Reviewer’s report

Title: Effects of Different Doses of Magnesium Sulfate on Pneumoperitoneum-related Hemodynamic Changes in Patients Undergoing Gastrointestinal Laparoscopy: a randomized, double-blind, controlled trial

Version: 0 Date: 15 May 2019

Reviewer: Francesco Barbani

Reviewer's report:

Thank you for the chance to review such an interesting contribution from Wei Tan and co-worker. The manuscript gives the opportunity to focus on hemodynamic response to surgical pneumoperitoneum and the ways to prevent it through the infusion of different dosages of magnesium sulfate. Hence, I read it with great interest and curiosity.

As the authors state in the paper, the present study provides direct evidence regarding the attenuation of the changes in CO, SVR, and MAP induced by pneumoperitoneum and maintenance of intraoperative hemodynamic stability by magnesium sulfate infusion, associated with a reduced change of vasopressin plasmatic concentration after pneumoperitoneum induction.

Adopting a double blind randomized prospective trial, comparing two different magnesium sulfate dosages with a placebo group, it can be stated that the study is well conceived to investigate the aim of the study. However, please find below my comments and questions.

Page 5, row 18 The primary outcome of the study is the difference in SVR between different groups, so it may be advisable to use the best hemodynamic monitoring devices to detect data at its best. How did the authors choose FloTrac/Vigileo among available devices? Since every patient has a central venous catheter in place (page 6, row 30), was transpulmonary thermodilution considered? What about other arterial waveform analyzers?

Page 7, row 27 Authors declare that anesthesia was maintained with propofol and remifentanil infusion in a very precise infusion rate range (4-6mg/kg/h and 0.25-0.35 mcg/kg/min, respectively); patients were monitored with pEEG, in a way to maintain bispectral index between 45-60. Were medication infusion rates varied even outer from given range? How did the investigators choose to vary propofol or remifentanil?

Page 7, row 41 Muscle relaxation was monitored by mean of Train of Four ratio, with cis-atracurium boluses (0.05 mg/kg) aimed to maintain TOF<25%. At the end of the surgery, block was reverted with a atropine/neostigmine mixture at a standard dosage (0.02mg/kg and 0.04 mg/kg, respectively), and patient extubated without declaring a TOF ratio in the paper. Since "time to extubation" has been evaluated among the three groups, it may be advisable to report these data. Moreover, since a profound muscle block during pneumoperitoneum has been reported to improve post-operative analgesia, it may advisable to report data around intra-operative TOF ratio in the
different groups, too.

Post-operative pain, assessed by mean of VAS at 5 min and at 20 min post extubation is considered a secondary outcome, but no information is provided around analgesia given. Is it multimodal (locoregional and/or systemic)? What kind of medications and dosages are infused?

Authors provide detailed information around management of possible intra operative complication. They define hypotension as MAP<60mmHg and state that investigators react with fluid boluses and vasoconstrictor, without taking in account data coming from pEEG, maybe suggestion possibility of hypotension due to oversedation. Please clarify this point.

Authors state they routinely use, as intraoperative fluids, sodium ringer lactate and hydroxyethyl starch, even in the case of stable hemodynamic condition and not overt bleeding patients. Please clarify this point.

Authors state they routinely use, as intraoperative fluids, sodium ringer lactate and hydroxyethyl starch, even in the case of stable hemodynamic condition and not overt bleeding patients. Please clarify this point.

Since the primary outcome from this study is the difference in SVR between different groups, it may be useful to consider baseline patients' medication history, especially in case of essential hypertension. Chronic beta-blockade, calcium antagonists or ACE inhibitors may interfere with hemodynamic response to pneumoperitoneum.

Authors state that patients from group H needed less a lower remifentanil infusion rate compared to patient from L and S group. This sentence may need to be supported with explanation on the way adopted in the study to manage remifentanil infusion rate among different investigators and patients.

**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

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

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license ([http://creativecommons.org/licenses/by/4.0/](http://creativecommons.org/licenses/by/4.0/)). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal