Reviewer's report

Title: Fluvoxamine for fatigue in primary biliary cirrhosis and primary sclerosing cholangitis: a randomised controlled trial.

Version: 1 Date: 24 May 2004

Reviewer: Martin I Prince

Reviewer's report:

General

The authors describe a double blind placebo controlled randomised trial of the use of Fluvoxamine in cholestatic liver disease. The importance of the problem of fatigue is well accounted for in the introduction. A rationale for using the trial drug (i.e. fatigue may be a manifestation of sub clinical depression or share a common aetiological pathway) is outlined. Consort statement reporting principles have been adhered to. Results are presented on an intention to treat basis. There was an initial difference in fatigue scores between the two groups due to random variation. It is unclear if this affected the negative outcome of the trial

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The main weakness of the trial is that it is severely underpowered. The power calculation is based upon very optimistic estimates of benefit with active drug and similarly optimistic estimates of difference between placebo and active arms. This point should be made more strongly in the discussion- the authors state that a small beneficial effect may have been missed. In a study of this size a substantial beneficial effect may have been missed although it would unlikely from the data presented. The methods for performing the power calculation are not stated, I presume that a non-parametric method has been used. It is important to state this, as it is necessary for the reader to see that a non-parametric method has been used in the power calculation as these statistics were then used in the analysis.

2. The authors state that subgroup analysis was performed analysing the data for patients with PBC and PSC separately. As there are no space constraints in this electronic journal, this data should be published. An important role for this paper is to inform future systematic reviews and meta analyses. These reviews are usually specific to individual diagnoses.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Figure 2 adds little additional data not contained in table 3 and may be removed. The text states that figure 3 contains both intention to treat and per protocol analysis. Only one set of data appears to be actually represented.

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Discretionary Revisions (which the author can choose to ignore)
1. It is probably worth noting that the Beck inventory was developed on patients without chronic non-psychiatric illness and may therefore not be specific in some patients with liver disease, for example four questions ask about fatigue, low energy, decrease appetite and decreased libido all of which may be features of liver disease per se.

2. There are no records of whether blinding was successful. If this data is available it should be included.

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

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No

**Declaration of competing interests:**

None