Reviewer's report

**Title:** Efficacy of vitamin C as an adjunct to fluoxetine therapy in pediatric major depressive disorder: a randomized, double-blind, placebo-controlled pilot study

**Version:** 2  **Date:** 18 December 2012

**Reviewer:** Martha Payne

**Reviewer's report:**

Manuscript Review
Efficacy of vitamin C as an adjunct to fluoxetine therapy in pediatric major depressive disorder: a randomized, double-blind, placebo-controlled pilot study

**Journal:** Nutrition Journal

**Type of article:** Research

This important study examined the potential for ascorbic acid supplementation to enhance response to fluoxetine treatment for pediatric depression. There is great potential for this approach to improve the generally low success of depression treatment. A number of minor issues should be addressed to improve interpretation and comprehension of this report.

**Minor Essential Revisions**

1. Vitamin C (Introduction and/or Discussion) – need to clarify that the role of vitamin C for treating a deficient (or insufficient) state likely differs from the role of vitamin C in a vitamin-sufficient state. Since this study did not examine serum vitamin C status, it is important to clarify this point and the fact that it is not clear which situation (deficient, insufficient or sufficient) applies to the study participants.

2. Vitamins and mood (Introduction) – discuss that studies have generally included vitamins/minerals in addition to vitamin C, so the specific role of vitamin C is unclear. Also, many studies examined mood in a healthy population rather than clinical depression.

3. Participants (Methods) – unclear why two subjects with hypomania were excluded (as this wouldn't typically be considered a neurological, psychotic, or substance abuse condition).

4. Participants (Results) – three subjects “withdrew from the trial due to noncompliance.” It is not clear what is meant by this. Were subjects removed from study due to noncompliance? Did they withdraw because they did not feel they could be compliant?

5. Participants (Methods/Results) – Methods section says there were 13 subjects in treatment group (14 in control), while Results say that there were 14 subjects in treatment (13 in control). This discrepancy needs to be fixed.
6. Instruments (Methods/Discussion) – An important finding is this study is that CDRS and CDI showed significant differences with vitamin C (vs. control), while CGI did not. It would be helpful to clarify who provided ratings for each assessment (child, clinician, parent, teacher) and how this difference may have influenced the results. CGI may have differed because it was the clinician who completed it (if, in fact, the clinician did complete), while other individuals completed the CDRS and CDI.

Discretionary Revision

1. Limitations seem overstated. A 6-month trial does not seem short. Combination of child/teen groups may not be ideal – but doesn’t seem a huge limitation given that ages did not differ between the two trial arms.

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests