Effectiveness of Oral 5-HT_3 Receptor Antagonists for Emetogenic Chemotherapy

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Purpose/Objectives: To review the efficacy and safety of the oral 5-hydroxytryptamine$_3$ (5-HT_3) receptor antagonists and the use of oral and IV antiemetic therapy during and after hospital admission.

Data Sources: Articles in medical and nursing literature

Data Synthesis: Use of oral antiemetics may help patients avoid potential complications associated with IV administration and be more convenient. They also are likely to lower staff and materials costs compared to IV formulations. Oral granisetron is the only oral antiemetic approved in the United States for use with highly emetogenic chemotherapy regimens. Oral dolasetron and ondansetron are indicated for use with moderately emetogenic chemotherapy

Conclusions: Oral therapy is preferable to IV formulations for most patients. The oral 5-HT_3 receptor antagonists approved for chemotherapy-induced nausea and vomiting include dolasetron, granisetron and ondansetron. Oral granisetron is differentiated for its safety, efficacy, and use in highly and moderately emetogenic chemotherapy

Implications for Nursing Practice: Oral antiemetics are preferable to IV antiemetics because of decreased total costs and greater convenience for patients who are able to ingest oral medication.

Key Points . . .

- The 5 HT_3 receptor antagonists are the newest generation of antiemetic drugs.
- Three currently are approved for use in the United States, but, because of cost, their use has been restricted to patients receiving particularly emetogenic chemotherapy.
- All three drugs are effective against mild to moderately severe nausea and vomiting, but only granisetron has been approved for use in patients receiving highly emetogenic drugs.[a]
- Use of all these drugs mandate careful patient assessment, patient education, and choice of the most appropriate route of administration to achieve the desired results in the most cost-effective manner.

As cytotoxic chemotherapy has evolved, so have the agents used to treat or prevent chemotherapy-induced side effects such as nausea and vomiting. The development of 5-hydroxytryptamine$_3$ (5-HT_3) receptor antagonists has greatly improved the control of acute vomiting (Ettinger, 1995; Perez, 1995). Three 5-HT_3 antagonists are approved for use in the United States: granisetron (Kytril , SmithKline Beecham Pharmaceuticals, Philadelphia, PA), ondansetron (Zofran , Glaxo Wellcome Inc., Research Triangle Park, NC), and, most recently, dolasetron mesylate (Anzemet , Hoechst Marion Roussel, Inc., Kansas City, MO).

The three agents marketed in the United States are available in injectable and oral formulations. Efficacy of IV formulations for the three agents is similar according to several comparative studies (Audhuy et al., 1996; Gebbia et al., 1994; Hesketh et al., 1996; Martoni, Angelelli, Guaraldi, Strocchi, & Pannuti, 1994; Navari et al., 1995; Noble et al., 1994; Ruff et al., 1994), but differences have been noted among the oral formulations. Oral ondansetron (recommended dosage 8 mg bid) and dolasetron (recommended dosage 100 mg qd) are approved in the United States for prevention of emesis associated with moderately emetogenic chemotherapy, such as carboplatin- and cyclophosphamide-based regimens. Only oral granisetron (2 mg qd) is indicated for preventing nausea and vomiting associated with highly and moderately emetogenic chemotherapy, including high-dose cisplatin (SmithKline Beecham Pharmaceuticals, 1997a)

Release of serotonin (5-HT) from enterochromaffin cells in the small intestinal mucosa contributes to acute nausea and vomiting associated with chemotherapy (Cubeddu, Hoffmann, Fuenmayor, & Finn, 1990). Serotonin activates receptors on vagal afferent fibers in the intestinal mucosa, which relays sensory information to discrete brain areas involved in nausea and vomiting (Cubeddu et al.; Ettinger, 1995). Oral 5-HT_3 receptor antagonists act by blocking the serotonin receptors in the gastrointestinal

[a] *Editor's note: Just prior to publication, we learned that Glaxo Wellcome Inc. recently received U.S. Food and Drug Administration approval for ondansetron as an indication also for highly emetogenic chemotherapy (24 mg tablet 30 minutes prior to chemotherapy). Please consult the ondansetron product literature for additional information.*

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