Research Brief

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Comparative safety and effectiveness of serotonin receptor antagonists in patients undergoing chemotherapy: a systematic review and network meta-analysis

Summary

We conducted a comprehensive systematic review and network meta-analysis on 5-HT_3 receptor antagonists for patients undergoing chemotherapy. All agents were effective for reducing risk of nausea, vomiting, and chemotherapy-induced nausea or vomiting. Our results suggest that most 5-HT_3 receptor antagonists were relatively safe when compared with each other, yet none of the studies compared active treatment with placebo for harms. However, dolasetron+ dexamethasone may prolong the QTc in children and adults compared to ondansetron+dexamethasone.

Implications

Overall, most 5-HT_3 receptor antagonists are effective for nausea and vomiting outcomes. The treatments were relatively safe when compared with each other, yet none of the studies compared active treatment with placebo for harms. Additional studies are needed to characterize the cardiac and cognitive safety of these treatments, particularly in relation to placebo. Until then, it would be prudent for clinicians to obtain baseline electrocardiographic tracings before prescribing these common antiemetics to patients undergoing chemotherapy.

Reference: Tricco AC, Blondal E, Veroniki AA, et al. Comparative safety and effectiveness of serotonin receptor antagonists in patients undergoing chemotherapy: a systematic review and network meta-analysis. BMC Med. 2016;14 (1):216.

PMID: 28007031

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What is the current situation?

- Chemotherapy is a major component of cancer therapy, though chemotherapy-induced nausea and vomiting (CINV) is common and very debilitating.
- Serotonin (5-HT_3) receptor antagonists are used to decrease nausea and vomiting in patients undergoing chemotherapy, though concerns have been raised that they may be associated with cardiac risk.

What is the objective?

- To determine the comparative safety and effectiveness of 5-HT_3 receptor antagonists for patients undergoing chemotherapy.

How was the review conducted?

- The protocol for the review was registered and published.
- MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials, conference abstracts, and trial registries were searched from inception until December 2015. The reference lists of included studies and relevant reviews were scanned.
- Studies comparing 5-HT_3 receptor antagonists (i.e. dolasetron, granisetron, ondansetron, palonosetron, ramosetron, tropisetron) with each other or placebo administered to patients undergoing chemotherapy were eligible.
- Screening of literature search results, data abstraction and risk-of-bias assessment were conducted independently by two reviewers.
- Outcomes of interest included the number of patients experiencing: arrhythmia, QTc prolongation, QRS interval prolongation, death, sudden cardiac death, delirium, no nausea, no vomiting, no CINV, and severe vomiting.
- Random-effects and network meta-analysis (NMA) were conducted.

What did the review find?

- 299 studies (with 58,412 patients) were included. None of the included studies reported harms for active treatment versus placebo.
- NMA on the risk of QTc prolongation showed a significantly greater risk for
- dolasetron+dexamethasone versus ondansetron+dexamethasone (4 RCTs, 3,358 children and adults).
- For NMAs on number of patients without nausea (44 RCTs, 11,664 adults), number of patients without vomiting (63 RCTs, 15,460 adults), and number of patients without chemotherapy-induced nausea or vomiting (27 RCTs, 10,924 adults), all agents were significantly superior to placebo.
- For NMA on severe vomiting (10 RCTs, n = 917 adults), all treatments decreased the risk, but only ondansetron and ramosetron were significantly superior to placebo.
- According to the rank-heat plot, palonesetron+steroid was ranked the safest and most effective agent overall.

Funded by CIHR

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada