Two Days of Dexamethasone Versus 5 Days of Prednisone in the Treatment of Acute Asthma: A Randomized Controlled Trial

Joel Kravitz, MD, FRCPSC, Paul Dominici, MD, Jacob Ufberg, MD, Jonathan Fisher, MD, Patricia Giraldo, MD

From the Department of Emergency Medicine, Community Medical Center, St. Barnabas Health System, Toms River, NJ (Kravitz); Department of Emergency Medicine, Albert Einstein Medical Center, Philadelphia, PA (Dominici, Giraldo); the Department of Emergency Medicine, Temple University, Philadelphia, PA (Ufberg); and the Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA (Fisher).

Study objective: Dexamethasone has a longer half-life than prednisone and is well tolerated orally. We compare the time needed to return to normal activity and the frequency of relapse after acute exacerbation in adults receiving either 5 days of prednisone or 2 days of dexamethasone.

Methods: We randomized adult emergency department patients (aged 18 to 45 years) with acute exacerbations of asthma (peak expiratory flow rate less than 80% of ideal) to receive either 50 mg of daily oral prednisone for 5 days or 16 mg of daily oral dexamethasone for 2 days. Outcomes were assessed by telephone follow-up.

Results: Ninety-six prednisone and 104 dexamethasone subjects completed the study regimen and follow-up. More patients in the dexamethasone group reported a return to normal activities within 3 days compared with the prednisone group (90% versus 80%; difference 10%; 95% confidence interval 0% to 20%; $P=.049$). Relapse was similar between groups (13% versus 11%; difference 2%; 95% confidence interval –7% to 11%, $P=.67$).

Conclusion: In acute exacerbations of asthma in adults, 2 days of oral dexamethasone is at least as effective as 5 days of oral prednisone in returning patients to their normal level of activity and preventing relapse. [Ann Emerg Med. 2011;58:200-204.]

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0196-0644/$-see front matter

doi:10.1016/j.annemergmed.2011.01.004

INTRODUCTION

Background

Asthma is the presenting complaint in almost 2 million emergency department (ED) visits annually and has been increasing in prevalence in the United States during the past 20 years.[1] Systemic steroid administration (either oral or intravenous) has long been a cornerstone in the emergency treatment of acute asthma exacerbation, instrumental in both avoiding admission and shortening length of stay, as well as avoiding relapse.[2,3]

Although much has been published on the equivalence of oral and intravenous steroid administration in these cases, little literature exists on the difference in effectiveness of various steroid preparations. Numerous policy statements recommend the use of systemic corticosteroids for patients with acute asthma exacerbations[2,4,5] but do not compare different steroid preparations.

Importance

Many clinicians use a brief course of prednisone for mild to moderate asthma. Dexamethasone has an equivalent bioavailability in oral and intravenous formats but a longer half-life (up to 72 hours) than prednisone. As a result, it has been proffered as an alternative to prednisone that may allow shorter treatment regimens and improved compliance. In recent pediatric studies, shorter regimens of intramuscular or oral dexamethasone have demonstrated equivalence to prednisone and prednisolone in children with acute asthma.[6,7] These same studies also found improved patient compliance with the shorter dexamethasone regimen.

Goals of This Investigation

The objective of this study is to compare the time needed to return to normal activity and the frequency of relapse after acute exacerbation of asthma between patients receiving 2 days of oral dexamethasone versus 5 days of oral prednisone.

MATERIALS AND METHODS

Study Design and Setting

This was a prospective, randomized, double-blind study conducted between 2004 and 2007 in the urban EDs at Albert Einstein Medical Center (census 75,000) and Temple University Hospital (census 70,000) in Philadelphia, PA. Both institutional review boards approved the study.

Editor's Capsule Summary

What is already known on this topic

Oral prednisone is commonly administered after acute exacerbations of asthma. Given its longer half-life, a shorter course of dexamethasone might be equally effective.

What question this study addressed

After acute exacerbations of asthma, is 2 days of oral dexamethasone superior to 5 days of oral prednisone in returning patients to normal activity and in preventing relapse?

What this study adds to our knowledge

In this randomized controlled trial of 200 adults, 10% (95% confidence interval 0% to 20%) more patients had returned to normal activities within 3 days in the dexamethasone group compared with the prednisone group (number needed to benefit=10). The frequency of relapse was similar between the 2 corticosteroids.

How this is relevant to clinical practice

A 2-day course of dexamethasone appears modestly more effective than 5 days of prednisone in returning patients to normal activity after acute exacerbations of asthma.

Selection of Participants

Patients aged 18 to 45 years, with a diagnosis of asthma for at least 6 months and a peak expiratory flow rate less than 80% predicted, were eligible for inclusion. Research assistants are present 24 hours a day, 7 days a week in the ED to screen and enroll prospective study patients and ensure that no eligible patients remain unscreened.

Patients were excluded from the study if they had received oral corticosteroids in the previous 4 weeks; if they experienced chronic obstructive pulmonary disease, congestive heart failure, pneumonia, or sarcoidosis; or if they were pregnant or breastfeeding. The age limit of 45 years was chosen to try to avoid enrolling people with a concurrent diagnosis of chronic obstructive pulmonary disease. Patients were also excluded if they gave a history of corticosteroid allergy, tuberculosis, systemic fungal disease, gastritis, or diabetes or if they were unable to either consent to the study or be available for follow-up. Patients admitted to the hospital for their asthma exacerbation were also excluded from the analysis. Written informed consent was obtained from each subject.

Interventions

Patients meeting enrollment criteria received an initial peak expiratory flow rate measurement before and after an initial treatment of 5 mg nebulized albuterol and 2.5 mg of nebulized ipratropium bromide. Subsequent albuterol and other asthma treatment were at the discretion of the treating physician.

A computerized randomization table maintained by the pharmacy department was used to assign patients to one of 2 treatment arms. Patients in the prednisone group received 5 medication packets labeled 1 through 5, each containing 60 mg of prednisone. Patients in the dexamethasone group received 5 identical medication packets; the first 2 contained 16 mg of oral dexamethasone in packets 1 and 2, with placebo doses in packets 3 through 5. Both the medications and the placebo doses were prepared in identical capsules by the hospital's pharmacy department so that neither the treating emergency physician nor the enrolling research staff could discern which study medication was administered. The first dose from each packet was received during the patient's ED visit, and patients were instructed to receive the medication in the packets in the correct numeric order on the subsequent 4 days.

Data Collection and Processing

Using a standard collection form, research associates collected baseline data, including age, sex, asthma history (including previous intubations, previous ICU admissions, recent ED visits, and hospital admissions for asthma within the past year), smoking history, and peak expiratory flow rate.

Patients were contacted by telephone 2 weeks after their visit. They were asked how many days were required before they returned to normal daily activities, the number of times albuterol was used per day in the week after their ED visit, and whether there was a relapse, defined as repeated ED or primary care provider visits or admission to the hospital for worsening of the asthma exacerbation within the 2-week follow-up period.

Primary Data Analysis

With 80% power and $\alpha=.05$ with a 2-tailed test, assuming that 80% of patients in the prednisone group would return to normal activity in fewer than 3 days, one would need 88 patients in each treatment group to detect a minimum of a 15% improvement in the dexamethasone group.

Outcome measures were analyzed with χ^2, using SAS statistical software (version 9.1.3; SAS Institute, Inc., Cary, NC). $P<.05$ was considered statistically significant.

RESULTS

Patient flow is shown in the Figure, and baseline characteristics were similar between study sites and between drug groups (Table 1).

Significantly more subjects returned to normal activity within 3 days with dexamethasone compared with prednisone, and the frequency of relapse was similar between groups (Table 2). The number of albuterol doses patients needed per day while receiving the study medication did not differ between the 2 groups (prednisone group: median 2 doses/day [interquartile range {IQR} 0 to 10]; dexamethasone group: median 2 doses/day [IQR 0 to 6]).

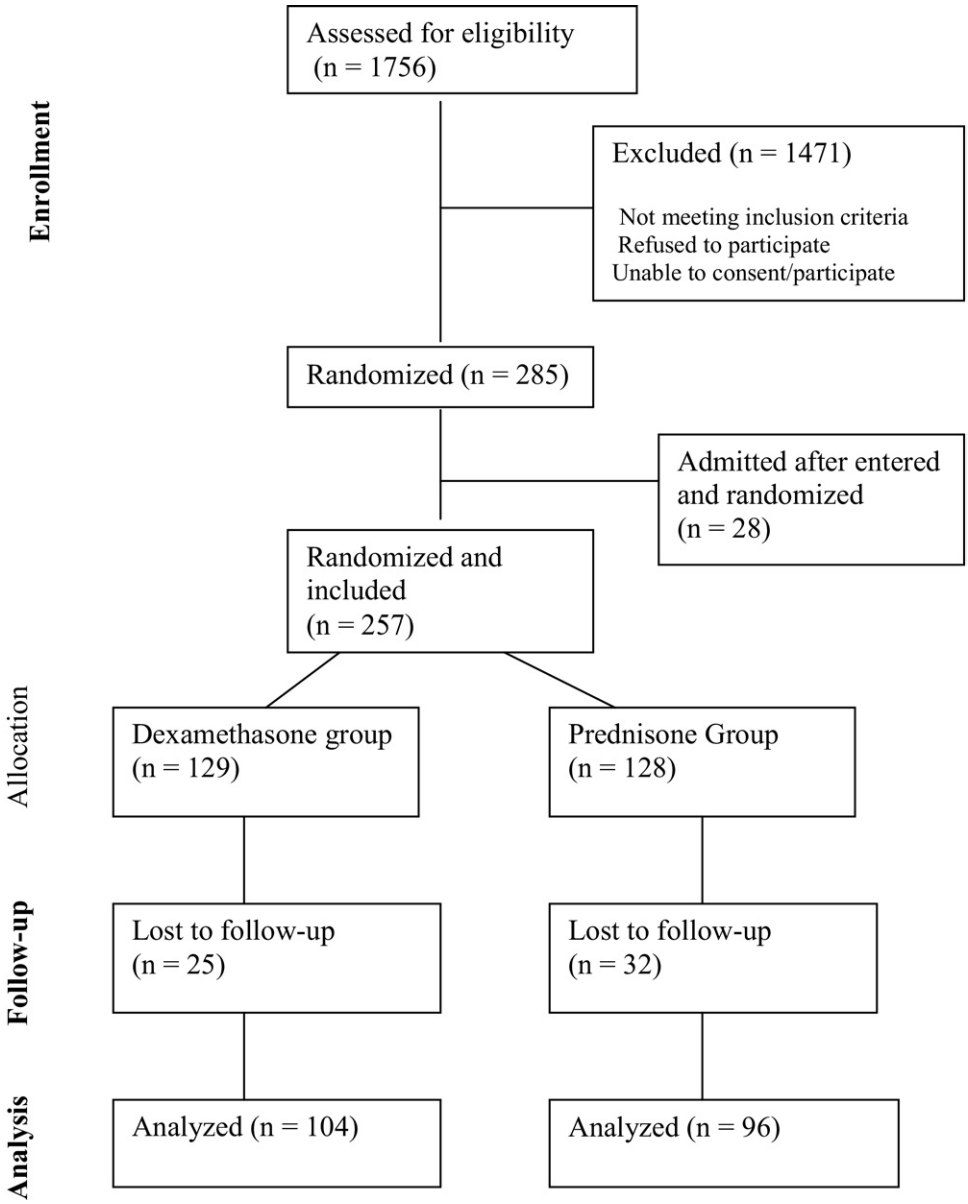

Figure 1. Patient enrollment, randomization and follow-up.

LIMITATIONS

We chose as a primary outcome to measure the number of days until patients believed they were able to return to their normal activities. Although some of the pediatric studies used calculated asthma scores as one of their outcome measures,[8] patients in our study were followed up by telephone, making a more formal scoring system impossible to implement. However, we submit that a patient's return to normal baseline activity is the endpoint of a measured improvement in asthma score and can thus be used as a surrogate marker for score improvement.

A second limitation is that 22% of enrolled patients were lost to follow-up, and it is unknown whether outcomes might have differed between those we could and could not contact.

DISCUSSION

Our results indicate that 2 days of oral dexamethasone is at least as effective as 5 days of prednisone in the treatment of mild to moderate asthma exacerbations in the ED. Relapse rates and treatment failures were equivalent in both groups. A statistically significant difference favoring the dexamethasone group was found in terms of returning patients to their normal activities within 3 days. This period was chosen according to the long 72-hour half-life of dexamethasone. Similar results have been observed in studies of pediatric asthma exacerbations. Qureshi et al[6] were the first to demonstrate a potential equivalence of 2 days of oral dexamethasone and 5 days of prednisone in acute pediatric asthma, showing no difference between the 2 groups

Table 1. Baseline patient characteristics.

Variable	Prednisone	Dexamethasone
N	96	104
Age, y, median (IQR)	30 (23–38)	28 (22–37)
Sex, female (%)	56 (58)	62 (60)
Peak flow initial, median (IQR)	230 (195–297)	230 (180–300)
Peak flow ideal, median (IQR)	488 (474–599)	488 (474–502)
Peak flow personal best, median (IQR)	400 (350–450)	400 (300–500)
ED visits in past 30 days (%)		
None	72 (75)	85 (82)
1	20 (21)	10 (10)
≥2	4 (4)	9 (9)
ED visits in past 12 mo (%)		
None	35 (36)	37 (36)
1–2	35 (36)	33 (32)
3–4	14 (15)	14 (13)
>4	12 (12.5)	20 (19)
Admissions in past 12 mo (%)		
None	76 (79)	85 (82)
1	11 (11)	12 (12)
>1	9 (9)	7 (7)
Smoke (%)	29 (30)	37 (36)
Intubation for asthma (%)	10 (10)	17 (16)
ICU for asthma (%)	16 (17)	27 (26)
Discharge peak flow, median (IQR)	350 (300–400)	350 (300–430)
Asthma severity score, median (IQR)	4 (3–4)	4 (2–4)

Table 2. Outcome measures.

Outcome Measure	Prednisone (%), N=96	Dexamethasone (%), N=104	Difference (%)	95% CI*
Days to return to normal, 0–3 days†	72 (80)	91 (90)	10	(0 to 20)
Any hospital admissions	1 (1)	3 (3)	2	(–6 to 2)
Any ED visits since discharge	6 (6)	5 (5)	1	(–5 to 8)
Any primary care provider visits since discharge	5 (5)	3 (3)	2	(–3 to 8)

*P=.049.
†Return to normal daily activity information missing for 6 prednisone and 3 dexamethasone patients.

with respect to relapse rates and symptoms persistence at 10 days after treatment. Relapse rates were observed to be similar in both the dexamethasone and prednisone groups (11% versus 13%; P=.67; difference 1.5%; 95% confidence interval –7% to 11%).

More recently, Gordon et al[8] compared a single dose of intramuscular dexamethasone to a 5-day course of oral prednisolone in children with acute asthma exacerbation. In their study, the 2 treatment regimens performed equally with respect to both the primary outcome (change in asthma score) and the secondary outcome measurements (asthma score at 4-day follow-up, admission rates and unplanned physician visits by 4-day follow-up). Altamimi et al[7] recently performed a randomized double-blind comparison of a single oral dose of dexamethasone versus a 5-day course of prednisone in patients aged 2 to 16 years with mild to moderate asthma exacerbation, in a study similar to our current protocol. Although that study did not complete sufficient enrollment to achieve the desired statistical power, their results did suggest equivalence between the 2 groups with respect to days needed to return to baseline.

Dexamethasone has well-known pharmacologic properties, including duration of action of up to 72 hours, a relatively long half-life, and excellent bioavailability.[9,10] In addition to these factors, one of the more attractive features of dexamethasone in the pediatric patient is the palatability; prednisone is known to be among the worst-tasting medications in the physician's armamentarium. The abovementioned pediatric studies could reasonably argue that this factor alone would contribute to improved patient compliance and thus help in the treatment of pediatric asthma exacerbation. This does not apply to the adult population, although a shorter treatment regimen might lend itself to improved compliance because research suggests that up to 28% of patients visiting the ED do not fill their prescriptions.[11,12] If the pediatric research ultimately is found to translate to the adult asthmatic patient, a single dose of dexamethasone may be sufficient, thus ensuring patient compliance by treatment in the ED itself.

Our study suggests that a 2-day course of oral dexamethasone is at minimum as effective as a 5-day course of oral prednisone in the treatment of mild to moderate asthma exacerbations in patients who are discharged from the ED and may return patients to a normal level of activity more rapidly. It is still unclear whether the statistically significant difference observed in this study translates to a true clinical benefit for dexamethasone over prednisone. These results corroborate similar findings in several pediatric studies. This study contributes to the growing body of evidence that equivalent potencies of different corticosteroid preparations are at least equally effective in the treatment of acute asthma exacerbation and that the convenient short-course dosing of dexamethasone makes it an attractive treatment option.

Supervising editor: Steven M. Green, MD

Author contributions: JU and JF conceived of and designed the study. JK, PD, and PG collected the data. JK refined the protocol for acceptance, obtained institutional review board approval, obtained research funding, drafted the article, and functioned as the primary investigator in terms of data analysis and article preparation. PD served as the research coordinator, assisting in performing much of the statistical analysis. PG provided assistance with institutional review board forms and logistics in the implementation of the study. All authors contributed to the refinement and final

preparations of the article. JK takes responsibility for the paper as a whole.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). This study was made possible by an unrestricted grant from the Albert Einstein Society of the Albert Einstein Medical Center, grant number 03-14.

Publication dates: Received for publication December 22, 2010. Revision received January 5, 2011. Accepted for publication January 11, 2011. Available online February 18, 2011.

Presented at the Society for Academic Emergency Medicine annual meeting, 2005, New York, NY; and the Society for Academic Emergency Medicine regional meeting, April 2005, New York, NY.

Address for correspondence: Joel Kravitz, MD, FRCPSC, Community Medical Center, Department of Emergency Medicine, Toms River, NJ, 08755; 609-923-9812; E-mail joel_kravitz@hotmail.com.

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