November 9, 2015

Re: World Journal of Gastroenterology, ESPS manuscript number: 22917

Dear Ya-Juan Ma and the editorial team at the *World Journal of Gastroenterology*,

The co-authors and I would like to thank you and your editorial team for your prompt and thorough review of our manuscript entitled '**A prospective study of efficiency/patient experience with anaesthesiologist assisted sedation for colonoscopy'**. The editorial comments were insightful and detailed and they are likely going to improve the quality and readability of our manuscript. Please find attached our detailed responses to each comment and our revised manuscript, with inputted changes highlighted in yellow.

Science editor comments:

SPECIFIC COMMENT:

1. The title must be informative, specific, and brief (Title should be no more than 10~12 words/60 bytes. Please revise it). Words should be chosen carefully for retrieval purposes. All nonfunctional words should be deleted, such as 'the', 'studies on', 'observations of', and 'roles of', *etc*.

> **RESPONSE:** Thank you for this suggestion. We agree the title was not specific enough as originally drafted.
>
> **CHANGE:** We have modified the title to, "Efficiency and Patient Experience With Propofol vs. Conventional Sedation – A Prospective Study"

SPECIFIC COMMENT:

2. Please provide a COMMENTS section

RESPONSE: Thank you for making the authorship aware of this requirement for our manuscript revision.

CHANGE: We have modified the revised manuscript to include the required COMMENTS section in the appropriate location within the document.

Reviewer #1 comments to the authors (reviewer's code – 03441951):

GENERAL COMMENTS:

1. This prospective non-randomized single-center study aims at evaluating the performance of anaesthesiologist-administered propofol sedation (AAP) versus endoscopist-administered conventional sedation (EAC). The overall findings suggest that total room time is increased with AAP although associated with less pain as perceived by the patient. The study is interesting and contributes to the ongoing discussion on the mode and delivery of sedation for colonoscopy.

RESPONSE: Thank you for your review. The authorship agrees this is an interesting study, which furthers discussion surrounding the ideal mode of sedation for colonoscopy.

CHANGE: None

SPECIFIC COMMENTS:

1. Who decided on whether the patient received an AAP-colonoscopy or an EAC-colonoscopy? Was it purely a choice by the patient? Did comorbidites have a say in it?

RESPONSE: At our institution, AAP-assisted colonoscopy and EAC are available to patients, however patients do not select a preferred sedation type. Thus, patients were enrolled as they presented to the endoscopy suite and there was no randomization or special consideration of patient factors inclusive of comorbidities when deciding on patients receiving EAC vs. AAP.

CHANGE: We have revised the Materials and Methods section to include, "We performed a prospective, non-randomized, comparative study recruiting patients during a three-month (12 week) consecutive period at a single high-volume Canadian academic outpatient endoscopy unit where both AAP and EAC are utilized. Bowel preparation protocols, colonoscopy indication, therapeutics performed and ASA class are identical for patients receiving both AAP and EAC and patients do not select the type of sedation they receive."

SPECIFIC COMMENTS:

2. On your multivariate analyses, what did you adjust for? It is not clear to me from the statistical methods section.

RESPONSE: We regret this oversight and have provided an update to the study methods.

CHANGE: We have revised the statistical methods section of the manuscript to include, "Multivariate analysis was utilized to normalize the collected data set. Adjustments were made for a non-normally distributed total room and total procedure time and between-group statistical tests are based on the log-transformed data."

SPECIFIC COMMENTS:

3. Many other aspects potentially affecting procedure-related pain and tolerance, intubation rates and total time are not accounted for at baseline, e.g. cap-assistance for the colonoscopies (1), magnetic endoscopic imaging devices (2), anti-spasmotic medication (3). This limitation deserves mentioning in the discussion if the raw data is impossible to collect.

RESPONSE: We agree this is an important consideration and represents a limitation of our current investigation as regrettably this data was not collected during the enrollment phase of the study.

CHANGE: We have revised the Discussion to include the following statement, "Its worth mentioning that some other factors that could potentially improve overall colonoscopy performance and patient experience – particularly for inexperienced endoscopists – such as cap-assisted colonoscopy, magnetic endoscopic imaging system and anti-spasmotic medication were not investigated in our study."

SPECIFIC COMMENTS:

4. Who made the phone calls to the patients? The endoscopist, a nurse, a third person? This might have implications to the validity of the answers.

RESPONSE: All post-procedure patient satisfaction surveys were administered by the study research assistant, who was not involved in the direct treatment of any patient. We regret that this was not clear in the initial methods section and have revised accordingly.

CHANGE: We have revised the Materials and Methods to include, "Throughout the study, a research assistant (PT) was available to answer participants' questions. The study research assistant was not involved in any direct care of study participants and was responsible for collecting patient written consent, recording study measurable and contacting patients post-procedure for the patient satisfaction survey."

SPECIFIC COMMENTS:

5. How did you define cecal intubation? By identification of the ileocecal valve, the appendiceal orifice, ileal intubation?

RESPONSE: We regret this was not clear as initially drafted and have revised accordingly.

CHANGE: We have revised the Results to include, "The cecum was intubated in all patients and confirmed by standard cecal landmarks and in most instances by intubation of the ileum and direct visualization of intestinal villi."

SPECIFIC COMMENTS:

6. Relatively few patients responded to the questionnaires. Do you have any information on the characteristics of these patients? Age, gender, BMI, etc.?

RESPONSE: We regret that we were not allowed to record data specific to participants responding to the patient satisfaction survey as outlined by our institution research ethics approval mandate for this specific study.

CHANGE: None

SPECIFIC COMMENTS:

7. In Table 2, you report that there were two adverse events in the AAP group (1.6%) and 0 in the EAC group (0%) with a corresponding p-value of < 0.001. Running a Fishers exact I find a two-sided p-value of 0.5. Please explain this discrepancy.

RESPONSE: We regret this error and thank you for drawing this to our attention.

CHANGE: We have repeated all other statistical analyses in the study to confirm accuracy as well and have removed Table 2 in accordance with reviewer #2's recommendation as outlined below.

SPECIFIC COMMENTS:

8. I enjoyed reading the manuscript and look forward to receiving a revised manuscript, considering the abovementioned enquiries.

> **RESPONSE:** Thank you for your careful review and insightful revisions. We have responded to your revisions and believe they have significantly enhanced the quality of our manuscript.

Reviewer #2 comments to the authors (reviewer's code – 03270846):

COMMENT:

GENERAL COMMENTS: This study includes different and interesting findings about sedation for colonoscopy procedure. The study results show that AAP is associated with less pain but total procedure room time is increased.

> **RESPONSE:** Thank you for your review. We agree that many important questions have arisen from our study and that future research is required to further elucidate the most effective sedation type to pursue for colonoscopy in future.

SPECIFIC COMMENTS:

1. In the section of "Materials and Methods", sample selection and data collection must be extended. For example, the following knowledge can be added to the section; *sample selection, number of the participants quitting the study, number of the participants that is not available post procedure. *verbal/written consent

from the participants, *the number of gastroenterologists participating to the procedure, *differences in the pre-procedure and procedure duration(bowel preparation, sedation modalities, deciding process to the patient receive propofol sedation or conventional sedation), *patient satisfaction status at the first 24 hours after the procedure(if you have evaluated), *rate of the telephone survey 48. hours post procedure and rate of the 72. hours post procedure, *evaluating patient satisfaction in different hours(48. Hours and 72. hours) might have limitations to the interpretation of the study results.

RESPONSE: We agree that this was not well outlined in the initial Materials and Methods section submitted and have revised accordingly.

CHANGE: We have added the following to the 'Materials and Methods' section, "Bowel preparation protocols are identical for patients receiving both AAP and EAC and patients do not select the type of sedation they receive…Patients were provided a contact telephone number and electronic mail address of the study research assistant who was available to answer study questions and remove participants from the trial at their request at any point during the study period. A total of five patients declined participation in the study and no participants requested to be removed from the study after enrolment… Six gastroentrologists participated in the study… To avoid recall biases and maximize group standardization, no participants were contacted prior to 48-hours post-procedure, nor were participants contacted beyond the 72-hour post-procedure time interval. Participant satisfaction data was combined according to the group represented by each participant (AAP or EAC). Patient satisfaction data was analyzed as a whole. Thus, stratification for difference between participants reached at the 48 versus 72-hour post-procedure time point was no performed. Throughout the study, a research

assistant (PT) was available to answer participants' questions. The study research assistant was not involved in any direct care of study participants and was responsible for collecting patient written consent, recording study measurable and contacting patients post-procedure for the patient satisfaction survey."

SPECIFIC COMMENTS:

2. In the "Results" section; reduce the number of tables. If you give all findings in the text you can exclude the related table(s). For example table 2.

RESPONSE: We agree with this recommendation.

CHANGE: We have removed Table 2 from the analysis.

SPECIFIC COMMENTS:

3. In the text, you must give tables only in a form. Using in different styles (Table 2 and Table II) will reduce the readability of the paper.

RESPONSE: We agree with this recommendation.

CHANGE: We have resolved this discrepancy within the text of the manuscript to report tables in the form of 'Table 1'.

SPECIFIC COMMENTS:

4. In the appendix, patient satisfaction survey is defined (24-72 hours) post procedure in the title. This will create a complexity. I think you can exclude the appendix because the survey questions are given in the table 5.

RESPONSE: We agree with this recommendation.

CHANGE: We have revised the manuscript to remove the appendix as recommended.

SPECIFIC COMMENTS:

6. The section of "Discussion" must be extended according to the results. Some of the findings have remained raw data. You must interpret all important findings that are presented in the results.

RESPONSE: We agree with this recommendation.

CHANGE: We have revised the discussion to further interpret the important results of our investigation.

SPECIFIC COMMENTS:

7. This manuscript includes important results on a controversial issue about colonoscopy sedation procedure. It was a great pleasure to examine your manuscript. After completing the revisions, I think it will be even better.

RESPONSE: The authorship agrees with this assessment and wish to thank you for your helpful revisions which we believe have further enhanced the quality of the manuscript.

We thank you again for your time and attention. We look forward to your reply.

Sincerely,

Nitin Khanna, MD, FRCPC