an inflamed joint. This usually results in rapid symptom relief, but is of limited benefit if the patient has an active polyarthritis.
- In a patient with active polyarthritis, an intramuscular injection (e.g. methylprednisolone 80—120 mg or triamcinolone acetonide 80—120 mg) may help symptoms while waiting for the benefits of DMARDs to evolve over the ensuing weeks.

There have been studies that use high-dose oral tapering regimens or intramuscular corticosteroids to control early active disease, yet no trial has demonstrated superiority of either regimen over the other in terms of efficacy or lack of adverse