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: 30 November 2007

Reviewer: Domenico Motola

Reviewer's report:

Major Compulsory Revisions

1) In the results section, second paragraph, the Authors state that "none of the patients started any other new medication at the time of starting sulfasalazine"; in the attached table, fourth column, concomitant drugs at the time of the adverse event (i.e. hepatic toxicity) were reported. This should be properly remarked in the manuscript text. Moreover, among the concomitant drugs, some of them can induce hepatic adverse event, namely paracetamol (used by 4 patients out of 10), diclofenac (used by 3 patients out of 10). A toxic liver effect, induced by a sinergistic action of two or more drugs (known to be hepatotoxic) used concomitantly cannot be ruled out and therefore this confounding factor should be properly remarked as a limit of this manuscript in the conclusion section.

2) In the results section, first paragraph, the Authors state that "...38 relating to sulfasalazine and 30 of these from our institution...". This appears as an important bias of the study, and it should be properly highlighted in the discussion.

3) The cases observed in this study are 10 (Five White British and 5 Black British): therefore, the last sentence of the conclusion (both in the abstract and in the text), concerning the intensive early monitoring of Black British people, is too strong on the basis of ten cases observed and therefore it should be rephrased.

Minor Essential Revisions

1) Abstract: in the section "Methods", replace the term "severe" (which concerns the intensity of a given adverse drug reaction) with the more appropriate term "serious";

2) Methods: the Authors should rephrase the sentence "this investigation was instigated when...";
3) Page 8: in this paragraph appears for the first time the acronym â##SASPâ## (sulfasalazine). This acronym should be shifted in the background section before the first appearance of sulfasalazine.

4) Conclusions, last paragraph: the Authors estimate of sulfasalazine induce hepatic toxicity is 0.4%. This figure can be classified in Europe as a â##ANCOMMONâ## adverse drug reaction (> 1/1000, < 1/100) and this should be remarked in the conclusion.

5) In the references, the citations 13 and 38 referred to the same published article (Lucena et al. Hepatology 2001;33:123-30). Delete one of the two citations and check all references.

Discretionary Revisions

1) In the assessing the causality assessment, the Authors used the Danan-Benichou method. This method seems to be not widespread in the determination of causality assessment of adverse drug reactions. The last citation of this method using PubMed is in 1993 (Access to PubMed, november 26th, 2007 using the key word â##Danan-Benichouâ##). The Author could use the WHO causality assesment or Naranjo methods to confirm their scores.

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 limited interest

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare no conflict of interest.