Anti-TNF-α therapy in Pain Management of Ankylosing Spondylitis

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Ankylosing spondylitis (AS) is a chronic inflammatory disease affecting the axial skeleton, peripheral joints and the entheses. It is characterized by inflammatory back pain and stiffness. In the later stage of the disease, radiographic sacroiliitis and spondylitis can be seen. Although other systemic manifestations, such as uveitis, may be the presenting condition, back pain is usually the major symptoms that result in significant disability and psychological stress.

A century ago, salicylates and opiates had been used to treat ankylosing spondylitis for their analgesic properties. In 1920s, radiation therapy was used with good result but discontinued due to its serious long term side effects. In 1940s, NSAIDs was introduced. Thereafter, different generations of NSAIDs have been developed. NSAIDs are very effective in reducing inflammatory back pain. In the following years, DMARDs were introduced, which include sulphasalazine and various immunosuppressive agents. While these agents are effective in rheumatoid arthritis, they are much less effective in AS.

The development of biologic therapy revolutionize the management of AS. The demonstration of good or very good efficacy of TNF blockers marked a breakthrough in the management of AS. Biopsies have confirmed the presence of abundant TNF-α mRNA in the inflamed sacroiliac joints. 1 In fact, TNF-α is one of the pro-inflammatory cytokines produced by monocytes, macrophages and activated T cells and is an important mediator in the inflammation in rheumatic diseases. Today, there are several TNF-α inhibitors available in the market, namely Infliximab, Etanercept and Adalimumab. They are administrated intravenously or subcutaneously. Although there is no head-to-head comparison study, current data suggest that these TNF-α inhibitors have similar efficacy.

In assessing the clinical efficacy of these agents in ankylosing spondylitis, a tool named “ASAS” is employed. It is designed by the Assessment of SpondyloArthritis international Society (ASAS). ASAS is widely used in both clinical trials and daily practice. There are four domains in the ASAS assessment tool, namely back pain, function, inflammation and patient global assessment. ASAS20 refer to 20 percent improvement in any three of the four domains.

In one of the landmark studies with Infliximab, it was demonstrated that after 24 weeks of treatment 123 of 201 patients (61.2%) in the infliximab group achieved ASAS20 response compared to 15 of 78 patients (19.2%) in the placebo group (P <0.001).2 The clinical effect was evident two weeks after the first infusion of Infliximab. Night pain, one of the four domains in the composite ASAS score, significantly improved in the treatment arm. Mean change in the visual analogue scale was -2.9 (-5.6,-0.8) in infliximab group versus -0.3 (-1.7, 0.9) in placebo group (P<0.001).

Similar clinical efficacy was demonstrated among different anti-TNF-α agents. At week 12 of trials, patients treated with the anti-TNF-α agents were 3.6-fold more likely, compared with those treated with placebo, to achieve 50 percent improvement.3 Approximately 80 percent of patients with AS responded to treatment with one of these agents and approximately one half attained at least 50 percent improvement in the composite index.4

Anti-TNF-α agents now become the treatment of choice for active AS patients who failed the NSAIDs therapy. It is an effective treatment to control inflammatory back pain and disease activity. The current international consensus is that any active patients (defined by BASDAI >=4) with axial spondyloarthropathy (traditionally termed ankylosing spondylitis) who do not respond to two NSAIDs for 4 weeks should consider anti-TNF-α therapy. BASDAI refers to Bath Ankylosing Spondylitis Disease Activity Index. It is a validated diagnostic test which allows rheumatologists to determine the disease activity by assessing patients' fatigue, spinal pain, joint pain or swelling, enthesitis, inflammation of tendons and ligaments, morning stiffness duration and severity.5

Currently, anti-TNF agents are non-standard drugs under Hospital Authority Drug Formulary. In the public setting, these drugs are prescribed as “self-financed items”. Patients who have financial difficulty will be subsidized by the Samaritan Fund. As of June 2011, 325 patients with ankylosing spondylitis have received anti-TNF treatment in Hong Kong, according to the Hong Kong Society of Rheumatology Biologics Registry.6

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