Author’s response to reviews

Title: Pharmacological methods for reducing coughing on emergence from elective surgery after general anesthesia with endotracheal intubation: protocol for a systematic review of common medications and network meta-analysis

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Author's response to reviews:

Dear Editor and Reviewers:

Thank you for your helpful comments in improving our protocol, “Pharmacological methods for reducing coughing on emergence from elective surgery after general anesthesia with endotracheal intubation: a protocol for a systematic review of common medications and network meta-analysis.”

In response to Reviewer #1’s comments:

1. Endotracheal tube cuff and anesthetic methods subgroup analysis: We agree that the endotracheal tube type and its cuff type may affect the likelihood of coughing. Given the wide variety of endotracheal tubes and brands available and variability of reporting on the type of endotracheal tube in studies, however, this may be difficult to analyze. Furthermore, upon the initial scoping review, data on endotracheal tube cuff are not frequently presented and thus we do not feel that we would have enough data to perform a subgroup analysis.

We do agree that total intravenous anesthetic (TIVA) and volatile anesthetic may affect the incidence and severity of emergence coughing. Given that it’s a pharmacological method in line with our overall research theme and data that we plan on collecting, we will do subgroup analysis on this issue.
2. Heterogeneity of dosages and infusions: We concur that the heterogeneity of dosages may affect the efficacy of study medications on reducing emergence cough. However, we are unable to find reliable studies that may help us determine what are considered, for instance, low, medium or high doses of a particular study medication.

Thus, what we plan to do to rectify this situation is to do a subgroup analysis by splitting the dosages obtained from the selected studies into two groups based on the median dosing regimen. Dosages that were less than the median would count as “low dose”, and dosages more than the median would count as “high dose”. For study medication with no clear median dosage, and/or a large degree of heterogeneity among dosing regimens preventing the creation of clear definitions, then that would be reported in the results section.

3. Gray Literature: Reviewer #1 commented how the gray literature, as a non-peer-reviewed document source with risk of bias, may negatively impact the reliability of the results. We believe in the importance of finding and including gray literature results in our meta-analysis. Published, peer-reviewed literature is not necessarily at lower risk of bias. Furthermore, by including the gray literature, we aim to reduce publication bias.

If the concern is that gray literature, such as abstracts, may be difficult to assess for bias, then we can perform a subgroup analysis of studies that are either high risk of bias or conference abstract abstracts (which often contain limited information) to help us evaluate the risk of bias of including such studies.

Regarding Reviewer #2’s comments:

1. Subgroup analysis: We agree on doing further subgroup analyses that may affect coughing incidence and severity, including total intravenous anesthetic (TIVA) versus volatile anesthetic.

2. Balloon pressure, type of endotracheal tube, patient position: We agree that balloon pressure and type of endotracheal tube may affect the coughing severity and incidence on extubation. To analyze both of these factors, however, may not add additional information. For balloon pressures, we believe that that the range of balloon pressures in these studies is likely to be narrow. Cuff pressures must be sufficiently high enough to minimize the leak during positive pressure ventilation, but at the same time, cannot be too high to cause mucosal ischemia, typically quoted at around 25~35 cm H2O. As such, the variability among cuff pressures are likely to be minimal.

Furthermore, given the wide variety of endotracheal tubes and brands available and variability of reporting on the type of endotracheal tube in studies, this may be difficult to analyze. Furthermore, upon the initial scoping review, data on endotracheal tube cuff are not frequently presented and thus we do not feel that we would have enough data to perform a subgroup analysis.
Please also see our revised manuscript reflecting the changes made in response to the reviewer’s suggestions.

Thank you again for your suggestions.

Sincerely,

Alan Tung