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Comment on dexmedetomidine systematic review and meta-analysis methodology

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Dear Editor,

We were reading a recently published systematic review and meta-analysis of dexmedetomidine in critically ill mechanically ventilated patients [1] and wanted to point out some areas that concerned us with respect to the methodology used. More importantly our issues with the methodology have important implications on the conclusions that may be drawn by the authors and the readers of this important piece of work. If our observations are indeed accurate, a re-analysis of the data might lead the authors (and readers) to come to a completely different conclusion regarding the efficacy and safety of dexmedetomidine in this patient population. Our concerns are outlined below.

First, we noticed that the Moldonado study (Ref. 32 in the article) was entered into the meta-analysis twice for the length of ICU stay outcome and the duration of mechanical ventilation. Our understanding is that this is incorrect because the patients who received dexmedetomidine were accounted for twice in these analyses. The more appropriate method would be to enter the study twice (i.e., once for each comparator) but for each entry use a denominator of 20 for dexmedetomidine (i.e., half the patients randomized to dexmedetomidine).

Second, the studies by Martin (Ref. 20 in the article) and Herr (Ref. 19 in the article) appeared to have measured the incidence of "agitation". However, the data from these trials were entered into the meta-analysis as "delirium". As far as we understand, delirium and agitation are not synonymous and cannot be analyzed together.

Third, the studies that were combined in Fig. 6 all measured delirium in substantially different ways, making the meta-analysis less meaningful. One study measured CAM-ICU positive patients plus those with an ADR of delirium or confusion, another measured CAM-ICU positives, and another measured CAM-ICU positives only when RASS scores were between -2 to +1. Either the reader should be alerted to the differences more explicitly or the appropriateness of pooling the data should be reconsidered (especially in

light of the significant statistical heterogeneity).

The fourth issue had to do with heterogeneity in general. Several of the meta-analyses found significant heterogeneity and the authors do mention several possible reasons for this. They do not, however, explore any of those reasons in detail (i.e., by conducting specific post hoc sensitivity analyses). In our opinion, if any of their explanations for heterogeneity are correct, then there may be a strong argument to not meta-analyze the data.

Conflict of interest None.

Reference

1. Tan JA, Ho KM (2010) Use of dexmedetomidine as a sedative and analgesic agent in critically ill adult patients: a meta-analysis. *Intensive Care Med* 36:926–939. doi:[10.1007/s00134-010-1877-6](https://doi.org/10.1007/s00134-010-1877-6)

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