Aprepitant: A New Modality for the Prevention of Postoperative Nausea and Vomiting: An Evidence-Based Review

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Purpose: *Postoperative nausea and vomiting (PONV) affects as many as 30% of surgical patients. Aprepitant, an antagonist of the neurokinin-1 receptor with a 40% half-life, may be effective for prophylaxis for PONV. This review describes the evidence of adding aprepitant to antiemetic therapy for PONV prophylaxis.*
Methods: *A literature search was conducted to answer the population-intervention-comparison-outcome-time (PICOT) question: In adult patients undergoing general anesthesia (P), does aprepitant (I) decrease PONV (O) postoperatively (T) as compared to patients receiving other antiemetic therapy or a placebo (C)?*
Results: *Eight randomized controlled trials, one prognostic study, and one post hoc analysis were appraised. Perioperatively, aprepitant decreased the severity and number of episodes of PONV.*
Discussion: *Aprepitant appears to be more effective in decreasing the incidence of PONV postoperatively as compared with ondansetron. It is recommended that aprepitant is used to treat patients at risk for PONV and for whom PONV could lead to catastrophic adverse outcomes.*

Keywords: *aprepitant, postoperative nausea and vomiting, neurokinin-1 receptor, antiemetic therapy, review.*

POSTOPERATIVE NAUSEA AND VOMITING (PONV) has been a long-standing problem in the postanesthetic period. It can affect up to 30% of all postoperative patients and up to 80% of high-risk patients.[1–4] PONV can increase health care costs related to unanticipated admissions and delayed postanesthesia care unit (PACU) or hospital discharge.[3] Risk factors for PONV are described as based on three categories: patient-specific, anesthetic related, and surgery related.[1] Patient-specific risk factors include female gender, nonsmoking status, and a history of PONV and/or motion sickness.[2,4,5] Anesthetic considerations include use of volatile agents, nitrous oxide, and postoperative opioids.[2,6] Surgery-related elements, such as the duration and type of surgery, are also of special concern (Table 1).[1,2]

It is standard practice to incorporate PONV prevention strategies for patients who present with moderate or high risk. As anesthesia practitioners are unable to avoid many risk factors in day-to-day practice, there is a large quantity of ongoing research to explore ways to lower the incidence of PONV. Lowering the incidence of PONV will potentially lower its costly and disastrous consequences such as fluid and electrolyte imbalance, surgical wound dehiscence, hemorrhage, aspiration pneumonia, delayed discharge, and hospital readmission.[3,4,6,7]

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Table 1. PONV Risk Factors in Adults

Patient Specific	Anesthesia Related	Surgery Related
• Female gender • Children • Younger than 50 years • Nonsmoking status • History of PONV and/or motion sickness	• Volatile agents (desflurane, isoflurane, and sevoflurane) • General vs regional • Nitrous oxide • Postoperative opioids	• Duration • Postoperative opioid use • Type of surgery: cholecystectomy, gynecologic, and laparoscopic procedures

PONV, postoperative nausea and vomiting.

In high-risk patients, research has shown that management should consist of a prophylactic rather than therapeutic approach.[1,2] Medications generally target the receptor-mediated triggers of PONV, although its origins are poorly understood. The five pathways generally accepted as having a role in PONV are the chemoreceptor trigger zone, the vestibular apparatus, the cerebral cortex, midbrain afferents, and vagal mucosal pathways in the gastrointestinal system.[4,8] Cholinergic, dopaminergic, histaminergic, and serotonergic receptors are stimulated via these pathways and are the target of traditional antiemetics on the market.[1,4] Unfortunately, common antiemetics used today tend to have a limited duration of action, variable reliability, and may reduce overall incidence of PONV by only 26%.[5,9] For this reason, there is a need to develop and use medications that act at a different receptor, have a prolonged effect, and have minimal adverse side effects in prevention of PONV.

Aprepitant targets neurokinin-1 (NK1) receptors in the mucosal pathways in the gastrointestinal system, with a 40 hour half-life.[2–5,7] NK1 receptors exist peripherally and centrally and combine themselves with substance P. Substance P is an endogenous ligand for NK1 receptors and plays a significant role in the vomiting center.[4,9] The combination of substance P and NK1 receptors produces a reaction in the vomiting center in the brain and gastrointestinal tract. By inhibiting the binding of substance P, nausea and vomiting are suppressed.

Aprepitant is the first NK1 receptor antagonist to be approved by the US Food and Drug Administration for PONV prevention. Aprepitant provides up to 72 hours of antiemetic action and has exhibited high efficacy among patients with chemotherapy-induced nausea and vomiting.[5,6] As with other antiemetic agents, aprepitant's safety profile has rare side effects consisting of fatigue, neutropenia, abdominal pain, and anorexia. Individuals with allergic reaction to NK1 antagonists or severe hepatic disease should not use aprepitant.[6]

Methods

The following PICOT question was used to search the literature: In adult patients undergoing general anesthesia (P), does aprepitant (I) decrease PONV (O) postoperatively (T) as compared to patients receiving other antiemetic therapy or a placebo (C)?

An extensive literature search was conducted using CINAHL, MEDLINE, EMBASE, and Google Scholar to include articles from 2007 to 2014. The following MESH search terms were used individually and in combination: aprepitant, neurokinin receptor, neurokinin-1 receptor antagonist, and postoperative nausea and vomiting. The level and quality of the research evidence was evaluated using the Hierarchy of Evidence for Intervention Studies (Table 2).[10] References from selected articles were also reviewed for relevant studies that could be included. Exclusion criteria included letters to the editor, research support papers, and articles addressing chemotherapy-induced nausea and vomiting.

Results

The search generated 23 articles, 10 of which were directly related to our PICOT question (Table 3). Eight randomized controlled trials, one prognostic study, and one post hoc analysis of pooled data