Reviewer's report

Title: Serum hyaluronate as a non invasive marker of hepatic fibrosis and inflammation in chronic HBV infection

Version: 1 Date: 26 April 2005

Reviewer: Edoardo Giovanni Giannini

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General

The study by Montazeri and Co-workers deals with an important issue in clinical hepatology. Chronic HBV infection is a major world-wide health concern. Non-invasive assessment of disease stage and liver inflammation can be of help for the management of patients with chronic hepatitis B. In this study the Authors assessed the accuracy of hyaluronic acid (HA) for the diagnosis of advanced fibrosis (and inflammation) in a group of patients chronically infected by HBV. They found that, on the average, HA levels are higher in patients with decompensated cirrhosis as compared to both chronic hepatitis patients and controls. Furthermore, among chronic hepatitis patients, those with advanced fibrosis have higher HA as compared to patients with mild fibrosis. However, HA serum levels of chronic hepatitis patients as a whole are not significantly different from those of health controls. Finally, the Authors evaluated, by means of ROC curves, the accuracy of different HA cut-offs for diagnosing advanced fibrosis or decompensated cirrhosis.

The results of the study are quite interesting, and I actually appreciated the cautious conclusions expressed by the Authors. There are some limitations to the study, mainly patients distribution and the limited usefulness of HA to discriminate between two conditions that can be easily discriminated on a clinical basis alone (chronic hepatitis versus decompensated cirrhosis).

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

1. The Authors evaluated a relatively small cohort of subjects. Eleven patients alone had advanced fibrosis and 68 mild fibrosis. They found a marked difference in mean HA levels between the two subgroups of patients (28 versus 309 ng/mL), and actually HA levels of patients with mild fibrosis are not different from those of healthy controls (20 ng/mL). This is likely due to imbalance in patients distribution. This is not a negligible point, since HA seems to be useful for identifying patients with advanced fibrosis (and therefore more in the need of anti-viral therapy), but falls short to identify patients with initial fibrosis. The Authors need to discuss this result.

2. The analysis of HA levels in patients with decompensated disease is important in order to show the progressive increase in HA as liver disease worsens. However, I am not sure that the detailed analysis of ROC curve and the identification of a HA cut-off able to discriminate between decompensated cirrhosis and chronic hepatitis adds something to the study. Indeed, these two clinical entities can be easily identified on clinical grounds, and therefore in this setting the use of HA seems to be redundant.

3. A group of patients with compensated cirrhosis is lacking. In fact, the Authors evaluated patients with fibrosis score up to 5 (i.e., probable cirrhosis, according to the Ishaks score) but no patients with fibrosis score 6. This is a major drawback of the study, since identification of the presence of compensated cirrhosis in patients with chronic liver disease is of fundamental importance for therapeutic and prognostic implications. The Authors need to detail the reasons for such exclusion. A further group of patients with compensated disease (and analysis of a HA cut-off able to separate
this sub-group from the others) would greatly improve the message of the study.

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. Criteria for selection of patients are not clear. It seems that the Authors retrospectively selected their patients rather assessing consecutive patients. Detailed description of criteria for inclusion and exclusion together with the number of patients excluded needs to be shown in the Result section of the manuscript.
2. In the Discussion section of the manuscript, the second statement is not supported by the study results. In fact, HA serum levels are not significantly higher in CHB patients as compared to controls (p=0.33).

Discretionary Revisions (which the author can choose to ignore)

1. Some abbreviations (such as CHB) need to be cited in the text (not in the abstract).
2. Reference #7 is not appropriate.
3. References #16 and #17 are not pertinent to the context in which they are cited.
4. Page 4, 5th line: propeptideds should be propeptides.
5. Page 5, 2nd paragraph, 2nd line: Pough should be Pugh and Percutneous should be percutaneous.
6. Page 6, Corgnix should be Corgenix.
7. Results: please express age of the patients as integer.
8. Page 8, 4th line from the end: phosphatease should be phosphatase.

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: Needs some language corrections before being published

Statistical review: No

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