clomethasone dosage on omalizumab (P < .001). There were also statistically significant differences in asthma symptom scores and number of puffs of rescue medication in favor of omalizumab. Incidence of adverse effects were similar in placebo and omalizumab groups.

Conclusion. These results indicate that omalizumab therapy safely improves asthma control in allergic asthmatics who remain symptomatic despite regular use of inhaled corticosteroids and simultaneous reduction in corticosteroid requirement.

Reviewer’s Comments. The role of immunomodulating therapies in the treatment of allergic disease and asthma has become an exciting area of investigation in recent years. This study provides promising results in that anti-IgE therapy may have a role in controlling asthmatics who remain symptomatic despite regular use of inhaled corticosteroids. This therapy also appears to have a steroid-sparing effect, which is desirable. However, I would be interested in seeing more studies comparing anti-IgE with some of the other inhaled steroid compounds, such as fluticasone and budesonide, as long-term follow-up, especially because this therapy would require shots every 2 to 4 weeks. Practically, compliance will be important factors, as well as efficacy and safety, as we continue to study these new therapies.

WANDA PHIPATANAKUL, MD
Boston, MA

IPRATROPIUM BROMIDE PLUS NEBULIZED ALBUTEROL FOR THE TREATMENT OF HOSPITALIZED CHILDREN WITH ACUTE ASTHMA


Objective. To ascertain whether the addition of repeated doses of nebulized ipratropium bromide (IB) to standardized inpatient asthma care for children with status asthmaticus would improve clinical outcome.

Study Population. A total of 210 children 1 to 18 years old admitted with acute asthma.

Methods. This was randomized, double-blind, placebo-controlled trial in which children with acute asthma were assigned to receive either ipratropium or placebo in addition to standard therapy consisting of nebulized albuterol, systemic steroids, and oxygen. The intervention group received 250 µg IB combined with each albuterol treatment by jet nebulization in a dosing schedule as determined an algorithm. The placebo group received isotonic saline instead of IB.

Results. There were no significant differences between the therapeutic groups in hospital length of stay (P = .46) asthma care pathway progression (P = .37) the need for additional therapy, or adverse effects. Children greater than 6 years (N = 70) treated with IB had a shorter mean hospital length of stay (P = .03) and progressed more rapidly in the asthma care pathway (P = .02) than children in the placebo group, although these differences were no longer significant after data were adjusted for baseline differences.

Conclusion. The addition of repeated doses of nebulized IB to a standardized regimen of systemic steroids and albuterol offers no significant advantage in terms of clinical outcome for the treatment of hospitalized children with acute asthma.

Reviewer’s Comments. The literature on IB in acute asthma remains unclear. Emergency room studies have yielded conflicting results, with some showing shorter lengths of stay and reduced rates of hospitalization and others showing no effect. This is an excellent study of inpatient asthma that demonstrates little effect, although there was a trend toward more effect in older children. There are likely to be individual patients who respond more to IB than others although it has not yet been possible to identify those patients before the initiation of treatment. It still seems reasonable to use IB in patients showing little response to their first β-agonist treatments to determine if that individual patient may benefit from its use.

CHRISTOPHER RANDOLPH, MD
Waterbury, CT

EFFICACY OF IV THEOPHYLLINE IN CHILDREN WITH SEVERE STATUS ASTHOMATICUS


Purpose of the Study. To determine if the addition of intravenous (IV) theophylline to an aggressive treatment regimen of inhaled and IV beta-agonists, inhaled ipratropium and IV methylprednisolone would enhance the recovery of children with severe status asthmaticus admitted to the pediatric intensive care unit (PICU).

Study Population. Forty-seven children with a diagnosis of status asthmaticus who were admitted to the Cardinal Glennon Children’s Hospital in St Louis PICU for ≥2 hours. All subjects were in severe distress with a modified Wood-Downes clinical asthma score (CAS) of ≥5. Subjects’ age range was 13 months to 17 years.

Methods. Subjects were enrolled who fulfilled the above criteria. In brief, the CAS includes measures of oxygenation, breath sounds, accessory muscle use, respiratory wheezing, and cerebral function. Admission to the PICU was determined by inadequate response to repeated albuterol treatments and the ED and critical care staff. Subjects were randomly assigned to receive in addition to their regular aggressive treatment (denoted above in purpose of study) either IV aminophylline 7 mg/kg loading dose followed by age adjusted rates of 0.5–0.65 mg/kg/hr or no additional treatment (controls). Theophylline levels were kept between 12 to 17 µg/mL. The CAS evaluations were performed by investigators blinded to the treatment and were performed twice daily by 1 of 4 investigators. The PICU attending and resident team were all aware of the treatment assignment and made all medical decisions related to the subjects. CAS was suspended in the event of intubation and resumed on extubation. Nursing staff was queried regarding side effects of the subjects.

Results. There was no significant difference between the theophylline and control groups with respect to age, sex, race, home medications, past use of hospital resources, origin (ED or ward), ED treatment, or time of admission. The baseline CAS scores were not different. Six subjects required mechanical ventilation (3 in each group), although the 3 control subjects were intubated after treatment and the 3 in the theophylline group before treatment was begun. Subjects receiving IV theophylline had a significant decrease in time to reach CAS ≤5 and a greater percentage change in respiratory rate than control subjects during the first 12 hours in the PICU. Theophylline did not significantly influence the time to meet PICU discharge criteria among patients not receiving mechanical ventilation, but in those requiring intubation, the PICU stay was reduced. There was no significant difference in adverse effects between the 2 groups, except and increase in complaints of emesis in the theophylline group and increase in tremor in the control group.

Conclusions. Contrary to the National Heart Lung and Blood Institute guidelines for treatment of status asthmatic-
cus in children, this study suggests that critically ill children with severe status asthmaticus may benefit from the addition of IV theophylline to β-agonist, anticholinergic, and corticosteroid therapies. Additional studies may examine the administration of theophylline to select patients in the ED unresponsive to conventional therapy or in patients known to be high risk for respiratory failure.

**Reviewer's Comments.** This is the first prospective randomized trial of IV theophylline limited to children admitted to the PICU. Other studies in hospitalized (noncritical care) asthmatic children failed to show a benefit with the addition of theophylline to conventional treatment. It is possible that the benefit of the addition of theophylline is dependent on the severity of their illness. Adult studies have shown the improvement in spirometry with the addition of a methylxanthine is related to the degree of airway narrowing. The addition of theophylline may serve to reduce the incidence of respiratory failure and mechanical ventilation in children with severe status asthmaticus. The authors note that not blinding the medical team to the treatment may have influenced the results to some degree, but for safety reasons, they did not feel that was warranted. The authors referred to this as a “controlled” study, but there was no reference to a placebo (ex: saline). It would be interesting to repeat this study with a placebo control and with some of the newer critical care treatments such as heliox.
### Efficacy of IV Theophylline in Children with Severe Status Asthmaticus

Mary Beth Bollinger

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