Treatment of rheumatoid arthritis and ankylosing spondylitis

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ABSTRACT

The treatment of the two most frequent inflammatory rheumatic diseases rheumatoid arthritis (RA) and ankylosing spondylitis (AS) has some similarities but in total more differences. Thus, therapy with non-steroidal anti-inflammatory agents (NSAIDs), conventional disease modifying anti-rheumatic drugs (DMARDs) and biologic agents has a different role in the management and different efficacy in AS and RA. This implies signs and symptoms, function, and structural damage. This is in part due to the different pathogenesis: (i) while the synovium is an important target in RA it is rather the bone in AS and (ii) while the pathology in RA is rather osteodestructive to cartilage and bone presenting with erosions, it is predominantly osteoproliferative in AS as indicated by syndesmophytes and ankylosis. Biologic agents targeting tumor necrosis factor (TNF-α) work clinically well in both diseases but, while they clearly inhibit structural damage in RA, they do not seem to have much influence on new bone formation in AS. DMARDs are efficacious in RA but less so in AS. NSAIDs are efficacious in both RA and AS, but they are considered first line of therapy in AS while they are rather adjunctive agents in RA. In AS, NSAIDs, potentially especially coxibs, may even prevent new bone formation due to their inhibitory effect on cyclooxygenase-2.

The motivation for this supplement originated from (i) the fascinating history of rheumatology and how the increasing knowledge about the two most frequent inflammatory rheumatic diseases rheumatoid arthritis (RA) and ankylosing spondylitis (AS) finally led to a clear separation after they had been considered one disease for quite some time. Indeed, the main differences in epidemiology and clinical picture are well established by now, and (ii) there is the recent experience that anti-TNF therapy, although clearly efficacious for both diseases, works differently in RA and AS: on the one hand TNF blockers are clinically even more effective in spondyloarthritides (SpA) than in RA, but on the other hand, they clearly inhibit structural damage (erosions) in RA but they do not seem to have major influence on new bone formation in AS.

All these points and more are very well illustrated and discussed in this supplement. This article is an introduction to the section on treatment of RA and AS, and provides a short overview on the different interventions.

The treatment of inflammatory rheumatic diseases is based on pharmacological and non-pharmacological therapies. Both of these may have a curative, rehabilative and even preventive character and aim at the improvement of pain, inflammation (disease activity), global health and quality of life, the amelioration and maintenance of function and structure – on both an individual and a society basis which implies utility and other socioeconomic aspects of disease. Among the non- pharmacological interventions physiotherapy and rehabilitation are essential and of major importance for patients with musculoskeletal and rheumatic diseases (1, 2).

The major pharmacological therapies in rheumatology are listed in Table I.

The role of these various drugs used in rheumatology is different for RA and AS. While non-steroidal anti-inflammatory agents (NSAIDs) are considered first line of therapy in AS with proven efficacy on clinical symptoms (3-5) and a possible disease modifying effect (6) with inhibition of new bone formation, their role in the treatment of RA is not well defined.

For systemic corticosteroids it is the other way around: they have a rather established role in RA (7, 8) but virtually none in AS. The situation is different for intraarticular injection therapy (9) which seems to work independent of the diagnosis and the origin of the inflammation. Some studies even indicate that intraar-

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Table I. Pharmacological therapies for rheumatic diseases.

1. Non-steroidal anti-inflammatory agents
2. Corticosteroids
3. Disease modifying anti-rheumatic drugs
4. Biologics
5. Analgetics

Table II. Disease modifying anti-rheumatic drugs.

- Methotrexate
- Leflunomide
- Sulfasalazine
- Hydroxychloroquine
- Gold
- Cyclosporine

Table III.

Biologics
- Anti-TNF agents
  - Etanercept
  - Infliximab
  - Adalimumab
  - Golimumab
  - Certolizumab
- Anti-IL-1 agents
- Anakinra
- Canakinumab

Anti-IL6 agents
- Tocilizumab

Anti Il12/IL-23 agents
- Ustekinumab

Anti-IL17 agents
- No agent approved

Anti T-cell activity
- Abatacept

Anti B-cell activity
- Rituximab

ticular steroids are also in patients with bone marrow oedema equivalents (10, seen by magnetic resonance imaging).

The role of conventional disease modifying anti-rheumatic drugs (DMARDs, Table II) is established in RA where several agents such as methotrexate (11) are available. In contrast, no DMARD is approved for AS but there might be some very limited efficacy of sulfasalazine and methotrexate, in early disease and for peripheral arthritis (12).

The combination of DMARDs and the use of treatment strategies (tight control, step up *vs*. step down, etc.) has been extensively studied in RA (9, 13) but not in AS.

Biologics (Table III) have been shown to be very efficacious in RA (14, 15) and also in AS (16) but for AS this is only true for the TNF-blockers. Other biologics such as rituximab, abatacept, or tocilizumab have not yet been tested in AS.

Anti-TNF agents may work even better in AS and other SpA than for RA (17, 18). However, while an inhibition of structural damage has been clearly demonstrated for TNF blockers in RA (19, osteodestructive lesions) this has not been shown in AS (osteoproliferative lesions) so far (20).

There is no difference for analgesics which are used to treat symptoms that are not related to inflammation but due to primary (comorbidity) and secondary degenerative changes.

In conclusion, there are clear differences in the treatment of RA and AS. This is subject to intensive review and detailed discussion in this supplement.

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