Reviewer's report

Title: Glutamine Therapy Reduces Endothelial Adhesion of Sickle Red Blood Cells to Human Umbilical Vein Endothelial Cells

Version: 1 Date: 2 February 2005

Reviewer: Marie J. Stuart

Reviewer's report:

General

The article by Nihara Y et al demonstrates that a total of 10 patients with HbSS who were given oral L-glutamine improved in vitro red cell-endothelial adhesion following administration of this drug. No mechanism(s) of action have been identified, and while the data presented is tantalizing, the absence of other hematologic parameters makes this an incomplete report which needs significant modification prior to publication.

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

1). We need to document that glutamine levels were increased when compared to baseline, following therapy in the longitudinal studies in each individual patient, otherwise we have no proof that the subject in fact ingested the medication.

2). Hematologic parameters in the cross-sectional and longitudinal studies must be tabulated, Hb / Hct / Reticulocyte / HbF levels etc. In addition, Hb / Hct / Reticulocyte / HbF and red cell indices pre and post therapy, in the longitudinal group, must be given for us to evaluate whether the adhesion-related changes were due to modulation in the proadhesive reticulocyte population, dense cell numbers etc.

3). For both Cr51 and gravity adherence adhesion studies, cpm and adherent cell counts respectively should be given in figure legends as raw numbers such that a more informed view of the assays employed may be obtained by the reader.

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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). Many references are inappropriate – Need to be gone over with the senior authors. For instance, why in #1 and 2 do we concentrate on the Latin-American population which forms a minority of HbSS patients? Why do we only give national history studies in Europe (#5) and in Jamaica (#6), and leave out Orah Platt's New Engl J Med reference from the 1980s? The authors can quote more pertinent references than #9 and #20 etc, etc.

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Discretionary Revisions (which the author can choose to ignore)

1). Figures 1 and 2 should be combined as Figure 1(a) and (b) for better readability. Similarly, Figures 4 and 5 should be combined as panels (a) and (b).

2). The discussion is a bit “rough” and again needs polishing by the senior authors.
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:
'I declare that I have no competing interests'