

Author Responses to Reviewers

Reviewer 00506481

The findings are very valuable and should be shared with the scientific community. The corrections are shown as green highlight in the manuscript. The conversion from prolonged intravenous fentanyl infusion to enteral methadone in critically ill children was studied methodically among two groups viz Rapid Conversion Group (RCG) and Slow Conversion Group (SCG) respectively. RCG = Rapid conversion group consisted of patients who were completely converted from fentanyl infusion directly to enteral methadone in 48 hours or less; SCG = Slow conversion group consisted of patients who were completely converted from fentanyl infusion directly to enteral methadone in more than 48 hours. It was observed that it is feasible to convert from intravenous fentanyl infusion directly to enteral methadone within a timeframe of 48 hours using a methadone:fentanyl dose conversion ratio of approximately 2.5:1 to minimize withdrawal and reduce need for rescue opioids.

Author response: We thank the reviewer for the supportive comments. We have highlighted the changes recommended by the reviewer in yellow (multiple instances).

Reviewer 00069139

The manuscript describes a retrospective review of analgesic conversion in a PICU setting. The study summarised that rapid conversion resulted in a lower withdrawal and shorter ICU stay. Designs and statistic are excellent (except for the retrospective nature). English language is spotless. The manuscript is highly recommended for publication.

Author response: We thank the reviewer for the supportive and helpful comments. We have highlighted the changes recommended by the reviewer in yellow (multiple instances).

1. How can we tell that the 'Rapidness' in RCG is an independent parameter. Is it possible that quick weaning was achieved because there was less withdrawal symptoms and those cases basically were easy-to-switch cases with less ICU stay.

Author response: We agree with the reviewer concern and have added the following statement (highlighted in yellow) to the limitations paragraph in the Discussion to address this concern. "Though it is possible that patients in the RCG happened to experience less withdrawal symptoms and were easier to wean compared to those in the SCG, both groups were well balanced with regard to age, illness severity, diagnoses,

and extent of exposure to IV fentanyl infusion (Table 1).” As the two groups were well balanced at the start of the conversion from IV fentanyl infusion to enteral methadone, it is likely that both groups were at similar risk for withdrawal and ease of/difficulty with conversion. We hope that this will be satisfactory to address the reviewer concern.

2. Four-digit p-value (Table 2-3) might be too much for this kind of paper.

Author response: We have revised all the 4 digit p-values in Tables 2 and 3 to < 0.05 (highlighted in yellow, multiple instances). We hope that this will be satisfactory to the reviewer.

3. Page 2 Line 11: "48-hour" needs a hyphen.

Author response: We have made the change as recommended (highlighted in yellow).

4. Discussion is informative, but a bit lengthy.

Author response: As suggested by the reviewer, we have shortened the Discussion by deleting material from the first and third paragraphs in the Discussion section. We hope that this will be satisfactory to the reviewer.

Author Responses to Editorial Comments

All comments by the Editor have been addressed and modifications have been made to the manuscript as recommended.

1. The postal code has been provided as requested

2. Signature attested statements have been provided for: Institutional review board statement, Informed consent statement, Conflict of interest statement, Biostatistics statement, Data sharing statement, Grant application form, and Scientific Research process

3. Copyright Assignment has been provided with signatures from all authors

4. Google scholar search results have been provided

5. Attestation of statistical analysis has been added to the Materials and Methods in the section on Statistical Analysis

4. Audio core tip has been provided

5. Comments have been provided

6. Figure Legend has been revised to provide a total title for Figure 1 followed by sub-titles