

## Comparative safety of serotonin (5-HT<sub>3</sub>) receptor antagonists in patients undergoing surgery: A systematic review and network meta-analysis

### Summary

We conducted a systematic review to examine the comparative safety of 5-HT<sub>3</sub> antagonists in patients undergoing surgical procedures. Using network meta-analysis we found that significantly more patients receiving granisetron and dexamethasone experienced arrhythmia. No other significant safety signals were identified for delirium, mortality, and QT prolongation.

### Implications

Overall, granisetron plus dexamethasone was found to carry the highest risk of arrhythmia of any of the 5-HT<sub>3</sub> antagonists assessed. Though no significant safety effects were found for other outcomes, a lack of consistent harm reporting among the included studies was noted. Further research in the use of 5HT-3 antagonists for surgical patients should focus on harm reporting as well as effectiveness.

**Reference:** Tricco AC, Soobiah C, Blondal E, et al. Comparative safety of serotonin (5-HT<sub>3</sub>) receptor antagonists in patients undergoing surgery: a systematic review and network meta-analysis. *BMC Med.* 2015;13:142.

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**For more information, please contact Dr. Andrea Tricco:**  
[triccoa@smh.ca](mailto:triccoa@smh.ca)

### What is the current situation?

- Serotonin (5-HT<sub>3</sub>) receptor antagonists are commonly used to decrease nausea and vomiting for patients undergoing surgery
- Some evidence exists that shows that 5-HT<sub>3</sub> receptor antagonists may also cause harm, such as arrhythmia
- The aim of this review was to conduct a systematic review and network meta-analysis (NMA) to determine the safety of 5-HT<sub>3</sub> receptor antagonists

### How was the review conducted?

- Eligible study designs included randomized clinical trials (RCTs) and non-randomized studies (e.g., cohort) examining 5-HT<sub>3</sub> antagonists (granisetron, ondansetron, dolasetron, tropisetron) vs. each other or placebo in patients of all ages undergoing surgery
- The outcomes of interest included arrhythmia, QT prolongation, PR prolongation and mortality
- Screening of the literature search results, data abstraction, and risk-of-bias assessment were conducted independently by two reviewers. Conflicts were resolved through discussion
- The protocol (or plan) for the review was registered and published
- Direct pairwise meta-analysis and network meta-analysis were conducted

### What did the review find?

- A total of 120 relevant studies were included, providing data on 27,787 patients
- NMA was conducted to examine arrhythmia (31 RCTs) and delirium (18 RCTs), and 2 meta-analyses were conducted to examine mortality (3 RCTs) and QT prolongation (2 RCTs)
- Significantly more patients receiving granisetron plus dexamethasone experienced arrhythmia compared to all other interventions and placebo
- No statistically significant differences in delirium frequency was observed across all treatment comparisons
- No statistically significant differences were observed regarding mortality and QT prolongation in meta-analysis
- No studies reported on PR prolongation or sudden cardiac death