Reviewer’s report

Title: Vitamin C as an adjuvant for treating major depressive disorder and suicidal behavior, a randomized placebo controlled clinical trial

Version: 2 Date: 15 September 2014

Reviewer: Andrew Hugh Ford

Reviewer’s report:

Thank you for asking me to review this small clinical trial of vitamin C as adjunctive treatment for major depression in adult patients. There have been very few trials in this area and as such this is a useful addition to the existing literature. The manuscript however needs substantial rewriting and I have some concerns with the way the data has been presented and analysed. The presentation could be improved by more closely following the Consort guidelines although the flow chart is helpful. My specific comments are as follows:

Abstract
• Please reword the sentence “The adverse effects were checked too.”

Introduction
• This is far too long and not well organized. It would be better to first state how vitamin C is an oxidant then discuss the oxidative stress model of depression, then talk about basic science studies of vitamin C and depression, then observational evidence and finally discuss the pediatric trial and the trial of depressed shift workers. The introduction doesn’t read well in its current form.
• Sentence 2, paragraph 1, page 4 needs to be reworded.
• The latter part of paragraph 1 needs to be reworded to be less definitive/adamant.
• 1st sentence, para 2 needs rewriting and a reference.
• Sentence 2, para 3, page 4 needs rewriting.
• It is unclear why the results of reference 14 are included in para 1 of page 5.
• Para 1, page 6 needs to be rewritten.
• In para 2, page 6 the authors say they “assume” that vitamin C improves depression from the existing evidence although they presented very little convincing evidence in their introduction?
• No hypotheses are stated.

Methods
• Page 6 – what is meant by “Enough information about the trial procedure…”?
• First sentence, page 7 – the trial is investigating the efficacy of vitamin C in addition to citalopram not on its own.
• Line 6, para 1, page 7 – I presume the authors meant citalopram where they wrote vitamin C?
• How was compliance checked?
• How was the dose of citalopram determined?
• Hypothyroidism is hardly a “severe medical condition”.
• The authors state that suicidal behavior was an outcome in the trial yet state that “suicidal attempt” was an exclusion criterion? I presume they mean suicidal ideation but they need to expand on this.

Results/Outcomes
• The outcomes of >49% or >24% on the HDRS are better written as # 50% etc. in my opinion.
• There is no attempt to do a multivariate analysis. I take the point that the groups were equal on baseline characteristic but the authors need to state why they did not attempt to adjust for any potential confounds.
• It is very odd that 68 people were randomized and allocated but only 43 received the allocated treatment? Please explain why this happened and discuss the potential bias this introduces.
• I would usually expect to see the significance level represented by a lower case p rather than capital.
• The authors should always stipulate whether the variance of their means is a SD or SEM i.e. the number in parentheses needs to be explained.
• The chi square symbol is not usually a capital X.
• Table 1 – the percentages for females in the placebo group and marital status in vitamin C groups are incorrect.
• Please add the number of participants at the top of each column so we know what the denominator is.
• The rows are inconsistently labeled with n (%) and mean (SD) missing on some.
• Why not present the change in HDRS and BDI as mean change from baseline and SD rather than % change?

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

Nil