Review of the preclinical pharmacology and comparative efficacy of 5-hydroxytryptamine-3 receptor antagonists for chemotherapy-induced emesis

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Authors' objectives
To examine the comparative effectiveness and safety of 5-Hydroxytryptamine-3 receptor antagonists in the prophylaxis of chemotherapy-induced emesis, and to examine patient preferences for different compounds used.

Searching
MEDLINE and CancerNet were searched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), including crossover studies, were included.

Specific interventions included in the review
The 5-hydroxytryptamine-3 (5-HT3) receptor antagonists granisetron, ondansetron and tropisetron.

Participants included in the review
Patients undergoing either moderate or highly emetogenic chemotherapy. In 5 out of 7 trials the patients in the treatment group were receiving cisplatin (n=2369).

Outcomes assessed in the review
Emetic episodes (typically, the number of vomiting episodes and/or retches), nausea, and patient preference were assessed.

How were decisions on the relevance of primary studies made?
The author does not state how the papers were selected for review, or how many of the reviewers performed the selection.

Assessment of study quality
The validity of the individual trials was assessed in terms of study design (open versus blinded, crossover versus parallel, method of randomisation), and the limitations of the individual studies were described in this context. The author does not state how the papers were assessed for validity, or how many of the reviewers performed the validity assessment.

Data extraction
The author does not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The studies were combined in a qualitative narrative, with the individual study details given in tabular format.

How were differences between studies investigated?
No quantitative test of heterogeneity was conducted: differences between the studies were described narratively.
Results of the review
Seven studies, five involving cisplatin chemotherapy and two involving non-cisplatin therapy, were included.

Ondansetron completely controlled vomiting in 45-89% of patients, granisetron controlled vomiting in 60-62% of patients and tropisetron controlled vomiting in 44-75% of patients in these comparative trials.

A single intravenous dose of granisetron (3mg) was found to be as effective as multiple (8mg x 3) or single (32mg) IV doses of ondansetron in preventing acute nausea and emesis.

The two moderately emetogenic clinical trials showed granisetron (3mg IV) to be as effective as ondansetron (8mg IV/24 mg orally) and tropisetron (5mg IV). Three of the four crossover trials showed a patient preference for granisetron.

Cost information
US costs of FDA-approved and non-FDA approved dosages of granisetron and ondansetron are reported. Separate costs for these two drugs are also given according to whether cisplatin or non-cisplatin chemotherapy is employed. However, the authors point out that these costs are likely to vary with individual institutional discounts. No detailed economic analysis is reported.

Authors’ conclusions
The three 5-HT3 receptor antagonists examined are equally effective in the prevention of emesis associated with mid-range and high-dose cisplatin. Difference in patient preference and cost should therefore be taken into account when selecting which agent to use.

CRD commentary
There are large differences between the included studies in terms of both the measurement of outcomes and in patient demographics. For example, trials vary from 90% female to 77% male, and vary in terms of the participants’ prior experience of chemotherapy. These factors are likely to influence the findings regarding the efficacy of these drugs. Although limitations of the included trials are discussed in the article, the variations in quality and design of trials may impair the generalisability of the findings.

The review also suggests that the studies published to date have lacked the statistical power to demonstrate a difference between the drugs, and much larger studies are required. The review therefore cannot exclude the possibility that differences in effectiveness between these drugs do indeed exist.

No dates or search terms are given for the databases searched, making it difficult to determine whether all relevant studies are likely to have been identified.

Bibliographic details

PubMedID
7707101

Other publications of related interest
Two other meta-analyses on this issue have been published:


Indexing Status
Subject indexing assigned by NLM

MeSH
Antiemetics /economics /therapeutic use; Antineoplastic Agents /adverse effects; Cisplatin /adverse effects; Granisetron /therapeutic use; Humans; Indoles /therapeutic use; Ondansetron /therapeutic use; Prognosis; Serotonin Uptake Inhibitors /economics /therapeutic use; Vomiting /chemically induced /drug therapy

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.