Preoperative Steroid Use and the Risk of Infectious Complications After Neurosurgery

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Abstract

Background and Purpose: The association between preoperative corticosteroid use and infectious complications after neurosurgical procedures is unclear. We aim to determine whether corticosteroids increase the risk of infectious complications after neurosurgery. **Methods:** We examined the association between preoperative corticosteroid use and postoperative infectious complications in a cohort of adults who underwent a neurosurgical procedure between 2005 and 2010 at centers participating in the National Surgical Quality Improvement Program. Corticosteroid use was defined as at least 10 days of oral or parental therapy in the 30 days prior to surgery. Our primary outcome was a composite of any infectious complications occurring within 30 days of surgery. We used propensity score analysis to examine the independent association between preoperative corticosteroid use and postoperative infections. **Results:** Among 26 634 neurosurgical procedures, 1228 (4.61%, 95% confidence interval [CI], 4.36-4.86) were preceded by preoperative corticosteroid use and 1469 (5.52%; 95% CI, 5.24-5.79) were followed by postoperative infections. In a propensity score analysis controlling for comorbidities, illness severity, and preexisting preoperative infections, corticosteroid use was independently associated with subsequent postoperative infections (odds ratio, 1.38; 95% CI, 1.11-1.70). Our results were unchanged in sensitivity analyses controlling for central nervous system tumors or active treatment with chemotherapy. **Conclusion:** Our results suggest that preoperative corticosteroid use is associated with an increased risk of infectious complications after neurosurgery. These findings may aid physicians with preoperative treatment decisions and risk stratification. Future randomized trials are needed to guide preoperative use of corticosteroids in this population.

Keywords

neurosurgery, infectious disease medicine, neurohospitalist, neurocritical care

Introduction

Approximately 48 million inpatient surgeries are performed annually in the United States, of which 2.1 million are neurosurgical procedures.^{1,2} Postoperative infectious complications such as surgical site infections and pneumonia can occur in neurosurgical patients and result in increased rates of morbidity and mortality, length of hospital stay, and cost.³⁻⁷ Known risk factors for infections include older age, diabetes mellitus, and use of intracranial monitoring devices.⁸

Corticosteroids are highly beneficial immunosuppressant medications that are frequently used in neurosurgical patients to decrease edema, inflammation, and pain.^{9,10} The benefits of corticosteroid use in the neurosurgical population are numerous and well known; they have been shown to decrease perioperative swelling, minimize inflammation, and improve functional outcomes following spinal cord compression.¹¹⁻¹⁵ Neurosurgical procedures therefore are often performed in the

setting of corticosteroid use because of their desired favorable effects; however, the risks of infections following preoperative steroid use are less well defined.

Corticosteroids have been studied in the overall general surgical population, with mixed findings regarding their effect on the risk of postoperative complications. In a recent observational analysis, approximately 3% of the general surgical population received preoperative steroids, which were

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associated with a 2- to 3-fold increased risk of infections and an almost 4-fold higher risk of death.¹⁶ On the other hand, in a recent randomized trial in patients undergoing cardiac surgery, corticosteroids decreased the incidence of postoperative infection, duration of ventilation, and length of hospital stay.¹⁷ The few studies that have evaluated the risk of corticosteroids specifically in the neurosurgical population have assessed small cohorts and have also shown mixed results.¹⁸⁻²⁰ We therefore examined the relationship between preoperative corticosteroid use and postoperative infectious complications after neurosurgical procedures.

Methods

Design

We assessed the relationship between the preoperative use of steroids and infectious complications after neurosurgery in a cohort of patients prospectively gathered from 2005 to 2010 by the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). National Surgical Quality Improvement Program has developed a national registry to promote quality improvement in surgical outcomes by allowing evaluation of a large group of surgical patients from multiple institutions.²¹ Patients are prospectively observed for a period of 30 days postoperatively in order to document any complications and/or mortality. Our analysis involved only deidentified data from the NSQIP database and was therefore exempt from evaluation by our institutional review board.

Patients

We included patients who underwent a neurosurgical procedure based on their NSQIP classification or a principal operative procedure with a Current Procedural Terminology (CPT) code between 22000 and 22999 or 61000 and 64999. We excluded pediatric patients (age <18 years).

Measurements

Trained NSQIP reviewers collect data by various methods such as medical chart review, telephone interviews with patients, and discussions with health care providers. National Surgical Quality Improvement Program is a well-validated data set, and audits of these prospectively collected data have shown >98% inter-rater agreement for all variables.²¹⁻²³ Prior studies have shown that outcome measures in the NSQIP database are more reliable than administrative data.²⁴

To control for potential confounders in the association between preoperative steroid use and postoperative infectious complications, we noted previously reported risk factors for postoperative complications in neurosurgical procedures using relevant variables as defined in the NSQIP database.²⁵⁻³⁴ A diagnosis of diabetes mellitus required treatment with either an oral hypoglycemic agent or insulin. Chronic obstructive pulmonary disease (COPD) included emphysema

or chronic bronchitis resulting in functional disability, hospitalization for an exacerbation, chronic bronchodilator therapy, or a diagnostic pulmonary function test. Tobacco use was based on self-report of active cigarette use in the year before surgery. Hypertension required blood pressure persistently >140/90 mm Hg or antihypertensive therapy for >1 month before surgery. Prior transient ischemic attack (TIA) was defined as a sudden onset transient focal neurological deficit reflecting a cerebral vascular distribution, and prior stroke was defined similarly but required more persistent deficits. Coronary heart disease was based on any history of percutaneous coronary intervention, a diagnosis of myocardial infarction within the 6 months before surgery, or angina within the month before surgery. Congestive heart failure required a new diagnosis or new signs or symptoms of heart failure within the month before surgery. Disseminated cancer included cancer that had spread to one or more distant sites. Renal insufficiency was defined as a creatinine of more than 3 mg/dL or a history of dialysis. Bleeding disorders included any known clotting deficiency or use of anticoagulant that put the patient at risk for excessive bleeding requiring hospitalization. Preoperative systemic sepsis was defined as the systemic inflammatory response syndrome and either a positive blood culture or clinical documentation of purulence or a positive culture from any site thought to be causative. Wound infection/open wound was defined as a wound that communicates with the air by direct exposure with or without cellulitis. Overall severity of illness was categorized according to the American Society of Anesthesiologists' classification.

In a sensitivity analysis, we also controlled for the presence of a central nervous system tumor or active receipt of chemotherapy. This was done for face validity, since these variables appeared likely to be confounders in the relationship between steroid use and postoperative complications. In addition, we performed exploratory subgroup analyses using relevant CPT codes to assess whether the effects of steroids varied across different neurosurgical procedures. The neurosurgical subgroups included spinal surgery, craniotomy for hematoma evacuation, craniotomy for brain tumor excision, aneurysm clipping, peripheral neuroplasty, and transsphenoidal pituitary excision.

Our main exposure variable was preoperative steroid use, defined as regular administration of either an oral or parenteral corticosteroid medication in the 30 days prior to surgery. Corticosteroids given via a topical, rectal, or inhalation route were not included. In addition, short courses of steroids (less than 10 days in the 30 days prior to surgery) were not included.

Our primary outcome was a composite of any infectious complications, for example, superficial site infections and pneumonia, occurring within 30 days of surgery. We then performed exploratory analyses on the individual end points making up our composite outcome. National Surgical Quality Improvement Program defines superficial surgical site infections as involving only skin or subcutaneous tissue of the incision with at least one of the following signs of infection:

Table 1. Baseline Characteristics of Cohort.^a

	Overall, N = 26 634	
Age, mean, y	55 (16)	
Female	13 292	49.9
Race		
White	20 409	76.6
Black	2124	8.0
Hispanic	1410	5.3
Asian	390	1.5
American Indian	2301	8.6
Coronary artery disease	1456	5.5
Stroke/TIA	1712	6.4
Congestive heart failure	78	0.3
Cancer	676	2.5
Hypertension	12 344	46.3
Diabetes	2511	9.4
Chronic kidney disease	127	0.5
Peripheral vascular disease	327	1.2
COPD	1005	3.8
Bleeding disorder	703	2.6
Preoperative sepsis	219	0.8
Preoperative wound infection	528	2.0
Central nervous system tumor	1823	6.8
Chemotherapy	171	0.6
Tobacco use	6807	25.6
ASA class		
1	1609	6.0
2	12 818	48.1
3	10 793	40.5
4	1331	5.0
5	83	0.3

Abbreviations: ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; y, year.

^a Data are presented as number and percentage unless otherwise indicated.

purulent drainage, organisms isolated from fluid or tissue from the superficial incision, pain; swelling; redness; or heat at the site leading to the incision being deliberately opened by the surgeon unless the incision was culture negative. A deep incisional surgical site infection was defined as infection of the fascial and muscle layers of the incision. An organ space surgical site infection was defined as an infection that appears to be related to the operation and that involves any part of the anatomy (organs or spaces) other than the incision. Pneumonia was defined as rales and dullness to percussion on physical examination and new onset purulent sputum or organisms isolated from blood culture or tracheal or bronchial isolate and no evidence of pneumonia present preoperatively. A postoperative urinary tract infection was defined as urinary urgency, urinary frequency, dysuria, or suprapubic tenderness and a urine culture with $>10^5$ colonies/mL of urine. A graft/prosthesis/flap failure was defined as mechanical failure of an extracardiac graft or prosthesis requiring return to the operating room, interventional radiology, or balloon angioplasty. Systemic sepsis was defined as the systemic inflammatory response syndrome and either positive blood culture or clinical documentation of purulence or positive culture from any

site thought to be causative. Systemic shock was defined as sepsis plus evidence of organ and/or circulatory dysfunction.

Data Analysis

On the basis of previously published reports,²⁵⁻³⁴ the following covariates were included a priori as potential confounders in our models: age, sex, race, coronary heart disease, prior stroke or TIA, congestive heart failure, disseminated cancer, hypertension, diabetes mellitus, renal insufficiency, COPD, bleeding disorders, preoperative sepsis, history of wound infection, smoking, and American Society of Anesthesiologists classifications.

We performed univariate comparisons using the chi-square test, and we report our results using odds ratios and exact binomial confidence intervals (CIs). We examined the association between preoperative steroid use and postoperative infectious complications by performing a propensity score analysis. A multiple logistic regression model was used to predict the likelihood (propensity score) of postoperative infections on the basis of the confounders listed previously. As our goal was to isolate the relationship between preoperative corticosteroid use and postoperative infections, rather than create a parsimonious prediction model, all covariates were left in place regardless of statistical significance. A separate multiple logistic regression was then performed to assess the relationship between our composite outcome and steroid use while accounting for the propensity score. Statistical significance was defined as a *P* value of less than .05.

Results

Of the cases included in NSQIP from 2005 through 2010, there were 26 634 neurosurgical procedures performed on patients of greater than 18 years of age. Among these patients, 1228 (4.61%; 95% CI, 4.36-4.86) had preoperative corticosteroid use and 1469 (5.52%; 95% CI, 5.24-5.79) developed postoperative infections.

The baseline characteristics of the cohort are listed in Table 1. Higher age, female sex, coronary heart disease, history of stroke or TIA, congestive heart failure, cancer, hypertension, diabetes, chronic kidney disease, peripheral vascular disease, COPD, bleeding disorder, preoperative sepsis, preoperative wound infection, and higher American Society of Anesthesiologists' classification were all associated with a higher rate of postoperative infection (Table 2).

In univariate analysis, preoperative corticosteroid use was significantly associated with subsequent postoperative infectious complications (odds ratio, 1.85; 95% CI, 1.52-2.26; Table 3). In a propensity score analysis controlling for possible confounders, the association between preoperative corticosteroid use and postoperative infectious complications remained significant (odds ratio, 1.38; 95% CI, 1.11-1.70). This association was unchanged in a sensitivity analysis that also controlled for the presence of a central nervous system tumor or active treatment

Table 2. Characteristics of Cohort Stratified by Postoperative Infectious Complications.^a

	Complication, N = 1469		No Complication, N = 25 165		P Value
Age, mean, y	59 (16)		55 (16)		<.001
Female	793	54.0	12 499	49.7	<.001
Race					<.001
White	1082	73.7	19 327	76.8	
Black	166	11.3	1958	7.8	
Hispanic	71	4.8	1339	5.3	
Asian	24	1.6	366	1.5	
American Indian	126	8.6	2175	8.6	
Coronary heart disease	116	7.9	1340	5.3	<.001
Stroke/TIA	242	16.5	1470	5.8	<.001
Congestive heart failure	16	1.1	62	0.2	<.001
Cancer	78	5.3	598	2.4	<.001
Hypertension	863	58.7	11 481	45.6	<.001
Diabetes	205	14.0	2306	9.2	<.001
Chronic kidney disease	19	1.3	108	0.4	<.001
Peripheral vascular disease	34	2.3	293	1.2	<.001
COPD	103	7.0	902	3.6	<.001
Bleeding disorder	95	6.5	608	2.4	<.001
Preoperative sepsis	35	2.4	184	0.7	<.001
Preoperative wound infection	73	5.0	455	1.8	<.001
Central nervous system tumor	145	9.9	1678	6.7	<.001
Chemotherapy	19	1.3	152	0.6	<.001
Tobacco use	348	23.7	6459	25.7	.091
ASA class					<.001
1	28	1.9	1581	6.3	
2	413	28.1	12 405	49.3	
3	758	51.6	10 035	39.9	
4	250	17.0	1081	4.3	
5	20	1.4	63	0.3	

Abbreviations: ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; TIA, transient ischemic attack; y, year.

^a Data are presented as number and percentage unless otherwise indicated.**Table 3.** Percentage Occurrence of Overall and Specific Complications Stratified by Steroid Use with Associated Odds Ratios.

Adverse Event	Steroid Patients, %	Nonsteroid Patients, %	Odds Ratio (95% CI)	P Value
Composite	9.45	5.33	1.85 (1.52–2.26)	<.001
Superficial SSI	1.47	1.18	1.28 (0.78–2.08)	.33
Deep SSI	0.57	0.63	0.74 (0.34–1.62)	.46
Organ space SSI	1.55	0.31	3.95 (2.29–6.79)	<.001
Pneumonia	2.93	1.24	1.60 (1.10–2.33)	.014
Graft failure	0.16	0.06	2.96 (0.64–13.87)	.17
UTI	3.83	2.09	1.30 (0.94–1.79)	.12
Septic shock	0.81	0.46	0.85 (0.42–1.72)	.65

Abbreviations: CI, confidence interval; SSI, surgical site infection; UTI, urinary tract infection.

with chemotherapy (odds ratio, 1.38; 95% CI, 1.11–1.71). Based on the exploratory analyses performed on specific neurosurgical populations, the adverse effects of steroids may only be seen in craniotomy for hematoma evacuation and spine surgery (odds ratio, 1.68; 95% CI, 1.27–2.21) and not in transsphenoidal pituitary resection, peripheral neuroplasty, aneurysmal clipping, or brain tumor excision (odds ratio, 0.76; 95% CI, 0.48–1.21; Table 4). In addition, corticosteroid use may be associated with organ space surgical site infection (odds ratio, 3.95; CI, 2.29–6.79) and

pneumonia (odds ratio 1.60; 95% CI, 1.10–2.33) but not other infectious complications (Table 3).

Discussion

In a large cohort of patients undergoing neurosurgical procedures, we found an association between the use of preoperative corticosteroids and postoperative infections. Although there are shared risk factors such as older age, female gender,

Table 4. Percentage Occurrence of Primary Outcome in Neurosurgical Subgroups Stratified by Steroid Use with Associated Odds Ratios.

Neurosurgical Subgroup	Steroid Patients, %	Nonsteroid Patients, %	Odds Ratio (95% CI)	P Value
Hematoma evacuation and spine surgery	9.85	4.89	1.68 (1.27-2.21)	<.001
Transsphenoidal pituitary resection, peripheral neuroplasty, aneurysmal clipping, brain tumor excision	6.70	7.44	0.76 (0.48-1.21)	.25

Abbreviation: CI, confidence interval.

and medical comorbidities, the relationship between preoperative corticosteroid use and postoperative infectious complications persisted after accounting for such potential confounders. Based on exploratory analyses, the adverse effects of preoperative corticosteroids may only be seen in spine surgery and intracranial hematoma evacuation. In addition, based on further exploratory analyses, corticosteroids were associated with both pneumonia and organ space surgical site infections but not other infectious complications.

Our results must be interpreted in light of the limitations of the study. First, this was a retrospective study of data elements in the NSQIP database. Prospective ascertainment or the availability of additional factors that were not collected or not analyzed may have influenced the outcomes. For example, as the focus of this study was on postoperative infections, it would have been useful to know the HIV status and transplant status of the patients but these variables were not included in the NSQIP database. Second, NSQIP is a voluntary registry, and not a community-based sample, and therefore these findings may not be generalizable to all neurosurgical patients. In addition, we lacked information on the type of corticosteroid used or the dosing, duration, and indication. We also could not examine the benefits of corticosteroids in terms of reducing edema, decreasing pain, or improving functional outcomes as we lacked detailed neurological examination and imaging data. Future studies may help determine whether the duration or dose of corticosteroid significantly alters postoperative infectious complications.

Despite these limitations, the use of the NSQIP database allowed for a comprehensive evaluation of the risks of corticosteroid use in a large population of neurosurgical patients. The previous validity of the NSQIP data set as well as the heterogeneous nature of both patients and institutions included in the data set argues that the present results may be some of the most valid on the topic at hand. The results of this study show that there should be further prospective studies and randomized clinical trials performed on corticosteroid use in this population. Future studies may indicate that clinicians should carefully consider the risks of starting corticosteroids in patients who may soon be undergoing neurosurgery. In addition, based on our exploratory analyses, further studies should be performed to clarify the risks of postoperative infections in specific neurosurgical procedures in order to allow clinicians to make better informed decisions regarding starting preoperative corticosteroids. In conclusion, corticosteroids have numerous well-known benefits when used in the neurosurgical

population; however, our study suggests that the preoperative use of corticosteroids may lead to an increased risk of infections in patients undergoing neurosurgery.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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