Reviewer’s report

Title: Hepatotoxicity associated with sulfasalazine in inflammatory arthritis: A case series from a local surveillance of serious adverse events

Version: 1 Date: 13 December 2007

Reviewer: Einar S Bjornsson

Reviewer’s report:

The paper by Jobanputra et al. is on an important and perhaps neglected topic of drug-induced liver injury (DILI) by other specialists than some hepatologists. The paper describes a local effort in the UK searching for hepatotoxicity in patients with rheumatological diseases. This is a very good effort but the paper suffers from several limitations and several inaccuracies in its current form. Many terms and conditions in the paper seems too local as these are not familiar to other than perhaps doctors working in the UK such as yellow cards and postcards

Specific comments:

1. In the Background of the abstract: please spell out DMARDs, a term that has not be introduced earlier. I would suggest that the word proactive is removed as this is not a study with intervention.

2. In the Methods of the abstract, it is stated that a published index has been used, it is perhaps better to say that a published causality assessment instrument was used.

3. In the Background: Please explain what a yellow card is. Not known to others than UK employes.

4. What and where is MHRA? In the UK?

5. Is reference 4 the correct one?

6. Carbamazepine is not correctly spelled.

7. In methods: One senior clinician, state within paranthesis who that was.

8. In Results: The first sentence: Our population serves of around 400,000. Where is this population? Explain.

9. It should be defined what the authors mean by serious hepatotoxicity. Is that symptomatic liver injury or is it hepatotoxicity with concomitant jaundice?

10. According to the Results, only 5 out of 10 had a known hepatitis status. I just wander which these 5 patients were and this should be included in the table. It
should also be included who of these patients had jaundice, preferably, the maximal elevation in serum bilirubin in times upper limit of normal. It should be acknowledged in the Discussion that this is a major drawback that the patients have had a very limited diagnostic work-up, and it should be pointed out that this is very important when performing a causality assessment of a suspected drug-induced liver injury.

11. Five patients had tests for CMV, it is not necessary to state that some tested for IgG.

12. What is the proportion of Black British of African or Caribbean descent in the cohort?

13. A very interesting finding is the high number of reports, 0.4% developed serious hepatotoxicity, which is far higher than previously reported for DILI. These figures, that is more than 1 per 10000 users is very high compared with previous figures on DILI in the literature. Some references on the reported incidence of DILI in the literature should be referenced to. Obviously underreporting can not be excluded which should be acknowledged by the authors.

14. At the bottom of page 9. In our cohort, drug toxicity did not appear to be linked to disease activity, the presence of ANA and other clinical characteristics. Was this looked at? I can not see that in the Results. If this has not been formally studied, this should be deleted.

On page 10: Four of our patients were given steroids. What pointed to that the steroid therapy affected prognosis? There is not any proof that steroids are effective in this situation and it should be acknowledged.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests"