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Letter

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Is there really a higher risk for infection with anti TNF-α agents or is there a selection bias?

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Abstract

A recent study suggests that rheumatoid arthritis patients treated with anti TNF-α agents and steroids are at a higher risk for hospitalization for infections compared to those treated with other disease modifying antirheumatic drugs (DMARDs). This conclusion is misleading since the results were clearly due to a selection bias, the comparator group using non-cytotoxic DMARDs having mild disease.

Key words: Anti TNF-α, agents, rheumatoid arthritis, infection

Dear Editor,

The relationship between anti TNF-α therapy and risk of infection is still unsettled: some studies show an increased risk of infections[1,2] but others do not.[3,4]

Recently, Lane et al. have looked at this association using the United States Department of Veterans Affairs national databases, retrospectively.[5] They divided the patients with rheumatoid arthritis into three groups based on the disease modifying antirheumatic drugs (DMARDs) they had received. The patients in Group I were on hydroxycholoroquine, sulfasalazine, auranofin, injectable gold, and penicillamine, designated by the authors as users of non-cytotoxic DMARDs. The treatment in the moderate group (Group II) included methotrexate, leflunomide, azathioprine, cyclophosphamide, cyclosporine, and anakinra. The patients in Group III were the TNF-α antagonist users. The obvious premise was that the patients had been allocated to these groups according to the increased disease severity.

In brief both the number of patients with infection and the number of hospitalizations for infection, the 2 primary study outcome measures, differed significantly between the 3 groups and the authors concluded that treatment with anti-TNF's increased the rate of infections mainly in Group III, the anti-TNF users. It is however important to note that, on closer scrutiny, these differences among the 3 groups were obviously due to the low frequency of infections among Group I only. There were no statistically significant differences (5.8%, 774/13367; 6.0%, 229/3796, χ^2=0.3, p=0.5 and 7.2%, 972/13367; 7.3%, 279/3796, χ^2=0.26, p=0.87) for either the number of patients or the total number of hospitalizations for infection between Groups II and III.

There is a potential selection bias not adequately addressed by the authors. The more severe patients with RA also have more frequent infections as was recently brought up.[6] Furthermore the similarity in the infection loads in groups II and III, not given the deserved emphasis, do not do justice to anti-TNF use.

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