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A Comparison of Oral Dexamethasone With Oral Prednisone in Pediatric Asthma Exacerbations Treated in the Emergency Department

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The aim of this study was to determine if 2 doses of oral dexamethasone are as effective as a 5-day course of oral prednisone in preventing relapse for pediatric asthma exacerbations. Patients presenting to the emergency department with an asthma exacerbation were randomized to receive 0.6 mg/kg of dexamethasone or 2 mg/kg of prednisone in a prospective, double-blind study. The primary outcome was relapse within 10 days, and the secondary outcome was vomiting in the emergency department. Eighty-nine patients completed the study: 38 in the prednisone group and 51 in the dexamethasone group. In all, 3 patients in the prednisone group (8%) and 8 patients in the dexamethasone group (16%) required an unscheduled follow-up visit (P = .27). In all, 7 patients in the prednisone group (18%) and 5 patients in the dexamethasone group (10%) had vomiting (P = .24). No difference was found in the relapse rate or incidence of vomiting between patients given prednisone and dexamethasone for pediatric asthma exacerbations.

Keywords: pediatric; asthma; prednisone; dexamethasone

Asthma, a common presenting problem to emergency departments (ED), accounts for nearly 700 000 pediatric ED visits annually.[1] The control of an acute asthma exacerbation centers on bronchodilator therapy as well as the use of corticosteroids to suppress the inflammatory cascade. Several studies have proven the efficacy of corticosteroids in the management of acute asthma exacerbations.[2-7] Currently, most physicians are treating pediatric asthma exacerbations with a 5-day course of oral prednisone. Problems with this regimen include poor patient or parent adherence, poor palatability, and side effects, especially emesis.[8] Dexamethasone is 5 to 6 times more potent and has 4 to 5 times longer half-life than prednisone, which may allow for the treatment of acute asthma exacerbations with a shorter course of steroids to improve compliance.

Recent studies have compared oral, intramuscular (IM), and inhaled dexamethasone with oral prednisone for the treatment of acute pediatric asthma.[8-12] Qureshi et al[8] concluded that 2 doses of oral dexamethasone provide similar efficacy with improved compliance and fewer side effects than 5 doses of prednisone for asthma exacerbations. Limitations to this study included a lack of blinding, a lower-than-typical dose of prednisone (1 mg/kg/d), and the dexamethasone-arm patients received the home study medicaiton at discharge while the prednisone arm received a perscription. Altamimi et al[9] recently concluded that a single dose of oral dexamethasone

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is no worse than 5 days of twice-daily prednisolone in their study of 117 children with mild to moderate asthma using a noninferiority design. Their primary outcome measure was the number of days needed to return to baseline as measured on an asthma self-assessment score assuming that the regimen with a single dose of dexamethasone was no worse than 1 additional day as compared with standard therapy.

The objective of this study was to compare the efficacy of 2 doses of oral dexamethasone with a 5-day course of oral prednisone in preventing relapse within 10 days for pediatric asthma exacerbations.

Methods

We conducted a prospective, randomized, double-blinded convenience study of children from 2 to 18 years old with a history of asthma (2 or more episodes of wheezing treated with β-adrenergic agonists) who presented to the ED with an acute exacerbation of their asthma. The study took place in an urban, tertiary care, academic children's hospital with an annual ED census of approximately 45 000 visits. Patients were enrolled between January 2004 and June 2005.

Exclusion criteria included the use of oral steroids in the past month; history of intubation for a previous asthma exacerbation; varicella exposure in the past 3 weeks; possible foreign body aspiration; any chronic lung disease (eg, cystic fibrosis) that would affect the patient's management; chronic heart, liver, or kidney disease; significant respiratory distress necessitating airway intervention (eg, intubation); previous enrollment in this study; no telephone for follow-up; and ≥2 episodes of emesis after steroid administration in the ED.

All patients with an acute asthma exacerbation were treated according to the institution's asthma clinical care guideline. A pediatric asthma score (PAS), modified from the one published by Kelly et al,[10] was documented for each child upon arrival to the ED and at set times throughout his or her ED course (Table 1). The asthma severity of the patient is considered mild if the PAS is between 5 and 7, moderate if the PAS is between 8 and 11, and severe if the PAS is between 12 and 15. Vital signs were also recorded. Children received 3 consecutive nebulizers with albuterol and ipratropium bromide. The dose of albuterol given was weight dependent (2.5 mg if <20 kg; 5 mg × 1 treatment, then 2.5 mg for subsequent treatments if 20-35 kg; and 5 mg if >35 kg). The dose of ipratropium bromide was 0.5 mg.

Patients were randomized to receive 0.6 mg/kg of oral dexamethasone (maximum dose 16 mg, rounded to the nearest 2 mg) or 2 mg/kg of oral prednisone (maximum dose 80 mg, rounded to the nearest 5 mg) during their nebulizer treatments. Block randomization (<7 years and ≥7 years) was performed in the hospital pharmacy. To ensure double blinding, the pharmacy prepared both drugs to look identical as a white powder in a clear capsule. Older patients swallowed the capsule and younger patients had the powder mixed with applesauce or pudding for ease of administration. Children who vomited the steroid preparation were redosed with the same dose of medication. All patients who vomited the second dose of steroids were excluded from the study.

The need for subsequent nebulizer treatments and final disposition from the ED was left to the discretion of the ED attending. At the time of discharge, patients in the dexamethasone arm received 1 dose of 0.6 mg/kg of dexamethasone (maximum dose 16 mg) to take the next day and placebo to take twice daily to complete a 5-day course. The patients in the prednisone arm received 1 mg/kg of prednisone (maximum dose 30 mg) to take twice daily for 5 days. All patients received their study medication in the ED prior to discharge. All the capsules, including the placebo, were identical in appearance and were placed in capsule bubble packets labeled dose 1 through 10 to ensure that patients in the dexamethasone group received the second dose of dexamethasone as their next dose and then started the placebo. At the time of discharge, patients received instructions to use their albuterol every 4 hours for 24 hours then as needed for symptom relief. Patients and their families were called 10 days after their ED visit for follow-up.

Demographic variables including age, sex, ethnicity, duration of asthma symptoms, number of previous ED visits, number of previous hospital stays, exposure to household smoke, and current medication usage were recorded. Clinical variables including vital signs on presentation and at discharge, PAS, number of inhaled treatments required, and any episodes of vomiting were recorded.

Our primary outcome was relapse within 10 days, defined as the need for subsequent hospitalization or an unscheduled visit with a medical provider (primary

Table 1. Pediatric Asthma Score

Score	1	2	3
Respiratory rate			
2-3 y	≤34	35-39	≥40
4-5 y	≤30	31-35	≥36
6-12 y	≤26	27-30	≥31
>12 y	≤23	24-27	≥28
Oxygen requirement	>90% on room air	85%-90% on room air	<85% on room air
Auscultation	Normal breath sounds to end-expiratory wheeze only	Expiratory wheezing	Inspiratory and expiratory wheezing to diminished breath sounds
Retractions	0-1 site	2 sites	3 or more sites
Dyspnea	Speaks in sentences, coos, and babbles	Speaks in partial sentences and short cry	Speaks in single words, short phrases, and grunting

care doctor, urgent care, ED, etc), due to continued or worsening asthma symptoms. As the primary outcome of our study was to assess relapse back to the hospital, we excluded all patients who required admission to the hospital from the ED. We also excluded patients whose stay in the ED/ED observation unit was ≥10 hours. Our secondary outcome was emesis with steroid administration in the ED.

Statistical Analysis

By using an α of .05 and a power of 0.8, we calculated that a sample size of 700 patients in each treatment group was needed for an equivalency trial between dexamethasone and prednisone. We used a baseline relapse rate of 10% for the prednisone group. We allowed up to a 14% relapse rate for the dexamethasone group to be considered equivalent to the prednisone group.

Continuous variables were analyzed with the Mann-Whitney *U* test as all distributions were found to be non-normal. Categorical variables were analyzed with a chi-square test. A P value < .05 was considered statistically significant. This study was approved by the Colorado Multiple Institutional Review Board. Informed consent was obtained from parents or guardians, and assent was obtained for children 7 years and older. Calculations were performed using SPSS for Windows, (version 14.0, 1999; SPSS Inc, Chicago, Illinois).

Results

Patient enrollment data are presented in Figure 1. The excluded patients had demographic and clinical characteristics similar to those of the study patients. There was also no difference in the study drug group assignment between the patients who completed the study and those who did not complete the study. The only significant difference between the 2 groups was the PAS, which was higher in the excluded patient group (median 7 vs 9, P < .001). Table 2 presents the data for the excluded and study patients.

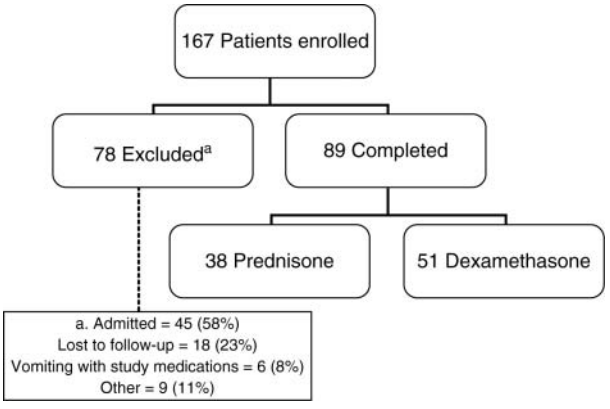

Figure 1. Flow of study participants.

Eighty-nine patients completed the study. In all, 38 patients received a standard prednisone course, and 51 patients received 2 doses of dexamethasone during the first 2 days of treatment. There was no difference between the prednisone and dexamethasone groups in sex, age, number of prior ED visits in the last year, number of prior hospitalizations for asthma in the last year, and exposure to smoke. Patients in the 2 treatment groups did not differ in the number of breathing treatments within the preceding 24 hours prior to presentation or their use of

Table 2. Characteristics of Excluded Versus Study Patients

	Study Patients (n = 89)	Excluded Patients (n = 78)
Dexamethasone (%)	51 (57)	38 (49)
Male (%)	49 (55)	52 (68)
Age, y (range)	6.8 (2-18)	5.9 (2-17)
Albuterol Rx in the past day (range)	3 (0-12)	3 (0-12)
Exposure to smoke (%)	29 (33)	33 (47)
Pulse oximetry (range)	92 (83-100)	90 (76-100)
PAS (range)[a]	7 (5-14)	9 (5-15)

Abbreviation: PAS, pediatric asthma score.
[a]$P < .01$.

Table 3. Demographics and Asthma Characteristics of the 2 Study Groups

	Prednisone (n = 38)	Dexamethasone (n = 51)
Male (%)	23 (61)	26 (51)
Median age, y (range)	6.2 (2-18)	4.5 (2-18)
Ethnicity		
Caucasian (%)[a]	3 (8)	12 (24)
African American (%)[a]	13 (34)	18 (35)
Hispanic (%)[a]	15 (40)	19 (37)
Other (%)[a]	7 (18)	2 (4)
Median days of symptoms (range)	2 (1-6)	2 (1-11)
Median number of visits to the ED for asthma in the last year (range)	1 (0-12)	1 (0-10)
Median number of hospitalizations in the last year (range)	0 (0-8)	0 (0-2)
Exposure to smoke (%)	16 (42)	13 (25)
Median number of albuterol treatments in the last 24 h (range)	1 (1-2)	1 (1-2)
Inhaled steroids (%)	16 (42)	13 (25)
Other medications (eg, Singulair and Claritin, %)	3 (8)	4 (8)

Abbreviation: ED, emergency department.
[a]$P = .01$.

other medications, such as inhaled steroids, singular, or Claritin (Schering-Plough HealthCare Products, Inc. Memphis, Tennessee). There were more Caucasians in the dexamethasone group and more patients who listed their ethnicity as "other" in the prednisone group ($P = .01$). The other ethnicity groups included Native Americans, Asians, Portuguese, and patients who listed more than one ethnicity. Table 3 presents the demographic variables and asthma characteristics of the 2 study groups.

Initial vital signs did not differ between the 2 study groups, including temperature, heart rate, respiratory rate, systolic blood pressure, and pulse oximetry. Of note, these pulse oximetry readings were performed at 5280 feet. The dexamethasone group had a higher median PAS score on presentation ($P = .003$), suggesting they had more significant lower airway obstruction. Table 4 presents the clinical variables at presentation for the 2 study groups.

There was no difference between the prednisone and dexamethasone groups in the primary outcome variable of need for unscheduled follow-up. In all, 3 patients in the prednisone group (8%) and 8 patients in the dexamethasone group (16%) required an unscheduled follow-up visit ($P = .27$). In addition, there was no difference in the incidence of vomiting between the 2 groups. In all, 7 patients in the prednisone group (18%) and 5 patients in the dexamethasone group (10%) had vomiting in the ED ($P = .24$).

Discussion

This study showed no difference between dexamethasone and prednisone in the outpatient management of acute pediatric asthma exacerbations. The use of corticosteroids is standard care for the treatment of asthma exacerbations. Previous studies have

Table 4. Clinical Variables at Presentation

	Prednisone (n = 38)	Dexamethasone (n = 51)
Median temperature in °C (range)	37.1 (35.5-40.2)	37.4 (36-39.8)
Median heart rate (range)	134 (70-174)	140 (79-195)
Median respiratory rate (range)	28 (16-76)	36 (16-70)
Median systolic blood pressure (range)	113 (81-134)	112 (90-140)
Median pulse oximetry on room air (range)	93 (87-100)	91 (83-98)
Median peak flow (12 patients/group, range)	190 (80-450)	135 (50-300)
Median PAS (range)[a]	6 (5-12)	8 (5-14)

Abbreviation: PAS, pediatric asthma score.
[a]$P = .003$.

shown that steroids reduce the rates of hospitalization and relapse for acute asthma exacerbations.[3-6] Studies have also demonstrated improvement in pulmonary function with the use of corticosteroids.[6,7] The National Institutes of Health (NIH) guidelines for the diagnosis and management of asthma recommend the use of oral steroids for those with moderate to severe asthma exacerbations.[11] We also found no difference in the rate of vomiting in the ED, a common side effect of steroids, between groups.

The pharmacological properties of dexamethasone (eg, longer half-life and more potent) compared with those of prednisone make it an appealing alternative for the treatment of acute asthma exacerbations. Importantly, these properties may allow for the use of a shorter course of steroids, which should increase compliance. Studies have demonstrated that better adherence to asthma regimens leads to improved outcomes.[12,13] Unfortunately, several studies have documented a low prescription pickup rate after ED visits. Overall, only 65% of high-urgency pediatric prescriptions were filled upon discharge from the ED,[14] and only 45% of Tennessee children covered by Medicaid had prescriptions for corticosteroids filled within 7 days of their ED visit for asthma.[15] Issues with noncompliance with filled oral prednisone prescriptions have also been documented.[8,12] Because asthma is a common presenting problem to the pediatric ED, any improvements in the current management of asthma have the potential to significantly impact a large volume of patients and improve patient outcomes.

Several previous studies demonstrated the efficacy of inhaled and IM dexamethasone in the management of asthma exacerbations.[16-18] More recently, 2 studies, Qureshi et al[8] and Altamimi et al,[9] evaluated the efficacy of oral dexamethasone. Our findings were similar to these 2 recent studies. The study of Qureshi et al[8] compared 2 doses of oral dexamethasone (0.6 mg/kg/dose) with 5 days of oral prednisone (2 mg/kg loading dose, then 1 mg/kg/d) in an unblinded study of 533 patients. The children in the prednisone group were given a prescription at discharge, whereas the children in the dexamethasone group were given the dose to take at home the next day. The Altamimi et al[9] study compared a single oral dose of dexamethasone (0.6 mg/kg) with 5 days of twice-daily prednisolone (1 mg/kg/dose) in 110 patients. We set out to improve previous study designs. Our study design included double blinding, a second dose of dexamethasone at home, twice daily dosing of prednisone, and each treatment arm received study drug at discharge.

The relapse rates for the dexamethasone and prednisone groups were 7.4% and 6.9%, respectively, in the Qureshi et al[8] study compared with the relapse rates for dexamethasone and prednisolone of 6.6% and 1.8%, respectively, in the Altamimi et al[9] study. Our study had a higher relapse rate for dexamethasone (16%) compared with the previous 2 studies. Our relapse rate for prednisone (8%) was slightly higher but similar to these previous studies. However, the difference in relapse rates between the dexamethasone and prednisone group in our study was not statistically significant. The dexamethasone group's initial median PAS was significantly higher, suggesting this group had a greater severity of illness on presentation. Patients with more significant lower respiratory tract obstruction may be at greater risk for requiring subsequent unscheduled visits. However, given our small number of patients, we cannot exclude that there may be a subtle difference between the effects of dexamethasone and prednisone in their anti-inflammatory roles for the treatment of acute pediatric asthma exacerbations.

The group of patients who were initially enrolled and later excluded had a higher PAS than the group of patients who completed the study. The majority (58%) of the excluded group were admitted to the hospital. Patients who require admission to the hospital would be expected to have a higher PAS or severity of illness upon presentation when compared with the group who completed the study and did not require admission.

Limitations

Given the small number of patients, we cannot exclude a type II error. Initially, we planned on enrolling 700 patients in each arm to complete an equivalency trial. The study was terminated secondary to several factors. A nursing guideline was instituted that permitted the initiation of steroid therapy prior to being seen by a physician, and approximately 30% of enrolled patients required admission, which resulted in their subsequent exclusion. Providers became reluctant to enroll patients in a study where, roughly one-third of the time, the patient required unblinding. We performed post hoc power calculations that revealed our power was <10% to detect a difference of 4% in relapse rates between groups.

Qureshi et al[8] and Altamimi et al[9] reported admission rates between 11% and 13%. Our admission rate was 27% (45/167). Our higher admission and relapse rates may indicate a higher disease severity of pediatric asthma patients treated at our institution. Our study was performed at an altitude of 5280 feet, significantly higher than the locations of the other 2 studies, a factor which also may have contributed to the higher admission and relapse rates. These factors may limit the external validity of our study.

Conclusions

We found no difference in the relapse rate or incidence of vomiting between patients given prednisone and dexamethasone in our study of pediatric asthma exacerbations. Although our results are encouraging and are consistent with similar recent literature,[8,9] we feel that a large multicentered trial powered for equivalency should be performed.

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