RESEARCH ARTICLE

Outcomes for Pediatric Asthmatic Inpatients After Implementation of an Emergency Department Dexamethasone Treatment Protocol

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ABSTRACT

OBJECTIVES: Evidence supports using dexamethasone for mild-to-moderate asthma exacerbations in the emergency department, but the effectiveness of dexamethasone versus prednisone for asthmatic patients who are hospitalized is unclear. Our aim was to compare outcomes for inpatients before and after our emergency department's adoption of dexamethasone for the treatment of acute asthma exacerbations.

METHODS: In this single-center retrospective cohort study, we employed interrupted time series analyses to control for secular trends while evaluating our outcomes of length of stay, total inflation-adjusted hospital charges, and ICU transfer rates for patients admitted with asthma.

RESULTS: Data were analyzed over 36 months (January 2014–April 2017) and included 1015 subjects (606 in the preprotocol change [pre-PC] group and 409 in the postprotocol change [post-PC] group). In the pre-PC group, prednisone only was used in 96% of subjects. In the post-PC group, prednisone only was used in 7% of subjects, dexamethasone in 65% of subjects, and a combination of the 2 steroids in 28% of subjects. Controlling for other variables in the interrupted time series model, we found no significant immediate differences between the pre-PC and post-PC periods for the outcomes of length of stay ($P = .68$), total charges ($P = .66$), and ICU transfers ($P = .98$). The rate of ICU transfers was stable pre-PC and increased by 10% (95% confidence interval: 2%–19%) per month (odds ratio = 1.10; 95% confidence interval: 1.02–1.19; $P = .02$) in the post-PC period.

CONCLUSIONS: After dexamethasone replaced prednisone as the most commonly prescribed steroid type for inpatients with asthma at our institution, we found no immediate changes in outcomes for asthmatic patients who were hospitalized but an upward trend in ICU transfers.

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Asthma affects 6.2 million children in the United States[1] and is the second most common reason for hospitalization in pediatrics.[2] Systemic corticosteroids are the standard of care to treat acute asthma exacerbations.[3] Historically, prednisone has been the most commonly prescribed steroid; however, dexamethasone is more palatable,[4–7] and given the longer duration of action and shorter treatment course, it may have improved medication compliance over prednisone. Recently, several studies conducted in the emergency department (ED) setting in which dexamethasone was compared with prednisone for children with mild-to-moderate acute asthma exacerbations revealed that dexamethasone was equally effective for the outcome of asthma relapse as well as more cost-effective than prednisone.[8–14] One survey study revealed that parents preferred a 2-day course of steroids compared with a 5-day course, making dexamethasone an attractive alternative to prednisone.[7]

However, despite growing evidence to support the use of dexamethasone for mild-to-moderate asthma exacerbations in the ED setting,[15] it is unclear whether dexamethasone is as effective as prednisone for the treatment of asthma exacerbations requiring hospitalization.[16] To our knowledge, there is only 1 study in which the authors examine the comparative effectiveness of dexamethasone versus prednisone for inpatients. In the multicenter retrospective cohort study, after employing propensity score matching within hospital, Parikh et al[17] found that the proportion of subjects with a length of stay (LOS) of ≥3 days was significantly smaller in the dexamethasone group compared with that in the prednisone group. In addition, they found that the dexamethasone group had a significantly lower index admission cost. They found no significant difference between groups for the outcomes of all-cause 7 and 30-day readmissions and for transfers to the ICU.[17] Although the findings of this study reveal that dexamethasone may be an alternative to prednisone for inpatients, all subjects with an All-Patient Refined Diagnosis-Related Group (APR-DRG) of moderate, major, or extreme were excluded in the study. In the previously discussed ED studies,[8–10,12,14] the patients with the highest exacerbation severity (ie, those admitted to the hospital from the ED) were also largely excluded; therefore, it is important to understand outcomes for this population.

In 2015, our institution's EDs and urgent cares (UCs) began using dexamethasone instead of prednisone for children presenting with an acute asthma exacerbation and meeting inclusion criteria for our asthma clinical care pathway (CCP). The protocol change occurred in our EDs and UCs only and happened over the course of 4 months. Change was facilitated by 4 changes: (1) adding dexamethasone to our ED institutional CCP, (2) updating our asthma triage procedures to include a standing order for dexamethasone on arrival to the ED or UC, (3) adding dexamethasone to the electronic health record asthma order set used by ED and UC clinicians, and (4) auditing and providing feedback to ED and UC clinicians.

Inpatient steroid treatment remained at the discretion of the inpatient clinician given the limited evidence for patients who were admitted. After the ED protocol change, for patients who were admitted, inpatient clinicians could choose to continue the dexamethasone course started in the ED or transition to prednisone. Inpatient providers were notified of the ED protocol change but not given any recommendations or guidance regarding inpatient steroid treatment. This resulted in a substantial increase in the number of inpatients treated with dexamethasone. In our study, we aimed to take advantage of this natural experiment to analyze outcomes for inpatients after our ED's protocol change. With our study, we add to what is already known by examining outcomes for inpatients across all illness severities. Primary outcomes were LOS and hospital charges for subjects with acute asthma exacerbations admitted to the inpatient service from our ED before and after the ED protocol change. Secondary outcomes or balancing measures were unintended consequences of the protocol change, including all-cause readmissions and transfers to the ICU. We hypothesized that patient outcomes, including unintended consequences, would not change. We employed interrupted time series (ITS) analyses to evaluate our outcomes while controlling for secular trends in the data.

METHODS

Study Population

Using an internal database of de-identified data extracted from the electronic health record, we retrospectively collected study variables on subjects admitted to inpatient or observation status from an ED or UC within our system of hospitals between January 2014 and April 2017 with a primary diagnosis of asthma defined by *International Classification of Diseases, Ninth Revision* (493.xx) and *International Classification of Diseases, 10th Revision* (J44.xx and J45.xx) discharge codes. Subjects were only included if they met inclusion criteria for our institution's asthma CCP.[18] Therefore, children <2 years of age were excluded, as were children with chronic lung disease, neuromuscular disease, congenital heart disease, and concurrent pneumonia as defined by the *International Classification of Diseases, Ninth Revision* and *International Classification of Diseases, 10th Revision* discharge codes. As a means of excluding subjects who received treatment at an outside hospital before presenting to our ED or UC, we only included subjects receiving both steroids and bronchodilators in our ED or UC before admission.

This study was approved by the Colorado Multiple Institutional Review Board.

Study Definitions

Patient level variables included the following: admission age, race, insurance, admitting service (hospital medicine versus pulmonology), and admission season. Subjects were classified as receiving or not receiving continuous albuterol, oxygen, and magnesium sulfate at any time for any duration during their hospital stay (ED, UC, or inpatient). First pediatric asthma score (PAS) category [18] was assigned by a trained respiratory therapist on presentation to the ED or UC and defined as low, moderate, or high on the basis of vitals and physical examination findings, including the following: respiratory rate, oxygen

requirement, auscultation, retractions, and degree of dyspnea. Steroid type was determined by the type(s) of steroid(s) administered for any duration during a given patient's hospital stay (including ED or UC and inpatient setting) and did not include steroids that were prescribed at discharge. Steroid type was defined 1 of 3 ways: dexamethasone only, prednisone only (including prednisone, prednisolone, and methylprednisolone) or a combination of dexamethasone and prednisone. To evaluate whether the ED protocol change affected the proportion of patients admitted, we measured the ED admission rate. The ED admission rate was defined as the total number of children admitted to the inpatient unit or ICU over the total number of children seen in the ED for an acute asthma exacerbation over the same period.

Outcome variables included LOS, total inflation-adjusted hospital charges, all-cause readmission within 30 days, all-cause readmission within 6 months, and transfers to the ICU after admission to the inpatient unit. Total adjusted hospital charges were adjusted for inflation to 2017 dollars by using the Consumer Price Index algorithm.

Analysis

For the analysis, the cohort was split into 3 groups: pre-protocol change (pre-PC) group (pre-July 2015), implementation phase (July 2015–October 2015), and post-protocol change (post-PC) group (post October 2015). Only the index admission for each subject during each study period (pre-PC and post-PC) was included in the analyses.

A series of pre-post analyses were done in which (1) patient characteristics, (2) outcome measures, (3) balancing measures, and (4) ED admission rates were compared between pre-PC and post-PC periods by using χ^2 tests for categorical variables and *t* tests or Wilcoxon rank tests for continuous variables. Steroid type was described as the proportion of subjects who received each steroid type pre-PC and post-PC. Observed steroid type and ED admission rate were analyzed as monthly proportions to illustrate change over time.

To reduce potential biases in the pre-post analyses,[19] we used ITS or segmented regression analyses to control for secular trends or variation over time in the data unrelated to the protocol change. The ITS was used to measure the impact of the protocol change on the primary outcomes (LOS in hours and inflation-adjusted total hospital charges), and balancing measure (proportion transferred to ICU after inpatient admission). The ITS design was used to evaluate both the immediate change (level change) and the change over time (change in slope) associated with the protocol change. Log γ models (for continuous outcomes) and logistic regression (for categorical outcomes) using generalized estimating equation methods with an autoregressive (Toeplitz) correlation matrix to account for repeated admissions of subjects were used to evaluate the relationship of the effect of the protocol change on outcomes. The primary explanatory variables included protocol period (pre-PC and post-PC), time in month, and the interaction of time × protocol period.

Multivariable ITS models were controlled for important covariates identified a priori, including the following: age, race, financial class, season, admitting service, first asthma score, and need for continuous albuterol. To measure the change in

TABLE 1 Characteristics of Asthmatic Patients Who Were Admitted in Pre-PC and Post-PC Groups

	Pre-PC Group, $N = 606$	Post-PC Group, $N = 409$	P[a]
Age, y, mean (SD)	7.6 (4.0)	8.0 (4.0)	.10
Race, % (*n*)			.08
White	45 (270)	52 (212)	
African American	26 (158)	23 (93)	
Other	27 (166)	24 (97)	
Unknown	2 (12)	2 (7)	
Insurance, % (*n*)			.81
Private or self-pay	38 (231)	39 (159)	
Government issued	62 (375)	61 (250)	
Hospital service, % (*n*)			.65
Hospitalist	81 (493)	80 (328)	
Pulmonary	19 (113)	20 (81)	
Season, % (*n*)			.01
Spring (March–May)	41 (248)	34 (138)	
Summer (June–August)	17 (106)	15 (61)	
Fall (September–November)	26 (158)	30 (121)	
Winter (December–February)	16 (94)	22 (89)	
APR-DRG severity, % (*n*)			<.01
Minor	52 (313)	72 (294)	
Moderate	45 (272)	22 (89)	
Major	3 (18)	5 (20)	
First PAS category, % (*n*)			.39
Low	15 (89)	18 (73)	
Moderate	60 (364)	57 (234)	
High	25 (153)	25 (102)	
Oxygen required during admission, % (*n*)	91 (550)	98 (400)	<.01
Continuous albuterol required during admission, % (*n*)	78 (473)	84 (342)	.03
Magnesium sulfate required during admission before ICU, % (*n*)	2 (10)	3 (11)	.25

[a] *P* values were calculated by using Pearson's χ^2 test.

intercept or the immediate effect of the protocol change, admissions during the implementation period, defined as the first 4 months after the protocol change (July 2015–October 2015), were excluded from regression analysis. Implementation strategies were actively deployed by the quality improvement team during this 4-month period, including education, decision support, clinical pathway revision, and provider audit and feedback.

For each of the outcomes (LOS, charges, and ICU transfers), aggregate data, observed monthly, were overlaid with the mean of predicted values from the unadjusted ITS model to evaluate for immediate changes in outcomes between the pre-PC post-PC periods as well as changes in the slope.

Data were analyzed by using SAS version 9.4 software (SAS Institute, Inc, Cary, NC). All statistical tests were performed as 2-sided tests, with a level of significance of 0.05.

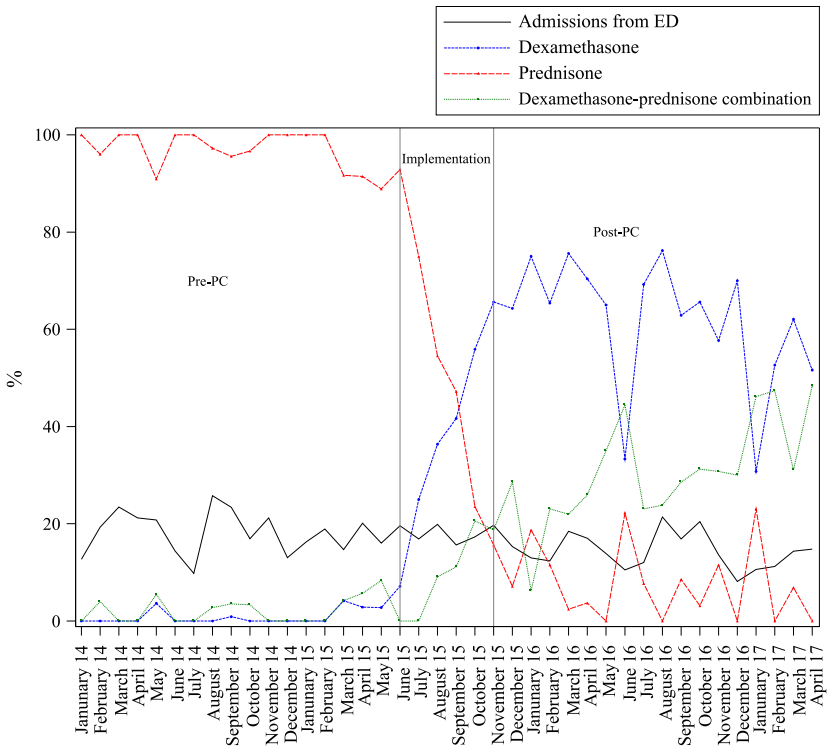

FIGURE 1 Graph of observed steroid type and ED admission rates as monthly proportions.

RESULTS

After excluding the implementation period, data were analyzed over the course of 36 months and included 1015 subjects. In the pre-PC group, there were 606 subjects with a total of 644 admissions over an 18-month period (January 2014–June 2015), and in the post-PC group, there were 409 subjects with a total of 435 admissions over an 18-month period (November 2015–June 2017). There was no difference between the pre-PC and post-PC groups for patient demographics or first PAS category (Table 1). There was a difference in season of admission. Compared with the pre-PC period, more subjects in the post-PC group received continuous albuterol and oxygen, and fewer subjects were classified as APR-DRG severity moderate (Table 1).

There was a difference in steroid type between the 2 groups. In the pre-PC group, prednisone was used in 96% of subjects. In the post-PC group, prednisone was used in 7% of subjects, dexamethasone in 65% of subjects, and a combination of the 2 steroids in 28% of subjects (Fig 1, Table 2).

In the bivariable analyses, compared with the pre-PC group, the post-PC group had a significantly longer LOS in days ($P = .01$) and significantly higher inflation-adjusted hospital charges ($P < .01$). There were no differences between the 2 groups for ICU transfers or 6-month all-cause readmissions. There were no children readmitted within 30 days in the pre-PC period, and 3 children were readmitted in the post-PC period ($P = .07$). The overall ED admission rate decreased after the protocol change (from 20% to 15%; $P \leq .01$). Although there was a decrease in the percent of children admitted from the ED to the inpatient unit (from 18% to 14%; $P \leq .01$), there was no difference in admissions directly to the ICU from the ED between the 2 groups.

The unadjusted ITS analyses for the outcomes of LOS, hospital charges, and ICU transfer rate are displayed in Fig 2. To see if the differences in outcomes seen in the bivariable analysis were associated temporally with the protocol change, we used the ITS design to evaluate both the immediate change (level change) at the time of protocol implementation and the change over time (slope) in outcomes before and after the protocol change. If the differences in LOS and charges seen in the bivariable analyses were associated temporally with the protocol change, we would expect to see an immediate (level) change in the ITS. With and without controlling for other variables in the ITS model, we found no significant immediate change (level change) between the pre-PC and post PC periods for the outcomes of LOS ($P = .68$), total charges

TABLE 2 Steroid Type by Study Period

	Pre-PC Group, $N = 606$	Post-PC Group, $N = 409$	P
Steroid type, % (*n*)			<.01
Prednisone	96 (584)	7 (28)	
Dexamethasone	1 (7)	65 (266)	
Any combination of dexamethasone and prednisone	2 (15)	28 (115)	

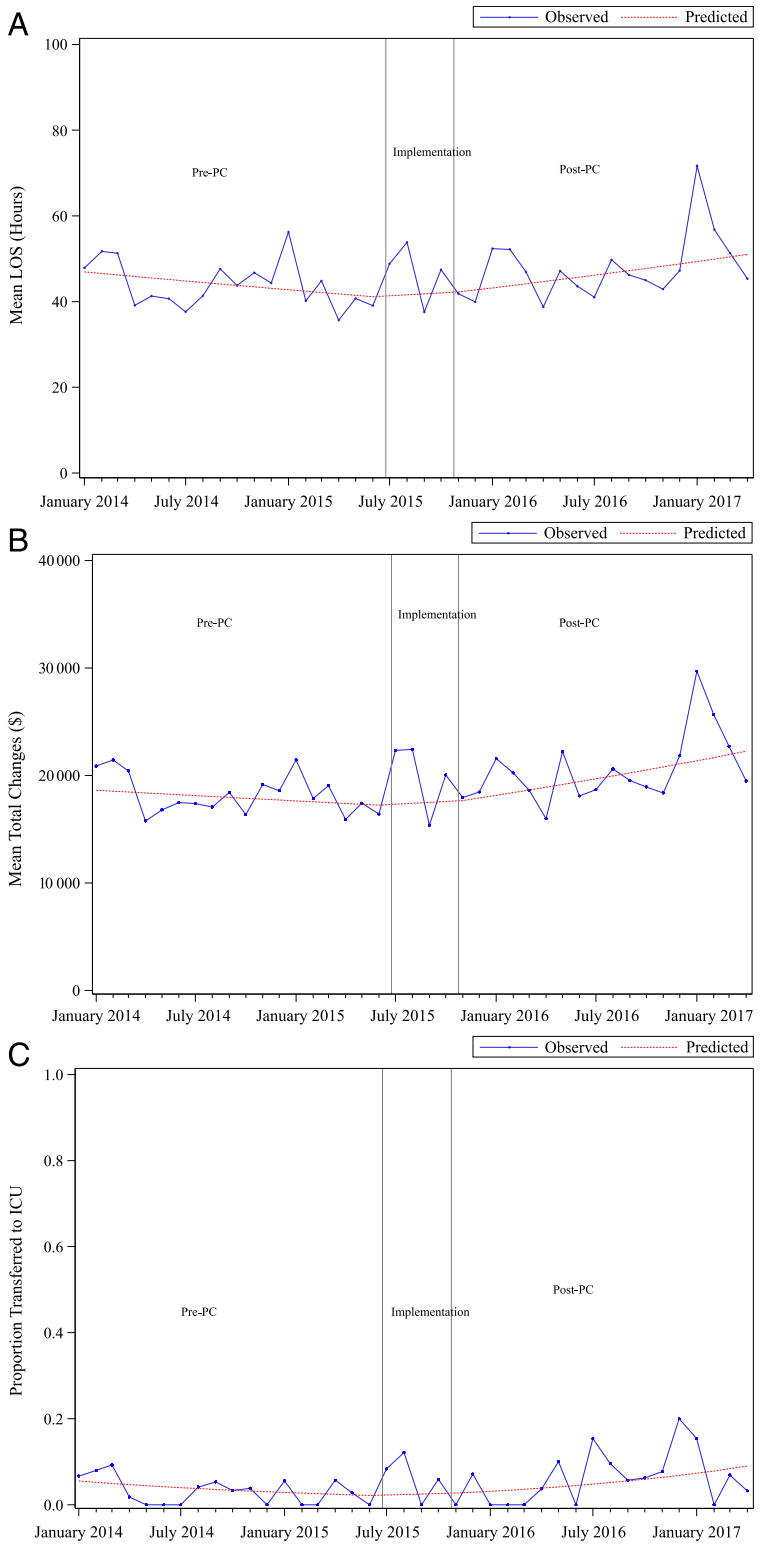

FIGURE 2 Unadjusted ITS. A, Mean LOS in hours. B, Mean total inflation-adjusted hospital charges. C, Proportion transferred to the ICU from the inpatient unit. Aggregate data were observed monthly and overlaid with the mean of predicted values from the unadjusted ITS model.

($P = .66$), and ICU transfers ($P = .98$), suggesting that there was no immediate change in outcomes associated with the protocol change.

There were changes in the slope or changes in outcomes over time between the pre-PC and post-PC periods for LOS and ICU transfers with and without controlling for other variables in the model. In the adjusted analysis for LOS, the slope pre-PC was stable, and the slope post-PC was increasing (1.01 [95% confidence interval (CI): 1.00–1.02]; $P = .03$). The slope change pre-PC versus post-PC was 1.01 (95% CI: 1.00–1.03; $P = .04$). In other words, there was a 1% (95% CI: 0%–3%) relative increase in the change in mean LOS per month in the post-PC period compared with the pre-PC period (Table 3). The slope for ICU transfers pre-PC was stable. The slope post-PC was increasing (odds ratio = 1.10 [95% CI: 1.02, 1.19]; $P = .02$), or in the post-PC period, the odds of ICU transfers increased by a rate of 10% (95% CI: 2%–19%) per month. The difference in the odds of ICU transfers pre-PC and post-PC was 1.16 (95% CI: 1.01–1.33; $P = .04$). For the total mean inflation-adjusted hospital charges, the change in slope was not significant when comparing pre-PC with post-PC.

DISCUSSION

Using dexamethasone instead of prednisone has important implications for inpatients. Studies have revealed that inpatients have low rates of corticosteroid prescription fills after discharge.[20] Given a longer duration of action and a shorter recommended treatment course,[21] the use of dexamethasone facilitates improved medication adherence compared with the use of prednisone for inpatients. Although the available evidence supports the use of dexamethasone for mild-to-moderate asthma exacerbations in the ED setting, the evidence for inpatients is limited. In this single-center retrospective study, we used a quasi-experimental study design to take advantage of a natural experiment to examine outcomes for asthmatic inpatients after a protocol change at our institution recommended dexamethasone instead of prednisone in the ED setting. Most patients at our institution received dexamethasone

TABLE 3 Adjusted and Unadjusted ITS Analyses

Outcomes and Predictors	Multivariable Log γ And Logistic Regression Models			
	Unadjusted ITS Model		Adjusted ITS Model[a]	
	Effect Estimate (95% CI)	*P*	Adjusted Effect Estimate (95% CI)	*P*
LOS				
Immediate change post-PC versus pre-PC	1.05 (0.90–1.22)	.56	0.97 (0.82–1.14)	.68
Slope pre-PC	0.99 (0.98–1.00)	.12	1.00 (0.99–1.01)	.45
Slope post-PC	1.01 (1.00–1.02)	.01	1.01 (1.00–1.02)	.03
Slope change post-PC versus pre-PC	1.02 (1.01–1.03)	<.01	1.01 (1.00–1.03)	.04
ICU transfers				
Immediate change post-PC versus pre-PC	1.46 (0.28–7.67)	.65	0.97 (0.15–6.23)	.98
Slope pre-PC	0.94 (0.86–1.04)	.25	0.95 (0.85–1.07)	.40
Slope post-PC	1.08 (1.01–1.15)	.02	1.10 (1.02–1.19)	.02
Slope change post-PC versus pre-PC	1.14 (1.02–1.28)	.03	1.16 (1.01–1.33)	.04
Inflation-adjusted total charges				
Immediate change post-PC versus pre-PC	1.03 (0.88–1.20)	.71	0.97 (0.85–1.11)	.66
Slope pre-PC	1.00 (0.99–1.00)	.35	1.00 (0.99–1.01)	.95
Slope post-PC	1.01 (1.00–1.02)	<.01	1.01 (1.00–1.02)	.02
Slope change post-PC versus pre-PC	1.02 (1.00–1.03)	.01	1.01 (1.00–1.02)	.14

[a] Adjusted for age, race, financial class, season, service, first asthma score, and need for continuous albuterol.

in the ED after the protocol change. After the protocol change, there was also a sizable increase in dexamethasone use for inpatients, with 65% of inpatients receiving dexamethasone alone and another one-third of inpatients receiving both dexamethasone and prednisone during their hospital course. With increased dexamethasone use, using an ITS analysis, we found no immediate changes in patient outcomes, including LOS or total hospital charges, or in unintended consequences, including ICU transfer rates and all-cause readmissions. Our findings are similar to the previous study's findings, but we add to the evidence by including all APR-DRG severities and using clinical data to control for patient severity in the analyses.[17] Differences in illness severity may affect outcomes, and considering a continuum of illness severity, inpatients with high severity are likely the most unlike the subjects included in previous ED studies on dexamethasone.

Despite no immediate changes in outcomes and balancing measures, we did note an increasing trend in LOS and ICU transfer rates in the post-PC period. Although the 1% relative increase in the change in mean LOS per month in the post-PC period compared with the pre-PC period was statistically significant, it is not likely clinically significant. However, the 10% increase per month in ICU transfers warrants more discussion. This trend in ICU transfer rates may be related to a potentially more severe population of inpatients in the post-PC period, but when taken together, differences in subjects between the pre-PC and post-PC periods make it difficult to determine if severity increased or decreased in the post-PC period. The ED admission rate, or the proportion of subjects presenting to the ED or UC who were hospitalized, decreased after the protocol change. It is plausible, with more subjects being discharged from the hospital from the ED, that those who were admitted to the hospital in the post-PC period may have represented a higher severity population. This is supported by the fact that significantly more inpatients in the post-PC period required oxygen and continuous albuterol compared with the pre-PC period. However, the data are mixed because more subjects were classified as APR-DRG severity mild and fewer as moderate during the post-PC period, which would indicate a less severe population post-PC.

It is interesting to note that the proportion of children treated with a combination of prednisone and dexamethasone trended up over the post-PC period, along with the ICU transfer rate. The subjects treated with both prednisone and dexamethasone may represent the patients with the most severe asthma in our study. Overall, one-third of subjects received a combination of dexamethasone and prednisone in the post-PC period. These subjects likely received dexamethasone in the ED and then prednisone as inpatients. In a previous survey study at our institution, researchers examined reasons for the differential adoption of dexamethasone for inpatients among inpatient providers and found that several factors influenced the use of prednisone versus dexamethasone. Inpatient providers were less likely to use dexamethasone for patients with severe asthma histories or presentations, and pulmonologists who cared for asthmatic patients who were the sickest were less likely to use dexamethasone compared with hospitalists, citing limited research in which the effectiveness of dexamethasone was compared with that of prednisone in the inpatient setting.[22] On the basis of these data, subjects in our study may have been more likely to receive combination therapy if they had high illness severity or if they

were admitted to the pulmonology service. The upward trend in the proportion of children who received both steroids (likely dexamethasone in the ED and prednisone after admission) may signal an upward trend in severity over the same period, which may explain the increasing trend in ICU transfers. However, we cannot exclude the possibility that dexamethasone is inferior to prednisone for the patients with the highest severity of asthma in the inpatient setting.

Our study has several limitations. First, it is a single-center retrospective study in which an asthma population with a relatively short LOS and low readmission rate is examined, which limits our ability to identify significant differences in these outcomes. We controlled for patient severity on the basis of first asthma score and the need for continuous albuterol. However, our data did not allow us to differentiate among subjects who required continuous albuterol (eg, subjects who required 3 hours of continuous albuterol and subjects who required 2 days of continuous albuterol). On the basis of how the data were collected, we were unable to distinguish what steroid type was prescribed during each segment of a patient's hospital course (ED versus inpatient floor), how many doses were given, or for what duration. Variation in steroid prescribing post-PC limits our ability to directly compare dexamethasone with prednisone. Lastly, although we controlled for season in our analysis, there are yearly variations in the severity of viral-induced illnesses (eg, outbreak of enterovirus D68 in the fall and winter of 2014), which were known triggers of asthma exacerbations and may alter severity of patient presentations and outcomes.

CONCLUSIONS

Evidence supports prescribing dexamethasone instead of prednisone for mild-to-moderate asthma exacerbations in the ED setting. There are potential benefits to prescribing dexamethasone versus prednisone for inpatients. After dexamethasone replaced prednisone as the most commonly prescribed steroid type for inpatients with asthma at our institution, we found no immediate changes in several key outcomes for children who were hospitalized. However, we did see an increase in ICU transfer rates over time. With our study, we provide further evidence that dexamethasone may be an acceptable alternative to prednisone in the treatment of asthma patients who are hospitalized, but we highlight the need for more data in which prednisone is compared with dexamethasone for patients with the highest severity of asthma.

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