

Comparative safety of serotonin (5-HT₃) 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-HT₃ 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-HT₃ 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-HT₃) receptor antagonists in patients undergoing surgery: a systematic review and network meta-analysis. *BMC Med.* 2015;13:142.

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What is the current situation?

- Serotonin (5-HT₃) receptor antagonists are commonly used to decrease nausea and vomiting for patients undergoing surgery
- Some evidence exists that shows that 5-HT₃ 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-HT₃ receptor antagonists

How was the review conducted?

- Eligible study designs included randomized clinical trials (RCTs) and non-randomized studies (e.g., cohort) examining 5-HT₃ 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