Reviewer’s report

Title: The beneficial use of ultramicronized palmitoylethanolamide as add-on therapy to Tapentadol in the treatment of low back pain: a pilot study comparing prospective and retrospective observational arms

Version: 1 Date: 04 Aug 2017

Reviewer: Dario Bugada

Reviewer’s report:

Abstract - methods section line 11 - please remove "treated" as it is repeated

Introduction: well written and clearly introduces the unmet needs. Proper length.

Methods:

the methods are well described. Inclusion and exclusion criteria are specified, and STROBE guidelines are used, and mentioned. The two arms are well described.

Actually, this is not a typical observational study since it is half retrospective and half prospective: as a reviewer, I'm not totally aware if specific tools and statistical methodologies should be applied in this case (the reason why I suggest additional opinion by an expert); however the methods used for the study are clear, and the statistical analysis appears to be appropriate. The only concern is the number of patients: it seems very low, probably configuring more a pilot investigation rather than an actual observational study (in the reviewer's opinion) Further, there is no mention of registration on ClinicalTrials.gov: was the study included in any Registry? This aspect further argues towards the definition of "pilot study" rather than a trial. Minor suggestions for the methods section: remove the daily mean dose of TP - it should be reported in the results, highlighting that the mean dose it is not statistically different between groups.

Results:

line11-13: please remove the sentence "there was..(Figure 3)". You can only add "in favour of the prospective group" at the end of the sentence at line 7, avoiding repetitions.

Line 42, page 6- line 50, page 7: I suggest to erase this part..it is very long and confusing, and it is a repetition of data reported in the table.

Table 1: is the difference in the incidence of dyslipidemia and venous insufficiency statistically different? Is it somehow able to influence the study results and their interpretation? This should be probably discussed.
Tables and figures: when a statistically significant difference exists between groups, it should be evidenced with a marker (like * or **) in the figure/table, to help the reader's understanding.

Discussion: well focused and findings are well described. Limitations are treated, as well.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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