Reviewer’s report

Title: Adding dexmedetomidine to morphine-based analgesia reduces early postoperative nausea in patients undergoing gynecological laparoscopic surgery: A randomized controlled trial

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Reviewer: Daniela Ghisi

Reviewer's report:

Summary

The article is well drafted, and the modality of the study is solid since it is a double-blind, randomized, controlled trial. The question of the trial appears to be flexible, interesting, ethical and relatively innovative since some articles already present in the literature on the use of dexmedetomidine as adjuvant to analgesia with PCA and as adjuvant in the prevention of post-operative nausea and vomiting (PONV).

The biologically rational behind the study appears to be solid, based on the prediction of a reduction in opioid consumption as a potential factor for a drop in the occurrence of PONV (other mechanisms could facilitate the decrease of PONV by dexmedetomidine).

The topic discussed and the choice of the primary endpoint (PONV reduction in the first 24 hours) appears to be relevant from the clinical point of view, representing post-operative nausea and vomiting, a stigma for gynecological surgery. We emphasize that only myomectomy and laparoscopy-assisted vaginal hysterectomy surgeries are part of the included population.

The study aims at demonstrating how an intra-operative bolus of dexmedetomidine (0.4 mcg/kg) followed by the association of dexmedetomidine at a concentration of 1 mcg/ml in PCA with morphine 0.5 mg/ml administered in an infusion modality baseline of 1 ml/hour and boluses of 2 ml with an 8-minute lock-out may reduce the incidence of post-operative vomiting compared to morphine PCA alone without intra-operative bolus of dexmedetomidine in patients undergoing gynecological surgery with TIVA general anesthesia with the use of dexamethasone as prophylaxis for PONV.

The use of dexmedetomidine has the dual purpose of improving post-operative recovery and decreasing PONV incidence.

The primary endpoint is not statistically significant since the reduction of PONV in the first 24 hours is only 21% compared to an expected 50%.

The study confirms that the use of a dexmedetomidine intra-operative bolus allows to reduce PONV in the early post-operative period (first two hours).
The reduction in the occurrence of PONV and the consumption of opioids, as well reported by the author, must be well weighed compared to the increase of bradycardia and sedation (dose-dependent dexmedetomidine side effect).

Major Issues

* In the paragraph of the abstract concerning the methods it would be interesting to find the use of dexmedetomidine intra-operative bolus and not only the setting of the PCA (line 17, page 2).

* In the paragraph of the abstract and the article concerning conclusions the authors presume that the addition of dexmedetomidine to morphine PCA is able to reduce the onset of early PONV. We believe that it is not possible to conclude that reduction in PONV results from the use of dexmedetomidine in PCA or the intra-operative bolus. Furthermore, as this is a secondary endpoint and the use of multiple tests is not reported in the statistical methods, we consider this result not justifiable from a statistical point of view.

* Line 54 on page 12 points out how the reduced consumption of opiates and, therefore, of dexmedetomidine may have influenced the outcome of the study. Considering that the consumption of morphine is equal in the two groups, how could incidence for PONV decrease without increasing the concentration and, therefore, the total volume administered of dexmedetomidine? What considerations regarding possible side effects?

Minor Issues

* In the calculation of the sample size an incidence reduction of PONV of 50% is estimated: it would be interesting to understand from which article this data is extrapolated because it's crucial in the statistical failure of the study.

* Drug preparation for the different study groups is entrusted to a study coordinator and not to an external service.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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