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Clinical factors associated with the use of dexamethasone for asthma in the pediatric emergency department

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ABSTRACT

Background: Dexamethasone is efficacious for the treatment of pediatric asthma exacerbations but is not specifically recommended by current national guidelines.

Objectives: To describe the factors associated with prescribed dexamethasone in a pediatric emergency department (PED) and upon patient discharge.

Methods: Retrospective chart review of patients aged 2 to 18 years discharged home from a PED with a diagnostic code for asthma (J45x). Descriptive statistics are reported and binary logistic regression with generalized estimating equations was used to examine the demographic and clinical factors associated with dexamethasone use in the PED and upon discharge.

Results: 594 children contributed 690 visits for asthma. Two-thirds of patients received prednisone in the PED ($n = 430$; 62%). Among 260 children who received dexamethasone, 76% ($n = 198$) were prescribed a second dose for post-discharge administration. Multivariable models showed that patients triaged as most urgent had a 50% reduction in the odds of receiving dexamethasone in the PED (OR = 0.5; 95% CI = 0.28–0.87). Patients seen by a pediatrician (OR 4.2; 95%CI 2.1–8.3) and those triaged as urgent (OR 2.9; 95% CI = 1.8–7.8) were more likely to receive a single dose of dexamethasone.

Conclusions: Dexamethasone is less commonly used in the PED for asthmatic patients triaged as most urgent. Triage acuity and level of training were associated with single-dose treatment of asthma in those receiving dexamethasone. Further studies are needed to clarify the use of dexamethasone across the spectrum of asthma severity.

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Asthma affects approximately seven million children under the age of eighteen in the United States, posing a significant health and economic burden that disproportionately affects minority children and those living in poverty (1). Respiratory disorders, including asthma, are the most common reason pediatric patients are brought to the emergency department (ED) for care (2). In an acute care setting, systemic corticosteroids (SCS) are recommended by the Global Initiative for Asthma (3), the British Thoracic Society (4), and the National Institutes of Health (5), as SCS improve lung function, reduce health service relapse, and decrease the rate of hospital admission from the ED (6).

Current asthma guidelines recommend the use of prednisone (or prednisolone), but the dose and length of treatment varies (3–5). Issues related to frequent dosing, palatability, and side effects negatively affect medication adherence following discharge from the ED, with many children failing to complete the oral corticosteroid (OCS) course as prescribed (7,8). Given the ongoing morbidity and mortality associated with acute asthma exacerbations (1), and the importance of SCS in mitigating these effects (6), there has been growing interest in the use of dexamethasone for acute pediatric asthma exacerbations (9–14). Although dexamethasone is not specifically recommended by any of the aforementioned organizing bodies (3–5), dexamethasone is a clinically and economically

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beneficial alternative to prednisone with the advantages of easier administration and improved patient compliance (9–15). In light of this emerging evidence, the objective of this study is to describe the patient and clinical factors associated with the use of dexamethasone in the pediatric emergency department (PED) for children experiencing an acute asthma exacerbation.

Materials and methods

Study design, sample and setting

Following approval by the institutional review board, this retrospective cohort study was conducted at an academic, urban, free standing children's hospital with approximately 85,000 PED visits and 10,000 inpatient admissions annually. The electronic medical record of patients discharged home from the PED between September 1 and December 31, 2017 with an *International Classification of Diseases, 10th Revision, Clinical Modification* code for asthma (J45x) were reviewed (Supplementary material, Appendix A). Patients aged 2 to 18 years with a history of asthma presenting with a respiratory complaint (e.g. cough, wheeze, or difficulty in breathing) and given an inhaled bronchodilator in the PED were included unless: (a) they had a co-morbid systemic disease (e.g. congenital heart disease) or (b) they were transferred from an outside facility. Patients presenting with their first episode of wheeze were also excluded as a history of recurrent wheeze is required for a diagnosis of asthma (5). As previously described, the final study sample underwent detailed chart review by trained medical professionals and data abstractors using a standardized collection tool (16). Demographic and clinically relevant variables were collected for the index PED visit and any asthma related visits that occurred within 14 days of discharge. Study data were collected and managed using REDCap software (17).

Variables and outcome measures

All factors examined in the multivariable model were selected based on extant literature in addition to clinical judgment, and included: triage acuity, history of asthma severity, the use of bronchodilators prior to PED presentation, the presence of respiratory distress, pulse oximetry (SpO₂) reading in triage and the triage respiratory rate. Triage acuity was measured using the emergency severity index (ESI) and was trichotomized: an ESI score of one or two was labeled as “most urgent,” an ESI score of three was labeled “urgent,”

and an ESI score of four or five was labeled “non-urgent” (18). A history of severe asthma was defined as a previous pediatric intensive care unit admission or endotracheal intubation. Respiratory distress was defined as the presence of any nasal flaring, grunting, or retracting documented by the treating health care provider. Both SpO₂ and respiratory rate were measured during the triage process, with SpO₂ measured as a percentage and respiratory rate measured as breaths per minute.

The primary outcome measure for this study was the administration of dexamethasone as the OCS of choice within the PED; thus, only patients prescribed an OCS were included in the analysis. The secondary outcome measure was single-dose treatment of acute asthma exacerbations with dexamethasone. Only patients who were treated with dexamethasone were utilized for this outcome. Both variables were measured as dichotomous outcomes.

Data analysis

Descriptive statistics were reported using general measures of frequency and central tendency. Baseline characteristics were only reported on the first PED visit occurring during the study period per patient ($n = 594$), and prior to any data imputation. A series of chi-square and Mann-Whitney U tests were conducted to provide an unadjusted comparison of clinical factors across type of OCS. Binary logistic regression with generalized estimating equations was used to examine the factors associated with dexamethasone use and single-dose prescription in the PED, while adjusting for relevant patient and clinical factors. An exchangeable correlation matrix was used to account for the correlation between multiple visits from the same patient. Analyses were performed using R version 3.6.0 with the “geepack” statistical package (19,20). Missing data were handled using multiple imputation (5 imputations) using the “mice” package (21).

Results

A total of 594 children contributed 690 visits to the PED for an acute asthma exacerbation. Overall, 0.7% of the data were missing, with missingness by variable ranging from 0.13% to 6.5%, and 7.2% of all records having at least one missing data point. As reported in Table 1, the median age of the sample was 6 years (interquartile range [Q1, Q3] 4–10). Most participants were male (60%), African-American (85%), and

Table 1. Sample characteristics.

Variable	No. (%) of patients <i>n</i> = 594
Age [^]	6 (4–10)
Sex	
Male	359 (60.4)
Female	235 (39.6)
Race	
African American	502 (84.5)
Caucasian	13 (2.2)
Other	79 (13.3)
Payer	
Medicaid	474 (79.8)
Private	91 (15.3)
Other	29 (4.9)
Triage acuity [‡]	
Most urgent	198 (33.3)
Urgent	293 (49.3)
Non-urgent	103 (17.3)
Provider type	
PEM physician	297 (50.0)
Pediatrician	196 (33.0)
Nurse Practitioner	101 (17.0)
PED length of stay (Minutes) [^]	172 (135–217)
Hospitalized for asthma [§]	
Yes	100 (16.8)
No	494 (83.2)
Previous severe exacerbation [¶]	
Yes	38 (6.4)
No	556 (93.6)

Note. PED = Pediatric Emergency Department; PEM = Pediatric Emergency Medicine.

[^]Median (interquartile range [Q1, Q3]).

[‡]Measured using the emergency severity index where: most urgent = scores of 1 or 2; urgent = scores of 3; and non-urgent = scores of 4 or 5.

[§]An asthma related hospitalization within one year prior to the index PED visit.

[¶]Previous pediatric intensive care unit admission or intubation for asthma.

insured through Medicaid (80%). Those assigned an urgent triage score (ESI 3) contributed the highest number of visits (49%), and most patients were evaluated and treated by a pediatric emergency medicine (PEM) physician (50%), as opposed to a pediatrician (33%) or a nurse practitioner (17%). The average length of stay in the ED was 172 min (interquartile range [Q1, Q3] 135–217).

Unadjusted analyses

Table 2 provides an unadjusted comparison of clinical characteristics between patients who received dexamethasone and those who received prednisone. None of the patients received both dexamethasone and prednisone. Two-thirds of patients in the sample received prednisone in the PED (*n* = 430; 62%). Of the 260 children who received dexamethasone, 76% (*n* = 198) were prescribed a second dose for post-discharge administration. Compared to those patients treated with dexamethasone, the cohort treated with prednisone had a higher percentage of males (64% versus 55%; *p* = 0.02), a higher proportion of patients

Table 2. Unadjusted comparison of clinical and visit characteristics by type of oral corticosteroid.

Variable	Prednisone <i>n</i> = 430 (62%)	Dexamethasone <i>n</i> = 260 (38%)	<i>p</i>
Triage acuity [‡]			0.001
Most urgent	171 (39.8)	59 (22.7)	
Urgent	194 (45.1)	150 (57.7)	
Non-urgent	65 (15.1)	51 (19.6)	
Provider type			0.24
PEM physician	213 (49.5)	135 (51.9)	
Pediatrician	147 (34.2)	74 (28.5)	
Nurse practitioner	70 (16.3)	51 (19.6)	
PED length of stay [^]	177 (137–219)	160 (125–206)	0.004
Hospitalized for Asthma [§]			0.1
Yes	100 (23.3)	46 (17.7)	
No	330 (76.7)	214 (82.3)	
Previous severe exacerbation [¶]			0.36
Yes	36 (8.4)	16 (6.2)	
No	394 (91.6)	244 (93.8)	
Medication prior to PED arrival [†]			0.79
Yes	313 (72.8)	186 (71.5)	
No	117 (27.2)	74 (28.5)	
Respiratory rate [^]	28 (24–34)	28 (24–32)	0.07
Pulse oximetry (<95%)			0.18
Yes	30 (7.0)	11 (4.2)	
No	400 (93.0)	249 (95.8)	
Respiratory distress*			0.02
Yes	143 (33.3)	63 (24.2)	
No	287 (66.7)	197 (75.8)	
Air entry			0.004
Normal	117 (27.2)	94 (36.2)	
Decreased at the base(s)	85 (19.8)	58 (22.3)	
Decreased at the apex/minimal	29 (6.7)	18 (6.9)	
Not documented	199 (46.3)	90 (34.6)	
Wheezing			0.4
Yes	361 (84.0)	211 (81.2)	
No	69 (16.0)	49 (18.8)	

Note. PED = Pediatric Emergency Department; PEM = Pediatric Emergency Medicine.

p = probability of accepting the null hypothesis at an alpha of 0.05.

[‡]Measured using the emergency severity index where: most urgent = scores of 1 or 2; urgent = scores of 3; and non-urgent = scores of 4 or 5.

[^]Mann-Whitney U test; median (interquartile range [Q1, Q3]).

[§]An asthma related hospitalization within one year prior to the index PED visit.

[¶]Previous pediatric intensive care unit admission or intubation for asthma.

[†]The patient received either albuterol or albuterol and ipratropium bromide prior to emergency department presentation.

*Defined as nasal flaring, grunting, or retracting upon emergency department presentation.

with a “most urgent” triage score (40% versus 23%; *p* = 0.001), and a higher median length of stay in the PED (177 min versus 160; *p* = 0.004). Fewer children treated with prednisone had normal air entry upon auscultation (27 versus 36%, *p* = 0.004). A comparison of asthma management strategies between children who received prednisone and those who received dexamethasone can be found in Table 3.

Adjusted analyses

Table 4 displays results from the logistic model comparing the probability of patients receiving dexamethasone within the PED and the use of a second

dose of dexamethasone. All multivariable models had a good fit when using the Hosmer-Lemeshow goodness-of-fit test. Patients assigned a “most urgent” triage score (ESI 1 or 2) had a 50% reduction in the odds of receiving dexamethasone in the PED as opposed to prednisone (OR = 0.5; 95% CI = 0.28–0.87). Pulse oximetry was also found to be associated with the use of dexamethasone; a 1% increase in SpO₂ was associated with a 12% increase in the odds of receiving dexamethasone as opposed to prednisone (OR = 1.12; 95% CI = 1.02–1.22). No other factors were found to be associated with the use of dexamethasone in the PED.

Patients who were evaluated by a pediatrician were 4.2 times more likely to be treated with a single dose

Table 3. Unadjusted comparison of pediatric emergency department management by type of oral corticosteroid.

Variable	Prednisone <i>n</i> = 430 (62%)	Dexamethasone <i>n</i> = 260 (38%)	<i>p</i>
Bronchodilator			0.79
Albuterol	30 (7.0)	16 (6.2)	
Albuterol + Ipratropium	400 (93.0)	244 (93.8)	
Minutes to 1st breathing treatment [^]	30 (17–51)	34 (21–48)	0.21
Number of breathing treatments			0.07
One	189 (44.0)	139 (53.5)	
Two	46 (10.7)	27 (10.4)	
Three	166 (38.6)	81 (31.1)	
Greater than three	29 (6.7)	13 (5.0)	
Minutes to oral corticosteroid [^]	37 (21–61)	42 (26–62)	0.06
Discharged with oral corticosteroid			0.32
Yes	344 (80.0)	201 (77.3)	
No	86 (20.0)	59 (22.7)	

p = probability of accepting the null hypothesis at an alpha of 0.05.

[^] Mann-Whitney U test; presented as median (interquartile range [Q1, Q3]).

Notes. (1) All statistical tests were conducted using a Pearson chi-square unless otherwise indicated. (2) All information for this table was collected in triage prior to treatment.

of dexamethasone (OR = 4.2; 95% CI = 2.13–8.2). Furthermore, patients who were assigned an urgent triage (ESI 3) score had 2.9 times the odds of being treated with a single dose of dexamethasone when compared to children who received a non-urgent triage score (ESI 4 or 5) (OR = 2.94; 95% CI = 1.1–7.8). No other factors were found to be associated with a prescription for a second dose of dexamethasone post-PED discharge.

Discussion

To our knowledge, this is the first study to examine predictors of dexamethasone use for acute asthma in the PED. In this single center retrospective study, we found that dexamethasone is less commonly prescribed for acute asthma compared with prednisone. Patients with a higher triage acuity score and lower initial pulse oximetry values were less likely to receive dexamethasone. Among the patients who received dexamethasone in the PED, those assigned an urgent triage score or evaluated by a pediatrician were more likely to be treated with a single-dose of dexamethasone. No other demographic or clinical variables were associated with use of dexamethasone in the PED or the dosing frequency.

SCS are the standard of care for acute asthma, recommended for patients who recently completed a course of OCS and those not responding to initial bronchodilator therapy⁵. Prednisone has historically been the OCS of choice, and with a biologic half-life of 12 to 36 h, doses of 1 to 2 mg/kg/day for 3 to 10 days are recommended by current guidelines (5,11).

Table 4. Predictors of dexamethasone use in the pediatric emergency department.

Predictor variables	Dexamethasone use (<i>n</i> = 690)	Single dexamethasone dose (<i>n</i> = 260)
Provider type		
Nurse practitioner	0.94 (0.6–1.46)	0.78 (0.3–1.9)
Pediatrician	0.69 (0.48–1.01)	4.2 (2.13–8.2)**
PEM physician (Reference)	–	–
Triage acuity [‡]		
Most urgent	0.5 (0.28–0.87)**	1.46 (0.48–4.4)
Urgent	1.01 (0.65–1.56)	2.94 (1.1–7.8)*
Non-urgent (Reference)	–	–
Previous severe exacerbation [¶]	0.81 (0.43–1.52)	1.1 (0.29–4.1)
Medication prior to PED arrival [#]	0.85 (0.7–1.42)	1.18 (0.42–1.71)
Pulse oximetry	1.12 (1.02–1.22)*	0.99 (0.84–1.18)
Respiratory rate	0.99 (0.98–1.02)	1.01 (0.97–1.05)
Respiratory distress [§]	0.87 (0.58–1.29)	0.77 (0.35–1.69)
Hosmer-Lemeshow goodness of fit	$\chi^2 = 6.8$; <i>p</i> = 0.56	$\chi^2 = 6.4$; <i>p</i> = 0.6

PED = Pediatric Emergency Department; PEM = Pediatric Emergency Medicine.

[‡]Measured using the emergency severity index where: most urgent = scores of 1 or 2; urgent = scores of 3; and non-urgent = scores of 4 or 5.

[¶]Previous pediatric intensive care unit admission or intubation for asthma.

[#]Received either albuterol or albuterol and ipratropium bromide prior to PED presentation.

[§]Defined as nasal flaring, grunting, or retracting upon emergency department presentation.

*Statistically significant at an alpha of 0.05.

**Statistically significant at an alpha of 0.01.

Dexamethasone, with increased potency and a biologic half-life of 36 to 54 h, can be given as 1 to 2 doses (11). Although not specifically mentioned in the current guidelines (5), randomized clinical trials comparing prednisone and dexamethasone in the ED management of asthma have examined a range of patient ages, drug doses, primary outcomes and follow up durations (9–13). Despite methodological differences amongst published trials, several meta-analyses concluded that dexamethasone is equivalent to prednisone in the ED setting (9,10,12,13). The most recent randomized trial highlights these conclusions, showing that there is no difference between patients receiving prednisone and those receiving dexamethasone in symptoms at 7 days following ED evaluation (22). Paniagua et al. reported that patients had a similar ED length of stay, with no differences in hospital admission, return visits, school absenteeism, or missed workdays (22). Adherence in the dexamethasone group, however, was higher and parents preferred the two-day treatment (22). Despite the growing body of evidence supporting the use of dexamethasone for asthma, prednisone is the preferred OCS for providers within our PED.

A preference for prednisone may be partly explained by a paucity of evidence supporting the use of dexamethasone for patients hospitalized with asthma (23). As has been reported previously, practice patterns at our institution vary by specialty regarding the use dexamethasone for hospitalized patients with asthma (24). Nationally, only 2.9% of patients hospitalized for asthma receiving dexamethasone (25). Similarly, in the inpatient setting, 66% of children hospitalized for asthma are treated with prednisone, with higher asthma severity scores associated with prednisone administration (26). Dexamethasone results in a shorter hospital length of stay with similar 7 and 30 day readmission rates compared to prednisone (25,26). However, exclusion of higher acuity patients, such as those requiring intravenous magnesium sulfate or high flow nasal cannula from randomized trials comparing dexamethasone and prednisone in the PED limits the translation of its efficacy to the inpatient pediatric population (9,10,12,13,25,26). Similar to other centers (24), patients in our institution who are given dexamethasone in the PED are often transitioned to prednisone while hospitalized; thus, prednisone is preferred in our PED for potential inpatients. As SCS are ideally administered within 60 min of ED triage, prior to completion of initial therapy (5), providers in our PED may elect to use prednisone over dexamethasone in those patients

triaged as most urgent for whom they are anticipating hospital admission. Additional prospective research is therefore needed to extend the evidence base for dexamethasone across the spectrum of asthma severity to enable consistent prescribing for patients transitioning from the ED to the inpatient setting.

As additional studies are planned to clarify the role of dexamethasone for inpatient asthma (27), providers discharging a patient home from the ED are left to decide whether one or two doses of dexamethasone are indicated, as both regimens are supported by the available evidence (9–14). In a single center retrospective study of over 13,000 ED visits for asthma, 52.7% of patients received prednisone and 12.1% received dexamethasone; interestingly, a single dose of dexamethasone was associated with a 36% relative risk reduction in ED relapse (28). As a result, some institutions have incorporated single dose dexamethasone into their asthma clinical care pathways (29), an approach preferred by parents and associated with a lower incidence of vomiting (9–13,30). At our institution, asthma management is not standardized, and patients are cared for by either a PEM physician, a pediatrician or a nurse practitioner. Our results corroborate that practice patterns vary by training (24,31,32), with pediatricians more commonly opting for a single dose dexamethasone. Further work is needed to understand the rationale for a discharge dose of dexamethasone among PEM physicians and nurse practitioners as clinical markers of asthma severity, such as pulse oximetry, respiratory rate or respiratory distress, were not predictive of a second dose of dexamethasone. Furthermore, our PED serves a population with a significant burden of disease in whom multiple courses of OCS may be prescribed for asthma (33). Thus, the routine use of two doses of dexamethasone for a lower acuity patient without evidence of respiratory distress warrants further examination in order to minimize the potential longer-term harms associated with a more potent SCS (22,34,35).

Limitations

The findings of this study need to be considered in light of several limitations. First, this is a single center study and therefore the results may not be generalizable to other settings. Second, data were retrospectively collected from the electronic medical record precluding analysis of providers' clinical decision making regarding OCS. Due to limitations inherent in electronic medical documentation, retrospective data collection limits accurate assessment of asthma

severity which was unevenly distributed across the two groups in our study. Finally, data collection was limited to a four-month period of time to ensure feasibility. While the season selected reflects our institutional and national peak for asthma visits, findings from this time period may not be generalizable to other seasons (36).

Conclusions

In conclusion, dexamethasone is less commonly used in the PED for asthma, particularly among patients triaged as most urgent. Among examined variables, only level of training and triage acuity predicted a second dose of dexamethasone upon PED discharge. Asthma is a heterogeneous disease, and further studies are needed to clarify the use of dexamethasone across the spectrum of asthma severity.

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Declarations of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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Contributor statements

Dr. DeLaroche conceptualized and designed the study, designed the data collection instrument, interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript. Mr. Mowbray carried out the analyses and reviewed and revised the manuscript. Ms. Parker collected data, coordinated and supervised data collection, and reviewed and revised the manuscript. Dr. Ravichandran collected data, coordinated and supervised data collection, and reviewed and revised the manuscript. Mr. Jones supervised the analyses and reviewed and revised the manuscript.

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Article summary

Why is this topic important?

Pediatric patients are commonly brought to the emergency department for asthma exacerbations, and systemic corticosteroids are recommended for acute management. Dexamethasone is equivalent to prednisone with the advantages of easier administration and improved patient compliance, but is not specifically recommended by national guidelines.

What does this study attempt to show?

The objective of this study is to describe the patient and clinical factors associated with the use of dexamethasone in

the pediatric emergency department for children experiencing an acute asthma exacerbation.

What are the key findings?

One-third of children received dexamethasone in the PED and 76% were prescribed a second dose for post-discharge administration. Patients triaged as most urgent (ESI 1 or 2) and those with a lower pulse oximetry value were less likely to receive dexamethasone in the PED. Patients evaluated by

a pediatrician and those triaged as urgent (ESI 3) were more likely to be treated with a single dose of dexamethasone.

How is patient care impacted?

Few demographic and clinical variables were associated with use of dexamethasone in the PED or upon discharge. Further studies are needed to clarify the use of dexamethasone across the spectrum of asthma severity.

Appendix A: ICD-10-CM codes for asthma

Asthma	J45
Mild intermittent asthma	J45.2
Mild intermittent asthma uncomplicated	J45.20
Mild intermittent asthma with (acute) exacerbation	J45.21
Mild intermittent asthma with status asthmaticus	J45.22
Mild persistent asthma	J45.3
Mild persistent asthma uncomplicated	J45.30
Mild persistent asthma with (acute) exacerbation	J45.31
Mild persistent asthma with status asthmaticus	J45.32
Moderate persistent asthma	J45.4
Moderate persistent asthma uncomplicated	J45.40
Moderate persistent asthma with (acute) exacerbation	J45.41
Moderate persistent asthma with status asthmaticus	J45.42
Severe persistent asthma	J45.5
Severe persistent asthma uncomplicated	J45.50
Severe persistent asthma with (acute) exacerbation	J45.51
Severe persistent asthma with status asthmaticus	J45.52
Other and unspecified asthma	J45.9
Unspecified asthma	J45.90
Unspecified asthma with (acute) exacerbation	J45.901

Unspecified asthma with status asthmaticus	J45.902
Unspecified asthma uncomplicated	J45.909
Other asthma	J45.99
Exercise induced bronchospasm	J45.990
Cough variant asthma	J45.991
Other asthma	J45.998