Author’s response to reviews

Title: The impact of dexmedetomidine added to ropivicaine for transversus abdominis plane block on stress response in laparoscopic surgery: a randomized controlled trial

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Reply/Response Letter

Dear Editor Tu,

Thank you very much for your letter and advice. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewer, and the amendments are highlighted in red in the revised manuscript. Point by point responses to the editor’s and reviewer’s comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

I look forward to hearing from you soon.

With best wishes,

Yours sincerely,
We would like to express our sincere thanks to the editor and the reviewer for the constructive and positive comments.

Replies to Reviewer

1. Information around patient's medical history and regular medications must be provided, regular beta-blocker, ACE-inhibitors and other cardiovascular medications, steroids, diabetes, etc.

Answer: Subjects didn’t suffered from hypertension, heart disease and diabetes. They had no medication history including regular beta-blocker, ACE-inhibitors, other cardiovascular medications and steroids. This information has now been provided in the revised manuscript (Methods section, line 145-147, page 7).

Furthermore, the information about patient's medical history and regular medications were also described in the exclusion criteria (Methods section, line 149-153, page 7).

2. Indication for surgery, cancer none-cancer surgery, preoperative cytostatic, radiation or further pretreatment.

Answer: Included procedures were myomectomy, ovarian cystectomy and diagnostic procedures, subjects were excluded if they had malignant tumors. Therefore they were none-cancer surgery. Subjects have not received preoperative cytostatic, radiation or further pretreatment (Methods section, line 147-149, page 7).

3. Fasting, time without drink and food. Nutritional status, BMI.

Answer: The fasting period for solids was 8 hours, and for clear liquids was 2 hours before surgery. All participants were in good nutritional status (Methods section, line 155-156, page 8). The patients’ BMIs were listed in Table 1.
4. Intraoperative course, fluid regime, handling of low blood pressure and or heart rate, amount of ephedrine, norepinephrine, phenylephrine, atropine etc.

Answer: A 20 gauge peripheral intravenous catheter was inserted under local anesthesia, and infusion of Ringer’s lactate was started at the speed of 6-8 ml/kg/h (Methods section, line 169-171, page 8).

If any, were treated as follows: bradycardia: atropine 0.5 mg was administrated intravenously; tachycardia: remifentanil 1 μg/kg was administrated intravenously in titrated dose; hypotension: ephedrine 6 mg was administrated intravenously in titrated dose; hypertension: propofol 20 mg was administrated intravenously in titrated dose and increasing the infusion rate of propofol and remifentanil (Methods section, line 213-218, page 10).

The amount of atropine during the surgery was higher in High DEX + ropivacaine group than the other groups (P < 0.05). But there were no significant differences about the intraoperative amount of ephedrine among the five groups (P > 0.05, Table 4) (Results section, line 288-290, page 13; The amounts of atropine and ephedrine during the surgery were added to the revised Table 4).


Answer: Blood loss were less 50 ml and no transfusion was performed during the operation in different groups (Results section, line 252-253, page 12).

6. Surgery performed

Answer: Included procedures were myomectomy, ovarian cystectomy and diagnostic procedures (Methods section, line 147-148, page 7).

7. The time points should be further discussed.

Answer: The time points have been further discussed in Discussion section.

In our study protocol we chose the following four observational time points: prior to induction (T0, baseline), prior to pneumoperitoneum (T1), prior to the end of pneumoperitoneum (T2), and at the end of surgery (T3). The time point of prior to induction means the period before patients received nerve block in the operating-room, as the baseline level. Based on the results (see Table 2), the baseline stress levels were consistent across the groups. We have focused on the effect of pneumoperitoneum and pain stimulus on stress response of body in our design. Therefore, we
chose 5 minutes before pneumoperitoneum as an observational time point to detect the stress level before pneumoperitoneum, which reflects the effects of incision and laryngoscopy/intubation, even or the TAP block on stress response. Five minutes before termination of pneumoperitoneum, the stress level was detected again indicated as the changing with pneumoperitoneum and pain stimulus. At the end of surgery, there were no surgical stimulus, and endotracheal tube was extubated. We have detected the stress level with no intervention and observed the recovery status. In fact, there was a strong stress response during the surgery as showed in Table 2 (Discussion section, line 392-405, page 18-19).

If a measurement was included shortly after pneumoperitoneum, it would provide more perfect change trend of stress level induced by pneumoperitoneum. It perhaps was another limitation in our study. To our surprise, the results of our research were not affected by the limitation (Discussion section, line 409-412, page 19).

8、Statistics, differences between groups should be better described. Adjustment for repeated tests should be commented.

Answer: Thanks for this reminder. The statistical methodology/analysis has been described in detail. We feel that post hoc Tukey multiple-comparisons test (despite it has limitation) could serve as proper adjustment test following repeated ANOVA and has now clearly stated this in the revised manuscript. Further, we have added the following detailed difference comparisons between groups in the revised manuscript.

Compared with Ropivacaine group, serum Cor, NE, E, IL-6 and Glu were significantly decreased from prior to pneumoperitoneum (T1) to the end of surgery (T3) in Low, Medium, and High DEX + ropivacaine groups (P < 0.05). All of the above stress parameters were significantly decreased from prior to pneumoperitoneum (T1) to the end of surgery (T3) in Medium and High DEX + ropivacaine groups compared with Low DEX + ropivacaine groups (P < 0.05). There were significant differences about these stress parameters from prior to pneumoperitoneum (T1) to the end of surgery (T3) between Medium and High DEX + ropivacaine groups (P < 0.05, Table 2) (Results section, line 261-268, page 12-13).

Additionally, MAP and HR levels from prior to pneumoperitoneum (T1) to the end of surgery (T3) in Control group were higher than the baseline, but decreased levels of MAP and HR in High DEX + ropivacaine group were shown in these three timepoints as compared with the corresponding baseline (Results section, line 276-279, page 13).

9、What’s more, another fund supported this study was supplemented in the revised manuscript (Funding section, line 435-436, page 20).