Traditional Schemes for Treatment of Psoriatic Arthritis

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ABSTRACT. Prior to the availability of biologic agents such as anti-tumor necrosis factor (TNF), traditional treatment schemes for psoriatic arthritis were not extensively evaluated. While it appears that the newer forms of treatment are more effective, conventional agents still need to be scrutinized with similar methodology and will still have a role in those patients with less progressive disease, in combination with biologic agents, and in patients where biologics are not tolerated or have failed. (J Rheumatol 2009;36 Suppl 83:49-51; doi:10.3899/jrheum.090224)

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The availability of biologic treatments has been a major advance in the treatment of psoriatic disease, and has unearthed the need to develop better mechanisms for measuring activity and progression of disease and response to effective treatment. It has also put the use of traditional treatment schemes into a new perspective, where prolonged use of conventional agents in patients with severely active disease is no longer acceptable without good reason. However, some traditional agents may not have had the advantage of large scale clinical studies afforded to biologic therapies. Therefore, there will remain a need to evaluate the role of traditional treatments, for instance in those patients with a milder course of disease, alongside or in combination with biologic treatments, and in those patients who have failed biologics or for whom biologic treatments are unacceptable.

The evidence base for traditional treatment schemes in psoriatic arthritis (PsA) has been the subject of several recent reviews[1-4]. Here, the evidence that has been compiled using the appropriate methods for literature review, evidence weighting, and treatment recommendations is briefly summarized. The summary is confined to conventional treatments for PsA, including peripheral arthritis[5], axial disease[6], enthesopathy[7], and dactylitis[8]. More detailed accounts of outcome methods used and of methodology have been published[5-8]. There have been some recent studies that are described in more detail[9-12], in which the need to evaluate traditional agents more fully is underlined.

Nonsteroidal antiinflammatory agents. Nonsteroidal antiinflammatory drugs (NSAID), often used as first choice agents, provide symptomatic relief[13-16]. Continued use in ankylosing spondylitis may slow radiological progression[17]. NSAID have ocasionally been reported to cause flare of skin psoriasis[18]. Celecoxib may offer some rapid symptomatic relief but has little benefit over placebo after 12 weeks treatment[9].

Corticosteroids. Surprisingly, there are no randomized clinical trials (RCT) of systemic or intraarticular corticosteroids in PsA, yet about 15% of patients entering recent multicenter trials with biologics were taking some form of corticosteroid. Systemic corticosteroids are occasionally required for severe flares of arthritis. Discontinuation of corticosteroids has been linked to rebound of skin psoriasis. On the other hand, use of intraarticular corticosteroid injection is widespread and is felt to be a valuable form of treatment, especially for persistent mono or oligoarthritis.

Sulfasalazine. Sulfasalzine (SSZ) has a modest effect in improving clinical symptoms of peripheral joint disease and is often the first disease-modifying antirheumatic drug (DMARD) used[1, 19-24]. Up to one-third of patients may suffer adverse events such as gastrointestinal intolerance, dizziness, or liver toxicity. SSZ is ineffective for the treatment of axial disease[25], and studies are inconclusive for enthesitis and dactylitis.

Methotrexate. Although methotrexate (MTX) is commonly used as a DMARD in PsA and skin psoriasis, there is a lack of controlled studies in either condition[26,27]. Liver toxicity may be more frequent with MTX in PsA than in rheumatoid arthritis (RA)[28]. Histopathological findings may not be predicted by liver function tests[29,30]. Levels of amino-terminal propeptide of type III procollagen may be used as a guide as to the necessity of liver biopsy in patients requiring MTX long term[31].

More recent indirect evidence for possible longterm benefits of MTX comes from a longitudinal observational cohort[10]. Joint counts improved more and radiological progression was less in a later cohort followed from 1994 to 2004, compared to an earlier cohort followed from 1978 to 1993. The later cohort had been treated with a higher mean dose of MTX and had lesser duration of disease. The authors concluded that earlier treatment

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with higher doses of MTX may confer greater benefit. In another study of MTX versus placebo in patients with oligo-enthesitis for less than 12 weeks, there was benefit in favor of MTX in terms of reduced swollen and tender joint count, although not for laboratory markers of inflammation[11]. These 2 studies encourage ongoing evaluation of the role for MTX and its timing in the disease course.

Cyclosporine. Cyclosporine is an effective agent for skin psoriasis but less often used for PsA, mainly because of its renal toxicity with chronic use. Cyclosporine appears to be superior in efficacy to SSZ[32], and has similar efficacy to MTX[33], but overall greater toxicity.

Leflunomide. A randomized control trial involving 190 patients with active arthritis (at least 3 tender and 3 swollen joints) demonstrated efficacy for leflunomide in improving clinical symptoms of arthritis and secondary measures including disability and skin psoriasis[34]. Serious adverse events were more common in the leflunomide treated group (13.5%) than in the placebo-treated group (5.4%). The most frequent adverse events with leflunomide were diarrhea (24%), increased liver enzymes (12.5%), flu-like syndrome (12.5%), and headache (11.5%).

Other disease-modifying agents. Most of the DMARD used for RA are occasionally used for PsA, although there are very few properly controlled studies. A recent systematic review and metaanalysis was performed using numbers withdrawn due to lack of effect to estimate efficacy and withdrawal due to adverse effects to estimate toxicity[3]. Risk ratios were derived for numbers needed to treat versus numbers needed to harm for DMARD and TNF inhibitors. Using this approach there was evidence that gold, SSZ, leflunomide, and TNF inhibitors were effective. Surprisingly, gold and TNF inhibitors showed the largest effect sizes. Efficacy/toxicity ratios were highest with TNF inhibitors, followed by leflunomide, gold, and SSZ. In terms of other agents, small studies of mycophenolate in PsA have been promising[35].

CONCLUSION

Altogether there is sufficient reason not to dismiss traditional agents for use in PsA because of lack of evidence. Also, due consideration has to be given to the considerable cost of biologic treatments versus traditional treatments. The role of combination therapy with TNF inhibitors is an important one, especially considering that 30%–40% of patients in the TNF inhibitor trials have been on MTX as concomitant medication. Note should be made of findings from RA, where combination therapy with MTX and TNF inhibitors was superior to either agent alone at all levels of perceived disease activity.

Finally, there may be a case for looking at an intermittent therapeutic strategy in psoriatic disease. In a 5-year prospective study, episodes of remission were significantly more frequent in PsA compared to RA (24% vs 7.5%, respectively) and lasted longer (31 vs 4 months)[12]. With cessation of therapy remission was also longer for PsA versus RA (12 vs 3 months). Remission was more frequent but lasted no longer with biologics compared to traditional agents.

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