Review: Intravenous aminophylline does not have additional benefit when added to β_2-agonists for acute asthma

Parameswaran K, Belda J, Rowe BH. **Addition of intravenous aminophylline to beta2-agonists in adults with acute asthma.** Cochrane Database Syst Rev. 2000;(4):CD002742 (latest version 19 Jun 2000).

QUESTION

In adult patients with acute asthma treated in the emergency setting, does the addition of intravenous aminophylline to β_2-agonists have an additional bronchodilation effect?

DATA SOURCES

Studies were identified using the Cochrane Airways Group register (derived from MEDLINE, EMBASE/Excerpta Medica, and CINAHL standardized searches up to 1999), by hand searching respiratory journals and meeting abstracts, and by reviewing the bibliographies of identified articles.

STUDY SELECTION

Studies were selected if they were randomized controlled trials comparing intravenous aminophylline with placebo in adults with acute asthma who were already being treating with β-adrenergic agonists with or without corticosteroids.

DATA EXTRACTION

Data were extracted on patient characteristics, treatment type and dose, main outcome measures, peak expiratory flow (PEF), FEV_1, and adverse effects.

MAIN RESULTS

15 trials met the selection criteria. Treatment groups did not differ for airflow outcomes at any time. Patients in the aminophylline group had higher values of PEF and FEV_1 at 12 and 24 hours, but treatment-group differences were not statistically significant (Table). Neither airflow limitation at baseline nor the use of steroids modified the effect of aminophylline. Patients in the aminophylline group reported higher rates of palpitations or arrhythmias and vomiting, but the groups did not differ for tremor or hospital admissions (Table).

CONCLUSION

In adult patients with acute asthma, the addition of intravenous aminophylline to β_2-agonists does not lead to additional bronchodilation, but some adverse effects were reported more frequently.

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Intravenous aminophylline (Am) vs placebo in adults with acute asthma*

Outcomes	Am	Placebo	Weighted mean difference (95% CI)	
PEF (L/min, 12 h)	194	184	8.3 (–21 to 37)	
PEF (L/min, 24 h)	216	209	22.2 (–57 to 101)	
FEV_1 (L, 12 h)	2.0	1.6	0.4 (–0.2 to 1.0)	
FEV_1 (L, 24 h)	2.2	1.8	0.4 (–0.1 to 1.0)	
			RRI (CI)	NNH (CI)
Arrhythmia/palpitations†	25%	10%	44% (4 to 29)	7 (4 to 24)
Vomiting†	31%	9%	225% (112 to 368)	5 (3 to 10)
Tremor†	44%	35%	29% (–7 to 67)	Not significant
			RRR (CI)	NNT (CI)
Hospitalized	21%	28%	35% (–1 to 61)	Not significant

*PEF = peak expiratory flow. Other abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article.
†Follow-up time not provided.

COMMENTARY

Intravenous aminophylline is commonly used in emergency settings in combination with other medications in the management of acute asthma. The benefit attributable to aminophylline added to β_2-agonists has been evaluated in the Cochrane review by Parameswaran and colleagues. The review pooled 15 mostly small randomized controlled studies that met selection criteria, although information about dropouts, blinding, and randomization methods were unclear in many of the studies. This review shows no respiratory benefit of intravenous aminophylline in terms of PEF or FEV_1 (either absolute or percentage predicted) at 0.5, 1, 12, and 24 hours. Indeed, at 30 minutes, FEV_1 is 0.26 liters (95% CI 0.029 to 0.491) lower in the aminophylline group. Only 2 studies could be pooled, however, for this 0.5-hour outcome. Furthermore, at baseline, the intervention group started with a lower FEV_1, according to 9 pooled studies (by 0.104 L, CI 0.017 to 0.191), suggesting that randomization was not fully successful, with patients who had more severe asthma entering the aminophylline group.

The review clearly shows that vomiting and palpitations were more common in the aminophylline group than in the control group (approximately 30% vs 10% of patients for each of these symptoms).

The findings do not support the addition of intravenous aminophylline to β_2-agonists in the management of acute asthma in adults.

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