Reviewer's report

Title: ALA-D activity is a reliable marker for oxidative stress in bone marrow transplantation patients

Version: 2 Date: 2 December 2008

Reviewer: Ana Coto-Montes

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The manuscript study the possible role of ALA-D as an adequate biomarker of oxidative stress in autologous and allogeneic bone marrow transplantation patients. Likewise, the manuscript shows the increase of oxidative stress in these patients by several procedures.

This is a very interesting article in which is possible to find habitual procedures of basic research developed in a clinical problem. This way is not very usual but it has always very good results. And this article is an example, since it is simple, direct, easy to read but also with interesting conclusions. I think that it could be accepted with minor changes.

Following the points the journal proposes for reviewing an article:

The initial questions have been clearly exposed and they are enough for developing the study.

Mostly of methods were appropriated but I have some questions about them:
- I don’t understand why authors have studied the activity of CAT and not glutathione peroxidase (GSH-Px) when this enzyme is the most abundant in erythrocytes. The results that they have obtained are very good but it is necessary to take into account that some of superoxide anions that SOD produces can be neutralized by GSH-Px, therefore its activity would be very useful in order to know whether SOD and CAT-GSH-Px are adjusted or not.
- Tandem protein-thiol and non protein thiol is not usual and it is interesting because of the reductor role of thiol groups but explanation about its meaning in material and methods would clarify the reasons of this procedure.

The results are clear but I have a few questions about:
- Why authors have included the characteristics of patients into results? I think that all these data have to be included into Material and Methods because they have described the population of the study without any transformation.
- Data from antioxidant enzymes (SOD and CAT activities) should be present by graphics. This is the usual way and it allows to compare them.
- In relation to ALA-D, the results that authors have offered are very clear and
interesting because they sow that the activity of this enzyme goes down after the treatment. However, decrease in activity could be due to general decline of the heme route, which doesn´t imply ALA accumulation. To solve this question is only necessary to study the activity of ALA-S (#-aminolevulinic acid synthase). This enzyme is the rate-limiting enzyme of heme synthesis and its activity study could indicate the existence (or not) of ALA accumulation.

The discussion is short but clear. However, the absence of any description of several problems of ALA accumulation could produce in patients is observed since this is an important prooxidant with huge effects in the organism as porphyria can shown.

In general the article is acceptable although some changes, above cited, could improved the manuscript. Mostly of my comments are discretionary revisions and authors can decide to follow the indications or not. However, some additional information about ALA-S, its activity or reasons for avoiding to do it should be included.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests