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SYMPOSIUM: COMPLICATIONS OF HIP ARTHROPLASTY

Antiemesis After Total Joint Arthroplasty

Does a Single Preoperative Dose of Aprepitant Reduce Nausea and Vomiting?

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Abstract

Background Postoperative nausea and vomiting (PONV) is frequent after joint arthroplasty; in addition to causing patient distress, it interferes with early mobilization and hospital discharge. Various antiemetic agents reduce PONV, but their action is limited by a short half-life. Aprepitant, an antiemetic developed for patients receiving chemotherapy, has a duration of action much longer than other antiemetics.

Questions/purposes We asked whether a single dose of preoperative aprepitant (40 mg orally) reduced postoperative nausea and vomiting after THA or TKA.

Methods Fifty patients who received a preoperative dose of aprepitant (study group) were matched demographically to 50 patients who did not receive aprepitant (control group) from a group of patients undergoing THA or TKA. Patients' charts were reviewed to identify episodes of PONV, number of doses of antiemetics needed for breakthrough PONV, and length of stay. Aprepitant side effects, and complications.

Results Aprepitant reduced the percentage of patients with PONV (39% of study and 70% of control patients). Moderate or severe PONV occurred in 22% of study and 40% of control patients. The number of episodes of PONV during hospitalization was 2.9 for the control group and 1.6 for the study group. Postoperatively, the control group required on average 1.3 doses of ondansetron compared with 0.6 doses for the study group. Hospital length of stay was reduced from 3.3 days for the control group and to 2.3 days for the study group.

Conclusions These data suggest a single preoperative dose of aprepitant reduces the number of episodes and severity of PONV, the need for additional antiemetics, and the length of stay.

Level of Evidence Level II, prognostic study. See guidelines for authors for a complete description of levels of evidence.

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.
Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research.
This work was performed at Riddle Memorial Hospital, Media, PA.

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Introduction

Anesthetic agents and narcotic analgesia commonly cause severe postoperative nausea and vomiting (PONV) after total joint arthroplasty (TJA) [3, 7, 9, 20, 26, 28]. PONV after lower extremity TJA has a reported incidence of 20 to 83% [14, 21]. Various antiemetic agents control PONV [8, 12, 13, 15, 16]. In addition to the discomfort and emotional distress inflicted on the patient, PONV can be immobilizing, potentially increasing the risk of

thromboembolic disease, interfering with physical therapy and delaying hospital discharge [1, 11, 23, 25, 31].

For minimally invasive TJA to result in a speedier recovery and shorter length of stay, the use of multimodal means focusing on surgical technique, pain control, early and intense physical therapy, and avoidance of PONV is necessary [4–6, 18, 22, 24, 27]. Presurgical administration of an antiemetic agent reportedly decreases the incidence of PONV after TJA [8, 13, 17]. Unfortunately, most antiemetic agents provide a short duration of action and breakthrough PONV after TJA often occurs. Aprepitant is a long acting antiemetic commonly prescribed following administration of chemotherapy. The efficacy of this medication for control of PONV has not been previously reported.

The purpose of this study was to determine if a single preoperative dose of aprepitant (40 mg orally) (1) reduced the number of episodes of PONV after lower extremity major TJA, (2) reduced the severity and number of interventions for breakthrough PONV, (3) reduced additional antiemetic administration, and (4) reduced hospital stay. Finally we determined whether (5) BMI, gender or race related to PONV.

Patients and Methods

We retrospectively reviewed the charts of 50 patients who underwent either primary THA or TKA (unilateral or bilateral) between September 7, 2006, and March 23, 2009, at Riddle Memorial Hospital, Media, PA. We excluded patients with unicompartmental knees or revision arthroplasties. Based on a change of standard protocol, aprepitant (Emend®; Merck and Co, Inc, Whitehouse Station, NJ) in the amount of 40 mg orally was first given in our hospital preoperatively, 2 hours before surgery, on January 18, 2007. Subsequently, all total joint patients were prescribed this medication preoperatively. Fifty patients were selected from the period before January 2007 (from September 2006 to January 2007) to serve as control subjects. All study and control patients were treated postoperatively with ondansetron 4 mg intravenously to relieve symptoms of PONV if it occurred. The number of doses of ondansetron given in the study and control groups administered postoperatively was recorded and compared. We included all patients with documented administration of aprepitant in the study. We had no set protocol for determining PONV and rather relied on information in the records. The control group of 50 patients who did not receive aprepitant was selected to best demographically match the study group based on gender, body mass index, and type of surgery (unilateral, bilateral, TKA, or THA) performed. We performed a power analysis for PONV with an alpha value of 0.05 and a beta value of 80%. The difference in means among the groups was 1.39 and the standard deviation was 3.05. The analysis suggested that we needed 40 patients in each group, though the actual number of patients used was 50 per group. Of the 100 patients, 53 were female and 47 were male. Patients' ages ranged from 44 to 94 years of age. The two groups were demographically similar except the study group averaged 5 years younger than the control group (Table 1). The protocol was reviewed and approved by the Main Line Hospitals Institutional Review Board, Bryn Mawr, PA.

We searched the MEDLINE (PubMed, from 1966) database using the MESH controlled vocabulary, which includes the Cochrane Controlled Trials Register. The terms "postoperative nausea and vomiting," "postoperative complications," "arthroplasty," and "replacement" were used. A comprehensive literature review was performed to determine the incidence of PONV after arthroplasty and ascertain the effectiveness of commonly prescribed antiemetic agents in reducing PONV.

To evaluate the efficacy of aprepitant in preventing or lessening the occurrence of PONV, daily postoperative chart notes recorded by physicians, nurses, and physical therapists for each patient in both the control and study groups were examined. Instances of PONV were noted for the entire length of hospital stay. PONV was classified as follows: none, mild (one to two episodes), moderate (three to five episodes), or severe (six or more episodes). In

Table 1. Demographics of control and study groups

	Control group (n = 50)	Study group (n = 50)	p value	Confidence interval (95%)
THA:TKA	31:19	33:17	0.8352	—
Bilateral THA	0	0	—	—
Bilateral TKA	7	9	—	—
Average age in years (range)	70.3 (46–98)	65.5 (44–86)	0.0001	3.85 to 4.85
Male:female	24:26	29:21	0.4230	—
Average BMI (range)	30.5 (19–56)	31.0 (21–46)	0.662	−2.73 to 1.75
Postoperative narcotics (MSO_4 equivalents)	43.9	49.0	0.370	−16.4 to 6.21
Anesthesia spinal:GETA	49:1	50:0	1.0	—

addition, the number of times an antiemetic (ondansetron 4 mg intravenously) was administered was also recorded. Additionally, the total number of days each patient remained in the hospital (length of stay) was recorded. Demographic data including body mass index, gender, and race were recorded.

Results

Patients who did not receive aprepitant before surgery experienced nearly twice as many episodes of PONV during the 2 days immediately after their surgery (2.73 average occurrences for controls versus 1.55 average occurrences for aprepitant recipients) and, similarly, nearly twice as many instances of PONV during the entire length of their stay compared with aprepitant recipients (2.94 average episodes versus 1.55 average episodes).

The severity of PONV for the 50 control patients (23 men, 27 women) who were not treated with aprepitant is as follows: 15 patients (30%) did not experience any PONV during the length of their hospital stay. Fifteen patients (30%) experienced one or two episodes of PONV (mild), 12 patients (24%) experienced three to five episodes of PONV (moderate), and eight patients (16%) experienced six or more episodes of PONV (severe) (Table 2). The severity of PONV among the study group of 50 patients (24 men and 26 women) who were treated with aprepitant preoperatively was reduced. Thirty-one patients (62%) experienced no documented instances of PONV during the length of their hospital stay. Nine patients (18%) experienced one to two episodes of PONV (mild), five patients (10%) experienced three to five episodes of PONV (moderate), and five patients (10%) experienced six or more episodes (severe).

The preoperative use of aprepitant lowered the need for additional antiemetic administration postoperatively. On average, aprepitant recipients took less than one dose of ondansetron (0.61 doses) while patients who did not receive aprepitant received an average of 1.25 doses of ondansetron postoperatively (Table 3).

Table 2. Episodes of PONV

	Controls (n = 50)	Study (n = 50)
None	15	31
Mild (1–2 episodes)	15	9
Moderate (3–5 episodes)	12	5
Severe (6+ episodes)	8	5
Average number of episodes PONV	2.7	1.6

PONV = postoperative nausea and vomiting.

Table 3. Instances of breakthrough PONV administration of antiemetics and length of stay study

	Controls	Study
Average number of times antiemetics administered (range)	1.25 (0–5)	0.61 (0–4)
Average LOS (days)	3.31	2.31

PONV = postoperative nausea and vomiting; LOS = length of stay.

The average patients' length of stay for the control group was 1 day longer than for the study group. For the control group, the average length of stay was 3.3 days. For the study group, the average length of stay was reduced to 2.3 days.

We found no relationship between instances of PONV and obesity, gender, or race.

Discussion

PONV is a common problem following major surgery. Pain relief is provided by a multimodal pain management approach after joint arthroplasty surgery [4–6, 18, 22, 24, 27]. This approach includes oral, parenteral, and spinal narcotics. Unfortunately, narcotic analgesia is associated with unwanted side effects such as PONV. Many other factors contribute to PONV, including polymethylmethacrylate use, blood loss, and surgical pain [3, 7, 9, 20, 26, 28]. PONV can occur during the entire hospitalization and can be severe and disabling. It can prevent early mobilization, likely increasing the risk for venous thrombosis or pulmonary embolus and increased hospital length of stay [1, 11, 25, 31]. It can also prevent ingestion of oral anticoagulants such as aspirin and coumadin, which may place the patient at additional increased risk for venous thrombosis or pulmonary embolus. We therefore determined whether a single preoperative dose of aprepitant (40 mg orally) could (1) reduce the number of episodes of PONV after lower extremity major TJA, (2) reduce the severity and number of interventions for breakthrough PONV, (3) reduce additional antiemetic administration, and (4) reduce hospital stay. Finally we determined whether (5) BMI, gender or race related to PONV.

Our retrospective study has certain limitations. First, the groups were not matched for comorbidities. However, since no other factors were altered for the two study groups, other than the preoperative use of aprepitant, we believe it likely this agent had a substantial antiemetic effect and diminished the incidence of PONV. Second, we had no set protocol or criteria to record or quantify PONV. It is therefore possible that mild episodes of PONV were underreported but we presume we captured from the records any major events or use of additional agents. Both control and study groups used ondansetron to relieve

symptoms of PONV. Third, the two study groups were demographically similar except the study group had a mean age 5 years younger than that of the control group. We presume this had no effect on the findings.

When spinal anesthesia is used for TJA, intrathecal narcotics are commonly added for long-lasting analgesia and these agents may also induce PONV [10, 19, 26, 29, 30]. Pain after TJA is reported as intolerable by many patients and frequent use of narcotic analgesia postoperatively is often necessary, further contributing to the incidence of PONV [4–6, 18, 22, 24, 27]. PONV after TJA reportedly ranges in incidence from 20% to 83% depending on the parameters of the study.

The concept of minimally invasive TJA has generated tremendous interest from both patients and surgeons. In general, minimally invasive TJA is defined as occurring when methods are used which decrease the time needed to recover after surgery. Recent investigations have revealed a combination of methods may shorten recovery time after TJA. These factors include surgical technique, analgesia efficacy, early mobilization, and control of PONV [2, 8, 13, 17]. Our data suggest an important antiemetic effect after TJA for patients receiving aprepitant preoperatively. Patients who were given aprepitant preoperatively reported a 50% reduction in PONV. This decrease in PONV allowed patients to more effectively participate in physical therapy. The length of stay decreased by 1 full day after institution of the use of preoperative aprepitant (from 3.3 days to 2.3 days). Both patients and surgeons have a strong desire to make TJA less invasive with an accelerated recovery. Effective control of PONV is an important parameter necessary to achieve this goal.

Aprepitant is a powerful antiemetic developed to control nausea and vomiting after the administration of chemotherapy in oncology patients. Additionally, this medication has a long duration of action, effectively providing antiemesis activity for more than 72 hours. The safety profile of aprepitant is similar to other antiemetic agents. Serious side effects are uncommon. Occasional and rare effects can include neutropenia, abdominal pain, fatigue, and anorexia. In our study, no patient developed a serious medication side effect. Contraindications to use of aprepitant include severe hepatic disease and prior allergic reaction to this class of drug.

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