Original research

A retrospective analysis of the use of intravenous dexamethasone for postoperative nausea and vomiting in total joint replacement

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ABSTRACT

Background: Multimodal perioperative pain-management protocols have contributed to the success of elective total joint replacement in orthopedic surgery. General or neuraxial anesthesia for arthroplasty is accompanied by complications such as pruritis, nausea, and vomiting. Dexamethasone has been demonstrated to be a safe perioperative antiemetic. This study evaluates the benefit of low-dose intravenous dexamethasone used in the perioperative period to prevent postoperative nausea and vomiting.
Methods: Two scheduled doses of 8 mg of dexamethasone 12 hours apart after total hip arthroplasty or total knee arthroplasty were given to a dexamethasone group (n = 492) and were retrospectively compared with a no-dexamethasone group (n = 364) based on the use of antiemetics in the postoperative period. Frequency of antiemetic use in both groups was compared using a zero-inflated fixed-model Poisson distribution. Additional analysis included need for opioid analgesic, administration of diphenhydramine, and postoperative infection rates at 30 and 90 days.
Results: The dexamethasone group was found to have a significant reduction in need for the rescue antiemetic ondansetron (P = .00194). There was an associated reduction in length of stay for the treatment group (mean 1.83 days) relative to the control group (mean 2.17 days) (P < .001). There was no significant difference in postoperative infection rates at 30 or 90 days after arthroplasty.
Conclusions: Dexamethasone is a safe adjunct to perioperative protocol that may reduce nausea, thus improving patient satisfaction. There is an associated reduction in length of stay that may reduce cost of hospitalization.
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Introduction

The implementation of rapid-recovery protocols such as multimodal pain management and preemptive analgesia allows for improved patient satisfaction and minimized hospital length of stay. Spinal anesthesia for total joint arthroplasty has been linked to shorter length of stay relative to general anesthesia alone [1]. Despite this benefit, spinal anesthesia may still be accompanied by nausea, vomiting, pruritis, hypotension, and spinal hematoma [2].

Postoperative nausea and vomiting (PONV) is particularly common, has multiple known associated etiologies, and can frequently inhibit patient mobilization with therapy. While linked to anesthetics, recent literature has associated this phenomenon with general anesthesia more than spinal anesthesia. Conflicting studies have found no difference between the 2 modalities [3]. Despite the increasing use of multimodal analgesia, PONV remains a challenge and continues to be observed in 60%-80% of patients who receive a neuraxial blockade [4]. Some recent studies suggest that the addition of glucocorticoids to rapid-recovery protocols may have the potential to further reduce PONV and pain without significant additional risks. In patients receiving spinal morphine, dexamethasone administered intravenously at a one-time dose has been shown to improve associated PONV but did not reduce pruritis [5]. There is also recent literature noting opioid-sparing benefits in patients treated with a single dose of dexamethasone from 1.5 to 20 mg [6-8]. In the past, surgeons had avoided the use of glucocorticoids in the postoperative period because of theoretical fear of

increased surgical site infections, increased rate of venous thrombosis, and potential for osteonecrosis. Recent studies have demonstrated that 10 mg of dexamethasone does not increase the length of stay or rate of postoperative infection [9,10]. Although alternatives such as ondansetron and scopolamine are also concomitantly used, these do not produce the anti-inflammatory benefit found while using glucocorticoids such as dexamethasone [11]. It is well established that dexamethasone may serve as an antiemetic alone or in combination with ondansetron, but it is still being evaluated for routine postoperative use in the total joint replacement population.

In this retrospective study, we aimed to explore whether the routine administration of postoperative dexamethasone as a standardized protocol change had any meaningful effect on reduction of the incidence of PONV and pain experienced after primary total joint arthroplasty. Given the theoretical concerns surrounding the administration of glucocorticoids at the time of surgery, we also compared early postoperative infection rates at 30 and 90 days. We hypothesized that the addition of perioperative dexamethasone would result in decreased incidence of PONV and less pain after total joint arthroplasty without a concomitant increase in early complications.

Material and methods

After receiving institutional review board approval, the institutional health-care analytics service was used to access inpatient demographic and medication administration data from a single institution's electronic medical record system. We retrospectively identified any patients receiving total hip arthroplasty (THA) or total knee arthroplasty (TKA) in a single tertiary care center from April 2015 to April 2016 during adoption of an updated protocol for PONV prophylaxis within a 4-surgeon Adult Reconstruction Division. This protocol change involved the routine administration of perioperative dexamethasone for all patients undergoing primary THA or TKA. Exclusion criteria included patients with a diagnosis of diabetes mellitus, patients with renal or hepatic failure, or patients with a known adverse response to corticosteroids. This was initiated by the senior author and eventually incorporated into the practices of all surgeons of the division. Of this population, we identified patients who were given intravenous dexamethasone for PONV prophylaxis after their surgical procedure and demographically matched patients who did not receive this intervention within the overlapping time frame. Demographic data collected were patient age, gender, body mass index, and surgical indication/procedure. Infection rates at 30 and 90 days were queried with the International Classification of Diseases-9/10 codes corresponding to infectious etiologies (T81.4XX, T84.5XX, B95.62). Thirty- and ninety-day analysis windows were selected because these are the expected ranges of time for which perioperative pharmacologic interventions would be expected to impact the likelihood for acute periprosthetic joint infection. Patients with an admitting diagnosis of fracture, dislocation, infection, loosening, or avascular necrosis were removed from the data set to specifically analyze the population undergoing elective joint replacement due to primary osteoarthritis. Patients were treated with narcotics commensurate to individual requirements, which transitions to full oral administration before discharge and tapered accordingly.

Medication administration records for all 856 patients during the study period were retrieved for standard doses of dexamethasone, diphenhydramine, hydromorphone, ondansetron, oxycodone, promethazine, and scopolamine. These medications were chosen due to their use in standard protocol to combat PONV or postoperative pain. The protocol change in question was the addition of 2 doses of 8 mg of dexamethasone 12 hours apart in the postoperative period. Treatment was to be given at 8 PM on the evening of surgery and readministered around 8 AM the next day. Data on frequency of rescue antiemetic use after the initiation of dexamethasone therapy were collected for each patient and adjusted from each patient's start time of surgery, controlling for variations in length of stay. Ondansetron, the primary first-line rescue antiemetic used at our institution, was categorized into 12-hour time periods for each patient's respective admission to determine the timeline of benefit with dexamethasone therapy. A zero-inflated fixed-model Poisson distribution was performed to compare intergroup differences. This statistical method was selected to account for the natural subset of patients that do not require pharmacologic therapy and create a high frequency of zero-value entries. Wilcoxon rank-sum test was used to compare complication rates among the observed groups.

Results

A total of 856 patients were queried for meeting the inclusion criteria of this study. Of these patients, 492 (57%) received the dexamethasone treatment compared with 364 (43%) demographically similar patients who did not. This study uses frequency of medication administration as a proxy for symptomatic PONV, itching, or pain. To conduct this analysis, the following assumptions were made: (1) treatment with medication was driven by presentation of a symptom; (2) PONV is defined as occurring within the first 24-48 hours after surgery; and (3) patients were discharged in stable condition after treatment or prevention of PONV. Table 1 compares the demographic characteristics of these 2 populations with respect to dexamethasone therapy. A statistically significant reduction in hospital length of stay was found with patients who received perioperative dexamethasone. Patients without dexamethasone therapy averaged 2.17 ± 1.03 days in the hospital, whereas those receiving dexamethasone were found to remain in the hospital for 1.83 ± 0.85 days ($P < .0001$).

Table 2 depicts the number of patients treated with each mode of antiemetic therapy. Promethazine and scopolamine administration between groups was not found to be statistically significant ($P = .44$ and $P = .93$, respectively). Among the antiemetics displaying significant differences, ondansetron was the only antiemetic with sufficient frequency of administration to be used for analysis ($P < .001$) because prochlorperazine was only used in 17 patients throughout the study. When all antiemetics in Table 2 were collectively analyzed, there was no statistically significant change in the need for antinausea medication ($P = .0635$), although the dexamethasone group did receive a decreased dose of

Table 1
Comparison of the dexamethasone treatment and control groups.

Clinical characteristics	All patients	Dexamethasone	No dexamethasone	P value
n	856	492	364	-
Age	66.59 ± 10.30	66.69 ± 10.02	66.45 ± 10.69	.7074
BMI	30.44 ± 5.44	30.50 ± 5.38	30.56 ± 5.43	.4905
LOS	1.97 ± 0.95	1.83 ± 0.85	2.17 ± 1.03	<.0001
Female gender	63.08%	65.04%	60.44%	.1911
Total hip	39.60%	35.77%	44.78%	.009503
Total knee	60.40%	64.23%	55.22%	.009503
General	77.22%	76.02%	78.85%	.3716
Spinal	73.48%	76.22%	69.78%	.04219

BMI, body mass index; LOS, length of stay.
There are significant differences in the length of stay, type of operation, and use of spinal anesthesia associated with dexamethasone administration.

Table 2
Various antiemetics used at our institution.

Antiemetic	Total (n = 856)[a]	Dexamethasone (n = 492)[a]	No dexamethasone (n = 364)[a]	No. of antiemetic doses per admission without dexamethasone[b]	No. of antiemetic doses per admission with dexamethasone[b]	P value
Ondansetron 4 mg IV/PO	329 (38.43%)	177 (35.98%)	152 (41.76%)	**0.709 ± 0.051**	**0.519 ± 0.036**	**.00194**
Promethazine 25 mg IV/PO	178 (20.79%)	105 (21.24%)	73 (20.05%)	0.257 ± 0.016	0.023 ± 0.010	.396
Scopolamine 1.5 mg TD	26 (3.04%)	19 (3.86%)	7 (1.92%)	0.019 ± 0.007	0.041 ± 0.009	.926
Prochlorperazine 5 mg IV/PO	17 (1.99%)	6 (1.21%)	11 (3.02%)	0.046 ± 0.016	0.023 ± 0.009	.201
All antiemetics	392 (45.79%)	217 (44.11%)	175 (48.08%)	1.024 ± 0.066	0.881 ± 0.052	.0635

IV, intravenous; PO, per os; TD, transdermal.

As per protocol, ondansetron was the first-line therapy for symptomatic nausea. The use of this medication differed significantly between the 2 groups. As a result, this medication was further analyzed to track the timeline of PONV.

Bold indicates statistically significant value.

[a] Percentage of patients using each type of antiemetic.

[b] The average number of doses of antiemetic taken during each admission.

antiemetics of 0.254 (standard error, 0.11-0.41) relative to the control group. Patients who did not receive dexamethasone required an average of 0.3 (standard error, 0.19-0.42) additional doses of ondansetron relative to the treatment group ($P < .0002$) (Fig. 1). In addition, the dexamethasone group demonstrated decreased use of diphenhydramine, with 0.675 ± 0.078 doses given in the control group compared with 0.537 ± 0.043 doses given in the treatment group ($P = .0286$). The frequency of oxycodone use was compared between dexamethasone and nodexamethasone groups. There was no statistically significant difference in administration of opioid analgesics ($P = .699$).

The zero-inflated fixed-model Poisson distribution showed that the dexamethasone group exhibited a significantly decreased requirement of ondansetron ($P = .00038$) relative to the control group, with general/spinal anesthesia, procedure, and gender used as covariates (Table 3). No association was found regarding the benefit of using dexamethasone in the setting of general vs spinal anesthesia ($P = .66890$ and $P = .20779$, respectively). Similarly, no disparity in the effect was seen between THA and TKA ($P = .43958$).

Infection rates at 30 and 90 days were compared between the 2 groups using the Wilcoxon rank-sum test. Results are summarized in Table 4. There was no statistically significant difference in infection rates between the 2 groups.

Figure 1. Average frequency of ondansetron administration in each 12-hour period. Patients were analyzed 48 hours after operation to identify frequency of need for antiemetic. Dexamethasone therapy was targeted to 12 hours after operation. Frequency of doses was compared with a zero-inflated Poisson distribution. Time axis refers to postoperative hours. Significant differences are seen at 24 hours ($P = .00335$), 36 hours ($P \leq 0.001$), and 48 hours ($P < .001$) after surgery. There was no significant difference between treatment and control groups at 12 hours ($P = .0921$). The presence of asterisks indicates statistically significant time frames.

Discussion

This retrospective cohort study suggests that the addition of dexamethasone perioperatively may provide an additional means of control for PONV, potentially improving patient satisfaction. Associated with this intervention was a decreased hospital length of stay. There was a statistically significant decrease in the requirement for rescue antiemetics in our study after the administration of scheduled dexamethasone in the early postoperative period. Although it is not surprising that the addition of a known antiemetic would diminish nausea, it is relevant that planned prophylaxis of PONV can potentially improve the postoperative course. In our facility, antiemetics are administrated in response to a patient's complaint of nausea. Therefore, the medication administration record is a useful surrogate for correlating this protocol change to the common complication of postoperative nausea.

Contemporary rapid-recovery protocols have transformed total joint arthroplasty by decreasing the length of stay without increasing the readmission rate [12]. Reductions in cost and rate of periprosthetic infections have also been observed [13]. We propose that slight improvements to institutional rapid-recovery protocols can be made with the addition of a prophylactic antiemetic such as dexamethasone. At the time of writing this article, an 8-mg solution of dexamethasone used in this study is priced at $6.97, demonstrating that this can be integrated into a perioperative protocol at a reasonable cost [14]. Further prospective studies need to be conducted to more clearly determine the extent to which dexamethasone may benefit an inpatient protocol while also improving the power of periprosthetic infection analysis. Alternatives to dexamethasone include the previously mentioned nausea medications that were used as rescue antiemetics
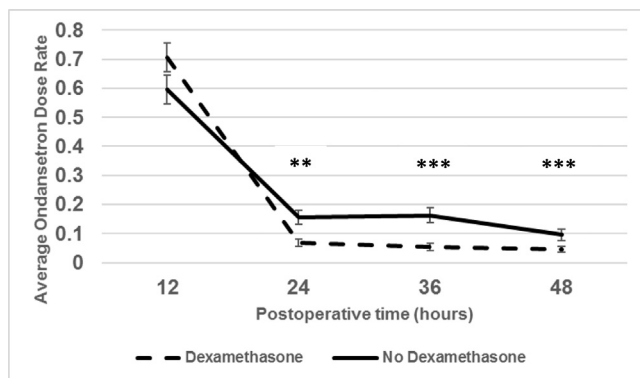
Table 3
Contribution of experimental variables to ondansetron administration.

Observed variable	Mean change in ondansetron doses per patient	Standard error interval	P value
Dexamethasone	−0.44	(0.3, 0.59)	**.00038**
General anesthesia	−0.05	(−0.17, 0.07)	.6689
Spinal anesthesia	−0.14	(−0.26, −0.03)	.20779
Male gender	−0.59	(−0.64, −0.53)	**<.001**
TKA operation	0.086	(−0.02, 0.21)	.43958

Without dexamethasone, there was an increase of 0.44 doses of ondansetron per patient admission, suggesting an increase in nausea. Male gender was significant for experiencing fewer episodes of PONV compared with female gender, requiring a mean of 0.59 less doses of ondansetron.

Bold values indicated statistical significants.

Table 4
Infection rates observed in this study.

Infection timing	Total	Dexamethasone	No dexamethasone	P value
30-day infection rates	0.70%	0.41%	1.10%	.2306
90-day infection rates	0.93%	0.41%	1.65%	.0622

There was no significant difference in infection rates between the 2 groups. Wilcoxon rank-sum test was used to compare the frequencies of both 30- and 90-day infection rates.

(ondansetron, scopolamine, promethazine, diphenhydramine) and preoperative aprepitant [4,15].

In this study, we also observed that dexamethasone therapy may be linked to a decreased hospital length of stay. This finding may have greater implications when considering the addition of dexamethasone to a perioperative protocol. Previous authors have suggested that dexamethasone's benefit toward reducing length of stay is rooted in the nausea-remitting properties of the drug when given perioperatively [6]. Pain associated with a surgery may also be closely linked to PONV. A randomized, controlled trial observing the effects of various operative interventions and their nature of inducing PONV found that orthopedic surgery only conferred a 0.91 relative risk of inducing PONV, whereas the use of postoperative opioids was the most significant modifiable risk factor for PONV, with a relative risk of 2.14 [16]. This study also recommended prophylaxis of nausea for moderate-risk patients, despite finding dexamethasone only to be beneficial at the start of the surgery. In this study, we found that the addition of dexamethasone after surgery may yield additional benefits. Whether a reduction in length of stay was due to improved nausea control, better pain control, or other factors, the significant differences found between the treatment and control groups are compelling indications for adding dexamethasone in the perioperative protocol.

This study solely examines the effect of perioperative dexamethasone on drug administration rates. Although a more direct assessment of postoperative nausea would have been to survey the patient, there are many aspects of the inpatient record that are particularly telling of this condition. Relative strengths of this study include the brief observation period, large cohort of patients, and small practice group. The time frame analyzed was limited to a year to reduce variability due to protocol changes. Second, patients' data are obtained from a practice in a high-volume institution spanning a large geographical catchment area, allowing for a high number of patients to be analyzed in the long term, as most return to the same institution for follow-up, while also providing accuracy to readmission parameters. Finally, it limits inclusion of cases to a small group of 4 surgeons conducting elective total joint arthroplasty with similar perioperative protocols to minimize the introduction of confounding variables. Weaknesses of this study include the nonrandomized retrospective cohort design used, limited generalizability given our specific protocol, inherent errors of the data source, underpowered periprosthetic infection analysis, inability to control for additional confounding variables, and selection bias. Among these factors, selection bias due to exclusion of diabetics is one of the design flaws of this study. In our institution, diabetics were typically not given dexamethasone because of fear of compromising blood sugar regulation. This may have led to a healthier population in the dexamethasone group despite having excluded diabetics from the study because clinicians may have withheld dexamethasone for a higher-risk patient. However, recent studies have not found diabetes to be associated with prolonged length of strength despite the association of prolonged wound healing with dysregulated blood glucose [17]. Surgeons historically may have had reservations to use dexamethasone because of the risk of elevating the blood sugar level. Nurok et al. [18] did not find an association between dexamethasone and postoperative glucose > 200 mg/dL, perhaps challenging this belief. Further confounding factors may be present from adjuncts to pain control. Nerve catheters were not tracked due to sporadic use among the patient population. Future studies should quantify to what degree nerve catheters decrease pain-induced nausea.

Conclusions

In this study, we have found statistically significant values suggesting benefits of incorporating postoperative dexamethasone for the purpose of reducing PONV. Choice of general or spinal anesthetic did not appear to impact the degree of nausea in the patient population. There was no statistically significant decrease in postoperative pain as measured by opioid use in the treatment and control groups, although perhaps postoperative itching was decreased in the dexamethasone group. Infection rates at 30 and 90 days were similar between the 2 groups, although analysis may be underpowered to accurately evaluate for periprosthetic joint infection. These findings further support dexamethasone as a safe and effective prophylactic for PONV.

In addition, dexamethasone therapy was observed to be associated with decreased length of stay between the 2 groups (1.83 vs 2.17 days). With patient satisfaction and episode of care costs now being closely monitored, publicly reported, and increasingly linked to reimbursement, dexamethasone may provide a safe and low-cost avenue to improving the patient experience while simultaneously decreasing hospital expenses. Further research should observe dexamethasone use prospectively to minimize bias and confounders. It should also further delve into the risk vs benefit of this therapy because it shows considerable promise as a low-cost adjunct to perioperative care.

References

[1] Basques BA, Toy JO, Bohl DD, Golinvaux NS, Grauer JN. General compared with spinal anesthesia for total hip arthroplasty. J Bone Joint Surg Am 2015;97(6): 455.

[2] Sculco PK, Pagnano MW. Perioperative solutions for rapid recovery joint arthroplasty: get ahead and stay ahead. J Arthroplasty 2015;30(4):518.

[3] Sansonnens J, Taffé P, Burnand B. Higher occurrence of nausea and vomiting after total hip arthroplasty using general versus spinal anesthesia: an observational study. BMC Anesthesiol 2016;16(1):44.

[4] Szarvas S, Chellapuri RS, Harmon DC, et al. A comparison of dexamethasone, ondansetron, and dexamethasone plus ondansetron as prophylactic antiemetic and antipruritic therapy in patients receiving intrathecal morphine for major orthopedic surgery. Anesth Analg 2003;97(1):259 (table of contents).

[5] Allen TK, Jones CA, Habib AS. Dexamethasone for the prophylaxis of postoperative nausea and vomiting associated with neuraxial morphine administration: a systematic review and meta-analysis. Anesth Analg 2012;114(4):813.

[6] Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth 2013;110(2):191.

[7] De Oliveira Jr GS, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology 2011;115(3):575.

[8] Salerno A, Hermann R. Efficacy and safety of steroid use for postoperative pain relief. Update and review of the medical literature. J Bone Joint Surg Am 2006;88(6):1361.

[9] Richardson AB, Bala A, Wellman SS, Attarian DE, Bolognesi MP, Grant SA. Perioperative dexamethasone administration does not increase the incidence of postoperative infection in total hip and knee arthroplasty: a retrospective analysis. J Arthroplasty 2016;31(8):1784.

[10] Backes JR, Bentley JC, Politi JR, Chambers BT. Dexamethasone reduces length of hospitalization and improves postoperative pain and nausea after total joint arthroplasty: a prospective, randomized controlled trial. J Arthroplasty 2013;28(8 Suppl):11.

[11] Smith C, Erasmus PJ, Myburgh KH. Endocrine and immune effects of dexamethasone in unilateral total knee replacement. J Int Med Res 2006;34(6):603.

[12] Stambough JB, Nunley RM, Curry MC, Steger-May K, Clohisy JC. Rapid recovery protocols for primary total hip arthroplasty can safely reduce length of stay without increasing readmissions. J Arthroplasty 2015;30(4):521.

[13] Köksal İ, Tahta M, Şimşek ME, Doğan M, Bozkurt M. Efficacy of rapid recovery protocol for total knee arthroplasty: a retrospective study. Acta Orthop Traumatol Turc 2015;49(4):382.

[14] Lexicomp (1978-2018). Dexamethasone (systemic): drug information. Accessed via UpToDate. https://www.uptodate.com/contents/dexamethasone-systemic-drug-information. [Accessed 12 February 2018].

[15] DiIorio TM, Sharkey PF, Hewitt AM, Parvizi J. Antiemesis after total joint arthroplasty: does a single preoperative dose of aprepitant reduce nausea and vomiting? Clin Orthop Relat Res 2010;468(9):2405.

[16] Apfel CC, Korttila K, Abdalla M, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004;350(24):2441.

[17] Sikora-Klak J, Gupta A, Bergum C, Zarling B, Markel DC. The evaluation of comorbidities relative to length of stay for total joint arthroplasty patients. J Arthroplasty 2017;32(4):1085.

[18] Nurok M, Cheng J, Romeo GR, Vecino SM, Fields KG, YaDeau JT. Dexamethasone and perioperative blood glucose in patients undergoing total joint arthroplasty: a retrospective study. J Clin Anesth 2017;37:116.