Reviewer’s report

Title: The relationship between the level of μ-opioid receptor (μORs) and postoperative analgesic use in patients undergoing septoplasty: A prospective randomized controlled trial.

Version: 3 Date: 23 May 2020

Reviewer's report:

The overall purpose of the study was to determine the number of mu-opioid receptors in patients treated with tramadol versus fentanyl. As a secondary objective, they showed a correlation between the amount of peripheral mu-opioid receptors observed (high 200.94-489.92 pg/mL; low 94.56-200.94 pg/mL) and postoperative pain levels quantified on the visual analogue scale (VAS) and the amount of drug used for pain relief. The reader can only obtain this description by reading the methodology and the results, since in the background it is not clear at all the problem to be investigated, the main and secondary objectives of this study.

Summary:

It's not clear what rescue painkiller was used. It was indicated for both study groups. I suggest detailing the sociodemographic data and the mean values with their standard deviations of the concentration of mu-opioid receptors omitting the writing of the highest and lowest values. In turn, I suggest adding the pain levels (VAS scale) in both groups. Please, you must correct the word "tradomal". It is not clear how many and how significantly different the number of analgesics required for pain control is between the two study groups.

Background:

Page 3, line 20, 29: I suggest to correct word "korticosteroids"; "analgesia".
Page 4, line 4-11: The sentences must be to add the reference. The problem to be investigated is not clear. While the cellular pharmacological effect of mu-opioid receptors is described, the novelty and impact of the research are not stated. In turn, it is not clear whether or not the model for measuring mu-opioid receptors in peripheral blood is valid for testing the analgesic effect of the drugs used in the study. It must be improved.

Method:

Page 5, line 30: It is not clear what was used for the induction of anesthesia in the group using tramadol, as it is important to determine the pharmacological effect of both drugs and to avoid intervention bias in outcomes.
Page 5, line 51. What is "ECG", all abbreviations must be explained.
Page 6, line 1: "classic septoplasty operation technique" must be referenced.
Page 6, line 2: How long after the study drug was administered were blood samples taken? Important to consider given the pharmacokinetics and bioavailability of both drugs in the peripheral blood. It is suggested that this be added.
Page 6, line 24: It is not clear how researchers ask patients about their pain level one hour after surgery, considering recovery time and cognitive ability to respond to VAS.

Page 6, line 35: Patients were given different drugs and their combinations for postoperative pain relief. It is not clear how often or how much was used, considering this variable as a possible confounding variable to the secondary objectives of this study. I suggest clarification.

In the sample size calculation, the unit of measure used for the sample calculation is not clear. The study used "Liu YC & Wang WS" measured the concentration of the allele frequency variant (118G) of the mu-opioid receptor gene (OPRM1) and the average pain measured on the VAS scale before and after the administration of tramadol/acetaminophen combination tablets (Ultracet) for treating oxaliplatin-induced painful neuropathy. So, did you do the calculation based on the amount of genetic variation in the gen receptor or at the pain level?

Nowhere in this section is it proven that the model of measuring mu-opioid receptors in peripheral blood is valid and reproducible for measuring the analgesic effect of drugs used in both study groups. It is suggested that details be provided in the Background and Methods sections.

Results:

Page 9, line 11-15: The researchers rewrite the doses of drugs used in both groups, these should be described in the Methodology. I suggest checking the units of measurement used according to the standards of use of international units of measurement indicated in the instructions of the authors of this journal (mg/kg; mcg? ml or mL?)

Page 9, line 18, to check word "tradomol".

Page 9, line 18: The authors state "a tradomol [? ] group requires a second painkiller later than patients..." what is meant by "later than...?" referring to time in hours, days, amount of drug... is not clear.

Line 51, Page 9: It is unclear whether the amount of patient vomiting is significant between groups. This variable was not explained above. It is suggested that a chi-square test be added and used.

Discussion:

In general, in this section the researchers guided the analysis of results based on the effect of multiple other drugs unrelated to those used in this research. On page 12, the researchers describe the expression of mu-opioid receptors in painful conditions. It is suggested that such a description be made earlier, supporting the main and secondary purpose of this study.

Final comments: The purpose of the study is interesting and novelty. However, it presents important lack information such as the problem to be investigated, use of a model for quantification of mu-opioid receptor expression in peripheral blood, operational definition of variables (independent, dependent, sub-analysis of data), explanation of control of risk of bias (intervention, measurement and analysis of results) and the analysis and bibliographic explanation of results. I suggest writing the manuscript according to CONSORT Statement Group guidelines.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

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.

No

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

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