Corticosteroids for Acute Orbital Cellulitis

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abstract

OBJECTIVES: Standard treatment of children hospitalized for acute orbital cellulitis includes systemic antibiotics. Recent data from single-center studies suggest the addition of systemic corticosteroids may hasten clinical improvement and reduce hospital length of stay (LOS). We investigate the potential relationship between corticosteroid exposure and duration of hospitalization for pediatric orbital cellulitis.

METHODS: Using Pediatric Health Information System registry data from 51 children's facilities, we performed a retrospective cohort study of children hospitalized for orbital cellulitis <18 years of age from 2007 to 2018. The primary study outcome was hospital LOS. Secondary outcomes included frequency of surgical interventions, PICU admission, and 30-day related-cause readmission.

RESULTS: Of the 5645 children included for study, 1347 (24%) were prescribed corticosteroids within 2 days of admission. Corticosteroid prescription was not associated with LOS in analyses adjusted for age; presence of meningitis, abscess, or vision issues; and operative episode and PICU admission within 2 days ($e^{\beta} = 1.01$, 95% confidence interval [CI]: 0.97–1.06). Corticosteroid exposure was associated with operative episodes after 2 days of hospitalization (odds ratio = 2.05, 95% CI: 1.29–3.27) and 30-day readmission (odds ratio = 2.40, 95% CI: 1.52–3.78) among patients with a primary diagnosis of orbital cellulitis.

CONCLUSIONS: In this database query, we were not able to detect a reduction in LOS associated with corticosteroid exposure during hospitalization for orbital cellulitis. Corticosteroid prescription was associated with PICU admission and operative episodes after 2 days of hospitalization. Before the adoption of routine corticosteroid use, prospective, randomized control trials are needed.

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WHAT'S KNOWN ON THIS SUBJECT: Recent data suggest a combination of intravenous antibiotics and systemic corticosteroids in the acute management of orbital cellulitis may result in reduced hospital stay. However, these studies are limited by their study design, corticosteroid dosing variance, and patient heterogeneity.

WHAT THIS STUDY ADDS: In contrast to existing reports, we found corticosteroid administration was not significantly associated with hospital length of stay.

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Acute orbital cellulitis, a bacterial infection common to children and young adults, is associated with severe acquired comorbidities such as vision loss, meningitis, abscess formation, sinus venous thrombosis, and mortality.[1,2] Standard management includes hospitalization for intravenous (IV) antibiotic administration and surgical interventions, as indicated, to prevent vision impairment, intracranial extension, and even death.[3]

Recent data suggest a combination of IV antibiotics and systemic corticosteroids may reduce inflammatory symptoms (eg resolution of fever, pain scores, orbital edema, chemosis, proptosis, and ocular mobility) in children hospitalized for orbital cellulitis.[4–7] Children provided adjuvant corticosteroids in an unmatched, prospective, single-center cohort study experienced a reduction in hospital length of stay (LOS) of 3 days.[4] In a multicenter retrospective study using the Pediatric Health Information System (PHIS) registry, 29% of children hospitalized for orbital cellulitis were prescribed corticosteroids.[8] However, clinical outcomes for those with and without exposure were not compared.

Current evidence is limited by sampling bias, corticosteroid dosing variance, and patient heterogeneity. As a result, knowledge gaps exist regarding corticosteroid efficacy and safety as adjunct therapy in this context. We aim to determine if differences in hospital LOS exist for children hospitalized for orbital cellulitis with and without exposure to systemic corticosteroids. Secondarily, we sought to determine if corticosteroid exposure was related to frequency of subsequent surgical interventions, PICU admissions, and disease related hospital readmission within 30 days of discharge.

METHODS

Data Source

We conducted a retrospective cohort study assessing inpatient encounters from January 2007 through December 2018 using the PHIS registry. This administrative database contains inpatient, emergency department, ambulatory surgery, and observation encounter-level data from >50 not-for-profit, tertiary care pediatric hospitals in the United States. These hospitals are affiliated with the Children's Hospital Association (Lenexa, KS). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. For the purposes of external benchmarking, participating hospitals provide discharge and encounter data including demographics, diagnoses, and procedures. Nearly all hospitals also submit resource use (eg pharmaceuticals, imaging, and laboratory) into PHIS. Data are deidentified at the time of data submission, and data are subjected to a number of reliability and validity checks before being included in the database. For this study, data from 51 hospitals were included.[8] This study was reviewed and approved by our local institutional review board (no. 197838).

Study Participants and Cohorts

Inclusion criteria were initial encounters from children 0 to 17 years of age hospitalized with orbital cellulitis identified by an *International Classification of Diseases Ninth Revision, Clinical Modification* (ICD-9-CM) discharge diagnosis code of 376.01 or equivalent *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) codes of H05.01, H05.011–13, and H05.019. Both primary and secondary diagnoses of orbital cellulitis were included to ensure capture of children with potential serious sequelae or complications resulting from orbital cellulitis. Patients were excluded for presence of 1 or more complex chronic conditions by using the pediatric complex chronic conditions classification system as they may impact hospital LOS.[9] Children with diagnoses associated with corticosteroid administration (eg asthma) were also excluded as previously described (Supplemental Table 6).[10] Children with viral or fungal infections and those who did not receive IV, oral, or intramuscular antibiotics (Supplemental Table 7) within 2 days of admission were excluded. Study cohorts were identified by prescription of systemic corticosteroids defined by specific agent (Supplemental Table 8) charged by the second day of the encounter to indicate providers' intention to treat.

Study Outcomes and Definitions

The primary outcome was hospital LOS measured in days. Secondary outcomes included (1) orbital cellulitis-related surgical interventions after the second day of admission; (2) PICU admission occurring after the second day of admission; and (3) 30-day inpatient readmission and/or emergency department visit with a discharge diagnosis code related to orbital cellulitis. Surgical interventions of interest were identified by *International Classification of Diseases* procedure code and included relevant ophthalmologic, otolaryngological, and neurosurgical procedures (Supplemental Table 9). Descriptive data included demographics and comorbidities associated with orbital cellulitis including meningitis, abscess formation, and

visual impairment (identified by using ICD 9-CM and 10-CM codes [see Supplemental Table 10]).[10] Orbital cellulitis associated with these comorbidities was defined as "complicated orbital cellulitis." Surgical interventions or PICU admission were limited to those that occurred after the second day of admission to ensure interventions occurred chronologically after steroid prescription.

Statistical Plan

Steroid prescription rates for each hospital were calculated and variations across hospitals was assessed by using funnel plots with 95% (2 SDs) and 99.8% (3 SDs) control limits.[11] Patient demographic and clinical characteristics were summarized by using standard descriptive statistics for continuous (mean, SD, median, interquartile range [IQR]) and categorical variables (count, percentage). Differences in distributions of characteristics and prescribing frequencies were evaluated by using 1-way analysis of variance or Kruskal–Wallis tests for continuous covariates and χ^2 or Fisher's exact tests for categorical measures. Potential associations between corticosteroids and primary and secondary outcomes were estimated by generalized estimating equations models with exchangeable correlation structures to account for correlations of patients within a hospital. Poisson distribution with log-link function was used for LOS. The binomial distribution with logit-link function was employed for secondary outcomes. Because disease-specific severity of illness is not recorded in a standardized method in PHIS, we performed a sensitivity analysis of associations between corticosteroid prescription and outcomes of interest after excluding patients with PICU admission within 2 days of admission. Because dexamethasone is a commonly used medication for perioperative nausea and vomiting in ophthalmologic procedures,[12] we performed a second sensitivity analysis excluding patients who were only prescribed corticosteroids on the day of a surgical procedure. Variables with an a priori significance of $P < .15$ from unadjusted analyses were included in adjusted analyses. All tests were 2-sided with type I error set at 0.05, and analyses were conducted by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

Sampling and General Characteristics

We identified 11 418 inpatient encounters that met inclusion criteria, and 5773 were excluded predominately for presence of chronic complex conditions or other medical comorbidities (Supplemental Fig 2). Of the 5645 remaining encounters, 4306 (76.3%) had a primary diagnosis of orbital cellulitis and 1347 (23.8%) were prescribed systemic corticosteroids (Table 1). Dexamethasone was the most frequently prescribed corticosteroid (n = 1196; 88.8%), with methylprednisolone (8.2%), hydrocortisone (0.07%), prednisolone

TABLE 1 Demographic and Clinical Characteristics for the Study Sample and by Cohorts Defined by Corticosteroid Exposure During Hospitalization

			Steroid Administration		
Variables	Level	Total, N = 5645	Yes, N = 1347	No, N = 4298	P^a
Continuous, median (IQR)					
Age at admission, y	—	6 (3–10)	8 (4–12)	6 (2–10)	<.001
LOS, d	—	3 (3–5)	4 (3–6)	3 (2–5)	<.001
Categorical, n (column %)					
Sex	Female	2006 (35.5)	469 (34.8)	1537 (35.8)	.53
	Male	3639 (64.5)	878 (65.2)	2761 (64.2)	—
Orbital cellulitis as primary diagnosis	Yes	4306 (76.3)	920 (68.3)	3386 (78.8)	<.001
	No	1339 (23.7)	427 (31.7)	912 (21.2)	—
Complicated orbital cellulitis	Yes	154 (2.7)	61 (4.5)	93 (2.2)	<.001
	No	5491 (97.3)	1286 (95.5)	4205 (97.8)	—
Meningitis	Yes	24 (0.4)	6 (0.5)	18 (0.4)	.90
	No	5621 (99.6)	1341 (99.6)	4280 (99.6)	—
Vision loss or blindness	Yes	19 (0.3)	8 (0.6)	11 (0.3)	.06
	No	5626 (99.7)	1339 (99.4)	4287 (99.7)	—
Abscess	Yes	121 (2.1)	50 (3.7)	71 (1.7)	<.001
	No	5524 (97.9)	1297 (96.3)	4227 (98.3)	—
Operative episode for orbital cellulitis during first 2 d of admission	Yes	1303 (23.1)	701 (52.0)	602 (14.0)	<.001
	No	4342 (76.9)	646 (48.0)	3696 (86.0)	—
PICU visit during first 2 d of admission	Yes	169 (3.0)	59 (4.4)	110 (2.6)	<.001
	No	5476 (97.0)	1288 (95.6)	4188 (97.4)	—

—, not applicable.

[a] The parametric P value is calculated by analysis of variance for numerical covariates and χ^2 test for categorical covariates.

(3.9%), and prednisone (2.6%) prescribed in only a small subset of patients. Children prescribed systemic corticosteroids were older (8 [IQR: 4–12] years versus 6 [IQR: 2–10] years, $P < .001$) and more frequently carried a secondary diagnosis of orbital cellulitis (31.70% vs 21.2%, $P < .001$). Complicated orbital cellulitis occurred more frequently in patients prescribed corticosteroids compared with those who did not (4.5% vs 2.2%, $P < .001$). When evaluated by component, the composite metric was primarily influenced by abscess frequency. Indeed, a greater proportion of patients with corticosteroid exposure were concurrently diagnosed with an abscess (3.7% vs 1.7%; $P < .001$; Table 1); however, statistically significant differences between rates of meningitis, visual impairment, or blindness were not observed between the study groups.

Regional Variation in Orbital Cellulitis Management

Variation in corticosteroid prescribing across 51 participating hospitals is displayed in Fig 1. Overall, wide prescribing variation were noted with institutional rates ranging from 1.9% to 73.7% (institutional mean during study period: 26.3% ±15.5%). Of note, 5 centers were above and 6 were below 3 SDs of the overall mean corticosteroid prescribing rates.

LOS

Children prescribed systemic corticosteroids experienced a longer median LOS compared with children without corticosteroid prescription (4 [IQR: 3–6] vs 3 [IQR: 2–5] days, $P < .001$). In unadjusted models, factors associated with increased LOS included corticosteroid exposure and older patient age; complicated orbital cellulitis and undergoing a surgical procedure or admission to the PICU were also associated with increased LOS (all $P < .001$) (Table 2). Overall, the unadjusted predicted mean LOS was 17.3% longer for children prescribed corticosteroids. After adjusting for patient age, complicated orbital cellulitis, surgical intervention for orbital cellulitis, and PICU admission (Table 3), corticosteroid exposure was no longer associated with LOS of stay in patients stratified by a primary ($e^{\beta} = 1.01$ 95% confidence interval [CI]: 0.97–1.06) or secondary diagnosis of orbital cellulitis ($e^{\beta} = 0.97$, 95% CI: 0.87–0.08). In sensitivity analyses, corticosteroid prescription was similarly not associated with LOS among patients without PICU admission within 2 days of hospitalization (primary diagnosis: $e^{\beta} = 1.00$ 95% CI: 0.96–1.05, secondary diagnosis: $e^{\beta} = 0.96$ 95%

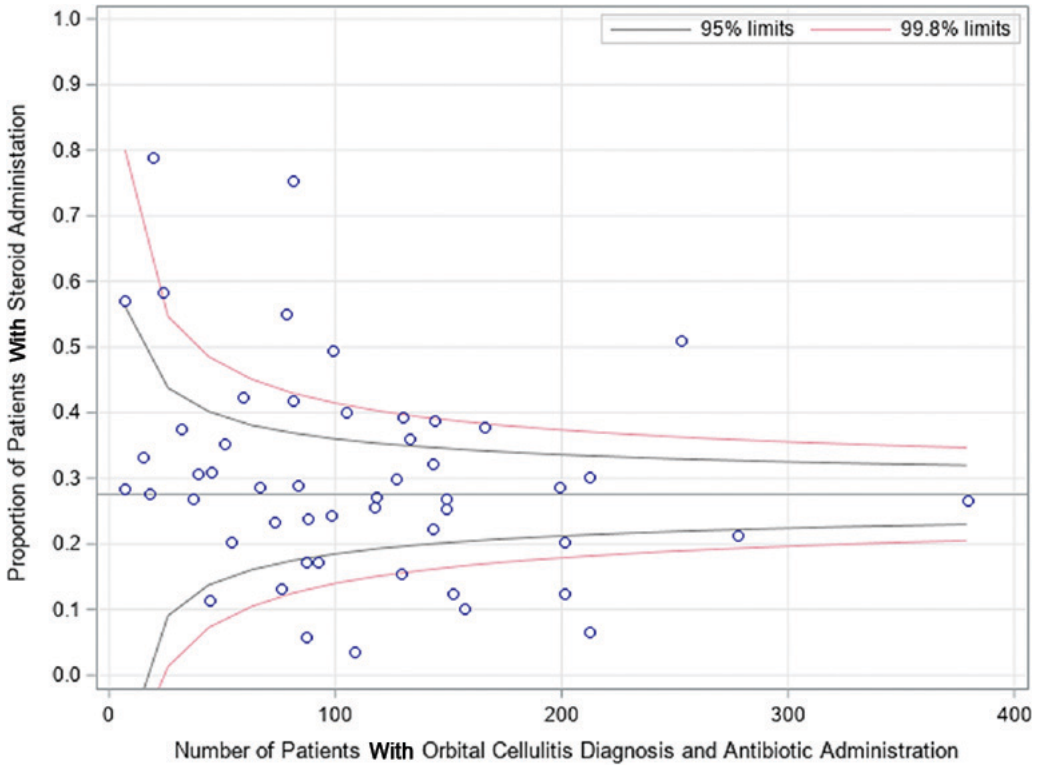

FIGURE 1
Hospital variation in steroid use among patients with orbital cellulitis. Wide variation in steroid use was observed across the 51 hospitals. The prevalence of steroid usage ranged from 1.9% to 73.7%, with an average of 26.3% (SD = 15.5).

TABLE 2 Unadjusted Associations Between Steroid Administration and LOS

Covariate	Level	Unadjusted, e^{β} (95% CI)[a]	*P*
Corticosteroid	Yes	1.17 (1.12–1.23)	<.001
	No	Reference	—
Older age	—	1.02 (1.01–1.02)	<.001
Sex	Male	1.01 (0.97–1.05)	.54
	Female	Reference	—
Orbital cellulitis as primary diagnosis	Yes	0.75 (0.70–0.79)	<.001
	No	Reference	—
Complicated orbital cellulitis	Yes	2.75 (2.44–3.10)	<.001
	No	Reference	—
Operative episode for orbital cellulitis during first 2 d of admission	Yes	1.51 (1.43–1.58)	<.001
	No	Reference	—
PICU visit during first 2 d of admission	Yes	2.12 (1.82–2.48)	<.001
	No	Reference	—

—, not applicable.

[a] Estimates represent the exponentiated regression parameter (95% CI) from Poisson regression with LOS in days as outcome.

CI: 0.90–1.02) or when excluding those only prescribed corticosteroids on the day of a surgical procedure (primary diagnosis: e^{β} = 1.06 95% CI: 1.00–1.11, secondary diagnosis: e^{β} = 1.03 95% CI: 0.91–1.16; all $P > .05$)

Secondary Outcomes

Among those with corticosteroid exposure, a greater proportion of patients underwent a surgical procedure (52.0% vs 14.0%, $P <$ .001) and were hospitalized in the PICU (4.4% vs 2.6%, $P < .001$) as compared with children not prescribed corticosteroids. Unadjusted logistic modeling revealed relationships between systemic corticosteroids and both operative episode for orbital cellulitis (odds ratio [OR] = 2.06, 95% CI: 1.44–2.95), PICU visit after second day of admission (OR = 3.25, 95% CI: 1.10–9.55), and 30-day related-cause readmission (OR = 2.70, 95% CI: 1.84–3.94, all $P < 0.05$) (Table 4). In adjusted analyses, corticosteroid exposure remained associated with operative episode after the second day of admission among patients with primary diagnosis of orbital cellulitis (OR = 2.05, 95% CI: 1.29–3.27) and with 30-day related-cause readmission among both patients with a primary (OR = 2.40, 95% CI: 1.52–3.78) or secondary diagnosis of orbital cellulitis (OR = 2.19, 95% CI: 1.08–4.45) (Table 5).

DISCUSSION

Among children hospitalized for orbital cellulitis, we did not observe the reduction in LOS for patients prescribed systemic corticosteroids as described previously in the literature. In adjusted analyses, corticosteroid prescription was not associated with LOS, whereas the presence of complicated orbital cellulitis, operative episodes, and PICU admission during the initial 2 days of hospitalization all were associated with longer hospitalization. We further determined that more patients with corticosteroid exposure underwent an operative episode related to orbital cellulitis after the second day of admission (9.3%) compared with those without (4.8%). Similarly, prescription of corticosteroids was associated with requiring readmission to the hospital or care in the emergency department within 30 days of discharge (OR = 2.70). These data suggest patients prescribed

TABLE 3 Adjusted Associations Between Steroid Administration and LOS Stratified by Primary and Secondary Diagnosis

		Primary Diagnosis		Secondary Diagnosis	
Covariate	Level	e^{β} (95% CI)[a]	*P*	e^{β} (95% CI)[a]	*P*
Corticosteroid exposure	Yes	1.01 (0.97–1.06)	.55	0.97 (0.87–1.08)	.57
	No	Reference	—	Reference	—
Greater patient age	—	1.00 (1.00–1.01)	.18	0.99 (0.98–1.01)	.43
Complicated orbital cellulitis	Yes	1.99 (1.54–2.56)	<.001	2.18 (1.82–2.61)	<.001
	No	Reference	—	Reference	—
Operative episode for orbital cellulitis during first 2 d of admission	Yes	1.40 (1.34–1.48)	<.001	1.17 (1.07–1.28)	<.001
	No	Reference	—	Reference	—
PICU visit during first 2 d of admission	Yes	1.34 (1.06–1.68)	.01	1.26 (1.07–1.57)	.04
	No	Reference	—	Reference	—

—, not applicable.

[a] Estimates represent the exponentiated regression parameter (95% CI) from Poisson regression with LOS in days as outcome.

TABLE 4 Unadjusted Associations Between Steroid Administration and Secondary Outcomes

Outcomes	Steroid, *n* (%)	No Steroid, *n* (%)	Unadjusted	
			OR (95% CI)[a]	*P*
Operative episode for orbital cellulitis after second day of admission				
Yes	60 (9.3)	176 (4.8)	2.06 (1.44–2.95)	<.001
No	586 (90.7)	3520 (95.2)	—	—
PICU visit after second day of admission				
Yes	4 (0.3)	4 (0.0)	3.25 (1.10–9.55)	.03
No	1284 (99.4)	4184 (99.9)	—	—
30-d orbital cellulitis-related readmission				
Yes	56 (4.2)	67 (1.6)	2.70 (1.84–3.94)	<.001
No	1291 (95.8)	4231 (98.4)	—	—

—, not applicable.
[a] OR (95% CI) comparing steroid administration to no administration (reference).

corticosteroids may represent a sicker population. Our findings are in contrast to previous reports and suggest prospective research is needed to establish the benefit and potential consequences of corticosteroid exposure in this population.

The potential etiology of disparate findings in this study are likely multifactorial and in part related to variable corticosteroid dosing regimens and cohort heterogeneity among existing reports. In a retrospective study of 23 patients, IV dexamethasone with variable dosing (0.33 to 1 mg/kg) and duration of therapy (12 hours to 7 days) resulted in decreased LOS as compared with children without steroid exposure (6.5 days versus 10 days) but failed to reach statistical significance.[7] Researchers of a prospective, single-blinded, interventional trial involving a standardized dosing regimen including a taper over 1 to 2 weeks reported a shorter mean LOS (14.1 vs 18.4 days) in the group who received adjunct therapy with corticosteroids.[5] However, patients were intentionally observed in the hospital until complete resolution of infection, which may not be generalizable or practical in clinical practice. More recently, reductions in LOS by 2.8 to 3.8 days for children receiving 3 days of IV dexamethasone (0.3 mg/kg per day) from the time of admission[4] or oral prednisolone (1 mg/kg) have been reported.[6] In a meta-analysis of 118 patients from these 4 studies, the pooled effect of corticosteroid administration was a shorter mean LOS of 2.9 days (95% CI: 2.73–3.07).[13] However, 99% of the measured effect on LOS was accounted for in 1 study.[4]

In contrast to these smaller, single-center studies, we found no significant difference in LOS when adjusting for age, complicated orbital cellulitis, operative episodes during the first 2 days of admission, and initial admission to the PICU. Although we cannot be certain why results differ from those previously published, we suspect the benefit appreciated in previous studies may be due to unmeasured confounders in previously publications,[7] steroid initiation timing, subjective or objective (ie laboratory evidence) clinical improvement on antibiotics alone,[4–6] or the inclusion of a control group that refused corticosteroid administration when approached for enrollment.[5] Furthermore, none of the prospective trials blinded providers to the intervention, introducing bias in patient selection. Although we cannot state definitively that certain populations with orbital cellulitis will not appreciate clinical benefit from corticosteroid administration, our results from a large cohort study of >5000 children and the

TABLE 5 Adjusted Associations Between Steroid Administration and Secondary Outcomes Stratified by Primary and Secondary Orbital Cellulitis Diagnosis

Outcomes	Primary Diagnosis		Secondary Diagnosis	
	OR (95% CI)[a]	*P*	OR (95% CI)[a]	*P*
Operative episode for orbital cellulitis after second day of admission	2.05 (1.29–3.27)[b]	.002	1.26 (0.65–2.45)[b]	.49
PICU visit after second day of admission	NA[c]	—	NA[c]	—
30-d orbital cellulitis-related readmission	2.40 (1.52–3.78)[d]	<.001	2.19 (1.08–4.45)[d]	.03

—, not applicable.
[a] OR (95% CI) comparing steroid administration with no administration (reference).
[b] Model includes age; meningitis, vision, abscess; and PICU visit during first 2 days of admission.
[c] Not calculated because low events.
[d] Model includes age, operative episode any time during admission, and LOS.

observation of others suggest a benefit is not yet broadly identifiable.[14]

The presence of severe comorbidities from orbital cellulitis (ie, meningitis, abscess formation, visual impairment) and associated need for surgical management of subperiosteal and other abscesses are important contributors to the overall LOS for orbital cellulitis. In our cohort, 2.7% of patients had complicated orbital cellulitis and 23.1% underwent an operative episode within the first 2 days of admission. Established recommendations by Garcia and Harris and others exist to guide the decision between operative and medical management for orbital cellulitis with and without subperiosteal abscess and intracranial extension.[15–17] In a recent systematic review of the management of pediatric orbital cellulitis, there was significant variability (14% to 93%) in surgical intervention rates,[18] with authors of multiple reports suggesting younger children more often respond to medical management alone.[15,19–21] In our adjusted analyses, both presence of complicated orbital cellulitis ($e^{\beta} = 1.99$; $P < .001$) and operative episodes ($e^{\beta} = 1.40$; $P < .001$) were independently associated with longer LOS and likely represent markers of severity of illness at the time of presentation. Although children prescribed corticosteroids were older (median age 8 years versus 6 years, $P < .001$), greater patient age was not associated with LOS, suggesting younger patients did not exhibit a better response to clinical management.

One of the proposed benefits of administering corticosteroids for orbital cellulitis is reduced inflammation that, in theory, may expedite recovery and hospital discharge.[4] Providers may hesitate to administer corticosteroids out of concern for immune suppression that could inhibit infection clearance or lead to the invasive spread of disease. This concern, and a lack of professional or societal guidelines supporting the standard use of corticosteroids, likely contributes to the wide prescribing variability noted in our study (1.9% to 73.7%).[10] Institutions that use corticosteroids more frequently may encounter more severe cases necessitating aggressive treatment or just be more comfortable with administering the medications. In contrast, centers with lower rates of prescribing may be related to insufficient evidence in this indication or a lack of familiarity. In previous publications, no patients were reported to have invasive spread of disease,[4–7] and researchers in only 1 study reported recurrences of a subperiosteal abscess; however, only a single patient in each of the corticosteroid exposure and control cohorts experienced this outcome.[6] The rates of intracranial extension, abscess reformation, and vision loss are lower than previous reports[14,22,23] and may reflect reduced disease severity. Existing studies are underpowered to detect these important adverse outcomes associated with corticosteroid administration for orbital cellulitis. In our study, we examined at what frequency patients underwent operative episodes for orbital cellulitis >2 days after admission, suggesting a failure of medical therapy. Overall, an operation was performed after the second day of admission on 5.5% of children and associated with the planned prescription of corticosteroids in adjusted analyses for primary (OR = 2.05, 95% CI: 1.29–3.27) but not secondary orbital cellulitis diagnoses (OR = 1.26, 95% CI: 0.65–2.45). Although the direction of association cannot be ascertained (ie, did corticosteroid prescription worsen disease or were patients with more severe disease prescribed corticosteroids), our data suggest the next appropriate level of evidence can be achieved with collaborative prospective trials that could measure differences in disease-relevant outcomes. A minority of patients (<1%) required transfer to the PICU after the second day of admission, suggesting children are unlikely to have progression of disease after initial management with or without the prescription of corticosteroids.

The use of a retrospective database has inherent limitations. The reliance on billing data yields a limited granularity needed to define cohorts, report rates of clinical outcomes, and determine their chronological relationship. The accuracy of coding from PHIS data is dependent on provider documentation and thus is subject to misclassification errors. We are not able to report the precise dosage or exact timing of administration of medications. Furthermore, the presence of billing data does not ensure that a patient received a treatment or therapy during hospitalization. As a result, we are unable to ascertain whether heterogeneity in treatment regimen biased our primary outcome to the null hypothesis despite certain regimens that may have greater efficacy. Our study is further limited by the fact that our study population included children with orbital cellulitis, with few or no other comorbidities, thus limiting the generalizability of our findings

to "healthier" children only. Although we found that patients with orbital cellulitis who received adjunct corticosteroids more frequently had subsequent operative episode after the second day of admission as well as 30-day orbital cellulitis readmission, we cannot determine causality. Although we used all available markers of disease severity, there does not exist a validated disease severity clinical score for pediatric orbital cellulitis.

Despite these limitations, our study has the advantage of a large sample size and in this way improves on the existing body of literature characterized by single-center experience and small sample size. In contrast to previous studies, we found corticosteroid administration was not associated with LOS among patients with orbital cellulitis. Despite the perceived safety of corticosteroids in those studies and low suspicion for immunosuppression, we found corticosteroid administration was in fact associated with potential adverse events such as an increased odd of operative episodes after the second day of admission and 30-day orbital cellulitis-related admissions. Given these findings and the limitations above, there is now a need for multicenter, prospective, controlled trials to further define the role and safety of systemic corticosteroids in the acute management of pediatric orbital cellulitis.

ABBREVIATIONS

CI: confidence interval
ICD-9-CM: *International Classification of Diseases Ninth Revision, Clinical Modification*
ICD-10-CM: *International Classification of Diseases 10th Revision, Clinical Modification*
IQR: interquartile range
IV: intravenous
LOS: length of stay
OR: odds ratio
PHIS: Pediatric Health Information System

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