Established criteria for disease controlling drugs in ankylosing spondylitis

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The ASAS recommendations for the initiation of DC-ART in AS are a good start

Ankylosing spondylitis (AS) is primarily an inflammatory arthritis of the back, affecting the sacroiliac and apophyseal joints. The age of onset is usually late teens with men being affected nine times more than women. Onset is gradual with pain and stiffness in the low back, characteristically at night or early morning. The natural history of AS is progression to affect the whole spine, resulting in spinal deformities. These include flattening of the lumbar lordosis, kyphosis of the thoracic spine, and hyperextension of the cervical spine, with eventual flexion contractures of the hips and knees and significant morbidity and disability. These clinical features are mirrored by the radiological changes of syndesmophytes and ankylosis of the spine as well as erosive changes, sclerosis, and eventual ankylosis of the sacroiliac joints.

Peripheral arthritis occurs uncommonly in AS, and when it occurs, it is usually late in the course of the arthritis. The development of peripheral arthritis early in the course of the disease is a predictor of disease progression. The arthritis usually presents in the lower extremities in an asymmetric distribution. Involvement of the “axial” joints, including shoulders and hips, is more common than involvement of more distal joints. In the shoulder, there may be a unique lesion of erosion at insertion of the rotator cuff. In the hips, progression deformity and eventual destruction of the joint may occur. In addition, enthesitis, or inflammation at sites of tendon insertion into bone, is common, affecting primarily plantar fascia and Achilles tendon insertion. The disease is often complicated by the presence of iritis (particularly anterior uveitis), cardiac manifestations (including dilatation of the root of the aorta and conduction defects), fibrosis of the upper lobes of the lungs, cauda equina syndrome (which results from multiple thecal diverticulae or dilated lumbar sacs), and later in the course of the disease, amyloidosis.

Longitudinal studies in patients with AS have shown that the deformities and disability occur within the first 10 years of disease. Survival is reduced among patients with AS compared with the general population, with a relative risk of 1.93. Causes of death include heart disease, cerebrovascular disease, malignancy, renal failure, pneumonia, and miscellaneous. Thus AS is not a benign condition.

TREATMENT IN AS

Treatment in AS is directed primarily at symptom relief—that is, control of pain and stiffness. The mainstay of treatment in AS is exercise to alleviate stiffness and maintain mobility, and non-steroidal anti-inflammatory drugs (NSAIDs) to control the inflammatory symptoms. Although there is some evidence that exercises work to relieve symptoms of AS, there is no evidence that progression of deformity and disability are slowed down. In the short term NSAIDs have been shown to improve pain and range of movement, but there is no evidence that they possess disease modifying effect.

“NSAIDs improve pain and range of movement but do not modify the disease”

Moreover, a proportion of patients with AS do not respond to these conservative measures and have a protracted course, which results in deformity and disability. Sulfasalazine has been used as a disease controlling agent with benefit in some trials, but the most recent and largest trial failed to demonstrate improvement in the spinal disease. Evidence for the efficacy of other systemic drugs, including methotrexate, corticosteroids, o-penicillamine, azuranofin, and azathioprine, is inconclusive.

NEW BIOLOGICAL TREATMENTS

The advent of biological treatment has provided promise for patients with AS. Recent studies have shown that anti-TNF agents alleviate both symptoms and signs of inflammation in patients with AS. Indeed, in AS, biological treatment may be considered to be the first line treatment after NSAIDs. Although these drugs appear relatively safe in the short term, there is concern about their long term toxicity. Moreover, these drugs are expensive, and indeed unavailable in some countries. Therefore, criteria for the judicious use of such treatment in patients with AS are necessary so that treatment is provided to appropriate patients.
considered for DC-ART. The list of 128 items relating to peripheral arthritis and 99 to axial disease were assigned to domains, which were subsequently reduced in a second round and identified as domains relevant to peripheral arthritis, axial disease, and enthesitis. In the third phase specific instruments to define the domains were identified, and finally, the group formulated the ASAS preliminary recommendations for considering initiation of DC-ART, particularly anti-TNF agents in AS.

“Recommendations for starting disease controlling antirheumatic treatment were developed by a three stage Delphi process”

These recommendations include lack of response to NSAIDs, and provide specific methods for evaluating persistent disease activity related to spinal disease, peripheral disease, and enthesitis. Both sets of recommendations for instituting DC-ART in AS require lack of efficacy to NSAIDs. This is clearly based on evidence that NSAIDs do work for symptom relief, but NSAIDs do work for symptom relief in almost half the patients. However, while the Canadian proposal leaves the decision about the use of anti-TNF agents to the doctor and patient, the ASAS proposal provides specific measures to ascertain the need for these drugs. It certainly would be easier for patients to ascertain the need for these agents to the doctor and patient, the ASAS proposal provides specific methods for evaluating persistent disease activity related to spinal disease, peripheral disease, and enthesitis. In the third phase specific instruments to define the domains were identified, and finally, the group formulated the ASAS preliminary recommendations for considering initiation of DC-ART, particularly anti-TNF agents in AS.

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