Discontinuation of Corticosteroids Following Initiation of Infliximab in Patients with Refractory Rheumatoid Arthritis

Norman B. Gaylis, M.D., F.A.C.P., F.A.C.R.¹

¹Arthritis & Rheumatic Diseases, Arthritis & Rheumatic Disease Specialties, Aventura, United States
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Norman B. Gaylis, M.D.

1 Arthritis & Rheumatic Diseases, Arthritis & Rheumatism Foundation of Michigan

Background

Rheumatoid arthritis (RA) is a chronic disease leading to progressive joint damage and functional decline. Historically, standard treatment of RA involved a step-up approach including NSAIDs, corticosteroids and DMARDs. However, corticosteroid therapy at both low and high doses can have rapid, long lasting, deleterious side effects such as osteoporosis and cataracts. Recently, novel treatment strategies have focused on blocking inflammatory mediators of RA, such as cytokines. The most effective new therapies have targeted tumor necrosis factor alpha (TNFα). Infliximab, an anti-TNFα monoclonal antibody, has proven to be highly effective in the treatment of DMARD resistant, methotrexate naïve, early RA patients. Treatment with infliximab plus methotrexate has provided clinical benefit while inhibiting the progression of radiographic damage, and preserving joint integrity in patients with active RA. Contemporary clinical trials assessing TNFα blockers have not permitted corticosteroid adjustments during the trial. However, considering the negative side effects associated with even short-term corticosteroid use, efficacious treatments allowing for steroid-tapering measures would be prudent. This retrospective analysis of RA patients analyzed the effects of a multidisciplinary treatment of corticosteroids, DMARDs, and or NSAIDs compared to combination treatment with infliximab where the steroid dose was not held static.

Objectives

To evaluate corticosteroid use in patients with refractory RA after initiation of infliximab therapy.

Methods

- Retrospective evaluation of 70 patients (5 male, 65 female) in a community rheumatology practice
- Inclusion criteria:
  - Diagnosis of RA consistent with American College of Rheumatology criteria
  - Unchanged or worsening symptoms despite treatment with standard therapy
- Defined as treatment with prednisone plus either methotrexate, nonsteroidal anti-inflammatory agents, or both
- Administration of a minimum of 4 infliximab infusions
- Infliximab was administered to all patients at a starting dose of 3 mg/kg and subsequently maintained or increased based upon clinical response
- All patients received initial infusions, in-office at 0, 2 and 6 weeks and then maintenance infusions every 8 weeks or as needed
- Assessments:
  - Daily prednisone dose before infliximab infusions
  - Daily prednisone dose 18 months after initiation of infliximab infusions
  - Infliximab dosing
Following Initiation of Infliximab Therapy Rheumatoid Arthritis

D., F.A.C.P., F.A.C.R.¹
Rheumatic Disease Specialties, Aventura, United States

Results
At baseline, the average daily prednisone requirement was 7.5 mg (range, 2.5 mg to 20 mg). The average infliximab dose during the first 18 months of treatment was 4.5 mg/kg (range, 3 to 8 mg/kg). After 18 months of infliximab treatment, 29 patients (41%) were able to completely discontinue prednisone therapy. Twenty-nine additional patients (41%) achieved a reduction in daily prednisone use. Twelve patients (17%) continued on the same prednisone dose as compared to baseline.

Conclusion
Our review demonstrated infliximab was effective in reducing signs and symptoms of RA in patients requiring corticosteroid therapy to maintain adequate levels of function and comfort. This improved response, following infliximab therapy, permitted the safe reduction or discontinuation of corticosteroids in the majority of patients. The ability to discontinue or reduce daily prednisone doses decreases the development of long-term adverse effects caused by corticosteroid therapy. Although decreased corticosteroid use has not traditionally been an outcome measure in RA patients, our review demonstrates this endpoint was significant in the majority of patients. In addition, it provides an important measurement of clinical response. As well as contributing to a more accurate measure of treatment, as the reduction of concomitant corticosteroids would permit the outcome measures standardly used (e.g., ACR, DAS, HAQ) to truly measure a biologic’s efficacy.

Therefore, in addition to other standard measures, changes in corticosteroid use following biologic therapy should be viewed as a key measure of clinical outcome in patients with RA.

References

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