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EBCH Summary

Summary of 'Intravenous aminophylline for acute severe asthma in children over two years receiving inhaled bronchodilators'

Jilleen Kosko[1]* and EBCH European editorial base[2]
[1]*Alberta Research Centre for Child Health Evidence, University of Alberta, Edmonton, Canada*
[2]*Emma Children's Hospital/Academic Medical Center, University of Amsterdam, The Netherlands*

This is a summary of a Cochrane review, published in this issue of EBCH, first published as: Mitta A, Bassler D, Goodman K, Lasserson TJ, Ducharme FM. Intravenous aminophylline for acute severe asthma in children over two years receiving inhaled bronchodilators. *The Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD001276. DOI: 10.1002/14651858.CD001276.pub2.

Can the additional use of intravenous aminophylline improve symptoms of acute severe asthma in children already receiving inhaled bronchodilators, glucocorticoids and oxygen therapy?

To answer this question, scientists working with the Cochrane Airways Group analysed seven trials involving a total of 380 children (aged two to 17 years) with acute severe asthma requiring hospital admission. Children were given oxygen, inhaled bronchodilators, and glucocorticoids from the beginning in all studies.

What are the possible benefits or harms associated with including aminophylline in the symptom management of acute severe asthma in children?

Acute asthma is a common pediatric emergency in many countries. In the past, intravenous aminophylline has been extensively used to reduce constriction of the airways and improve airflow to the lungs of children suffering from severe asthma symptoms. However, its use has declined as drugs that produce fewer side effects and are easier to use have become available. Today, the most commonly used treatments to reverse asthma involve inhaled bronchodilators (to open the airways), glucocorticoids (steroids; to reduce inflammation of the airways), and oxygen therapy.

In children with very severe asthma symptoms not responding to maximum levels of current treatments, admission to intensive care and possibly intubation (insertion of breathing tube) may be required. For these patients, even a small improvement in lung function (breathing) might be important, and there has been a renewed interest in using intravenous aminophylline for particularly severe asthma. Therapeutic levels of aminophylline have been established (10–20 mg/dl); among its benefits are bronchodilation (opening of airways), improved lung function, and improved mental alertness. However, exceeding this narrow therapeutic range can cause toxic side effects, including headache, excessive urination (diuresis), low blood potassium levels (hypokalaemia), insomnia, vomiting, rapid heart beat (tachycardia), irregular heart beat (cardiac dysrhythmia), convulsions, and sudden death.

How effective is aminophylline in improving symptoms of acute severe asthma in children?

Patients receiving the additional intervention of aminophylline showed significant greater improvements in lung function (compared to placebo) at 6–8 h, 12–18 h, and 24 h. The addition of aminophylline was not associated with a significant reduction in the number of bronchodilator treatments and length of hospital stay. There is insufficient evidence to confirm whether aminophylline use improves oxygenation, reduces admission rates and/or lengths of stay in intensive care unit, or lowers rates of mechanized intubation. Though there was no significant difference in incidence of headache, tremor, or seizures, patients who received aminophylline treatment were nearly four times more likely to experience vomiting. While aminophylline appears otherwise safe, the discomfort associated with increased vomiting for children already suffering severe symptoms should be acknowledged.

*Correspondence to: Jilleen Kosko, Alberta Research Centre for Child Health Evidence, University of Alberta, Edmonton, AB, Canada.
E-mail: jilleenk@shaw.ca

What is the bottom line?

In children suffering severe acute asthma symptoms who are unresponsive to maximized treatment with inhaled bronchodilators, steroids (glucocorticoids), and supplemental oxygen, the additional intervention of intravenous aminophylline improves lung function within 6–8 h of treatment. Improvement in symptoms may continue up to 24 h after therapy. There was no apparent difference between groups regarding number of medicinal treatments received, length of hospital stay, or in rates of admission to intensive care unit. Aminophylline use resulted in a three-fold increased risk of vomiting. Aminophylline may have a role in managing severe acute asthma; however, these results are based on a small number of children and further work in this area is required.

Table I. Characteristics of the systematic review and included randomized controlled trials (RCTs)

Systematic review			Quality of included RCTs			
Total N of	**N of Authors**	**Use of intention-to-treat analysis (ITT)**	**Concealment of allocation**	**Blinding of care providers and patients**	**Blinding of outcome assessors**	**Completeness of follow-up**
RCTs 7	For selection of RCTs Search: one author	No	Adequate 5/7	Adequate 7/7	Adequate 1/7	All studies varying numbers of withdrawls: 2–16%
Included children 380	Full text articles: two independent authors		Unclear 2/7		Inadequate 3/7	
					Unclear 3/7	
Comparisons 1	For data extraction not mentioned					
	For quality assessment more than one author					

Table II. Key findings based on selection of outcomes

Comparison/Included patients
Aminophylline + B2-agonists & systemic steroids versus placebo + B2-agonists & systemic steroids/Children with acute severe asthma, 2–18 years old.

Outcome	N of Studies	N of Children	Method	Result	Inference
Clinical relevant outcomes					
Death	6	326	Description	No events	No evidence of effect
ICU admission rates	1	163	Relative Risk (fixed) 95% CI	0.74 [0.52–1.06]	No evidence of effect
Patients with mechanically ventilation	1	163	Relative Risk (fixed) 95% CI	0.09 [0.01–1.64]	No evidence of effect
Length of hospital stay	3	231	Mean Difference (Fixed) 95% CI	−2.10 [−9.45, 5.25]	No evidence of effect
Other outcomes					
Change in % predicted FEV1 after 6–8 h	3	65	Mean Difference (Fixed) 95% CI	8.37 [0.82, 15.92]	Favours aminophylline
Change in % predicted FEV1 after 24 h	3	62	Mean Difference (Fixed) 95% CI	8.87 [1.25, 16.50]	Favours aminophylline
Side effects					
Vomiting	5	305	Relative Risk (Fixed) 95% CI	3.69 [2.15, 6.33]	Favours placebo

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