COMPARISON OF BENZALKONIUM CHLORIDE CONTAINING ALBUTEROL VERSUS PRESERVATIVE FREE ALBUTEROL FOR THE TREATMENT OF STATUS ASTHMATICUS

BACKGROUND

In 2014, the Centers for Disease Control and Prevention reported approximately 6.3 million children in the United States with a diagnosis of asthma.[1] According to the National Heart, Lung, and Blood Institute, inpatient management of an acute asthma exacerbation may include continuous albuterol administration.[2] Due to higher dosing requirements over an extended duration of time, continuous albuterol administration requires a larger volume of albuterol solution, which is often obtained from a multi-dose vial containing benzalkonium chloride (BAC). BAC is a common preservative used in pharmaceuticals, but also considered to be a potent bronchoconstrictor. BAC doses as low as 124 micrograms have been shown to cause bronchoconstriction. This effect is cumulative, prolonged, and correlates directly with basal airway responsiveness.[3] The multi-dose albuterol vials currently used for continuous albuterol administration contain 50 micrograms of BAC per 2.5 milligrams of albuterol. A patient receiving continuous albuterol inhalation at 20 milligrams per hour will receive 400 micrograms of BAC per hour. In the 1999 study conducted by Asmus et al., the mean concentration of BAC required to provoke a 20% drop in FEV1 was 300 micrograms (range 124 to 1947 micrograms).[4] This raises concern that the bronchoconstricting effects of BAC may antagonize the therapeutic goals of albuterol therapy among patients receiving continuous albuterol inhalation for extended periods of time.

OBJECTIVE

The primary objective of this study is to compare the length of continuous albuterol administration between patients receiving BAC-containing albuterol (BAC-albuterol) versus preservative free albuterol (PF-albuterol). Secondary objectives include comparison of therapy escalation, asthma scores, forced expiratory volume in one second (FEV_1) at discharge, length of hospital stay, and cost.

METHODS

A prospective, patient-blinded, randomized study will be conducted comparing patients admitted to Norton Children's Hospital for an asthma exacerbation. There will be no active recruitment of patients; however, eligible patients will be those who present to our emergency department in status asthmaticus. Patients will be randomly assigned to a patient room on 5 West versus 5 East upon admission based on bed availability. The Pyxis on 5 West will contain the standard multi-dose albuterol vial which contains BAC (current standard of care), while pharmacy will be preparing and dispensing PF-albuterol to patients on 5 East who are enrolled in the study. The treatment of patients will not vary between groups, nor deviate from the standard of care currently implemented at the institution. If a patient consents to study enrollment, he/she will receive PF-albuterol while awaiting bed assignment in the emergency department. This is essential to avoid confounding the results of the study, as BAC has a

prolonged half-life and may have clinical consequences even after a patient is randomized to receive PF-albuterol.

Informed consent will be required for all patients, and assent will additionally be required for patients between 7 and 17 years of age. The study will be explained by a study investigator or respiratory therapist (under the supervision of the respiratory therapy director) and informed consent/assent paperwork will be provided to the patient/caregiver while in the emergency department. Approximately 10-20 minutes will be allotted for the consent/assent process. The difference between groups is the formulation of albuterol being used, and both formulations have FDA approval for use in status asthmaticus.

INCLUSION AND EXCLUSION CRITERIA

Patients will be included in the study if they are admitted to the 5th floor at Norton Children's Hospital for the treatment of an acute asthma exacerbation, initiated on continuous albuterol inhalation therapy, and are between 3 and 17 years of age.

Patients will be excluded from the study if they are transferred to the 5th floor from any other unit except the emergency department, admitted for any indication other than acute asthma exacerbation, or exposed to BAC prior to admission.

DATA COLLECTION

Demographic information collected will include age, gender, weight, and ethnicity.

Data gathered pertaining to continuous albuterol administration will include albuterol formulation, dose, length of therapy, cost of medication administered, and amount of BAC administered.

Additional parameters obtained will include admission asthma score, escalation of therapy related to asthma exacerbation, time on supplemental oxygen, transfer to higher acuity care, total hospital length of stay, and discharge FEV1.

A data collection document will be used by the respiratory therapist to collect start/stop time of continuous albuterol, evidence of patient non-adherence, and re-initiation of continuous albuterol. After completion, this document will be stored in a binder, in a cabinet, within a locked office. All data (from the data collection form and from the electronic medical record) collected will be stored in an Excel spreadsheet for data analysis. The data collection sheet to be used is attached. Data collected will be stored on a password protected computer, within a locked office, and will be restricted to the primary investigator. All information will be de-identified once entered into the data collection sheet.

STATISCIAL ANALYSIS

A power analysis will be conducted in order to determine the sample size needed to detect a statistical difference between groups. Descriptive statistics will be used to evaluate population demographics, while comparison data will be analyzed using a two-tailed student t-test.

CITATIONS

1. National Center for Health Statistics. Asthma, United States, 2014: Morbidity: Children (under age 18 years). Hyattsville, Maryland. 2014
2. Guidelines for the Diagnosis and Management of Asthma (EPR-3). NHLBI, NIH. National Institutes of Health, July 2007
3. Zhang YG, Wright WJ, Tam WK, Nguyen-Dang TH, Salome CL, Woolcock AJ. Effect of Inhaled Preservatives on Asthmatic Subjects: II. Benzalkonium Chloride. Am Rev Respir Dis American Review of Respiratory Disease 141.6 : 1405-408. 1990
4. Asmus MJ, Sherman J, Hendeles L. Bronchoconstrictor additives in bronchodilator solutions. J Allergy Clin Immunol 104:S53-S6. 1999