Editorial

Current treatment for Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic, inflammatory chronic disease affecting approximately 0.5% of the population in the world. RA is commonly occurs in women at any age, with peak incidence at ages 50 to 60 years. The mainly prominent feature is symmetrical joint swelling in feet, hands and knees. RA is a clinical syndrome encompassing numerous disease subsets, each concerning inflammatory cascades that usually lead to joint and organ damage if left untreated. The diagnosis is made upon a pattern of symptoms and physical examination findings, with and often without any radiographic or serologic abnormalities. Although progressive disability and a shortened lifespan were seen in the past, the outlook has improved substantially over the past 2 decades. These improvements are the result of earlier diagnosis, aggressive proactive (rather than reactive) treatment, widespread use of methotrexate, availability of biological agents, and perhaps a secular trend to milder disease (Van Nies et al., 2010).

Diagnosis

Rheumatoid arthritis should be considered in any patient with joint pain and swelling for more than a few weeks. The joint pain of RA is typically polyarticular and symmetrical, but may be pauciarticular (involving 2 to 4 joints) or even monoarticular at onset. In general, the distal interphalangeal joints are not involved. Although not specific for RA, morning stiffness that improves through the day, in the presence of symmetrical joint swelling, is characteristic of RA. Patients with synovitis and symptoms for more than 6 weeks are more likely to develop progressive disease versus a self-limited process (Aletaha et al., 2010; Thabet et al., 2009). Physical examination reveals softtissue swelling due to synovitis, fluid, or both, which, when severe, is obvious on inspection and palpation. However, mild joint swelling may be subtle and difficult to recognize, particularly in obese patients. Patients with long-standing, inadequately treated RA historically developed joint damage and deformities, including characteristic ulnar deviation, swan neck, and boutonniere deformities of the hands, and flexion contractures of the knees and elbows. These "classical" findings of RA fortunately are now far less common, because of preventive (rather than reactive) therapeutic strategies and better medications. Rheumatoid arthritis is a multi system disease, and may present with or be complicated by extraarticular manifestations.

Radiographic changes are not required to establish a diagnosis or initiate therapy for RA. Indeed, the goal of treatment at this time is to prevent radiographic changes. Rheumatoid arthritis may be diagnosed in many patients whose radiographs are normal or reveal only juxtaarticular osteopenia in the hands or feet. Classical radiographic findings include juxtaarticular osteopenia, joint-space narrowing, and. In early arthritis, these changes typically occur in the feet before the hands. More erosive joints are present in persons who are likely to develop RA rather than self-limited polyarthritis, but the predictive value of a single erosion is limited (Visser et al., 2009).

Ultrasonography and magnetic resonance imaging (MRI) have greater sensitivity than plain radiographs for the detection of soft-tissue synovitis before joint damage, but with lower specificity. However, their role in usual clinical care remains to be further characterized. The absence of synovitis by ultrasonography or MRI in a patient with a positive rheumatoid factor or ACPA test result may suggest the absence of a progressive inflammatory arthritis. It may be reasonable to obtain baseline radiographs of the feet and hands.

Drug therapy in RA

Pharmacologic treatment of RA should be directed at tight control of inflammation toward low disease activity and remission. A proactive, preventive (rather than reactive) strategy is required.

Methotrexate is an anchor drug for treatment of RA, because it is better more effective, more tolerated and less cause adverse effects than other disease modifying anti-rheumatic drugs (DMARDs). Biological mediators suggest new options for targeted therapies in patients with scarce responses to oral DMARDs. Non-steroidal anti-inflammatory drugs (NSAIDs) are not necessary therapy and are usually used as needed for pain relief. The older approach of "step-up" therapy, in which NSAIDs were used with DMARDs used later only if response is inadequate, is inferior to the early initiation of DMARD therapy.

*Address for Corresponding Author:
Dr Santram Lodhi
Guru Ramdas Khalsa Institute of Science and Technology (Pharmacy), Jabalpur, M.P., India
Email: srlodhi78@gmail.com

Applications of DMARDs for RA

Methotrexate

Methotrexate is the appropriate first-line agent for most patients with RA (Van der Heijde et al., 2006). Low-dose methotrexate has anti-inflammatory effects, rather than the antimetabolite effects seen at higher doses used to treat neoplastic diseases (Pincus et al., 1992). For RA, methotrexate at low doses (≤25 mg/wk) does not usually lower leukocyte or platelet counts, and almost all patients seem to benefit from an anti-inflammatory effect. About half of all patients have little or no radiographic progression, although 20% to 30% require biological agents to control radiographic progression. Methotrexate at 10 mg/wk or more is tolerated by 70% to 80% of patients. Patients intolerant to these doses are often treated by rheumatologists with the maximum tolerated dose, even 5 or 2.5 mg. Long-term treatment with metho -trexate is safe for most patients with RA. Methotrexate therapy is far more likely to be continued 5 years after its initiation than any other DMARD (Yazici et al., 2005) (50% to 80% of courses over 5 years compared with 10% to 30% of courses of all other DMARDs).

Methotrexate therapy may be continued even when liver enzymes are elevated 2- to 3-fold above normal, as long as frequent monitoring is performed and, at times, the dose is lowered. Liver function often returns to normal levels when the dose is lowered; it may also normalize in some patients without a change in dose, suggesting probable intercurrent infection or the effects of other medications. Liver biopsy is not required before initiating methotrexate therapy for RA except when preexisting liver disease is suspected. In the experience of most rheumatologists, alcohol consumption need not be absolutely prohibited in patients taking methotrexate at the doses used to treat RA (Haagsma et al., 1997). Moderate alcohol consumption (≤ 2 drinks/d) may be allowed in the absence of other contraindications.

Hydroxychloroquine

Hydroxychloroquine is used in some patients, particularly those with a positive antinuclear antibody, negative anti-CCP, and negative rheumatoid factor test results, who may overlap clinically with patients meeting criteria for systemic lupus erythematosus. Hydroxychloroquine alone rarely leads to adequate control of symptoms, but often is used in combination with methotrexate, initiated simultaneously or as add-on therapy in patients with incomplete response to methotrexate.

Sulfasalazine

Sulfasalazine, designed to combine an aspirin-like drug and an antimicrobial in the belief that RA was an infectious disease, includes salicylate and sulfa moieties. In clinical trials, sulfasalazine may have efficacy equal to methotrexate, 10 to 15 mg/wk over 1 year (Maillefert et al., 2003), but is far less effective over 5 years, particularly compared with methotrexate, 20 to 25 mg/wk (O'Dell et al., 1996). Triple therapy with hydroxychloroquine, sulfasalazine, and methotrexate may be beneficial in some patients compared with methotrexate alone (Van Vollenhoven et al., 2009). Nonetheless, responses vary significantly, and reliable means of identifying the best regimen for each patient with RA are not available. Addition of hydroxychloroquine and sulfasalazine may be considered in patients with inadequate responses to methotrexate, although addition of a biological agent seems more effective (Strand et al., 1999).

Leflunomide and cyclosporine

Leflunomide is not as well-tolerated as methotrexate in most patients, but has similar efficacy in clinical trials (Stein et al., 1994). Leflunomide is an option in patients who have adverse effects or poor efficacy with methotrexate, although biological agents are used more often in this setting. Cyclosporine can be used to treat acute disease flares, but is limited for long-term use by renal toxicity (Van den Borne et al., 1999; Tanner et al., 1990).

Role of NSAIDs in RA

In patients with RA, NSAIDs are now used primarily for controlling pain. They are not believed to have disease-modifying properties, such as the prevention of joint destruction. They are used by approximately half of patients with RA, sometimes regularly but often on an as-needed basis.

Although some patients with RA report diet as an important factor in improving or worsening their clinical status, no evidence supports specific dietary recommendations, vitamin supplements, or complementary–alternative therapies for all patients with RA.

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