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Spirometry and PRAM severity score changes during pediatric acute asthma exacerbation treatment in a pediatric emergency department

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Abstract

Objectives—To examine time-dependent changes of spirometry (percent-predicted FEV₁[%FEV₁]) and the Pediatric Respiratory Assessment Measure (PRAM) during treatment of acute asthma exacerbations.

Study design—We conducted a prospective study of participants ages 5–17 years with acute asthma exacerbations managed in a Pediatric Emergency Department. %FEV₁ and the PRAM were recorded pretreatment and at 2 and 4 hours. We examined responses at 2 and 4 hours following treatment and assessed whether changes of %FEV₁ and of the PRAM differed during the first and second 2-hour treatment periods.

Results—Amongst 503 participants, median [IQR] age was 8.8 [6.9, 11.4], 61% were male and 63% African-American. There was significant mean change of %FEV₁ during the first (+15.4%; 95% CI 13.7, 17.1; P<0.0001) but not during the second 2 hour period (+1.5%; 95% CI –0.8, 3.8; P=0.21), and of the PRAM during the first (–2.1 points; 95% CI –2.3, –1.9; P<0.0001) and second (–1.0 point; 95% CI –1.3, –0.7; P<0.0001) 2 hour periods.

Conclusions—Most improvement of lung function and clinical severity occur in the first two hours of treatment. Amongst pediatric patients with acute asthma exacerbation the PRAM detects significant and clinically meaningful change of severity during the second 2-hours of treatment, whereas spirometry does not. This suggests that spirometry and clinical severity scores do not have similar trajectories and that clinical severity scores may be more sensitive to clinical change of acute asthma severity than spirometry.

Keywords

Asthma; spirometry; pulmonary function tests; pediatrics; PRAM score

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INTRODUCTION

Asthma management guidelines recommend percent-predicted forced expiratory volume in 1-second (%FEV₁) by spirometry or peak expiratory flow measurement to assess severity and response to treatment during acute exacerbations.(1;2)However, spirometry frequently is not available or cannot be obtained on pediatric patients during these episodes, and PEF may not accurately measure lung function during exacerbations.(3–5)Acute asthma severity scores can be obtained on all patients, including young children. Amongst proposed scores, the Pediatric Respiratory Assessment Measure (PRAM) has been validated for assessing acute asthma exacerbation severity.(6–8)For validation the PRAM developers used respiratory resistance measured by forced oscillation as the criterion standard. Further evidence that an acute severity score provides clinically meaningful information comparable to %FEV₁ may be informative for both clinical care and expert asthma guideline development.

There is limited information on the changes of %FEV₁ or the PRAM during treatment for acute asthma exacerbations in the emergency department.(9;10) Greater knowledge of these time-dependent changes might better inform decision making and improve resource utilization.

Our objective was to examine whether changes of %FEV₁ and the PRAM during the first 2 hours of treatment differed from those during the second 2 hours of treatment in pediatric patients with acute asthma exacerbations.

MATERIALS AND METHODS

Study Participants

This study was undertaken as part of an ongoing, prospective investigation of participants with acute asthma exacerbations in an urban, academic children's hospital emergency department (PED).(11)Between the hours of 7am and 10pm, we recruited patients ages 5 to 17 years who had doctor-diagnosed asthma and signs or symptoms of an asthma exacerbation,(12) were treated with systemic corticosteroid (CCS) and inhaled albuterol by the clinical team.

We excluded participants who had been treated with systemic CCS prior to presentation because of possible interference with the rate of change of %FEV₁ and PRAM during the first 4 hours of treatment in the PED. We also excluded participants who were previously enrolled or who had clinical or radiographic evidence of pneumonia or other reason for pertinent signs and symptoms. Asthma assessment and treatment in our PED follows a collaborative protocol based on expert consensus guidelines.(1;13)The clinical team made all management decisions and was blind to the results of our testing. The Institutional Review Board approved the study (protocol #080058). Written informed consent was obtained from a parent or guardian of each participant and written assent or consent, as appropriate, from each participant. The principal investigator (DHA) had full access to all data for the study and takes responsibility for the integrity of the data and accuracy of the analyses.

Measurements

A dedicated research assistant recruited and enrolled participants and was trained in spirometry performance and other study procedures.(11) Study data were acquired at three time points: pretreatment (before systemic CCS and albuterol treatment) and again at 2 and

4 hours after CCS administration if the participant remained in the PED at those times. All data were entered into a secure online database.(14)

The PRAM was developed by Chalut, Ducharme and colleagues and has face and criterion validity in pediatric patients with acute asthma exacerbations.(6;7) The PRAM is comprised of suprasternal and scalene muscle retractions, air entry, wheezing, and oxygen saturation with a score range of 0 to 12 points, 12 being the greatest severity (Table 1). Components of the PRAM were recorded separately, and scores were calculated electronically.

All participants present at each time point were asked to perform spirometry. We used a MicroDirect MicroLoop spirometer (Micro Medical, Kent, England),calibrated daily using a 3-liter syringe. A nose clip was applied, and we instructed each participant to perform FVC maneuvers in accordance with American Thoracic Society (ATS) and European Respiratory Society (ERS)spirometry standards.(15;16)

Some participants could not perform 3 FVC maneuvers at each time point that met full ATS criteria. Some of these trials included at least one FVC maneuver with volume-time and flow-volume curves meeting ATS criteria for start-of-test and end-of-test. A standing pulmonary function test oversight committee reviewed these trials and determined whether the data was of high quality and should be included for analysis.(11) The committee is comprised of a certified pediatric pulmonary function technician and a pulmonary physiologist. Each member recorded their determination of whether a non-ATS trial should be retained for analysis based on the volume-time and flow-volume curves and spirometry calculations of the available FVC maneuvers. Each member was blinded to the other's determination and to all other participant data. A trial was included if both members determined independently that it was high quality.

The observational outcomes examined were time-based differences in the proportionate change of %FEV₁ and of the absolute change of the PRAM from pretreatment to 2 hours (1st time period) and from 2 to 4 hours (2nd time period).

Statistical Analysis

Descriptive statistics are presented as mean (SD) or median [IQR] as appropriate. Race and ethnicity were identified by the parent and categorized in accordance with NIH guidelines. (17) Some participants who could not perform pretreatment spirometry were able to do so at later time points, and some who were able to do so before treatment were not present at later time points. With these considerations in mind, %FEV₁ values are presented for all studies available at each time point (all available data) as well as for those participants who provided studies at all three time points (complete data).

Using all available data, we performed a multivariable generalized least square regression analysis that accounted for the correlation of the repeated measures of %FEV₁.(18)Models were adjusted for the *a priori* specified covariates age, gender, race, continuous albuterol treatment during each 2 hour treatment period, and pretreatment %FEV₁ or PRAM as appropriate. Time dependent changes are reported using beta coefficients with 95% confidence intervals (CI). The coefficient indicates absolute change where the null value is zero and is considered statistically significant when the corresponding 95% CI does not include zero. These effect sizes estimate the changes at 2hours from pretreatment and at 4 hours from 2 hours. These repeated measures regression analyses were also performed for absolute change of the PRAM during the two treatment periods. A two-sided significance level of 0.05 was used for all statistical inferences. Analyses were performed using R-software v. 2.12.1.(19)

RESULTS

During the study period, April 8, 2008, to March 10, 2011, 806 patients who met inclusion criteria were approached for study participation, 770 were enrolled, 267 were excluded because of duplicate enrollment, prior treatment with systemic CCS, or pneumonia, and 503 are included for analyses (Figure 1). The demographic and asthma characteristics of participants are presented in Table 2.

Before treatment 303 (60%) participants performed full ATS criteria spirometry, and an additional 28 (6%) performed high quality studies. Full ATS or high quality studies were performed by 229 (70%) of those present at 2 hours and by 105 (71%) of those present at 4 hours (Tables 3 and 4). These tables include all available data as well as complete data, as defined in the Statistical Analysis section above.

There was statistically and clinically significant improvement %FEV₁ during the first 2 hour (adjusted mean difference: [+15.4%; 95% CI 13.7, 17.1; P<0.0001]) but not during the second 2 hour period (+1.5%; 95% CI -0.8, 3.8; P=0.21) in the multivariable repeated measures analyses adjusted for age, gender, race, continuous albuterol treatment, and pretreatment %FEV₁ (Figure 2). PRAM values are displayed in Table 5. There were statistically and clinically significant improvements in PRAM scores after the first (-2.1 points; 95% CI -2.3, -1.9; P < 0.0001) and second (-1.0 point; 95% CI -1.3, -0.7; P < 0.0001) 2 hour periods after adjustment for age, gender, race, continuous albuterol treatment, and pretreatment PRAM score.

DISCUSSION

The results of this study suggest that, amongst pediatric patients with acute asthma exacerbations, most clinically meaningful improvements of lung function measured using %FEV₁ and a clinical severity score can be expected to occur in the first 2 hours of treatment. Specifically, we observed an overall 15.3% increase of %FEV₁ during the first 2 hour treatment period and none during the second, and a 2 versus 1 point improvement of the PRAM. One might speculate that the mechanisms for this may include that activation of pulmonary β_2 -receptors is rapid and complete and that bronchodilation plateaus after the first 2 hours. As well, β_2 -receptor desensitization may have occurred in some participants during this period of sustained activation.(20;21) These findings are clinically relevant to practitioners in emergency departments and other acute care settings and may facilitate efficient and appropriate decision-making.

Moreover, improvement of the PRAM was noted after both the first and second 2-hour treatment periods. That continued improvement of this bedside severity score was detected, whereas that of %FEV₁ was not, may have resulted from bias as a result of missing %FEV₁ values, noted below.,

Although expert consensus guidelines continue to recommend %FEV₁ measurement for acute asthma assessment, this measure is frequently not available in acute care settings and not possible in young children or those in respiratory distress. (1)) Langan and Spiro obtained reproducible spirometry during exacerbations in 73% of 34 children with median age 12 years, and our participants achieved a rate of 60% (median age 8.8 years).(3) As such, a substantial proportion of patients are not able to perform spirometry during exacerbations.

We believe our findings also support the value of validated, effort-independent, bedside measures of acute asthma severity because these measures can be obtained in all patients and because they may better represent the clinically severity of children in respiratory

distress than spirometry. There may also be clinical improvement that is not fully captured by spirometry. The PRAM is effort independent and can be obtained on all patients whereas spirometry requires considerable cooperation and coordination on the part of the patient. Although our findings indicate that a bedside acute severity score may be of greater use to clinicians in the emergency department, spirometry nonetheless provides an objective measure of lung function that is of great value in other clinical settings.

Limitations of our study include missing spirometry data that may introduce bias as some subjects were either unavailable because of disposition decisions or unable to perform spirometry at each time point. These participants may have had different asthma characteristics than those available or able to perform testing.(22) An additional limitation is the infrequency of PRAM scores over 8 in our cohort. This resulted from the infrequency of assigning 2-points for scalene muscle contractions or 3-points for completely absent breath sounds. This finding is at variance with that of Chalut, Ducharme and colleagues, who noted that all 5 components of the score contributed to the PRAM in their derivation and validation studies, although scalene muscle use was noted in only 2% of participants in the PRAM derivation study.(6;7) Notwithstanding the infrequency of scalene muscle use, significant and clinically meaningful change was noted for the PRAM during both the first and second 2-hour treatment periods.

In conclusion, our findings that most improvement of lung function and clinical severity occur in the first two hours of treatment suggests that disposition decisions for the pediatric patient with an acute asthma exacerbation can generally be made within 2 hours following initiation of systemic CCS and inhaled albuterol treatment. Equally important, this data suggests that spirometry and clinical measures of disease severity do not have similar change trajectories, and that clinical assessment tools may be more sensitive to change of severity. Although their improvement trajectories differ, spirometry and clinical measures of disease severity may both be important in assessing disease outcomes because they measure different physiological and clinical domains of acute exacerbation severity. This knowledge may improve resource utilization and decrease the burden of this illness on patients and families. In addition, expert management guidelines for acute asthma might consider the PRAM in place of FEV₁ or PEFr testing for acute pediatric asthma assessment.

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ABBREVIATIONS

CCS	Corticosteroid
%FEV ₁	Percent-predicted forced expiratory volume in 1-second
PRAM	Pediatric Respiratory Assessment Measure

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Figure 1.

^aOverall population of patients presenting to pediatric emergency department with final diagnosis of asthma exacerbation during study period

^bNot mutually exclusive

^cAble to perform spirometry meeting full ATS criteria or of high-quality as n (%) of participants available at time point

Figure 2.

% FEV₁ in participants available for testing who could perform spirometry before treatment (n = 331) and after 2-hours (n = 229) and 4-hours (n = 105) of treatment with continuous albuterol. Error-bars represent adjusted mean value bounded by 95% confidence intervals from multivariable model. Values for percent change of %FEV₁ are at top.

Table 1

Pediatric Respiratory Assessment Measure (PRAM) severity score components and values assigned by severity of each component^(1,2)

	Component values			
	0	1	2	3
Signs				
Suprasternal retractions	No		Yes	
Scalene contraction	No		Yes	
Air entry ^a	Normal	Decreased at bases	Widespread decrease	Absent or minimal
Wheezing ^a	Absent	Expiratory only	Inspiratory and Expiratory	Audible without stethoscope or silent chest
O ₂ saturation	95%	92–94%	< 92%	

^aMost severe side is used for rating if asymmetry is noted between right and left lung.

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TABLE 2**Demographic and Asthma Characteristics of Study Participants**

Characteristic	Study Sample (N = 503)
Demographic	
Age, years	8.8 [6.9, 11.4]
Male	306 (61)
Race ^a	
African-American	315 (63)
White	187 (37)
Hispanic ethnicity ^a	37 (7)
Medicaid insurance	319 (63)
Asthma	
Currently using inhaled CCS	193 (38)
Prior PICU admission for asthma	90 (18)
Prior ETI for asthma	20 (4)
PED disposition	
Discharge to home	429 (85)
Admit to floor bed	55 (11)
Admit to PICU	19 (4)

Data are presented n (%) or median [IQR] where IQR = interquartile range.

CCS = corticosteroid; PICU = pediatric intensive care unit; ETI = endotracheal intubation

^aRace and Hispanic ethnicity are categorized in accordance with NIH guidelines and are not mutually exclusive.

TABLE 3FEV₁ for participants ages 5 to 17 years with acute asthma exacerbations

	Absolute value, %FEV ₁		
	Pretreatment	2 hours	4 hours
All available data ^a	52 [36, 73]	65 [47, 80]	60 [44, 76]
Complete data ^b	37 [26, 47]	54 [42, 63]	55 [43, 71]

Values are median [IQR]

^aAll values meeting ATS or high quality spirometry criteria available at each time point (pretreatment, n = 331; 2hr, n = 229; 4hr, n = 105)^bValues for only those participants who were available and able to provide ATS or high quality criteria spirometry pretreatment and at 2 and 4hr (n = 51)

TABLE 4Proportionate change of %FEV₁ values for participants aged 5 to 17 years with acute asthma exacerbations

	Proportionate change, %FEV ₁	
	1 st 2 hours	2 nd 2 hours
All available data ^a	29 [10, 65]	4 [-3, 14]
Complete data ^b	34 [12, 72]	5 [-6, 16]

Values are median [IQR]

^a All values meeting ATS or high-quality spirometry criteria available at each time point (pretreatment and 2 hours, n = 199; 2 and 4 hours, n = 98)^b Values for only those participants who were available and able to provide ATS or high quality criteria spirometry pretreatment and at 2 and 4hr (n = 51)

TABLE 5

Pediatric Respiratory Assessment Measure (PRAM) severity score values for participants aged 5 to 17 years with acute asthma exacerbations

	Assessment time point during treatment		
	Pre-treatment ^a	2 hrs ^b	4 hrs ^c
PRAM value	3 [1, 5]	1 [0, 4]	1 [0, 2]
	1 st 2 hours ^b	2 nd 2 hours ^d	
Change of PRAM	-2 [-4, -1]	-1 [-3, 0]	

Values are median [IQR]

Participants available for PRAM measurement at each time point or for each time interval: ^a503; ^b 327; ^c146; ^d146