Academic Journal of
Pediatrics & Neonatology
ISSN 2474-7521

Research Article
Volume 14 Issue 3 - September 2024
DOI: 10.19080/AJPN.2024.14.555944

Acad J Ped Neonatol

Does Nebulized Ipratropium Bromide Affect PICU Length of Stay? A Single Center Retrospective Chart Review

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Submission: September 13, 2024; **Published:** October 04, 2024

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Abstract

Objective: To determine whether the addition of ipratropium bromide to nebulized albuterol and systemic corticosteroids affected length of stay in pediatric intensive care unit patients (PICU) with acute asthma exacerbation.

Methods: Single center retrospective chart review. Ninety-one patients (aged 2-18 years old) were admitted to PICU because of acute asthma exacerbation. We divided patients into a group that received nebulized albuterol only and a second group received a combination of nebulized albuterol and ipratropium bromide. Both groups received supplemental oxygen and systemic corticosteroids.

Results: Patients who received a combination of inhaled ipratropium bromide and nebulized albuterol stayed longer in PICU (p=0.0001) and longer in hospital (p=0.0017) than patients who received nebulized albuterol only.

Conclusions: Adding ipratropium bromide to nebulized albuterol prolonged PICU length of stay and hospital length of stay in hospitalized children with acute asthma exacerbation.

Keywords: Ipratropium Bromide; Acute Asthma Exacerbations; Length Of Stay; Systolic Corticosteroids; Spirometry Parameters

Abbreviation: LOS: Length of Stay; PICU: Pediatric Intensive Care Unit; Hr: Hours; Hx: History; SABA: Supplemental oxygen, short acting B-agonists

Introduction

Severe acute asthma exacerbations can be life threatening [1]. Supplemental oxygen, short acting B-agonists (SABA), systemic corticosteroids and monitoring response to therapy with continuous clinical assessment is the main treatment recommended by the National Asthma Management and Education Program [2]. Adjunctive treatments like inhaled helium-oxygen gas mixture, anticholinergics, magnesium sulphate, methylxanthines, systemic B-agonists, and positive pressure (invasive and non-invasive) ventilation are also common, but it's use is very variable and institution-dependent [3]. Anticholinergics are commonly used in inpatient and outpatient setting with short acting B-agonists to treat asthma exacerbations in children and adults in the emergency care setting to decrease the length of stay in the emergency department and rate of hospitalization. There are few publications about the use of inhaled or nebulized anticholinergics in hospitalized children, but there are no clear treatment guidelines for asthma exacerbation of patients in PICU. This study is meant to examine the effect of adding an inhaled anticholinergic to short acting B-agonists on length of stay in a PICU setting.

Materials and Methods

This study is a single center retrospective chart review performed in the PICU of Children's Memorial Hermann Hospital in Houston, Texas. IRB (HSC-MS-18-0186) was obtained from Children Memorial Hermann Hospital Review Board at Houston, TX prior to starting data collection and patient's parental consent was waived. Patients enrolled were 2 to 18 years old and were admitted to PICU with a diagnosis of asthma exacerbation between January 2016 to December 2018. Patients with viral or bacterial pneumonia, cystic fibrosis exacerbation, wheezing due to intrathoracic foreign bodies, sickle cell disease with acute

chest syndrome, inhalational injuries, acute respiratory distress syndrome, cyanotic congenital heart disease and tracheostomy were excluded from the study. Patients were divided into two groups: a cohort that received continuous nebulized albuterol 20 mg/hr. without nebulized ipratropium bromide and a cohort received a combination of continuous nebulized albuterol 20 mg/hr. with nebulized ipratropium bromide 0.25-0.5 mg every 6 hours. All our patients in this study received supplemental oxygen and systemic corticosteroids. Stata Corp. 2017 (Stata Statistical Software: Release 15. College Station, TX: Stata Corp LLC) was used for statistical analysis. Value of $P<0.05$ was considered statistically significant. Two-sample Wilcoxon rank-sum (Mann-Whitney) test was used to compare numerical variables (age, weight, height, PICU length of stay, hospital length of stay), and Chi square or Fisher's exact test was used to compare nominal variables (gender, ethnicity, history of inhaled corticosteroids use, family history of asthma, history of tobacco exposure).

Results

The total number of patients enrolled in this study was 91 patients, divided into a group received albuterol-only (Alb-only, n=39, 43%) and a group received a combination of albuterol and ipratropium bromide (Alb-IB, n=52, 57%). Both groups received oxygen and systemic corticosteroids. The Alb-IB group had more African American patients, and patients were older and taller than in the Alb-only group. There were no differences in gender, weight, history of preventative inhaled corticosteroid use, family history of asthma, and history of tobacco exposure (Table 1).

Table 1: Clinical characteristics of albuterol only group (Alb-only) and albuterol + ipratropium bromide (Alb-IB).

	Alb-only n=39 (43%)	Alb-IB n=52 (57%)	P value
Gender	F=15 (38.5%)	F=24 (46%)	0.46
Age (yrs)	Median 6, IQR 3-8	Median 9, IQR 4-12	0.004
Weight (kg)	Mean 29.41, SD 18.5	Mean 37.53, SD 21.9	0.053
Height (cm)	Mean 111.4, SD 29.9	Mean 129, SD 29.8	0.005
Ethnicity	African American=15 Hispanic=14 Caucasian=5 Not documented=5	African American=37 Hispanic=6 Caucasian=5 Not documented=4	C=0.01
FMHx asthma	N=9 (23%) Y=28 (72%) Not documented=2 (5%)	N=18 (34.5%) Y=34 (65.5%)	0.12
Hx ICS	N=23 (59%) Y=14 (36%) Y (non-compliant) =2 (5%)	N=28 (54%) Y=15 (29%) Y (non-compliant) =9 (17%)	0.2
Hx tobacco exposure	N=26 (67%) Y=8 (20%) Not documented=5 (13%)	N=29 (56%) Y=20 (38%) Not documented=3 (6%)	0.12

LOS in PICU and LOS in hospital were measured in hours (hrs.). The Alb-only group stayed less hours in the PICU (Median 33, IQR 16-48) than the Alb-IB group (median 60, IQR 32-86.5), P=0.0001. Also, the Alb-only group stayed less hours in hospital (median 58, IQR 41-86) than the Alb-IB group (median 91.5, IQR 56-123.5), P=0.0017 (Table 2).

Table 2: LOS in hours in PICU and hospital.

	Alb-only n=39 (43%)	Alb-IBn=52 (57%)	P value
PICU (hrs.)	median=33	median=60	0.0001
	IQR (25-75) =16-48	IQR (25-75) =32-86.5	
Hospital (hrs.)	median=58	median 91.5	0.0017
	IQR (25-75) =41-86	IQR (25-75) =56-123.5	

How to cite this article: Haitham Al-Wahab* and Kostantinos Boukas. Does Nebulized Ipratropium Bromide Affect PICU Length of Stay? A Single Center Retrospective Chart Review. Acad J Ped Neonatol 2024; 14(3): 555944. DOI: 10.19080/AJPN.2024.14.555944

Discussion

At the time of conducting this report, there were no published studies evaluating the benefits of adding ipratropium bromide to nebulized albuterol on length of stay in PICU as a primary outcome. Most pediatrics studies are focused on asthma clinical scores when evaluating clinical improvement in acute asthma exacerbation, while adult studies evaluate spirometry parameters as metrics of clinical improvement. A systematic review by Vezine et al of hospitalized children outside ICU showed no benefit in hospital length of stay when anticholinergics are added to B-agonists [4]. A randomized double-blind control trial by Craven et al from 2001 included a similar cohort to our patients admitted to an asthma unit and followed an asthma care algorithm, showed no clinical outcome benefit of adding ipratropium bromide beyond that of using standard B-agonists, oxygen and systolic corticosteroids [5].

The evidence of beneficial effects of anticholinergics in the emergency room is controversial and focused on prevention of hospitalization as a primary outcome. A large systematic review with meta-analysis by Rodrigo et al from included pediatric and adult studies showed significant improvement in spirometry parameters when combined therapy is used in the emergency care setting [6]. Other randomized control trials showed reduction in the duration of treatments to discharge from the emergency room [7] and a significant improvement in pulmonary function test [8] after combined therapy in the emergency room as well. On the opposite end, a randomized controlled trial by Watanasomsiri et al showed no significant improvement in peak expiratory flow rate (PEFR) when ipratropium bromide was added to inhaled B-agonist (salbutamol) in children 3-15 years in emergency care setting [9]. A small, randomized control trial done in adults by Salo et al showed that adding ipratropium to continuous albuterol did not decrease the rate of admission from the emergency room nor improve peak expiratory flow rate (PEFR) [10].

Other medications used in a few of our patients were intermittent intravenous magnesium sulphate, intravenous terbutaline infusion, intravenous aminophylline infusion, and one patient received subcutaneous epinephrine at time of admission. It is also worth mentioning that respiratory support varied between patients, including facemask oxygen, high flow nasal cannula, positive pressure ventilation and sometimes mechanical ventilation. Our PICU uses continuous albuterol in patients with severe asthma exacerbation which has been safe and cost effective [11,12]. Our study had more African American children in the Alb-Ib cohort, who may have more severe asthma exacerbation but no association with LOS [13].

Conclusion

Our study showed adding inhaled ipratropium bromide to continuous albuterol increased LOS in PICU and in hospital. Our study is a retrospective cohort analysis. It was done in one institution and therefore the results cannot be generalized. A larger prospective randomized control study is needed to evaluate the effect of ipratropium bromide on length of stay in PICU. We did not evaluate the adverse events of ipratropium bromide, but most of the studies reported a safe profile of the medication. Also, we do not routinely use spirometry parameters as a marker of clinical improvement in our PICU due to compliance difficulties in the young patients.

Acknowledgments

We acknowledge Saad Tariq, MD who did data collection, Weng Lam PharmD who provided patient samples from pharmacy, and Cynthia Bell who did statistics.

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