Reviewer's report

Title: Artificial liver support for acute liver failure: improvement of hepatic encephalopathy treated by on-line hemodiafiltration: a case series study

Version: 1 Date: 27 December 2009

Reviewer: Norman Sussman

Reviewer's report:

The article by Arata et al. describes their experience with HDF in 17 patients with acute liver failure.

1. The question is sound: Liver support for acute liver failure is urgently needed, and has been addressed in numerous publications over the past 5 decades. In this case series, the authors relate their results over a period of 7 years. Their accrual is slow, in keeping with the rarity of the disease.

2. Are the methods appropriate and well described?
   a. The authors define acute liver failure as a disease lasting <24 weeks. Looking at Table 1, I suspect that some of their patients had chronic liver disease. For example, the AST in patient #3 (HBV infection) was only 29 IU/mL. He improved, and then deteriorated and died when he could not get transplanted. In our experience, acute liver failure is associated with high transaminases, and resolves completely if the patient gets over the initial crisis. I also think patient #11 had a diagnosis other than alcohol – acute alcoholic hepatitis is generally associated with low enzyme levels, and occurs on a background of cirrhosis. I suspect acetaminophen since the patient had very high enzymes and recovered spontaneously. I would like more assurance that this group really has acute liver failure.

   b. I would also like to voice concern about personal experience. Various techniques of filtration have proven ineffective over a very long period of time. One is reminded of a situation at King’s College in which charcoal hemoperfusion was considered so effective that a clinical trial was deemed unethical. When the trial was finally conducted, hemoperfusion was found to be no more effective than standard of care. In the final analysis, I don’t think another anecdotal account advances this field.

3. Are the data sound? Although I believe the outcomes as reported, I do not feel these can be generalized to other centers. For this reason, I do not believe the data are sound. I would like the authors to distinguish between patients with underlying chronic liver disease and those with true, acute liver failure. I would also like them to explain the difference between HBV and HBV carrier (Table 1).

4. The manuscript adheres to relevant standards of reporting although many of the references are quite old. Some of these should be updated.

5. Balance: The discussion should address why many others have failed to achieve these dramatic results, and admit that this is an uncontrolled trial
6. The writing is good – I congratulate the authors on their clarity.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I do not have competing interests.
1. I was the founder of a Hepatix Inc., a bioartificial liver company - I no longer hold an interest.
2. I am a Board member of Stem Cell Innovations - no artificial liver anticipated in the near future
3. I am a Board member of HepaHope, a bioartificial liver company. HepaHope is in pre-clinical testing. I do not believe this sways my opinion of the manuscript under review.