# Intravenous Glycopyrrolate And Asthma

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## A. Introduction

Despite improved understanding of the pathophysiology and treatment of asthma, significant morbidity and mortality exist for patients. The symptoms of acute asthma are produced by severe airflow obstruction resulting from airway inflammation that causes a combination of bronchospasm, mucosal edema and increased mucus secretion. Inhaled beta-agonists, systemic corticosteroids and oxygen are the mainstay of therapy for acute asthma. The two major groups of drugs available for treatment of bronchospasm are the beta-agonists and the anticholinergics. Inhaled anticholinergics, however, have been shown to be less bronchodilatory and have a delayed onset of action. Some studies have attributed this to an initial bronchoconstricting effect of the anticholinergics. [pratropium bromide (Atrovent) is the most commonly used anticholinergic agent, however it's effect is limited in the acute setting.

No studies have been published on the use of intravenous anticholinergic agents in the management of bronchospasm , except one case report. The anticholinergic agent, glycopyrrolate, has been used intravenously for many years in general anesthesia with its safety being well documented.

The purpose of this study is to investigate whether the addition of a single intravenous dose of glycopyrrolate to a standard regimen results in a greater . mprovement in pulmonary function than treatment with standard regimen alone 'in patients with acute asthma.

## B. Research Methods

This will be a prospective, randomized, double-blinded, placebo controlled trial designed to study the percent improvement in FEVI produced by intravenous glycopyrrolate and standard therapy vs. standard therapy alone in acute asthma. Patients with a history of asthma who present to the emergency room in acute respiratory distress will be treated according to standard asthma protocol (as per NIH panel report). When the patient is assessed to have poor response to standard treatment by a physician, he/she will be randomized to receive .2 ing I.V. of glycopyrrolate or 1cc of normal saline (control). FEV1 will be measured on initial evaluation (pretreatment) and 30 minutes post -treatment with the study drug or placebo. Statistical analysis of the data will be accomplished using an independent T-test on the percent change of FEV1 pre to post-treatment.

## C. Study Procedures

Patients will be managed in the Asthma Area of Area B as per standard protocol with nebulized beta-agonists, I.V. steroids and oxygen. The following are additional study procedures required of the patients: pre and post-treatment

1. FEV1 measurements: Patients will be asked to perform forced expirations into a portable spirometer. This procedure is not significantly different from the usual peak flow measurement obtained several times with standard treatment.
2. Subjectively assesses a group of symptoms
3. Vital sign measurements: respiratory rate, blood pressure, heart rate, and pulse oximetry

Admission to the Allen Asthma Service for 24 hours is not an additional requirement for study patients since poor response to treatment is a standard reason for admission.

The duration of the entire study will be approximately 4 months. Patient participation in the study should require no more than 24 hours, which is mostly time for observation and standard treatment of their asthma.

**D. Study Drug**

The study drug glycopyrrolate (robinul) is a quaternary amine thought not to cause CNS toxicity because of it's inability to cross the blood-brain barrier. Radioreceptor assay for the measurement of anticholinergics have shown the distribution half-life to be 2-3 minutes and the elimination half-life to be 45-60 minutes.

The study drug will be given as a single intravenous bolus of .2 mg via a heplock, followed by a NS flush of 5cc.

Side effects include urinary retention, tachycardia (mild), dry mouth(mod), blurred vision.

IND pending.

**E. Medical Devices**

Spirometer.

**F. Study Questionnaires**

Study questionnaire will not be used.

**G. Study Subjects**

Fifty asthma patients who present to the CPMC emergency department with acute exacerbation will be identified by a triage nurse who will place a random study packet into the potential patient's chart. Informed consent will be obtained by physicians with a witness.

Inclusion/Exclusion criteria: Patients with a history of asthma diagnosed according to the standards of The American Thoracic Society will be included in the study. Patients will be excluded from the study if their initial spirometry demonstrates an FEV1 of >70% predicted normal value; if they have clinical or radiographic evidence of pneumonia, congestive heart failure, or pneumothorax; or if they have lung carcinoma. In addition, patients will be excluded if they have contraindications to the administration of glycopyrrolate, including glaucoma, obstructive uropathy, ileus, ulcerative colitis or toxic megacolon, myasthenia gravis, hepatic disease, renal disease, cystic fibrosis. Patients less than age 18, pregnant, nursing mothers will also be excluded.

**H. Confidentiality of Study Data**

All data will be stored in the office of the Principal Investigator and will be accessible only to the investigators. All study subjects will have a unique code number.

**I. Location of the Study**

The study drug will be administered in AREA B of the CPMC emergency department. Patients will be admitted to the Allen Asthma Service.

**J. Potential Risks**

For study subjects receiving the intravenous dose of glycopyrrolate there will be a small risk of urinary retention and tachycardia and a moderate risk of dry mouth. This drug has been used for decades in anesthesia and gastroenterology and its safety is well documented at the dose being used in this study.

**K. Potential Benefits**

The study of the efficacy of I.V. glycopyrrolate in acute asthma is undertaken for the purpose of developing more specific targeted pharmacologic agents and continuing to refine the management of acute asthma in hopes of decreasing morbidity and mortality in the future. K. Alternative therapy will be as per standard protocol at CPMC which includes beta agonists, inhaled anticholinergics, ix. steroids and intubation as needed. L. No compensation will be provided. M. This study will not involve minors. N. This study will not include contact of patients with radiation or radioactive substances.