Oncology Patient Evidence-Based Notes (OPEN): Antiemetics for Chemotherapy-Induced Nausea and Vomiting

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Introduction

Oncology Patient Evidence-Based Notes (OPEN), the new format of this column, will present a clinical oncology question followed by a review and synopsis of a relevant evidence-based guideline.

Which antiemetic regimen will prevent or reduce acute and delayed nausea and emesis associated with chemotherapy administration?

Review of Evidence

Since the 1990s, new antiemetic agents have significantly reduced the incidence of nausea and vomiting associated with chemotherapy. Specifically, these agents are the serotonin receptor antagonists and consist of dolasetron (Anzemet®, Aventis Pharmaceuticals, Bridgewater, NJ), granisetron (Kytril®, Roche Pharmaceuticals, Nutley, NJ), ondansetron (Zofran®, GlaxoSmithKline, Research Triangle Park, NC), and tropisetron (Navoban®, Novartis Pharmaceuticals, Auckland, New Zealand [this product currently is not marketed in the United States]). A new class of agents, substance P/neurokinin 1 receptor antagonists, also is being used in combination with other antiemetics to prevent acute and delayed chemotherapy-induced nausea and vomiting. An example of this type of agent is aprepitant (Emend®, Merck & Co., Inc., Whitehouse Station, NJ).

As a result of the numerous agents now available, the American Society of Clinical Oncology developed an expert panel consisting of individuals from medical oncology, oncology nursing, radiation oncology, pediatric oncology, and oncologic pharmacy practice to review the literature on antiemetic therapy and create evidence-based clinical practice guidelines for the use of antiemetics during oncologic treatment (Gralla et al., 1999). A MEDLINE® literature search was performed by the panel using the following keywords or phrases: antiemetics, neoplasms, adverse effects, anticipatory plus nausea, anticipatory plus vomiting, serotonin antagonists, phenothiazines, butyrophenones, cannabinoids, corticosteroids, and metoclopramide. Based on the best available evidence and the panel’s best clinical judgment, clinical guidelines with levels of evidence were developed. Level I is the strongest evidence and is composed of randomized, controlled trials or meta-analyses of well-designed, controlled trials. Level V is the weakest evidence and is composed of expert opinions or case reports (Agency for Health Care Policy and Research, 1994) (see Figure 1).

Acute Emesis

For acute emesis that occurs within 24 hours of chemotherapy administration, granisetron, ondansetron, dolasetron, and tropisetron have equivalent antiemetic activity when administered as a single dose according to the established, proven dosages and may produce similar side effects, including mild headache, transient asymptomatic transaminase elevations, and constipation (level of evidence: I). Oral agents, in comparison to agents administered via IV, have equivalent antiemetic effectiveness and are recommended because of their cost and convenience benefits (level of evidence: I). Corticosteroids, such as dexamethasone, methylprednisolone, or prednisone, have equivalent antiemetic activity (level of evidence: IV and expert consensus) and are recommended as a single-dose administration (level of evidence: II). Dexamethasone doses greater than 20 mg do not provide any additional antiemetic activity. Other classes of agents, such as metoclopramides, phenothiazines, butyrophenones, and cannabinoids, are not recommended as first-line antiemetic therapy for chemotherapy with high emetic risk (level of evidence: I). Benzodiazepines and antihistamines are not recommended as single agent antiemetics; however, benefit has been shown in combination with antiemetic drugs (level of evidence: II). The most effective combination of antiemetics is a corticosteroid and a serotonin receptor antagonist (level of evidence: I).

Key Words: nausea, vomiting, antiemetics

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I. Meta-analysis of randomized, controlled trials
II. At least one well-designed randomized, controlled trial
III. At least one well-designed quasiexperimental study
IV. Well-designed nonexperimental studies (comparative, correlational, other descriptive studies)
V. Expert committee reports, expert opinions, case studies, consensus statements, expert judgment

FIGURE 1. EVIDENCE HIERARCHY
Note. Based on information from the Agency for Health Care Policy and Research, 1994.

Patient characteristics and emetic risk of chemotherapy agents should be considered when prescribing and administering antiemetic regimens. Patient factors shown to predict greater emetic risk are poor emetic control with prior chemotherapy, female sex, younger age, and a history of low alcohol intake. Emetogenic potential of a chemotherapy agent is classified by experience rather than scientific data. When administering chemotherapy with high emetogenic risk, either cisplatin or non-cisplatin regimens, a combination of a 5-HT antagonist and a corticosteroid is recommended prior to chemotherapy administration (levels of evidence: I, II, III, and expert consensus). When administering chemotherapy with intermediate emetogenic risk, a corticosteroid is recommended (levels of evidence: III, IV, and expert consensus). When administering chemotherapy with low emetogenic risk, no antiemetic agent is recommended (levels of evidence: V and expert consensus).

Delayed Emesis

For delayed emesis occurring more than 24 hours after chemotherapy administration, fewer agents have been investigated in comparison to agents used for acute emesis. Unless contraindicated, corticosteroids are recommended as a single-agent antiemetic regimen administered at an oral dose of 8 mg for two to three days after chemotherapy. Side effects may include elevated serum glucose and insomnia. Combinations of antiemetic agents are recommended in patients receiving chemotherapy with high emetogenic potential; however, research does not support a specific combination regimen. Patient factors and emetogenic potential of chemotherapy agents identified for acute emesis are identical for delayed emesis. When administering cisplatin chemotherapy, a corticosteroid such as dexamethasone 8 mg twice daily for three to four days with metoclopramide 30–40 mg two to four times per day for two to four days or a 5-HT antagonist for two to three days is recommended (level of evidence: I). For highly emetogenic, noncisplatin chemotherapy, a corticosteroid or a corticosteroid with metoclopramide or a 5-HT antagonist is recommended using the same dosage schedule as cisplatin regimens (levels of evidence: III, IV, and V). When administering chemotherapy agents with intermediate and low emetogenic risk, no specific antiemetic agents are recommended (levels of evidence: V and expert consensus).

Conclusion

Nurses must note that the recommendations should be used as guidelines and individual patient factors must be incorporated when developing an antiemetic regimen. Although significant improvement in chemotherapy-induced nausea and emesis has occurred, only a limited number of patients have achieved the ultimate goal of complete absence of nausea and emesis while receiving chemotherapy. Ongoing research is needed to investigate the physical, psychological, and emotional mechanisms of nausea and vomiting and specific antiemetic regimens.

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- The most effective combination of antiemetics is a corticosteroid and a serotonin receptor antagonist.
- Granisetron, ondansetron, dolasetron, and tropisetron have equivalent antiemetic activity.
- Corticosteroids, such as dexamethasone, prednisone, or methylprednisolone, have equivalent antiemetic activity.
- Dexamethasone doses greater than 20 mg do not provide additional antiemetic activity.
- For acute or delayed emesis, patient factors shown to predict greater emetic risk include poor emetic control with prior chemotherapy, female sex, younger age, and a history of low alcohol intake.
- For delayed emesis with cisplatin chemotherapy, prophylactic use of dexamethasone 8 mg twice daily for three to four days with metoclopramide 30–40 mg two to four times per day for two to four days or 5-HT antagonists for two to three days is recommended.
- For delayed emesis with highly emetogenic, noncisplatin chemotherapy, prophylactic use of dexamethasone 8 mg twice daily for two to three days with metoclopramide 30–40 mg two to four times per day for two to three days or 5-HT antagonists for two to three days is recommended.

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References