Reviewer's report

Title: The TOZAL study: multi-site trial of taurine, omega-3 fatty acids, zinc, antioxidants, and lutein in the treatment of atrophic age-related macular degeneration

Version: 2 Date: 28 November 2006

Reviewer: Frank Eperjesi

Reviewer's report:

General

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

I several concerns with this paper. The control group were evaluated using a Snellen chart and visual acuity (VA) values have been reported in Snellen for this group. I assume that these values have then been converted to logMAR values. Information is lost when the Snellen system is used to measure VA and further information is lost during the conversion of Snellen values to logMAR values. It is likely that that the VA values were corrupted during the conversion process, and as the difference between the VA of the control group and the VA of the study group is very slight this possible corruption needs to be accounted for and described at least as a limitation of the study. Also the inclusion/exclusion criteria mention Snellin VA, I don't think it is appropriate for VA to be discussed in Snellen and logMAR in the same paper, this leads to confusion. An example of this is in the second paragraph (entitled Visual acuity outcomes) of the results section where the placebo arm is described as having a mean negative Snellen line change of 1.49 lines and the study group a positive change of 0.0541 logMAR. This is not a comparison of like for like. Furthermore in fig 2 the placebo VA is noted as a Mean EDTRS line change.

In the second paragraph of the discussion there is mention that an AREDS type formulation is the standard of care in AMD. To my knowledge the AREDS formulation had no affect on bilateral non-exudative AMD, the affect was only for patients with intermediate or advanced AMD in one eye.

It would be useful to know which form the zinc was in eg oxide or acetate and if the lutein was pure or esterified.

The LAST study did show an increase in many aspects of visual function for the study group including VA so the TOZAL study is not the first to report this.

The change in VA for the study group may be statistically significant but it is not clinically significant and this point should be made. Clinicians usually aim for an improvement of 2 lines of logMAR VA before recommending an intervention.

I would also like to have more information on the microcurrent stimulation (MCS), in particular what was the sham MCS. Could this have had an affect on VA of the study group?

Could the author explain why the study group was not given the intervention at visit 1. Also why was the VA and the contrast measured again at visit 2, which was only a week after visit 1. Why were the subjects recalled a week later to have VA and contrast measured again?

Were all the subjects advised to take the supplement with food?

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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)

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Discretionary Revisions (which the author can choose to ignore)
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

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