


5 Bozovich G, Gurfinkel E, Barreiro D, et al. Reduction of hospital costs for patients with acute non-Q-wave myocardial infarction or unstable angina treated with enoxaparin compared to standard heparin [abstract]. Eur Heart J 1999; 20:545


To the Editor:

The study of Mark et al1 was based on the 655 US patients with available economic data, out of the total of 936 US patients in the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events (ESSENCE) trial. The overall cost reduction associated with enoxaparin use was statistically significant at 30 days among the US patients. Amongst the total study cohort, there was a trend toward reduced costs, but it was not statistically significant. These data underlay our statement that “an economic assessment of the ESSENCE results showed significant cost savings in US hospitals, but not across those in other countries with the cost saving mainly attributable to fewer cardiac catheterization procedures.”

Fox and Goodman, in their letter, refer to economic analyses of non-US national subpopulations drawn from the ESSENCE trial, the results of which are consistent with the nonsignificant trend toward cost savings with enoxaparin use reported in the article to which we referred.1 Although the outcome data for the TIMI 11B trial (references 10, 11, and 12 in their letter all relate to this trial) are similar to those in the ESSENCE trial, we are not aware of any published procedural data or economic analyses based on this trial.

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REFERENCE


Status Asthmatics in Children

Evidence-Based Recommendations

To the Editor:

We read with interest the review by Werner, entitled “Status Asthmatics in Children,”1 that appeared in the June 2001 issue of CHEST. In this nonsystematic review, we found that important statements are not evidence based.

Werner examined the data and rationale for the use of corticosteroids (CCS) in children with acute asthma. On the basis of an incomplete literature search, the author stated, “There does not appear to be a role for aerosolized steroids in acute severe asthma in children.” As a result, all the evidence about the use of inhaled CCS in acute asthma was ignored. Most of this is new literature (mid-1990s), and its quality is very high. Therefore, Edmonds et al2 conducted a systematic review of the literature with meta-analysis to determine the benefit of inhaled CCS for the treatment of patients with acute asthma managed in the emergency department. On the basis of six randomized controlled trials (six adult, two pediatric), the authors found that patients treated with inhaled CCS were less likely to be admitted to the hospital (odds ratio, 0.33; 95% confidence interval, 0.17 to 0.64); additionally, they demonstrated a significant improvement in FEV1 at 2 h of treatment.

In the section on anticholinergics, Werner appropriately stated that “anticholinergics are now an integral part of the treatment of acute asthma in children.” However, a “recommended dose” of 250 to 500 μg at 6-h intervals does not seem acceptable. On the contrary, there is strong evidence that supports the use of high and increasing doses of inhaled anticholinergics (ipratropium bromide) added to β2-agonists in the treatment of children and adults with acute asthma.1 3 Examination of the protocols reveals that repeated doses of nebulized ipratropium bromide were usually administered as 250 to 500 μg per dose every 20 min or four puffs (80 μg) every 15 to 20 min via metered-dose inhaler and spacer. So, routine emergency department treatment of acute severe asthma involves repeated doses of β2-agonists and ipratropium bromide administered over the first hour.

Werner recommended the use of “high-flow supplemental oxygen”; the assertion that “in the absence of preexisting chronic
To the Editor:

I appreciate the thoughtful comments by Rodrigo and Rodrigo on my review of severe asthma in children. Rodrigo and Rodrigo disagree with my statement that, currently, there is no role for inhaled corticosteroids in treatment of acute, severe asthma in children. Should inhaled steroids be added to, or even replace, parenteral steroids in children with status asthmaticus? No literature exists to support such practice. They cite a recent meta-analysis in the Cochrane library on the benefits of inhaled corticosteroids in children with life-threatening asthma do not need to be changed. The analysis included three heterogeneous pediatric studies, none of which enrolled children with severe asthma. The majority of studies in this analysis compared inhaled corticosteroids to placebo, not to parenteral steroids. When comparing inhaled steroids to parenteral steroids, the meta-analysis found no difference. Parenteral steroids remain the avenue of choice in children with acute, severe asthma.

Rodrigo and Rodrigo further state that the recommended dose of 250 to 500 μg ipratropium pfd is insufficient. They quote five articles to support their assertion. Of these articles, four are available in the English language. None of them, including their own, supports their statement. None of these reports compared routine ipratropium doses to higher doses, nor did they compare more frequent to less frequent application. The only article attempting to address this issue is by Schuh et al. In this double-blinded, three-armed trial, the investigators administered ipratropium to asthmatic children and compared the effects of 250 μg administered three times within an hour, 250 μg as a single dose, and placebo. The group receiving three doses experienced the greatest improvement in pulmonary function. Davis et al had shown nicely that the dose-response curve for ipratropium in asthmatic children flattens between 75 μg and 250 μg. The maximal response of inhaled ipratropium develops over 30 to 90 min, and may persist for > 4 h. In summary, we know that ipratropium is better for severely asthmatic children than no ipratropium. It has not been shown that doses > 500 μg are necessary. It may be beneficial to start treatment with three doses of ipratropium every 20 min, then repeat it every 4 to 6 h.

Rodrigo and Rodrigo disagree with the statement regarding suppression of respiratory drive by administration of supplemental oxygen. There is no evidence to indicate that otherwise normal children experience respiratory depression with administration of oxygen. The report quoted by Rodrigo and Rodrigo offers an interesting observation in adult asthmatics (mean age, 43 years), in whom oxygen administration leads to a mean increase in PaCO2 by 2.5 mm Hg. It is nearly impossible to establish cause and effect from these data; bronchodilators were withheld during the observation period, and no attempt was made to see if the small trend would reverse after withdrawal of oxygen. Oxygen administration is a crucial element of first-line treatment of the asthmatic child. Children have less oxygen reserve compared to adults, as their resting oxygen consumption may be two to three times that of an adult. Unfounded fear may lead to misguided withholding of oxygen for the child with asthma.

We still have much to learn about pediatric asthma. It differs from adult asthma in many respects, such as etiology, epidemiology, and pathophysiology. Not all knowledge gained from adult asthmatics can be transferred readily to the pediatric patient.

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5 Rodrigo GJ, Rodrigo C. First-line therapy for adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. Am J Respir Crit Care Med 2000; 161:1862–1868

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2 Rodrigo GJ, Rodrigo C. First-line therapy for adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. Am J Respir Crit Care Med 2000; 161:1862–1868