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Original contribution

Dexamethasone and perioperative blood glucose in patients undergoing total joint arthroplasty: A retrospective study

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ABSTRACT

Study objective: Perioperative dexamethasone is commonly used to prevent nausea. It can also increase blood glucose levels, and recent concern about its blood glucose-elevating effect in humans has been raised. This study aimed to demonstrate relationships between dexamethasone administration and elevated perioperative blood glucose in patients undergoing total joint arthroplasty.
Design: Retrospective study.
Setting: Academic, orthopedic hospital.
Patients: A total of 625 patients (18–99 years) who underwent total hip or total knee arthroplasty with an ASA ≤3 were included in the study.
Interventions: Patients who received dexamethasone perioperatively were compared to those who did not receive dexamethasone.
Measurements: The primary outcome, which was any postoperative glucose >200 mg/dl, was compared between groups using multiple logistic regression. Demographic information, intraoperative information, incidence of postoperative nausea and vomiting, white blood cell count, medication use, and length of stay were also collected.
Main results: Perioperative dexamethasone (median [1st quartile, 3rd quartile] dose = 4 [4, 8] mg) was administered to 76% of patients. Only 5.6% (95% CI: 3.8–7.5) of patients had postoperative glucose levels >200 mg/dl. After covariate adjustment, there was no evidence of a difference in odds of experiencing postoperative glucose levels >200 mg/dl (odds ratio [95% CI]: 0.76 [0.28–2.07]; P = 0.594) and maximum glucose levels (P = 0.518) between groups. Dexamethasone-treated patients had greater changes in white blood cell count between baseline and postoperative days 0–1. There was no evidence of a difference in wound healing and length of stay between groups.
Conclusions: There was no evidence of an association between perioperative dexamethasone administration and the odds of having postoperative glucose levels >200 mg/dl or higher maximum glucose levels. However, these findings may not be generalizable to patients having different baseline characteristics or procedures.

1. Introduction

Dexamethasone is a corticosteroid that is commonly used to treat postoperative nausea and vomiting (PONV) and pain in the orthopedic setting [1,2]. However, dexamethasone has been shown to increase blood glucose in animal models [3,4], and a similar effect has been suggested in humans [5,6]. Concerns regarding the potential for perioperative dexamethasone-induced hyperglycemia to negatively influence postoperative outcomes in patients and the harm that even a slight increase in blood glucose may impose in patients without diabetes have been raised. Thus, anesthetic regimens involving dexamethasone may need to be re-evaluated to prevent postoperative hyperglycemia-induced adverse effects [7], which can outweigh the benefits of dexamethasone administration.

There are limited data demonstrating a clear relationship between dexamethasone administration, elevated perioperative blood glucose, and postoperative outcomes in patients undergoing orthopedic surgery. This study aimed to evaluate the relationship between dexamethasone administration and elevated perioperative blood glucose in patients undergoing total joint arthroplasty. We hypothesized that dexamethasone administration would be associated with increased odds of elevated perioperative blood glucose. The primary outcome was any

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postoperative blood glucose level >200 mg/dl. The secondary outcomes included maximum blood glucose, the area under the curve (AUC) of blood glucose measurements, changes in white blood cell (WBC) count from baseline, average numerical rating scale (NRS) pain score, wound healing, and length of stay.

2. Materials and methods

2.1. Ethics

This retrospective study of prospectively collected data was approved by the Institutional Review Board at Hospital for Special Surgery (HSS) on November 14, 2013 (#2013-103), and waiver of consent was obtained. The study began in January 2014 and ended in July 2014. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983.

2.2. Patient enrollment

Patients aged 18–99 years who underwent unilateral total hip arthroplasty (THA) or total knee arthroplasty (TKA) were included. The exclusion criteria were 1) intraoperative administration of stress-dose steroids, 2) organ dysfunction, 3) American Society of Anesthesiologists Classification (ASA) >3, 4) revision arthroplasty, and 5) additional concurrent procedures.

2.3. Selection process

Patients were selected on a weekly basis. All patients who underwent surgeries 2 weeks prior to the day of screening and met the inclusion criteria were recorded. Anyone who fit the exclusion criteria or had documents missing from their charts, which would prevent adequate screening and data collection, was excluded. Of the remaining patients, 625 THA and TKA patients were randomly selected by a research assistant who was not otherwise involved in the study.

2.4. Study conduct details

Medications, blood glucose levels, WBC counts, and NRS pain scores that were prospectively recorded at baseline (preoperative period), postoperative day (POD) 0, POD 1, and POD 2 were collected from patients' electronic charts. Blood glucose levels were measured via laboratory assessments or point-of-care devices. Information about anesthesia and intraoperative medications was collected from the patients' anesthesia records. Anesthesia start times and hospital discharge times were collected to calculate length of stay. All data were entered into Research Electronic Data Capture, which is a secure, web-based application for building and managing online surveys and databases [8], hosted at HSS.

2.5. Blood glucose handling

For diabetic patients, point-of-care blood glucose measurements were conducted upon arrival to the holding area. Glucose levels <70 mg/dl or >200 mg/dl warranted treatments, as decided by an internist or anesthesiologist. Measurements of glucose were taken using a point-of-care device every 6 h while on a soft diet and immediately before meals and at 10 PM while on a consistent carbohydrate diet. Serum glucose levels were measured once daily. The inpatient glucose goal was 140–180 mg/dl; if necessary, insulin was given to maintain these goals. Blood glucose levels >400 mg/dl warranted the administration of 5–6 units of insulin and notification of the House Officer. For all other patients, serum glucose levels were measured once daily as part of the basic metabolic panel (e.g., potassium, sodium, etc.), along with complete blood count tests.

2.6. Statistical analysis

We estimated that 33–64% of patients would be administered dexamethasone, and that 22% of patients not given dexamethasone would experience postoperative blood glucose levels >200 mg/dl. This was based on the following estimates: (1) 10% of patients will have diabetes [9]; (2) 20% of patients without diabetes who do not receive dexamethasone will have perioperative elevated blood glucose [10]; and (3) 40% of patients with diabetes who do not receive dexamethasone will have perioperative elevated blood glucose [11]. We calculated that a total of 625 patients would provide at least 80% power at a two-sided alpha level of 0.05 to detect a 20% difference in the percentage of patients that experience elevated postoperative blood glucose levels using multiple logistic regression, anticipating that model covariates would explain 70% of the variability in dexamethasone administration (i.e., model R [2] would be 0.7 if dexamethasone administration were regressed on model covariates). The threshold of 200 mg/dl was chosen to ensure good separation between groups and to prevent against the likelihood of missing signals due to stress-induced hyperglycemia in patients who have not received dexamethasone. This narrow separation has been documented in previous studies [12].

Continuous and ordinal variables are expressed as means with standard deviations or medians with 1st and 3rd quartiles, depending upon the distribution of the data. Categorical variables are expressed as counts and percentages. The association between dexamethasone administration and study variables was assessed using *t*-tests or Wilcoxon rank-sum tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Outcomes with a single measurement per patient were compared between groups using robust regression via Huber's M-estimator [13] for continuous variables and multiple logistic regression for categorical variables. For the analysis of postoperative glucose outcomes, the last measurement to be included was the one closest to the 48-hour cut-off time; any measurements after that were eliminated to reduce large variations in time between first and last glucose measurements. Longitudinal measures were compared using regression based on the generalized estimating equations (GEE) approach [14,15] with an autoregressive [AR(1)] correlation structure. The GEE method accounts for the correlation between repeated measurements on the same patient, where the AR(1) correlation structure assumes a greater degree of correlation among measurements recorded closer in time. Models for each outcome initially included an interaction term between the treatment group and time point. If no evidence of an interaction was found, the model was refit without an interaction term, and results were reported as the overall difference in means between groups or odds ratio with 95% confidence intervals (CI). In addition, a stratified analysis based on diabetes status was performed to determine if dexamethasone was associated with the odds of having postoperative glucose levels >200 mg/dl.

A propensity score analysis was performed to test the robustness of regression results. Propensity scores were calculated via logistic regression using dexamethasone administration as the outcome and age, body mass index (BMI), diabetes, daily insulin use, ASA status, white race, procedure, preoperative antiepileptic drug use, preoperative oral antiglycemic agent use, preoperative non-insulin injectable medication use, preoperative antiemetic use, and baseline blood glucose level as predictors. Patients who did not receive dexamethasone were matched in a 1:1 ratio to patients who received perioperative dexamethasone. Matching was performed exactly on diabetes status and by the nearest neighbor method without replacement on propensity score. Two patients with type I diabetes who did not receive dexamethasone were excluded from analysis because they could not be matched exactly on diabetes status to any patient in the dexamethasone group. Covariate balance was assessed by calculating standardized differences on both the original and matched samples and using the suggested cut-off of 0.1 to indicate a negligible difference between groups [16]. Outcomes with a single measurement per patient were compared between groups in the matched sample using paired *t*-tests for continuous variables and