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Factors affecting the use of salbutamol before hospital admission in children with asthma exacerbation

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Abstract
Background: Early home intervention for asthma exacerbation (AE) in children is associated with more favorable outcomes. Inhaled short-acting beta$_2$ agonists (SABA) are the cornerstones of AE treatment.
Objectives: We aimed to determine what proportion of parents administered salbutamol to their children to treat asthma exacerbation at home, and the factors affecting the decision to administer the medication. Additionally, we also aimed to examine the parents' level of knowledge regarding salbutamol use.
Methods: Asthma patients who were admitted to pediatric allergy outpatient clinics due to AE were included in the study. Parents' knowledge related to home salbutamol use was evaluated using a questionnaire. Modified Pulmonary Index Score was used to evaluate AE severity.
Results: The study included 177 children (64.4% males) with a median age of 6.16 years. Of these, 86 patients (48.6%) had not administered salbutamol before hospital admission, and parents of 69 (80%) patients stated that they knew salbutamol should be administered but they did not want to administer it without consulting a doctor. Of the 91 patients who had used salbutamol before hospital admission, 28 (30.7%) had administered the incorrect dose, 2 (2.2%) used the incorrect technique, and 9 (9.9%) had the incorrect dose and incorrect technique. In multivariate logistic regression analysis, history of hospitalizations (odds ratio [OR]: 6.35; 95% confidence interval [CI]: 3.07-13.9; P < 0.001), history of more than five exacerbations (OR: 4.51, 95%CI: 1.94-10.48; P < 0.001), and presence of sputum (OR: 2.54; 95%CI: 1.10-5.87; P = 0.028) were the main predictors of salbutamol use.

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Conclusion: Asthma patients and their parents should be better educated and actively encouraged on the use of SABA at home during an AE.

Introduction

Asthma is a chronic childhood disease that affects approximately 14% of children globally, with a rising prevalence worldwide.[1] Acute asthma exacerbations are common in children with asthma and are a major factor responsible for morbidity and even mortality.[2] Acute asthma exacerbations and poor asthma control are causes of pediatric emergency department visits, hospitalizations, missed school days, and low academic success among school-aged children.[3-5]

Environmental monitoring, trigger avoidance, and home symptom self-management are critical for preventing severe exacerbations.[4-5] According to the Global Initiative for Asthma (GINA), a key to initial home management of asthma exacerbations in children is providing a written action plan to enable the child's family members and caregivers to recognize worsening asthma and initiate treatment.[6]

Inhaled short-acting beta$_2$ agonists (SABA) are the cornerstones of treatment for patients with acute asthma.[7,8] The initial treatment for asthma exacerbations to be administered at home consists of inhaled SABA delivered using a mask or spacer.[6]

Children generally need assistance from family caregivers for asthma management.[4,5] Practices that promote early home intervention for children with asthma exacerbation are reported to be strongly associated with reduced risk of adverse outcomes.[9] Therefore, parents' level of knowledge about the management of asthma attacks (including SABA use) is important for this age group.

In this study, we aimed to determine what proportion of parents administered salbutamol to their children to treat asthma exacerbation at home before presenting to the hospital, and the factors affecting the decision to administer salbutamol at home. We also aimed to examine the parents' level of knowledge regarding the use of salbutamol.

Materials and Methods

This study was conducted in two different pediatric allergy and immunology outpatient clinics (Ankara and Malatya) between April 2017 and December 2018. Patients with a diagnosis of asthma who had been followed up for at least 1 year and presented to the pediatric allergy outpatient clinic with asthma exacerbation during the study period were included.

At the patient's first outpatient visit, parents were given a written asthma action plan including the specific signs of worsening asthma, the medications that should be initiated, and when and how to seek medical care.

At the patient's outpatient visit for asthma exacerbation, the patients were examined and a detailed history was taken. In the pediatric allergy and immunology clinics, in which our study was conducted, patients can be admitted to the outpatient clinic when they have complaints without going through the referral chain if they are already under follow-up in these clinics. The duration and characteristics of the symptoms presented during the current asthma exacerbation were recorded. The patient's age, gender, age at asthma diagnosis, follow-up period, medications used for asthma control, severity of asthma exacerbation, number of asthma exacerbations, and history of hospitalizations were also recorded. In addition, the parents' education level was recorded, and they completed a questionnaire regarding their knowledge and habits about using salbutamol before hospital admission. The questionnaire was created by the researchers of the present study (Table S1).

Written informed consent was obtained from the caregivers of all patients. This study was approved by the ethical review committee of Ankara Child Health and Diseases Hematology and Oncology Training and Research Hospital (EC number:2017-015).

Asthma diagnosis

Asthma was diagnosed according to the GINA criteria.[6] In patients under 5 years old, the diagnosis was based on the presence of recurrent symptoms (wheeze, cough, breathlessness, and nocturnal symptoms or awakenings) and risk factors for asthma development, with therapeutic response to asthma controller treatment.[6]

Assessment of asthma exacerbation severity

The severity of asthma exacerbation was evaluated using the modified Pulmonary Index Score (mPIS).[10] This scoring system assesses six factors (heart rate, respiratory rate, accessory muscle use, inspiratory-to-expiratory flow ratio, degree of wheezing, and oxygen saturation), with each factor graded on a scale of 0–3 points. The maximum score is 18, with mPIS scores of 6–9 points interpreted as moderate exacerbation and scores over 10 points as severe exacerbation.[10] The patients' mPIS was assessed by a physician at the time of hospital admission.

Spirometry

Spirometry was performed pre- and post-bronchodilator in older study participants who were able to comply with the American Thoracic Society standards.[11] The patients were seated in an upright position and at least three acceptable maneuvers were obtained. The best forced expiratory

volume in the first second (FEV_1) of these three trials was used. Testing equipment was calibrated daily to ensure accuracy and precision.

Statistical analysis

Statistical analysis was performed using SPSS version 22.0 statistical software package for Windows (IBM, Armonk, NY, USA). Continuous variables were expressed as means and standard deviation for normally distributed data and as median and interquartile range (IQR) for non-normally distributed data. The chi-square test was used to compare nonparametric data; the Mann-Whitney U test and independent samples t-test were used for the comparison of non-normally distributed continuous variables and normally distributed continuous variables, respectively. Logistic regression analysis was performed to determine the factors affecting salbutamol use. Factors with values of 0.20 or lower in univariate analysis were included in the multivariable analysis. The results were presented as odds ratio and 95% confidence interval. A value of $P < 0.05$ was considered statistically significant in all analyses.

Results

A total of 177 children (64.4% males) with a median age of 6.16 years (IQR: 3.64–8.56 years) were included in our study. The median follow-up period of the patients was 24 months (IQR: 18–42). Demographic characteristics of patients are given in Table 1.

Asthma controller drugs were used by 162 (91.5%) patients, while the remaining 15 did not regularly use a controller drug but used salbutamol as and when needed.

The median duration of symptoms before hospital admission was 2 days (IQR: 2–4 days). Admitting symptoms were cough in 161 patients (91%), wheezing in 63 (35.6%), sputum in 61 (34.5%), shortness of breath in 55 (31.1%), and fever in 32 patients (18.1%).

The parents of 86 patients (48.6%) had not administered salbutamol before hospital admission. Of these, 69 (80%) stated that they knew that salbutamol should be used but did not want to give the drug without consulting a doctor. The reasons cited by the parents for not giving salbutamol are shown in Figure 1.

The other 91 patients (51.4%) used salbutamol before hospital admission. When the factors associated with salbutamol use before hospital admission were evaluated, it was found that the group of patients that used salbutamol

Table 1 Demographic and clinical characteristics of the patients.

Sex, n (%)	
Female	63 (35.6)
Male	114 (64.4)
Age (years)	
Median (IQR)	6.26 (3.68–8.55)
Follow-up period (months)	
Median (IQR)	24 (15.5–42)
Symptom duration (days)	
Median (IQR)	2 (2–4)
Education level of mother, n (%)	
High school or higher	65 (36.7)
Education level of father, n (%)	
High school or higher	103 (58)
Number of asthma exacerbations, n (%)	
< 5	130 (73.4)
> 5	47(26.4)
Hospitalization history	
Yes	102 (57.6)
No	75 (42.4)
mPIS score	
Median (IQR)	4 (2–7)

IQR: Interquartile range; mPIS: Modified Pulmonary Index Score.

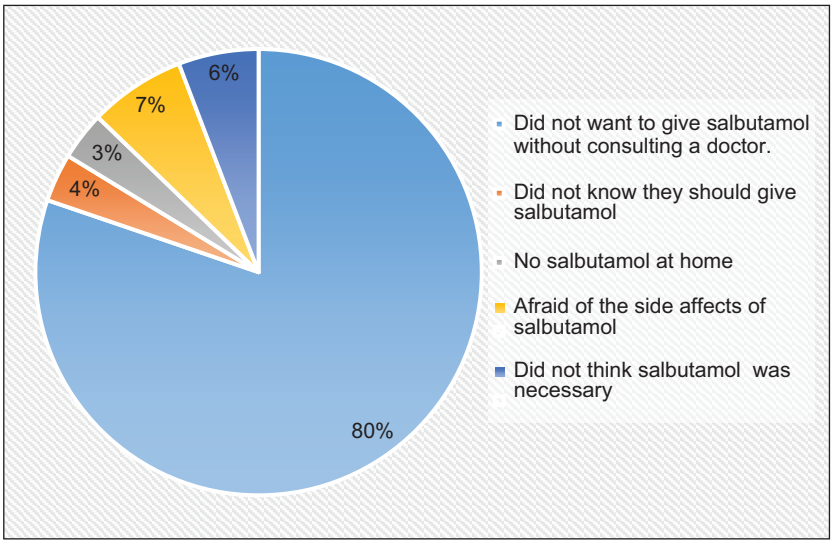

Figure 1 Parents' reasons for not administering salbutamol to their child during asthma exacerbation.

was significantly older (P = 0.023). The presence of cough (P = 0.001) and sputum (P = 0.032) was more common in salbutamol users. In addition, salbutamol users had longer symptom duration (P = 0.024) and follow-up time (P = 0.014), higher number of exacerbations (P = 0.002) and a higher prevalence of previous hospitalization (P < 0.001; Table 2). The rate of moderate and severe (mPIS > 6) asthma exacerbations was lower in salbutamol users than in patients who did not use salbutamol (P = 0.043; Table 2).

In univariate logistic regression analysis, a history of hospitalization, a history of more than five exacerbations, presence of cough or sputum, symptom duration longer than 2 days, and age older than 5 years were associated with using salbutamol. The high rate of moderate and severe (mPIS > 6) asthma exacerbation was associated with the non-usage of salbutamol in univariate analysis. In multivariate logistic regression analysis, history of hospitalization, sputum, and history of more than five exacerbations were significant predictors of salbutamol use. Fever was associated with the non-usage of salbutamol in both univariate and multivariate analyses (Table 3).

Of the 91 patients who received salbutamol before hospital admission, 58 (63.7%) used a spacer, 22 (24.2%) used a nebulizer, and 11(12.1%) used salbutamol metered-dose inhaler without a spacer. However, 28 (30.7%) of the 91 patients had administered the incorrect dose, 2 (2.2%) had used the incorrect technique, and 9 (9.9%) used both the incorrect dose and the incorrect technique. All children who took the incorrect dose of SABA were undertreated. As a result, only about 30% (n = 52) of our patients had used salbutamol with the correct dosage and technique before hospital admission. In the comparison of patients who had administered salbutamol with the correct dosage and technique with those who had not, it was found that the former group had a higher prevalence of previous hospitalization (P = 0.03; Table 4).

The parents of ninety-two (52%) patients stated that they had a nebulizer at home, and 22 (24.2%) of them stated that they used a nebulizer during the present asthma exacerbation. Eighteen (81.8%) of these 22 parents stated that they used the nebulizer as they considered it more effective, 2 (9%) used it on the doctor's recommendation, 1 (4.5%) because of its easy usage, and 1 (4.5%) because a salbutamol inhaler was not available at home. All parents stated that they applied the nebulizer mask fully adhered to their child's face.

Parents of 5 (208%) patients did not know when to administer salbutamol to their children, and 13 (7.3%) said that it was necessary to ask a doctor. The remaining 172 parents stated that salbutamol should be given when the child had shortness of breath (50.3%), cough (27.7%), wheezing (4%), shortness of breath and wheezing (4.5%),

Table 2 Comparison of the patients who used salbutamol and those that did not use salbutamol.

	Patients who used salbutamol (n = 91)	Patients who did not use salbutamol (n = 86)	P
Sex, n (%)			
Female	26 (28.6)	37 (43)	0.052
Male	65 (71.4)	49 (57)	
Age (years)			
Median (IQR)	7 (4.66-9.66)	4.9 (3-8.1)	**0.023**
Follow-up period (months)			
Median (IQR)	29 (18-48)	24 (12-36)	**0.024**
Symptom duration (days)			
Median (IQR)	3 (2-4)	2 (1-4)	**0.014**
Education level of mother, n (%)			
High school degree or higher	36 (39.6)	29 (33.7)	0.42
Education level of father, n (%)			
High school degree or higher	49 (53.8)	54 (62.8)	0.22
Hospital admission symptoms, n (%)			
Cough	89 (97.8)	72 (83.7)	**0.001**
Wheezing	36 (39.6)	27 (31.4)	0.25
Shortness of breath	32 (35.2)	23 (26.7)	0.2
Sputum	38 (41.8)	23 (26.7)	**0.036**
Fever	12 (13.2)	20 (23.3)	0.082
Number of asthma exacerbations, n (%)			
≤5	59 (64.8)	72 (83.7)	**0.002**
>5	32 (35.2)	15 (16.3)	
Hospitalization history n(%)	66	36	**<0.001**
mPIS score			
<6	67	51	**0.043**
≥6	24	35	

IQR: Interquartile range; mPIS: Modified Pulmonary Index Score.

Table 3 Predictors of using SABA before hospital admission by parents.

Parameters	Univariable			Multivariable		
	OR	95% CI	P	OR	95% CI	P
Age (> 5 years)	1.935	1.056-3.546	**0.033**	-	-	-
Symptom duration (>3 days)	1.858	1.023-3.375	**0.042**	-	-	-
Cough	9.401	2.081-42.473	**0.004**	-	-	-
Wheezing	1.430	0.770-2.658	**0.258**	-	-	-
Sputum	1.964	1.042-3.701	0.037	2.546	1.104-5.872	**0.028**
Dyspnea	1.486	0.781-2.825	**0.227**	-	-	-
Fever	0.501	0.228-1.101	0.085	0.344	0.131-0.906	**0.031**
Number of exacerbations (>5)	2.789	1.363-5.709	0.005	4.519	1.949-10.480	**0.000**
History of hospitalization	5.042	2.623-9.690	0.000	6.537	3.074-13.903	**0.000**
Exacerbation severity (mPIS ≥ 6)	0.522	0.277-0.984	**0.045**			

IQR: Interquartile range; mPIS: Modified Pulmonary Index Score.

Table 4 Comparison of the patients who used salbutamol at the correct dose and technique and those that did not use salbutamol at the correct dose and technique.

	Patients who used salbutamol at the correct dose and technique (n = 52)	Patients who did not use salbutamol at the correct dose and technique (n = 39)	P
Sex, n (%)			
Female	14 (27)	12 (30)	0.81
Male	38 (73)	27 (70)	
Age (years)			
Median (IQR)	7 (4.66-9.66)	4.9 (3-8.1)	**0.023**
Follow-up period (months)			
Median (IQR)	29 (18-48)	24 (12-36)	0.42
Symptom duration (days)			
Median (IQR)	3 (2-4)	2 (1-4)	0.25
Education level of mother, n (%)			
High school degree or higher	22 (37.2)	14 (35.9)	0.66
Education level of father, n (%)			
High school degree or higher	30 (57.6)	19 (48.7)	0.4
Hospital admission symptoms, n (%)			
Cough	51 (98)	38 (87.4)	0.83
Wheezing	23 (44.2)	13 (33.3)	0.38
Shortness of breath	14 (27)	18 (46)	0.07
Sputum	25 (41.8)	13 (33.3)	0.19
Fever	7 (13.4)	5 (12.8)	0.92
Number of asthma exacerbations, n (%)			
≤5	29 (55.7)	28 (71.8)	0.13
>5	23 (44.3)	11(28.2)	
Hospitalization history n (%)	26 (50)	10 (25.6)	**0.03**
mPIS score			
<6	37 (71)	30 (77)	0.63
≥6	15 (29)	9 (23)	

IQR: Interquartile range; mPIS: Modified Pulmonary Index Score.

shortness of breath and cough (4.5%), tachypnea (1.1%), and shortness of breath, cough, and wheezing (0.6%) Eighty-six parents (48.6%) commented that salbutamol should be administered in children using a metered dose inhaler with spacer, 80 (45.2%) with a nebulizer, 9 (5.1%) with a metered dose inhaler without a spacer, and 2 (1.2%) with either a spacer or a nebulizer. Eighteen (10.2%) of the parents did not know the dosage of salbutamol to be administered during an asthma exacerbation, while 33 parents (18.6%) stated an incorrect dose.

Discussion

This study examined the use of salbutamol in children with asthma exacerbations before presenting to the hospital, and it was revealed that nearly half of the patients did not use salbutamol and two-fifths of the patients used an incorrect dosage and/or an incorrect technique. Most of the parents who did not give salbutamol to their children stated that they knew it should be used but did not want to give it without consulting a doctor. The main predictors associated with the use of salbutamol before hospital admission were previous hospitalization, sputum, and history of more than five exacerbations.

Early treatment initiation is the most effective strategy for asthma exacerbation, and the use of SABA is one of the cornerstones of this treatment.[12] Although parents face challenges when managing their children's asthma, the barriers to ideal asthma management at home are often unclear.[4,13,14] Garbutt et al. evaluated the use of salbutamol at home during asthma exacerbations in children and 113 (99%) out of 114 parents replied that they would use salbutamol if their children showed asthma exacerbation symptoms.[15] Gibson et al. interviewed the parents of 15 school-aged patients who were hospitalized for asthma and found that parents generally had a sense of indecisiveness regarding asthma management.[16]

The present study determined that nearly half of the children admitted to the hospital due to an asthma exacerbation had not used salbutamol at home. Most of the parents of children who had not used salbutamol were aware that salbutamol should be used but were hesitant to administer the drug without doctor consultation. This indicated that parents have difficulty deciding on whether to initiate home salbutamol therapy by themselves or not. In the pediatric allergy and immunology clinics, where our study was conducted, patients can be admitted to the outpatient clinic in case of complaints without going through the referral chain if already under follow-up in these clinics. Our findings depend on this easy access to pediatric allergy specialists, and this rate may differ in countries where access to pediatric allergy and immunology clinics is more difficult.

In the study by Gibson et al., one of the parents stated that their knowledge level and self-confidence increased as their child's asthma follow-up continued and that they learned new things during their child's hospitalization.[16] Accordingly, in the present study, we observed higher rates of home salbutamol use among patients with a history of hospitalization and longer follow-ups. Additionally, patients who used salbutamol at the right dose and technique had a higher incidence of previous hospitalization. This may be attributable to the parents' education and experience acquired during follow-up and hospitalization. Although asthma education is usually provided in outpatient clinics, it can also be provided during hospitalization.[17] Nurses also educate parents while their children are hospitalized, and they gain experience in drug administration.[18]

In addition, we observed a higher prevalence of cough and sputum in the patient group that used salbutamol. The presence of clear symptoms such as cough and sputum may have helped parents get over their uncertainty about salbutamol use. Parents may have noticed the exacerbation more easily and initiated salbutamol in older children. Salbutamol may be easier, and parents may be less concerned about the side effects of salbutamol treatment.

In our study, the severity of asthma exacerbation was higher in patients who did not use salbutamol, and the increased severity of exacerbation in these patients might be due to the non-usage of the drug.

Our study found that 42% of the parents who administered salbutamol at home used the incorrect dosage and/or the incorrect application technique. However, since we did not know the severity of asthma exacerbations at home, we could not assess whether salbutamol was used at the correct frequency or not.

Some studies have shown that having an asthma action plan may not be enough for the appropriate use of SABA during asthma exacerbations.[5,19,20] Similarly, even though all of our patients were given an asthma action plan at the start of the follow-up period, half of the patients had not used salbutamol during their exacerbation of asthma, and 42% of the patients used it with incorrect dosage and technique. In addition, when inquired about how salbutamol should be administered in children when needed, the technique and/or dosage stated by 42 parents (23%) was incorrect.

In most children, the administration of SABA via a spacer is more effective than with a nebulizer.[21] In our study, a quarter of the patients who received salbutamol at home used a nebulizer, and most parents incorrectly stated that they found the nebulizer more effective. We believe that parents must be better informed about this subject.

One of the limitations of our study is that we were unable to assess the appropriateness of the frequency of salbutamol used by the patients at home, as we did not know the severity of their asthma exacerbation while at home. Another limitation is the small number of patients. The importance of children using salbutamol during an asthma exacerbation is known, but there is limited information on parents' knowledge of home salbutamol use. Despite its limitations, this study is important because it provides valuable insight into the proportion of parents who administered salbutamol to their children to treat an asthma exacerbation at home. As we know, this is the first real-life study on this subject.

Conclusion

Our findings demonstrate that there are still inaccuracies in dosage and administration among patients using salbutamol. In addition, the majority of the parents in our study who did not administer salbutamol to their children were aware that it should be used. Therefore, we believe that in addition to providing education and awareness and an asthma action plan to patients and their parents, parents must also be actively encouraged to use salbutamol at home.

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Supplementary

Table S1 Questionnaire completed by the parents of pediatric asthma patients.

Q1. Education level
- ○ Primary school
- ○ High school
- ○ University

Q2. Did your child use salbutamol before coming to the hospital?
- ☐ Yes
- ☐ No

Q3. If no, why not?
- ○ I did not know that my child should use salbutamol
- ○ I knew that my child should use salbutamol but was afraid of the adverse effects of the drug
- ○ I did not consider it necessary to use salbutamol
- ○ There was no salbutamol at home
- ○ There was no device (aerochamber/nebulizer) with which to administer salbutamol at home
- ○ I did not want to give the drug without asking a doctor
- ○ My child refused to take the drug

Q4. If yes, what dose and frequency was used?
Specify:

Q5. Do you give salbutamol with a nebulizer or spacer during attacks?
Specify:

Q6. When and how often do you think salbutamol should be given?
Specify:

Q7. Is there a nebulizer at home?
- ○ Yes
- ○ No

Q8. How many ml of medicine do you put into the nebulizer?
Specify:

Q9. How far from the face do you/your child hold the nebulizer mask?
Specify: