Review Article

GENERAL PRINCIPLES FOR THE TREATMENT OF EARLY RHEUMATOID ARTHRITIS

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ABSTRACT

The main goals of the treatment of a patient with rheumatoid arthritis (RA) are: reducing pain, joint swelling and constitutional symptoms such as fatigue; improving joint function; stopping progression of bone-cartilage damage; preventing disabilities; and reducing morbidity and mortality. In recent years, the therapeutic concept of early RA (first 12 months of symptoms) has undergone major changes. Three aspects in particular have become the basis of the new treatment paradigm: early diagnosis, immediate beginning of Disease Modifying Antirheumatic Drugs therapy (DMARD) and strict control of the inflammatory activity. In this article, the authors review the general principles of management of patients with early RA.

Key words: Arthritis rheumatoid. Therapeutics. Biological therapy.

Introduction

The objective of RA treatment must always be guided by the search for minimal disease activity or remission, whose definition is controversial. Remission would be the only way to prevent the evolution to erosive and potentially deforming forms. Detecting the parameters that may indicate activity and prognosis of the disease is, therefore, of vital importance for the conduction of an adequate treatment.[1]

The main objectives of the treatment of an RA patient are: reducing pain, joint swelling and constitutional symptoms such as fatigue; improving joint function; stopping progression of bone-cartilage damage; preventing disabilities; and reducing morbidity and mortality.[2]

In the last years, the therapeutic concept of early RA (first 12 months of the symptoms) has undergone great changes.[3] Three aspects in particular came to be the basis of the new paradigm for treatment: early diagnosis, immediate onset of Disease Modifying Antirheumatic Drugs therapy (DMARD) and strict control of the inflammatory activity.[4]

Acknowledgement of diagnosis importance and early treatment for RA

Once most of erosive lesions establish themselves in the first years of the disease, acknowledging and adequate treatment in this phase may prevent or slow down the disease's progression.[5]

It is established that patients treated with DMARD in the first weeks of the disease present a better evolution than those who initiate the treatment later.[6]

The concept of 'window of opportunity' emphasizes the need of immediate use of DMARD, associated to corticosteroids, aiming at the early control of the intra-articular inflammatory process, prevention of *pannus* formation and destruction of the damaged articulation.[7]

Importance of risk stratification and evolution to severe forms

There are different subgroups and subpopulations of patients with RA that will evolve in a diverse manner, with higher or lower severity. Today there is the attempt of establishing stratification models in order to treat the patient with a worst prognosis more agressively.[7]

Change in the form of prescription of therapeutic schemes

The old pyramid (sequential use of antiinflammatories, slow-action drugs and immune-suppressive drugs) was replaced by the combined therapy of multiple DMARDs, since diagnosis. This approach prevents the patient with a more severe condition (presenting erosive potential) from long periods without receiving proper treatment.[8]

Use of new therapeutic agents, including biological response modifiers

One of the most impressive of recent advances in terms of RA therapy was the development of biological response modifiers (biological agents). Although these drugs seem now the most effective medications for controlling RA, long term safety studies are still necessary. The use of biological agents as first therapeutic option in early RA, although already assessed in some studies, is rather controversial.[9]

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Currently the more widely used biological agents are tumor necrosis factor (TNF) antagonists. TNF is a potent inflammatory cytokine expressed in big amounts in synovial serum and liquid of individuals with RA. It promotes the release of other inflammatory cytokines, particularly interleukins (IL) IL-1, IL-6, and IL-8 and stimulates the production of proteases. The inhibition of this cytokine has proved to be an effective and quick way of controlling the disease activity.[10-12] Three anti-TNF drugs are available for clinical use: infliximab (chimerical anti-TNF monoclonal antibody - human/murine)[13], etanercept (fusion protein composed by the TNF soluble receptor region Fc of the IgC)[14] and adalimumab (human antibody against TNF).[15]

Other biological therapies being used include the IL-1 receptor antagonist (anakinra)[16], anti-lymphocytes B - anti-CD20 antibodies (rituximab)[17-19], inhibitors of costimulatory molecules, as CTLA4-IgG fusion proteins (abatacept)[20-22] and anticytokines, as the interleukin-6 soluble antireceptor antibody (tocilizumab).[23-25]

All the biological agents are effective in controlling articular manifestation and hindering the disease's radiological progression, although there may be a therapeutic failure, especially with continuous treatment, in as much as 30 to 40% of the patients. A biological agent's failure does not necessarily predict the absence of response to other drug of the same class, and the attempt of a new drug after the failure of the first is acceptable.[9]

The possible occurrence of multiple adverse effects, above all a higher susceptibility to various infections, including, in some cases, tuberculosis[26], should be carefully assessed.

Another factor to be considered, especially in our milieu, is the high cost of these medications. More analyses of drug-economy, including cost-effectiveness, cost-utility, and cost-benefit of these therapy are needed, moreover in the early phases of the disease.[27]

Conclusion

There is no formal consensus on the sequence of introduction of medications in early RA, varying according to the severity of the case and the response obtained. The Update on the Brazilian Consensus for the Diagnosis and Treatment of Rheumatoid Arthritis recommends that the choice and chronology of the biological agent to be prescribed be individualized, following the physician's criterion.[28]

In short, the very early use of effective DMARDs is a key-issue in the treatment of patients with the risk of developing persistent and erosive arthritis. Intensive treatment in an early phase of the disease, such as the combination of DMARD with steroids or even biological therapies, may induce high rates of remission and control radiological progression.[29]

This aggressive approach responds for a better prognosis than monotherapy with DMARD in early RA, and it must be considered very early for these patients. Besides that, strict monitoring of the disease activity, radiographical progression and prognosis assessment are mandatory, with the finality of adapting the therapeutic strategy whenever necessary.

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