Direct Observed Therapy of Inhaled Corticosteroids for Asthma at School or Daycare

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Background: Poor adherence with inhaled corticosteroid (ICS) medication is common in the pediatric population and can result in poor asthma control with increased frequency of asthma-related complications. The purpose of this study was to determine whether or not the initiation of ICS administration twice per day at school/daycare in patients with poor medication adherence at home improves asthma health care outcomes.

Methods: We retrospectively selected patients followed by our Pediatric Pulmonology Clinic who had poorly controlled asthma and had been assigned to receive ICS twice daily at school/daycare due to poor adherence with ICS therapy. We analyzed the number of short courses of oral corticosteroids, hospital admissions, emergency department visits, and intramuscular methylprednisolone administrations for asthma exacerbations for the year before and after the intervention. The Wilcoxon signed rank test with continuity correction was used in the primary analysis.

Results: Forty-nine patients who met the inclusion criteria were identified, but only 40 actually started the intervention. The number of oral corticosteroid courses per year decreased from 1.35 ± 1.1 before the intervention to 0.68 ± 1.2 ($P=0.008$) postintervention, hospital admissions per year decreased from 0.45 ± 0.7 to 0.10 ± 0.3 ($P=0.006$), emergency department visits per year decreased from 0.55 ± 0.8 to 0.28 ± 0.6 ($P=0.084$), and intramuscular repository methylprednisolone injections per year for asthma exacerbations decreased from 0.20 ± 0.4 to 0.10 ± 0.3 ($P=0.23$).

Conclusion: These results indicate that school/daycare administration of ICS may be an effective option to improve indicators of asthma exacerbations in children with poor adherence to ICS at home.

Keywords: adherence, pediatric asthma, direct observed therapy, inhaled corticosteroid therapy

Introduction

THE PREVALENCE OF ASTHMA in the pediatric population is estimated to be 9% in the United States, with asthma medication adherence rates ranging from 30% to 70%.^{1,2} The medical consequences for poor adherence to inhaled corticosteroids (ICSs) in the setting of asthma can include poor asthma control (resulting in the frequent need for systemic corticosteroid courses, emergency department visits, and hospitalization), frequent absence from school, missed workdays/lost wages for parents, inability to participate in sports, and on rare occasion death.¹ ICSs are critical in controlling persistent asthma. Using them correctly and at the recommended frequency is necessary for optimal medication effectiveness.

A previous investigation into directly observed administration of ICSs in school suggested that school administration is of benefit for asthma symptom control.³ However,

this prior study included only children 3–10 years of age and only students in 1 school district. Another study had similar favorable conclusions but only involved students of 1 specific school.⁴ A third study included students of numerous schools, but only examined the use of a dry-powder budesonide inhaler that was administered once daily.⁵ Our study is unique because it examines pediatric patients over a broad age range who attended multiple schools and received 2 doses per day in school.

We hypothesized that initiation of ICS administration twice per day at school/daycare in patients with poor medication adherence at home improves asthma outcomes. The primary objective of this study is to test this hypothesis.

Materials and Methods

We conducted a retrospective case–control study on patients followed by our pediatric pulmonology clinic who had

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been assigned to receive ICSs twice daily at school/daycare due to poor adherence with ICS therapy at home. We chose a retrospective case-control study model as the intervention being studied had already been undertaken with reliable data available from before and after the intervention for statistical analysis of the effectiveness of the intervention on patient outcomes. We chose reliable markers (frequency of systemic corticosteroid use, emergency room visits, and hospitalizations) that were objective, quantifiable, and could be statistically compared before and after the assessed intervention.

We obtained approval from the University of Florida-Gainesville Institutional Review Board (IRB) for this study to be conducted with a waiver of informed consent (IRB No. 201500978). We examined the charts of all patients known to the study investigators who met the criteria for inclusion. To be included in the study, the patient had to be <18 years of age and assigned to receive their prescribed twice-daily ICSs. We specifically studied patients who used ICS formulations with twice-daily dosing. Patients who were taking an ICS with once-daily dosing were not examined in this study. The parents had to agree to administration at school/daycare Monday through Friday and also to give the medication at home on Saturdays, Sundays, and holidays. Selection was based on poor adherence with ICS medication at least 1 year before data collection.

Poor adherence was determined by assessment of refill histories collected from the pharmacies utilized by the patients and by assessment of pulmonary function testing data if available. The school/daycare was called before the intervention being conducted for each patient to determine whether or not the nurse, health aid, or office staff was willing to supervise or assist with administration of the medication. A follow-up letter was sent describing the technique, quantity, and frequency of ICS that was to be given. The recommended ICS doses were given upon arrival to school/daycare and again before leaving toward the end of the day. Samples were provided for the parents to administer to the patients on Saturdays, Sundays, and holidays as many insurance plans will not cover separate inhalers for both school and home.

Each patient served as his or her own control. The data were collected from our electronic medical record. For each patient, it consisted of the number of systemic oral corticosteroid courses, the number of hospital admissions due to asthma exacerbation, the number of emergency department visits due to asthma exacerbation, and the number of intramuscular repository methylprednisolone administrations that occurred in the year before the month when the ICSs were assigned to be administered at school/daycare. The use of methylprednisolone is routine in our clinic when the prescriber suspects that the parents will not or have not followed through with the oral regimen. The dose for this intervention is 7.5 mg/kg to a maximum of 400 mg. The interventional data consisted of 1 year after the month when the ICSs were assigned to be administered at school/daycare compared with the control period, 1 year before the intervention. The month during which ICSs were assigned to be administered at school/daycare was not included due to the time required to set up the intervention and to allow time for the ICSs to have optimal effect.

We used the "R" statistical software (version 3.4.4) for the statistical analysis.⁶ Shapiro-Wilk testing for normality indi-

cated that our data were not normally distributed ($P < 0.05$), so we performed Wilcoxon signed rank tests with continuity correction to determine whether or not there were statistically significant differences in the examined indicators of asthma outcomes before and after the intervention. The threshold of statistical significance and rejection of the null hypothesis was considered to be a P value of <0.05 . Data are presented as mean $\pm$ SD, unless otherwise noted.

Results

We initially included 49 patients in the study. However, we discovered on chart review that there were 9 patients initially included who did not actually start the ICSs at school as prescribed, so we did not include them in the final statistical analysis. We collected available patient demographic and baseline information, including patient ages at the start of the interventional period, race/ethnicity, and comorbidities. An African American predominance was noted with a wide range of ages and patient comorbidities (Table 1). All patients included used a formulation of ICS with twice-daily dosing (Table 2). For the 40 patients who had started the ICSs at school as prescribed, the number of oral corticosteroid courses per year decreased from 1.35 ± 1.1 before the intervention to 0.68 ± 1.2 ($P = 0.008$) postintervention, hospital admissions per year decreased from 0.45 ± 0.7 to 0.10 ± 0.3 ($P = 0.006$), emergency department visits per year decreased from 0.55 ± 0.8 to 0.28 ± 0.6 ($P = 0.084$), and intramuscular repository methylprednisolone administrations per year for asthma exacerbations decreased from 0.20 ± 0.4 to 0.10 ± 0.3 ($P = 0.23$) (Fig. 1). There was not a statistically significant difference between the number of pediatric intensive care unit admissions in the year before the intervention (0.18 ± 0.65) as compared with the year after the intervention (0.05 ± 0.58) ($P = 0.15$). Also, there was not a statistically significant difference between the total length of time spent in the hospital in hours in the year before the intervention (63.7 ± 50.9) as compared with the year after the intervention (21.3 ± 39.4) ($P = 0.07$) for those who were hospitalized during either study period.

Discussion

The statistically significant decreases in the average number of oral systemic corticosteroid courses and hospital admissions due to asthma exacerbations suggest that the initiation of direct observed therapy at school/daycare of

TABLE 1. PATIENT DEMOGRAPHICS AND COMORBIDITIES

Median age in years (range in years)	10 (1.5–15)
Race (n)	
African American	33
White	6
Hispanic	1
Comorbidity (n)	
Allergies	40
Eczema	29
Obstructive sleep apnea	18
Gastroesophageal reflux disease	16
Obesity	11

TABLE 2. TYPE AND DOSE OF INHALED CORTICOSTEROID OR INHALED CORTICOSTEROID/LONG-ACTING BETA AGONIST COMBINATION USED

Type and dose	Start of interventional period (n)	End of interventional period (n)
Fluticasone propionate		
44 mcg/puff 2 puffs twice daily	10	9
110 mcg/puff 2 puffs twice daily	8	4
Beclomethasone dipropionate		
40 mcg/puff 2 puffs twice daily	2	1
80 mcg/puff 2 puffs twice daily	5	5
Mometasone furoate		
220 mcg/puff 1 puff twice daily	2	2
Budesonide and formoterol fumarate dehydrate		
80–4.5 mcg/puff 2 puffs twice daily	1	3
160–4.5 mcg/puff 2 puffs twice daily	4	4
Fluticasone propionate and salmeterol xinafoate		
115–21 mcg/puff 2 puffs twice daily	4	6
230–21 mcg/puff 2 puffs twice daily	0	2
Fluticasone propionate and salmeterol inhalation powder		
250–50 mcg/puff 1 puff twice daily	2	1
Mometasone furoate and formoterol fumarate dehydrate		
100–5 mcg/puff 2 puffs twice daily	2	1
200–5 mcg/puff 2 puffs twice daily	0	1

ICS improves control of persistent asthma and reduces the frequency of asthma exacerbations. These findings support our hypothesis. The decreases in the average number of emergency department visits and intramuscular repository methylprednisolone administrations likely did not reach statistical significance because the sample size was too small to have sufficient power to detect small differences in the presence of the observed variability. This therapy is uncommon since we reserve it for patients who have not re-

sponded to a short course of oral steroids or in those who it is unlikely that they will be given an oral course if prescribed, consistent with current evidence.⁷

The results of this study are consistent with the conclusions of prior studies examining the effect of administration of ICS therapy at school on asthma control.^{3–5} Our study increases the generalizability of these conclusions to a larger portion of the pediatric population and confirms that these conclusions also apply to patients who use ICSs that require

FIG. 1. Mean and standard deviation of the number of clinical interventions required per patient per study period for all 40 patients who met the criteria for analysis (including those with zero clinical interventions).

twice-daily dosing. Strengths of this study include that each patient served as his/her own control. We were also able to examine a broad age range of pediatric patients, attending different schools in multiple school districts, which increases the generalizability of the conclusions.

This study does have limitations, however. We were not able to verify whether or not each patient continued to receive ICSs for the remainder of the first year after initiation of the intervention, a limitation of the retrospective study design. A future prospective study assessing whether or not there is a correlation between duration of direct observed ICS therapy at school and improved patient outcomes is indicated. Also, in determining the number of oral and intramuscular steroid courses, the number of hospitalizations, and the number of emergency department visits that occurred for each patient, we were only able to review the patient charts that were present at our own institution. Thus, we were unable to determine whether or not any patients received systemic corticosteroid courses from providers outside our institution, were hospitalized for asthma exacerbation, or went to the emergency department for asthma exacerbation at institutions that were not directly using our electronic medical record.

We were not able to consistently determine from chart review why 9 patients did not actually start the ICS at school per the study protocol due to the retrospective nature of the analysis. It is unlikely that the parents began giving the medication at home more consistently. It was also noted that 9 patients had the strength of their asthma controller medication stepped up, 3 patients had the strength of their asthma controller medication stepped down, 1 patient changed to a different brand of asthma controller medication of equivalent strength and dose, and 27 patients had no change in their asthma controller medication brand or dose during the intervention period. This is a possible confounding factor in our analysis. These weaknesses commonly occur in retrospective chart reviews. In addition, we had a relatively small number of study subjects.

Potential limitations to the school-based direct observed therapy for ICS administration include potential lack of school nurse willingness to participate (school nurses in 2 of 18 districts in our area declined participation) and in the inability of children to receive the ICS therapy during school vacations and holidays. Insurance companies may not cover the additional inhaler needed to administer the ICSs at both home and school, and not all medical centers may have access to samples that can be given for the family to administer at home on days when the child is not in school. Direct observed therapy can, however, sometimes be arranged to be conducted during summer school and summer camps. It is also possible that some families may increase adherence at home if the patient has a positive clinical response to direct observed therapy while in school. The Hawthorne effect, which could result in improved adherence to not only ICSs but also to household environmental optimization efforts by the family, improved adherence to medications for asthma control other than ICSs, and earlier response by the family in response to asthma exacerbation symptoms due to the families being under direct observation during the interventional period, is another possible confounding factor as there was not a period of observation after direct observed therapy was ended.

The results of this retrospective chart review suggest that direct observed therapy at school/daycare is likely to im-

prove asthma control in patients with poor adherence to ICS therapy. It is likely to decrease health care costs for these patients. Since the frequency of death from asthma is decreased with increased ICS adherence, this intervention could potentially save a life.⁸

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Disclaimer

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Author Disclosure Statement

None of the authors have a conflict of interest to disclose.

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