Table 3

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Rothlin <i>et al</i> , 1993, Switzerland	Adults (aged 15–88 years) with blunt thoracic or abdominal injuries. Ultrasound scan by surgeons compared to the patients' clinical outcome and other diagnostic techniques	Prospective study	Clinical utility of ultrasound to detect haemothorax	Sensitivity 81%	Poor gold standard. Not performed by emergency physicians. Some of the beginner surgeons initially forgot to check for haemothorax, accounting for 5 of the 11 cases of false negative reports by ultrasound. Some of the effusions developed only after the first 24 h and therefore would not have been visible on the initial ultrasound scan
Ma <i>et al</i> , 1995, USA	245 adult (18 years +) patients presenting to the emergency department with major blunt or penetrating torso trauma. Diagnosis with ultrasound was compared to a combination of results of other diagnostic techniques including CT scan, supine chest x ray, formal two-dimensional echocardiography or tube thoracostomy	Diagnostic cohort	Clinical utility of rapid ultrasound assessment at detecting the presence of haemothorax	Sensitivity 96%, specificity 100%, accuracy 99%	Composite gold standard
Ma and Mateer, 1997, USA	240 adults (aged 18 years+) presenting to the emergency department with a major blunt or penetrating torso trauma. Accuracy of ultrasound compared with that of initial plain supine chest x ray for the detection of haemothorax using a combination of CT and tube thoracostomy as the gold standard	Retrospective analysis of a prior prospective study	Clinical utility of ultrasound vs initial plain supine chest x ray for the detection of haemothorax	Sensitivity 96.2% vs 96.2%, specificity 100% vs 100%, accuracy 99.6% vs 99.6%	The same patients as reference 2
Sisley <i>et al</i> , 1998, USA	Patients with suspected blunt or penetrating torso injury who required a chest radiograph for a complete evaluation	Prospective study	Clinical utility of ultrasound vs supine chest x ray at detecting the presence of haemothorax	Sensitivity 97.5% vs 92.5%, specificity 99.7% vs 99.7%, PPV 97.5% vs 97.4%, NPV 99.7% vs 99.1%	The results of ultrasound were compared to those of supine chest x ray rather than them both being compared to an independent "gold standard". Emergency physicians did not perform the ultrasound scan
Abboud and Kendall, 2003, USA	Blunt trauma patients who underwent CT scan of their chest as part of their clinical assessment	Prospective study	Clinical utility of ultrasound	Sensitivity 12.5%, specificity 98.4%	None of the haemothoraces detected by CT but not on ultrasound were large enough to be clinically relevant. The interval between the ultrasound scan and the CT scan was up to 4 h
Brooks <i>et al</i> , 2004, UK	Patients triaged to the resuscitation room with thoracic trauma (blunt or penetrating). Ultrasound findings were compared against a combination of other diagnostic methods including supine chest x ray, intercostal drain, CT or tube thoracotomy	Prospective study	Clinical utility of ultrasound at detecting the presence of haemothorax	Sensitivity 92%, specificity 100%, accuracy 98%, PPV 100%, NPV 98%	Composite gold standard

CT, computed tomography; NPV, negative predictive value; PPV, positive predictive value.

► CLINICAL BOTTOM LINE

Ultrasound is a sensitive, specific and accurate method to detect the presence of haemothorax in trauma patients. It cannot, however, replace chest radiography because there is additional information on the x ray that ultrasound cannot provide.

Rothlin M, Naf R, Amgwerd M, *et al*. Ultrasound in blunt abdominal trauma. *J Trauma* 1993;**34**:488–95.

Ma OJ, Mateer JR, Ogata M, *et al*. Prospective analysis of a rapid trauma ultrasound examination performed by emergency physicians. *J Trauma* 1995;**38**:979–95.

Ma OJ, Mateer JR. Trauma ultrasound examination versus chest radiography in the detection of hemothorax. *Ann Emerg Med* 1997;**29**:312–5.

Sisley AC, Rozyyeki GS. Rapid detection of traumatic effusion on using surgeon-performed ultrasonography. *J Trauma* 1998;**44**:291.

Abboud PA, Kendall J. Emergency department ultrasound for hemothorax after blunt traumatic injury. *J Emerg Med* 2003;**25**:181–4.

Brooks A, Davies B, Smethurst M, *et al*. Emergency ultrasound in the acute assessment of haemothorax. *Emerg Med J* 2004;**21**:44–6.

Aminophylline in bradyasystolic cardiac arrest

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doi: 10.1136/emj.2007.051342

Abstract

A short cut review was carried out to establish whether aminophylline improved return of spontaneous circulation rates and eventual

Table 4

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Mader TJ <i>et al</i> , 1997, USA	22 adults with non-traumatic asystolic out-of-hospital cardiac arrest. 14 aminophylline vs 8 control	Prospective, randomised, double-blind, placebo-controlled trial	ROSC Return of electrical activity defined as the occurrence of regular QRS complexes at a rate of ≥ 40 beats/min for at least 60 s, within 5 min of the study drug and before the administration of further drugs	5 vs 1 ($p=0.35$) 0 vs 7	Very small study. Results did not show any statistical improvement in ROSC. Disparity in presenting rhythm—control group contained significantly more patients with an initial rhythm of VF or PEA ($p=0.008$) Small trial
Mader TJ <i>et al</i> , 1999, USA	82, non-pregnant, normothermic adults suffering non-traumatic out-of-hospital cardiac arrest with asystole. 37 aminophylline vs 45 control	Randomised, double-blind, placebo-controlled trial	ROSC (defined as a palpable pulse of any duration)	27% (14–44%) 20% (10–35%)	Small trial
Mader TJ <i>et al</i> , 2003, USA	112, non-pregnant, normothermic adults (>21 years) suffering non-traumatic out-of-hospital cardiac arrest with asystolic arrest for 2 min after administration of both atropine and epinephrine (doses not specified). 66 aminophylline vs 45 control	Prospective, randomised, double-blind, placebo-controlled trial	ROSC Reversal of asystole	22.7% (13–35%) vs 15.6% (6–29%) 40.9% (29–54%) vs 26.7% (15–42%)	Small trial
Abu-Laban <i>et al</i> , 2006, Canada	971 patients older than 16 years with asystole or pulseless electrical activity at fewer than 60 beats/min, and who were unresponsive to initial treatment with epinephrine and atropine. 486 aminophylline vs 485 control	Double-blind randomised controlled trial	ROSC Survival to hospital admission Survival to hospital discharge	24.5% vs 23.7% NSD NSD	Average delay of 13 min from paramedic arrival to drug administration. Adequacy of CPR not controlled for

CPR, cardiopulmonary resuscitation; NSD, no significant difference; PEA, Pulseless Electrical Activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation.

outcome in bradycardiac arrest. A total of 1154 papers were found using the reported searches, of which four presented the best evidence to answer the clinical question. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of these four papers are summarised in table 4. It is concluded that aminophylline offers no benefit in this situation.

Three-part question

In [adults with bradycardiac arrest] does [the use of aminophylline as second line agent] [increase restoration of spontaneous circulation (ROSC) and improve long terms survival]?

Clinical scenario

A 59-year-old man has a witnessed out-of-hospital cardiac arrest and immediate bystander cardiopulmonary resuscitation (CPR). When the paramedic ambulance crew arrive after 8 min the first recorded rhythm is asystole. Resuscitation continues according to current advanced life support (ALS) guidelines. The patient is intubated, ventilated with high flow oxygen and receives 1 mg of epinephrine (adrenaline) and 3 mg of atropine intravenously. He remains in asystole after a further cycle (2 min) of CPR. You have heard that other agents may be useful at this stage and wonder if there is any evidence that intravenous aminophylline is effective.

Search strategy

Medline 1950 to May week 5 2007, Embase 1980 to 2007 week 22, Cinahl 1982 to June week 1 2007: [exp xanthines/methylxanthines.mp OR exp aminophylline/aminophylline.mp OR exp theophylline/theophylline.mp] AND [exp bradycardia/bradycardia.mp OR exp heart arrest/asystole.mp OR bradycardiac arrest.mp OR cardiac adj arrest].

The Cochrane Library Issue 2 2007: (aminophylline):ti,ab,kw AND (cardiac arrest):ti,ab,kw 4 articles (duplicated in table).

Outcome

A total of 1154 papers were found from Medline, Embase and Cinahl databases, of which four were relevant and of a sufficient standard of evidence to appraise critically. Cochrane identified the same four articles and no additional articles. All relevant papers are summarised in table 4.

Comments

Aminophylline acts as adenosine antagonists on A1/A2 receptors. Adenosine is an endogenous purine nucleoside that depresses the sinoatrial node, blocks atrioventricular conduction, inhibits the pacemaker activity of the His-Purkinje system and attenuates the effects of catecholamines. Adenosine is produced and released by myocardial cells during ischaemia and hypoxia. Aminophylline blocking the actions of adenosine may therefore be useful in the treatment of bradycardiac arrest.

Out of the four relevant randomised controlled trials available, none show a significant difference between the treatment and control groups with respect to ROSC.

Since these trials were completed we now know that the quality of CPR is an important determinant of outcome from CPR. Unfortunately in these studies and all previous drug studies in cardiac arrest patients there is no measure to ensure the patients received good quality CPR.

► CLINICAL BOTTOM LINE

Aminophylline does not improve survival from bradycardiac arrest.

Mader TJ, Gibson P. Adenosine receptor antagonism in refractory asystolic cardiac arrest: results of a human pilot study. *Resuscitation* 1997;**35**:3–7.

Mader TJ, Smithline HA, Gibson P. Aminophylline in undifferentiated out-of-hospital asystolic cardiac arrest. *Resuscitation* 1999;**41**:39–45.

Mader TJ, Smithline HA, Durkin L, *et al*. A randomized controlled trial of intravenous aminophylline for atropine-resistant out-of-hospital asystolic cardiac arrest. *Acad Emerg Med* 2003;**10**:192–7.

Abu-Laban RB, McIntyre CM, Christenson JM, *et al*. Aminophylline in bradycardiac arrest: a randomised placebo-controlled trial. *Lancet* 2006;**367**:1577–84.