Reviewer’s report

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

Version: 3 Date: 2 December 2014

Reviewer: Manuella P Kaster

Reviewer’s report:

In my point of view there were great improvements in the new version of the manuscript. The authors addressed the points raised by the referees and the discussion is much better in this revised version. I still have some considerations especially in the organization of the introduction. My suggestions are listed below.

Minor essential revisions:

Abstract

There is a spelling mistake in line two... depressive.
In the conclusion the word acid after citalopram should be removed.
I think that the authors should standardize the use of vitamin C or ascorbic acid in the manuscript.

Background

I still think that the introduction is confusing. The authors should start with a more general sentence... for example: In the past decades, several clinical and pre-clinical works reported that changes in oxidative stress parameters and in the activity of antioxidant enzymes might be involved in pathophysiology of MDD. In addition, it always should be mention if the work is clinical or pre-clinical and evidence in humans and animal models should be organized.

In the first sentence.. the authors should add .. are increased in major depressive disorder patients".. to highlight that this is a clinical work.

In the second sentence... this result is in an animal model of depression induced by stress? Is the activity of SOD increased or decreased by stress?

In the third sentence... the authors should change “in the animal” for in pre-clinical models.

In the end of first paragraph... references 3 and 4 are in patients with MDD? This should be described in the sentence.

The authors should reorganize this section: “Ascorbic acid the same as fluoxetine reverses brain oxidative damage [7]. Antidepressants may decrease the
increased level of oxidative stress in MDD patients [8]. Treating MDD with fluoxetine and citalopram decreased the increased levels of SOD and serum MDA [1].” In my suggestion it would be better: Antidepressants are capable to reverse the changes in oxidative stress parameters in MDD patients. A clinical trial demonstrated that the peripheral activity of the antioxidant enzyme SOD and the levels of the oxidative marker MDA were higher in MDD patients. These changes were accompanied by a reduction in the levels of ascorbic acid and were reverted after the treatment with fluoxetine and citalopram, further reinforcing the role of ascorbic acid in the MDD [1]. In addition, ascorbic acid had an effect similar to fluoxetine in an animal model of depression, reverting not only the behavioral profile induced by stress but also the oxidative damage [7].

“There are some promising reports about the effect of vitamin C for treating depression in animals.” This statement should be change since animal models are never considered depression in animals. Please change to... There are some promising reports about the beneficial effect of vitamin C in animal models of depression.

“Nevertheless, supplementary vitamins C (1000 mg/day) did not decrease depression in type 2 diabetic patients in a randomized, single-blind, placebo-controlled trial [15].” The authors should change depressi

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

**Quality of written English:** Needs some language corrections before being published

**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.