Randomized Trial of Dexamethasone Versus Prednisone for Children with Acute Asthma Exacerbations

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Objective To determine whether 2 doses of dexamethasone is as effective as 5 days of prednisolone/prednisone therapy in improving symptoms and quality of life of children with asthma exacerbations admitted to the emergency department (ED).

Study design We conducted a randomized, noninferiority trial including patients aged 1-14 years who presented to the ED with acute asthma to compare the efficacy of 2 doses of dexamethasone (0.6 mg/kg/dose, experimental treatment) vs a 5-day course of prednisolone/prednisone (1.5 mg/kg/d, followed by 1 mg/kg/d on days 2-5, conventional treatment). Two follow-up telephone interviews were completed at 7 and 15 days. The primary outcome measures were the percentage of patients with asthma symptoms and quality of life at day 7. Secondary outcomes were unscheduled returns, admissions, adherence, and vomiting.

Results During the study period, 710 children who met the inclusion criteria were invited to participate and 590 agreed. Primary outcome data were available in 557 patients. At day 7, experimental and conventional groups did not show differences related to persistence of symptoms (56.6%, 95% CI 50.6-62.6 vs 58.3%, 95% CI 52.3-64.2, respectively), quality of life score (80.0 vs 77.7, not significant [ns]), admission rate (23.9% vs 21.7%, ns), unscheduled ED return visits (4.6% vs 3.3%, ns), and vomiting (2.1% vs 4.4%, ns). Adherence was greater in the dexamethasone group (99.3% vs 96.0%, $P < .05$).

Conclusion Two doses of dexamethasone may be an effective alternative to a 5-day course of prednisone/prednisolone for asthma exacerbations, as measured by persistence of symptoms and quality of life at day 7. *(J Pediatr 2017;191:190-6).*

Clinical Trial Registration clinicaltrialsregister.eu: 2013-003145-42.

Asthma is the most common chronic childhood disease and the leading cause of chronic disease-related morbidity, as measured by school absences, visits to the emergency department (ED), and hospitalizations.[1,2] Asthma exacerbations account for nearly 5% of ED visits, and approximately 15% may require admission.[3-6]

Treatment of exacerbations is based on rapid reversal of bronchospasm and reducing airway inflammation. International guidelines recommend corticosteroids as an essential part of the treatment.[1] They reduce inflammation and enhance the effects of bronchodilators, preventing relapses, admissions, and the need for β_2-agonist therapy.[7-9]

Traditionally, oral prednisone/prednisolone was the corticosteroid used, twice daily for 5 days, because the half-life is 12-36 hours. However, this treatment regimen, its bitter taste, and the incidence of vomiting may lead to poor adherence, with an increased risk of persistent symptoms and hospitalization.[10-13] In contrast, dexamethasone presents the advantage of a 2-dose regimen, due to its longer biologic half-life of 36-72 hours, and is a more palatable option.[14,15]

Previous randomized controlled trials proposed dexamethasone as an equivalent therapy to prednisone/prednisolone for asthma exacerbations, without differences in hospital admission, unscheduled returns, and with less vomiting.[16-23] A recent meta-analysis recommended to consider dexamethasone as a viable alternative to prednisone/prednisolone.[24] However, there are limitations to each of the trials included in terms of study design, dosing regimen, sample size, and age of patients enrolled.[24,25] Most important, all these studies have used different clinical scores, relapse, and admission rates, as main outcome variables. Thus, potential differences between the 2 treatments on the persistence of symptoms and quality of life after the ED visit remains unclear. For this reason, more evidence could help to safely introduce this change in clinical practice.

ARQoL	Asthma-Related Quality of Life
ED	Emergency department
ns	Not significant
O_2 sat	Oxygen saturation
PACT	Pediatric Asthma Control Tool
PS	Pulmonary score

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We aimed to determine whether 2 doses of oral dexamethasone (experimental treatment) is as effective as 5 days of oral prednisolone/prednisone (conventional treatment) in improving symptoms of non–life-threatening asthma exacerbations and quality of life at day 7. The secondary objectives were to evaluate whether the experimental treatment is as effective as the conventional one in preventing hospital admissions and unscheduled returns to ED. Adherence to treatment and vomiting, school and work absenteeism, and parental satisfaction also were analyzed.

Patients and Methods

We conducted a prospective, randomized, open-label, noninferiority controlled trial (clinicaltrialsregister.eu: 2013-003145-42) to compare the effectiveness of the experimental treatment vs the conventional one in an acute-care teaching tertiary hospital near Bilbao, in the Basque Country (Spain). Our ED provides care to children <14 years of age, with a mean of 55 000 visits a year with approximately 3000 (5%) of these visits due to asthma exacerbations.

The treating physician identified the eligible participants who were children aged 12 months to 14 years old with asthma exacerbations who presented to the ED from September 2014 to October 2015. Asthma was defined as either previous medical diagnosis of asthma or at least 2 previous episodes of β_2-agonist–responsive wheeze or a first episode of wheezing in children over 2 years and history of atopy. An exacerbation of asthma was defined as acute asthma that prompts ED assessment, with any or all of the following clinical features: dyspnea, wheeze, acute cough, increased work of breathing, and/or increased requirement for bronchodilators from baseline use.[17-19,22,23] Parents or legal guardians of eligible participants received oral and written information about the study before written informed consent was obtained. When applicable, informed assent was obtained from the patient.

Children were excluded for any of the following reasons: presentation with critical or life-threatening asthma exacerbation, reported use of oral or parenteral corticosteroids in the previous 4 weeks, or presentation with respiratory failure that needed further support such as intravenous steroids, intravenous magnesium sulfate, and/or high-flow oxygen and admission to the pediatric intensive care unit. The treating physician was permitted to exclude patients if time constraints made enrollment unfeasible.

Before the trial, the research team was trained to conduct the follow-up interviews and performed information sessions for ED and ward staff. Primary Care pediatricians received an information letter.

After written informed consent was obtained, enrolled patients were randomized to 1 of 2 treatment groups. Randomization was performed by the statistical team with the software nQuery 7.0 (Statsols, Cork, Ireland). The randomization list generated by this process was concealed and safeguarded by the statistical team. The research team and treating physicians did not have access to this list. Allocation concealment was maintained by the use of sequentially numbered opaque envelopes containing a letter A (experimental treatment) or B (conventional treatment), following the randomization list. They were kept in the ED and opened by the treating physician after enrollment.

Interventions

All patients presenting to our ED with asthma exacerbations were managed according our current asthma protocol. To summarize, using the pulmonary score (PS)[26] and oxygen saturation (O_2 sat), patients were classified into 1 of 3 levels: mild (PS ≤3, O_2 sat >94%), moderate (PS 4-6, O_2 sat 91%-94%), or severe (PS > 6, O_2 sat <91%). Children received the first 2-3 β_2-agonist (albuterol) inhalations at 20-minute intervals, and subsequent doses or the addition of ipratropium bromide were given as ordered by the physician in charge according to the current protocol in our ED. Supplemental oxygen was administered to maintain O_2 sat ≥93%. Oral corticosteroids were prescribed during the first hour of treatment.

Patients allocated to the experimental treatment received an oral dose of dexamethasone (1 mg/mL) in the ED (0.6 mg/kg, maximum 12 mg), followed by a second dose in 24 hours. The selected dose of dexamethasone was based on previous asthma trials.[19,22] The pharmacy department prepared the oral formulation of dexamethasone. All patients allocated to dexamethasone arm received such oral formulation.

Patients allocated to the conventional treatment received a first dose of oral prednisone/prednisolone of 1.5 mg/kg in ED (maximum 60 mg), followed by 1 mg/kg/d (maximum 60 mg), twice-daily, on days 2-5, based on previous asthma guidelines.[1,22] Both the solution and tablet was the standard oral preparation. The choice between liquid or tablet was based on the age and preference of the child.

The dose of either medication was readministered orally if the patient vomited within 30 minutes. No further systemic steroids were prescribed before discharge.

Lack of response to treatment and/or persistent hypoxemia was a criterion for hospitalization. At discharge, families received prepackaged doses to take at home (with an extra dose if vomiting) and a follow-up by primary healthcare pediatricians in 24 hours was recommended in both groups. Our healthcare system provides free, universal, and comprehensive coverage. Albuterol inhalations were recommended on a 2- to 6-hour basis for the first day, then as ordered by primary care pediatricians. If children were admitted, randomized treatment was continued, and the dosing of β_2-agonist was at the discretion of the medical team.

Methods of Measurement

The research team completed standardized data collection sheets to record demographic and clinical variables. Data of unscheduled returns to ED and primary healthcare follow-up were retrieved from electronic records of the Basque Health Service.

The research team contacted study patients by telephone at day 7 and day 15 after the ED visit. At day 7, they performed a structured interview using validated questionnaires to assess the persistence of symptoms (using the pediatric asthma control

tool [PACT]) and quality of life (using asthma related quality-of-life [ARQoL] instrument).[27-30] PACT is a 6-item instrument for persistent symptoms that was developed from the National Asthma Education and Prevention Program guidelines and previously validated.[28,29] Each response was scored from 0 to 5 points with a maximum score of 30 points. Symptom scores for each domain were dichotomized into intermittent and persistent based on the National Asthma Education and Prevention Program guidelines, which define persistent symptoms based on frequency. Results were expressed as percentage of patients with persistent symptoms. ARQoL is an 8-item, asthma-related quality-of-life instrument including daytime and nighttime symptoms. Quality-of-life scores were summed and calculated as a percentile as described by Bukstein et al, where the greater the score, the better the quality of life.[27] Both questionnaires were translated into Spanish by the translation department of our hospital and were used in a previous study of our group.[30] Both questionnaires also were completed by parents during the ED visit, at baseline. Parents also answered about adherence with treatment, vomiting, unscheduled returns to ED, visits to primary healthcare, school and work absenteeism, and their satisfaction with the treatment. At day 15, data of revisits and school and work absenteeism were completed. Any adverse event was noted during follow-up.

Outcome Measures

The primary outcome measures were the percentage of patients with asthma symptoms at day 7 and their quality-of-life score. Secondary outcome measures were vomiting, adherence to treatment, and parental satisfaction at day 7. Other outcomes were the admission rate, unscheduled returns to ED, hospital readmissions, visits to primary healthcare, and school and work absenteeism at day 7. At day 15, unscheduled returns to ED, visits to primary healthcare, and school and work absenteeism were remeasured. Health record data rather than parent recall was used for the outcome of revisits, including situations in which there were discrepancies between parent report and the health record.

Statistical Analyses

The sample size calculation comparing dexamethasone and prednisone/prednisolone at day 7 assumed that dexamethasone is noninferior to prednisone/prednisolone if the PACT score at day 7 for dexamethasone group was not more than 6% greater than for the prednisone/prednisolone group.[30] Assuming a similar effectiveness for dexamethasone and prednisone/prednisolone, a sample size of 556 patients, would be sufficient to conclude noninferoirity with a power of 80%, considering expecting dropouts of 10%. This assumes a type I error rate of 0.05 and a noninferiority margin of 6% on the PACT score. We used descriptive statistics to compare baseline characteristics between the 2 groups: frequency tables for categorical variables and means with SD for continuous variables with 95% CIs. Analysis of the primary outcome was performed with the χ^2 test. For the secondary variables contrasts exploratory hypotheses were constructed with the Fisher or χ^2 for categorical variables and the Student *t* test or the nonparametric Mann-Whitney *U* test for continuous variables. Data were analyzed on an intention-to-treat basis with IBM SPSS Statistics 23.0 (IBM Corp, Armonk, New York).

This trial was approved by the ethics committee of the hospital and authorized by the Spanish Agency for Medication and Healthcare Products. The study was registered in The European Union Clinical Trials Register (EudraCT Number: 2013-003145-42) before enrollment of the first subject.

Results

A total of 57 865 children received care in our ED during the study period (September 5, 2014, to October 5, 2015). Of these, 2956 patients (5.1%) were diagnosed with asthma. Patients presenting with severe or mild exacerbations with no need of corticosteroids were excluded. Other reasons for exclusion were reported use of oral or parenteral corticosteroids in the previous 4 weeks or enrollment unfeasible due to time constraints. Seven hundred ten patients who met the inclusion criteria were invited to participate in the study, and, finally, a total of 590 patients underwent randomization (294 received experimental treatment with dexamethasone, 296 received conventional one with prednisone/prednisolone). Of the 120 patients not enrolled, 116 refused to participate and in 4 cases enrollment was not feasible because of a language barrier. There were 14 patients (7 in each group) who had exclusion criteria that had been overlooked mistakenly during the enrollment process, resulting in exclusion from the study. No re-enrollment was within 4 weeks of a previous enrollment. Telephone follow-up was completed in 281 patients (97.9%) in the dexamethasone group and in 276 patients (95.5%) in the prednisone/prednisolone group. Primary outcome data were available in 557 patients. A flowchart of study participants is presented in the **Figure**.

There were no differences in demographic and clinical characteristics between the 2 trial arms at enrollment. Both groups presented a similar percentage of persistent symptoms (43.8% in dexamethasone group vs 37.7% prednisone group, not significant [ns]) and similar quality-of-life score (79.4% vs 79.5%, ns). Baseline characteristics of patients included in the study are shown in **Table I**. There was also no difference between patients included and excluded in terms of demographic characteristics or initial severity.

In relation to the primary outcome, there was no significant difference in the percentage of patients with persistence of symptoms at day 7 between the dexamethasone and prednisone/prednisolone group (56.6%, 95% CI 50.6-62.6 and 58.3%, 95% CI 52.3-64.2, respectively). There were no differences between the 2 trial arms regarding the rest of the items of PACT questionnaire. Asthma symptoms most frequently reported by parents were cough (55%) and mucus in chest (19%). Regarding quality of life, both groups referred similar score (80 vs 77.7, ns) (**Table II**).

Table III (available at www.jpeds.com) shows the primary outcome for post-hoc selected subgroups of clinical interest

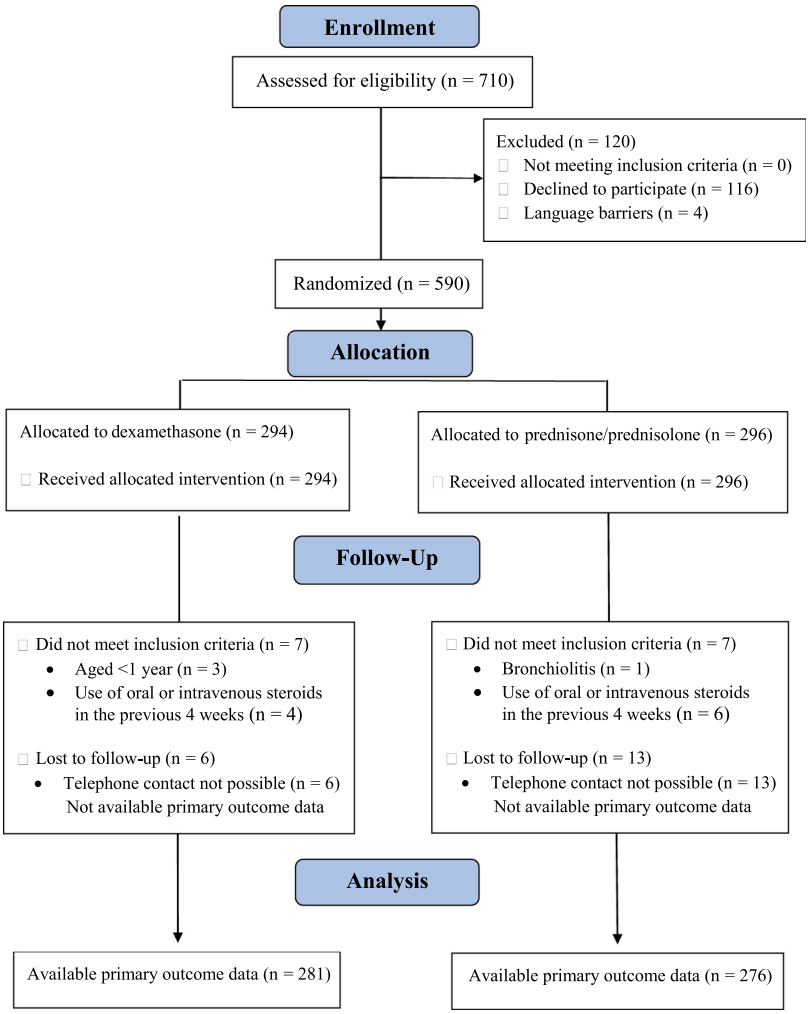

Figure. Flowchart of study participants.

such as patients with a first asthma episode, patients with mild-to-moderate exacerbations, admitted patients, patients with maintenance treatment, and patients aged 12-24 months. There was no significant difference in the primary outcome between the 2 study groups for each of these subgroups. Patients who received further doses of steroids, in the 7 days after enrollment, presented worse short-outcome without differences among the 2 arms of treatment (**Table III**). There were 22 (7.8%) patients in dexamethasone group who received further systemic steroids, compared with 16 (6.2%) in the prednisone/prednisolone group; however, this difference was not significant. Of those receiving additional steroids, patients in the dexamethasone group were significant older than those in conventional group (6.5 vs 3.9, $P < .05$). There were neither more differences between these patients in terms of sex, medical history, initial severity, or treatment received in ED, nor persistence of symptoms or quality of life (**Table IV**; available at www.jpeds.com).

Regarding secondary outcomes (reported as dexamethasone vs prednisone/prednisolone group), no differences were found in relation to episodes of emesis (2.1% vs 4.4%, ns); however, adherence was greater in the dexamethasone group (99.3% vs 96%, $P < .05$). There was no significant difference between the 2 arms of the study in the length of stay in ED (4.9 vs 4.8 hours, ns), admission rate to observation unit (20.3% vs 19.2%, ns), and admission to ward (3.6% vs 2.5%, ns). Both study groups presented a similar rate of return visits (4.6% vs 3.3%, ns) and return visits with admission (0.4% vs 0.7%, ns). The 2 trial arms had similar school absenteeism and a similar number of missed workdays. A high percentage of parents in the 2 groups expressed a preference for the 2-day treatment (93.8% vs 94.7%) (**Table V**). No adverse events attributable to the study medications were noted.

Discussion

In a study population of 557 children aged 1-14 years with asthma exacerbation, 2 doses of dexamethasone showed similar effectiveness to a 5-day course of prednisone/prednisolone on

Table I. Baseline characteristics of patients included in the study

Variables	Dexamethasone group (n = 281)	Prednisone group (n = 276)	P
Sex, male	169 (60.1%)	166 (60.1%)	ns
Age, y*	4.7 (3.4)	4.5 (3.4)	ns
Medical history			
Asthma	228 (81.1%)	227 (82.2%)	ns
Allergies	70 (24.9%)	54 (19.6%)	ns
Atopic dermatitis	43 (15.3%)	34 (12.3%)	ns
Maintenance treatment	67 (23.8%)	62 (22.5%)	ns
Exacerbation characteristics			
β_2-agonist in previous 24 h	210 (74.7%)	213 (77.2%)	ns
PS at arrival*	4.5 (1.2)	4.5 (1.3)	ns
O_2 sat*	95.6 (5.8)	95.6 (5.4)	ns
Supplemental oxygen	100 (35.6%)	94 (34.1%)	ns
>3 doses of β_2-agonist in ED	80 (28.5%)	81 (29.3%)	ns
Ipratropium bromide	163 (58%)	155 (56.2%)	ns
PACT at arrival			
Persistent symptoms	123 (43.8%)	104 (37.7%)	ns
While sitting quietly	12 (4.3%)	13 (4.7%)	ns
With light activity	23 (8.2%)	19 (6.9%)	ns
With sports	40 (14.2%)	31 (11.2%)	ns
While asleep at night	100 (35.6%)	90 (32.6%)	ns
In the morning	17 (6.0%)	19 (6.9%)	ns
Need of bronchodilator	38 (13.4%)	30 (10.9%)	ns
ARQoL at arrival*	79.4 (17.9)	79.5 (17.5)	ns

*Values are expressed as the mean ± SD.

the endpoints of persistence of asthma symptoms and quality of life on day 7. Also, there were no observed differences in other outcomes, including length of ED stay, hospital admission, and unscheduled return visits. These findings are clinically relevant and provide robust evidence of the role of dexamethasone as a valuable alternative to prednisone/prednisolone in the management of nonlife-threatening asthma in the ED setting.

Persistence of asthma symptoms and quality of life were predefined main outcomes of the trial. These patient-oriented measures were preferred over relapse and hospital admission rates, because they were considered better surrogate markers of disease

Table II. Primary outcome in all patients included in the study

Variables	Dexamethasone group (n = 281)	Prednisone group (n = 276)	P
Persistence of symptoms by PACT at day 7	159 (56.6%)	161 (58.3%)	ns
	95% CI (50.6%-62.6%)	95% CI (52.3%-64.2%)	
Persistent symptoms			
While sitting quietly	16 (5.7%)	24 (8.7%)	ns
With light activity	41 (14.6%)	44 (15.9%)	ns
With sports	75 (26.7%)	91 (33%)	ns
While asleep at night	127 (45.2%)	123 (44.6%)	ns
In the morning	30 (10.7%)	34 (12.3%)	ns
Need of bronchodilator	242 (86.1%)	252 (91.3%)	ns
ARQoL at day 7*	80.0 (16.8)	77.7 (18.5)	ns

*Values are expressed as mean ± SD.

Table V. Secondary outcomes in all patients included in the study

Variables	Dexamethasone group (n = 281)	Prednisone group (n = 276)	P
OU admission	57 (20.3%)	53 (19.2%)	ns
ED LOS, h*	4.9 (5.4)	4.8 (5.7)	ns
Hospital admission	10 (3.6%)	7 (2.5%)	ns
Unscheduled return to ED	13 (4.6%)	9 (3.3%)	ns
Hospital readmission	1 (0.4%)	2 (0.7%)	ns
Visits to primary care	212 (75.4%)	196 (71%)	ns
Parental satisfaction	210 (93.8%)	179 (94.7%)	ns
Vomiting	6 (2.1%)	12 (4.4%)	ns
Adherence to treatment	279 (99.3%)	265 (96%)	<.05
Further systemic steroids administered	22 (7.8%)	16 (6.2%)	ns
School days missed*	1.8 (1.8)	2 (1.9)	ns
Work days missed*	0.3 (0.9)	0.3 (0.8)	ns

LOS, length of stay.
*Values are expressed as mean ± SD.

severity, as well as more helpful indicators for assessing morbidity after acute asthma attacks.[31] Hospital admission and relapse rates may be influenced by a number of factors, such as medical decisions, criteria for inpatient care, local accessibility to the healthcare system, or implementation and updating of treatment protocols.[6,32] Previous studies of asthma morbidity have used clinical scores on days 4 or 5 as primary study variables.[18,20,21,23] Although it may be argued that more objective information on the course of exacerbations are derived from clinical scores, a single measure at a particular time point may be insufficient to assess the overall evolution of the episode. Taking into account the protective effect of oral corticosteroids during the first 7-10 days of treatment, which could even be prolonged up to 3 weeks due to its biological effects, we selected measuring symptoms on day 7. This different perspective would complement findings of previous trials focused on clinical scores,[8] because persistence of symptoms and impact on the quality of life could be well considered improvement-associated variables other than clinical scores.[6,31,33]

This adds to previous research that used persistence of asthma symptoms and quality of life as primary endpoints of the study. These variables also were measured via validated instruments (PACT and ARQoL questionnaires). Other randomized trials in pediatric asthma in which treatments with dexamethasone and prednisone were compared have used patient-reported symptom persistence or other quality of life–related variables. In the study by Qureshi et al, persistence of symptoms was a secondary outcome measure and assessed by a research assistant who contacted each patient's family 11-14 days after discharge.[22] In this study, differences between dexamethasone and prednisone were not found. In the study by Altamimi et al, the mean number of days needed for Patient Self-Assessment Score to return to baseline (primary outcome) was 5.22 in the dexamethasone group and 5.21 days in the prednisone group.[17] In the study by Cronin et al, differences between dexamethasone and prednisone in secondary outcomes, including return visits to a healthcare provider and number of days of restricted activity, were not reported.[23] All these

findings, although based on different methods, are consistent with our results.

A notable observation of the study was the high percentage of 60% of patients with persistent asthma symptoms 1 week after ED consultation. This poor outcome of acute asthma episodes in children has been also documented by others,[33-35] with high morbidity attributed to inadequate patients' follow-up in the outpatient setting or suboptimal use of controller medications for asthma. At enrollment, approximately 40% of the patients presented with persistent asthma symptoms, which is consistent with data of previous studies.[31,36,37] Although these patients are more likely to experience severe exacerbations, less than one-quarter of patients were receiving regular maintenance therapy. More efforts are needed to identify patients with persistent asthma, as well as to optimize the use and adherence to controller medications.[34]

Some peculiarities of the inclusion criteria should be commented on. Children >2 years with a first episode of wheezing and history of atopy were included in the study, as were children between 12 months and 2 years of age who had responded to β_2-agonist therapy in previous wheezing episodes. In these patients, the diagnosis of asthma is uncertain and may have a worse response to corticosteroids,[38] but they usually are treated according to standard management protocols for asthma in the ED setting.[1] Dexamethasone and prednisone/prednisolone were equally effective in these patients, which also agrees with previous studies.[18,20]

Another issue of interest is that the shorter course of the treatment with dexamethasone allows the possible need for extra doses, a fact that has been related to a traditional preference for prednisone by providers.[23] Interestingly, patients in both groups who received further doses of steroids showed a worse short-term outcome as compared with the overall study population but without differences between dexamethasone and prednisone/prednisolone. This less favorable outcome reported by families in this subset of patients would probably lead to primary care pediatricians to prescribe further doses of steroids.

Dexamethasone also has been shown to be more palatable than prednisolone to children presenting in the ED with asthma exacerbations.[12,15] However, the liquid presentation of dexamethasone requires a high volume because of its concentration. In our study, vomiting was not significant among children in the dexamethasone group. Moreover, differences in taste between treatments had no influence on adherence, which was notably high in both study groups.

This study has some limitations. This was an open-label study, both doctors and families knew the intervention and it may have limited the trial's internal validity. However, data managers and the statistical team were blinded. Second, it was carried out in a single urban ED; thus, our results should be interpreted cautiously in other settings. Third, the primary outcomes of the study, persistence of asthma symptoms and quality of life, were subjective measures, without an independent validation, and the lack of placebo in the experimental arm may have limited the results. However, these outcomes were measured by a trained medical team using validated questionnaires through structured interviews. These interviews were conducted by phone call to facilitate feasibility and not to increase work absenteeism to families. Both the PACT scale and ARQoL questionnaires were completed by parents, and a tool administered to children would have yielded a different result. However, parent response may tend to minimize the potential bias across age groups.

In addition, 43% of children included in the study were <5 years, which is an important disadvantage of self-reporting focused on symptoms. Fourth, although PACT is a tool initially designed to assess baseline symptoms, it has been validated in the ED setting and constitutes an objective questionnaire to assess the persistence of symptoms. Nevertheless, the use of PACT at enrollment and at day 7 may have overestimated the frequency of symptoms as the result of overlap between baseline and follow-up. However, many patients reported some symptoms not present at the moment of enrollment, which supports the discriminative capacity of the questionnaire. Fifth, the high adherence rate should be interpreted taking into account that families received prepackaged doses of medication to take at home, there was no control of empty packets, and there was no placebo in dexamethasone arm. In addition, adherence was self-reported, and we were reliant on the accuracy of their reporting for this outcome, with no independent validation.

Sixth, as commented in the discussion, we included patients aged as young as 12 months in whom the diagnosis of asthma is more uncertain. This population may not respond completely to corticosteroids, although this aspect is still controversial.[38-42] Seventh, subgroup analysis was not preplanned and not completely powered for the findings. Finally, children with critical or life-threatening asthma exacerbations in which greater doses of intravenous steroids are recommended were excluded from the study. Patients aged between 15 and 18 years were not included as they are not managed in our ED. For this reason, our findings should not be extrapolated to this population.

To conclude, two doses of dexamethasone were not inferior to a 5-day course of prednisone/prednisolone in children with mild-to-moderate asthma exacerbation treated in the ED setting. Therefore, this adds evidence for the use of dexamethasone for mild-to-moderate asthma exacerbations. The use of validated patient-oriented measures supports reproducibility of results focused on family-centered care. These findings are not applicable to patients with severe asthma attacks. ■

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Table III. Primary outcome in post-hoc selected subgroups of interest.

Variables	Dexamethasone group	Prednisone group	*P*
Patients <2 y (n = 117)			
PACT at day 7	32/56 (57.1%) 95% CI 56-79	42/61 (68.9%) 95% CI 44-69	ns
ARQoL* day 7	79.4 (17.1)	75.3 (21.5)	ns
First asthma episode (n = 102)			ns
PACT at day 7	26/53 (49%) 95% CI 36-62	31/49 (63.2%) 95% CI 49-75	
ARQoL*day 7	79.9 (15.4)	81.1 (15.2)	ns
With maintenance treatment (n = 129)			ns
PACT at day 7	42/67 (62.7%) 95% CI 50-73	40/62 (64.5%) 95% CI 52-75	
ARQoL* day 7	77.2 (14.6)	72.6 (20.4)	ns
PS <3 at arrival (n = 119)			ns
PACT at day 7	35/59 (59.3%) 95% CI 46-70	36/60 (60.0%) 95% CI 47-71	
ARQoL* day 7	78.5 (16.2)	79.1 (16.9)	ns
PS >3 at arrival (n = 438)			ns
PACT at day 7	124/222 (55.9%) 95% CI 49-62	125/216 (58%) 95% CI 51-64	
ARQoL* day 7	80.4 (17.0)	77.4 (18.9)	ns
OU admission (n = 110)			ns
PACT at day 7	34/57 (59.6%) 95% CI 50-75	32/53 (60.4%) 95% CI 46-72	
ARQoL* day 7	76.3 (18.3)	74 (20.5)	ns
Further systemic steroids administered (n = 38)			ns
PACT at day 7	16 (72.7%) 95% CI 51-86	13 (81.2%) 95% CI 57-93	
ARQoL* day 7	62.6 (25)	66.2 (23.2)	ns

OU, observation unit.
*Values are expressed as mean ± SD.

Table IV. Baseline characteristics of patients who received further doses of steroids

Variables	Dexamethasone group (n = 22)	Prednisone group (n = 16)	*P*
Sex, male	14 (63.6%)	10 (62.5%)	ns
Age, y*	6.5 (3.7)	3.9 (3.0)	<.05
Medical history			
Asthma	21 (95.4%)	13 (81.2%)	ns
Allergies	6 (27.2%)	3 (18.7%)	ns
Atopic dermatitis	4 (18.1%)	3 (18.7%)	ns
Maintenance treatment	6 (27.2%)	3 (18.7%)	ns
Exacerbation characteristics			
$\beta_2$agonist in previous 24 h	19 (86.3%)	10 (62.5%)	ns
PS at arrival*	4.5 (1.4)	5.1 (1.0)	ns
O_2 sat*	92.1 (19.2)	93.9 (2.7)	ns
Supplemental oxygen	10 (45.4%)	9 (56.2%)	ns
>3 doses of β_2-agonist in ED	7 (31.8%)	4 (25%)	ns
Ipratropium bromide	11 (50%)	11 (68.7%)	ns
PACT at arrival			
Persistent symptoms	13 (59%)	8 (50%)	ns
ARQoL at arrival*	75.4 (18.6)	80.8 (12.7)	ns

ARQoL range is 0-100; PACT is expressed as a percentage.
*Values are expressed as the mean ±SD.