Case Report

Fosaprepitant for the Treatment of Refractory Postoperative Nausea and Vomiting

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Abstract

Postoperative nausea and vomiting (PONV) is a debilitating condition that occurs in approximately 30% of patients undergoing general anesthesia. Premedication with 5-HT₃ receptor antagonists and glucocorticoids is effective in clinical practice; however, 10% to 20% of patients still develop PONV. Currently, little is known about the treatment of refractory PONV. We present a case that illustrates the use of fosaprepitant for the treatment of refractory postoperative nausea and vomiting.

Key Words—breakthrough, *Emend*, fosaprepitant, nausea, postoperative, refractory, vomiting

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Postoperative nausea and vomiting (PONV) occurs in approximately 30% of patients undergoing general anesthesia without antiemetic prophylaxis.¹ With antiemetic prophylaxis, 10% to 20% of patients experience PONV. With placebo, 65% to 86% of patients experience emetic symptoms after the first incident of PONV.² The prevention of PONV has been well studied; however, there is little knowledge available for the treatment of PONV. The main pharmacological classes of drugs used in the treatment of PONV as single agents or combination therapy include 5-HT₃ receptor antagonists, glucocorticoids, antihistamines, cholinergic antagonists, butyrophenone, phenothiazines, and benzamides.³ In general, a drug possessing a different mechanism of action from the prophylactic regimen should be used for the treatment of PONV. As demonstrated by Kovac and colleagues, in patients who received ondansetron for the prevention of PONV, additional ondansetron for the treatment of PONV was ineffective.⁴ Furthermore, less is known about the treatment of refractory PONV, and it has yet to be studied. We present a case of fosaprepitant used in the treatment of refractory PONV.

CASE REPORT

A 51-year-old male with a history significant for diabetes mellitus, hypertension, and chronic renal insufficiency suffered a traumatic fracture of his right ankle in 2003 requiring multiple surgical procedures. Unfortunately, his course was complicated by an infected nonunion and osteomyelitis of his right ankle. He presented in August 2013 for removal of antibiotic beads in his right ankle and fusion with placement of left iliac crest bone graft. Given his history of PONV due to sensitivity to anesthesia medication, a scopolamine patch was placed prior to surgery. Intraoperatively, the patient received midazolam 1 mg intravenous (IV), fentanyl 250 mcg IV, propofol 170 mg IV bolus followed by an infusion at a rate of 75 to 125 mcg/kg/min (total dose, 1,029.26 mg), and remifentanyl infusion at a rate of 0.05 to 0.08 mcg/kg/min (total dose, 742 mcg). Approximately 15 minutes prior to turning off the propofol and remifentanyl infusions, a single dose of ondansetron 8 mg IV was administered. In the postanesthesia care unit (PACU), the patient experienced PONV, and he was given ondansetron 16 mg IV, metoclopramide

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10 mg IV, and prochlorperazine 10 mg IV without resolution of symptoms. For pain in the PACU, he received a total of fentanyl 75 mcg IV and hydromorphone 1 mg IV. Postoperatively, for surgical prophylaxis, he received cefazolin 2 g IV every 6 hours for 4 doses. On postoperative day (POD) 1, the patient experienced 4 more episodes of emesis, and he was given ondansetron 8 mg IV every 6 hours for 4 doses and prochlorperazine 10 mg IV for 2 doses without resolution of symptoms. The patient was unable to tolerate his oral blood pressure medications, which included hydralazine, atenolol, lisinopril, nifedipine, furosemide, and clonidine. As a result, the patient's course was complicated by hypertensive urgency with blood pressures of up to 210 mm Hg systolic over 100 mm Hg diastolic, which was unsuccessfully managed with IV hydralazine, metoprolol, and labetalol. Given the refractory PONV, an IV dose of fosaprepitant 150 mg was administered on POD1, which improved his symptoms and his blood pressures. For pain on POD1, he received a total of acetaminophen 1 g orally (PO) and 2 g IV, hydromorphone 1.4 mg IV, oxycodone extended release (ER) 30 mg PO, and oxycodone immediate release (IR) 25 mg PO. The patient was also started on bupivacaine 0.25% nerve block at 6 mL/h (total dose, 292.5 mg). On POD2, his PONV completely resolved. His home regimen of oral antihypertensive medications was restarted. For pain on POD2, he received a total of oxycodone ER 20 mg PO, oxycodone IR 5 mg PO, and tramadol 200 mg PO. In addition, bupivacaine was changed to ropivacaine 0.2% at 6 mL/h and then discontinued on POD3 (total dose, 516 mg). Similarly, on POD3, he received a total of oxycodone ER 20 mg PO, oxycodone IR 25 mg PO, and tramadol 200 mg PO. The patient was discharged on POD4.

DISCUSSION

Aprepitant is a selective high-affinity antagonist of substance P/neurokinin 1 (NK1) receptors. It is available in PO and IV formulations, aprepitant and fosaprepitant, respectively. Fosaprepitant, a prodrug of aprepitant, rapidly converts to aprepitant when administered intravenously. Both formulations have been found to be effective and are US Food and Drug Administration (FDA) indicated for the prevention of acute and delayed nausea and vomiting associated with moderately and highly emetogenic chemotherapy in combination with other antiemetics. Unlike fosaprepitant, aprepitant is also FDA approved for the prevention of PONV.

Use of aprepitant has been found to be effective for the prevention of PONV in several studies. In patients undergoing general anesthesia for major surgeries, preoperative dosing of aprepitant 40 mg PO is more effective than ondansetron 4 mg IV for all the following endpoints over 0 to 24 hours: no significant nausea (56.4% vs 48.1%; $P = .009$), no nausea (39.6% vs 33.1%; $P = .035$), no vomiting (86.7% vs 72.4%; $P < .001$), no nausea or vomiting (38.3% vs 31.4%; $P = .023$), and no nausea, no vomiting, and no use of rescue therapy (37.9% vs 31.2%; $P = .027$).⁵ Preoperative dosing of aprepitant 125 mg PO compared to ondansetron 4 mg IV resulted in more patients achieving all endpoints, but statistical difference was only observed in no significant nausea (55.1% vs 48.1%; $P = .027$) and no vomiting (90.2% vs 72.4%; $P < .001$) endpoints.⁵ In laparoscopic gynecological patients undergoing general anesthesia, preoperative aprepitant 80 mg PO was effective in lowering acute PONV (13% vs 19%; NS) and delayed PONV (0% vs 8%; $P < .05$) when compared to no drug used. Moreover, the aprepitant group used significantly less postoperative analgesic medications compared to the control group.⁶ In patients receiving extended-release epidural morphine following unilateral primary total knee arthroplasty, the incidence of PONV was significantly less in the preoperative aprepitant 40 mg group compared to multimodality antiemetic therapy group (ondansetron 4 mg IV + dexamethasone 4-6 mg IV + either metoclopramide 10 mg IV, diphenhydramine 25 mg IV, or prochlorperazine 5 mg IV every 6 hours) (25% vs 75%; $P = .039$).⁷ A single-center, randomized, double-blind, double-dummy, parallel-group study is currently underway to compare and evaluate the efficacy of preoperative aprepitant 40 mg PO versus ondansetron 4 mg IV (in addition to dexamethasone 10 mg IV and promethazine 25 mg IV) in neurosurgery patients undergoing general anesthesia.⁸

Our case demonstrates the potential use of fosaprepitant as a treatment option for refractory PONV. However, prospective randomized controlled trials to further investigate the use of fosaprepitant in this setting are lacking.

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