

Repeat dosage of adrenaline in cardiac arrest

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Abstract

Background: Differing protocols exist as to whether the dose of adrenaline should be increased in children in cardiac arrest who have not responded to an initial dose of adrenaline.

Clinical Question: In children in cardiac arrest who do not respond to an initial standard dose of adrenaline (0.01mg/kg), does an increased second dose improve survival rates when compared to a repeat of the same dose?

Methods: We included all trials in children published in English. Studies in adult patients were excluded.

We searched The Cochrane Library, including The Cochrane Database of Systematic Reviews, DARE, CENTRAL and HTA in April 2005. We also searched Medline and Embase and several key guideline websites.

Studies were selected and appraised by one reviewer in consultation with colleagues, using inclusion, exclusion and appraisal criteria established a priori.

Results: One relevant randomised controlled trial with 68 participants was identified¹. This study did not find any benefit of high-dose (0.1mg/kg) adrenaline compared with standard dose (0.01mg/kg) after failure of an initial standard dose. Survival at 24 hours was lower in the group who received a high dose of adrenaline (2.9%) than in the group who received a standard dose (20.6%).

Conclusions: There is no evidence to suggest that a second high dose of adrenaline improves outcomes in children in cardiac arrest who do not respond to an initial dose of adrenaline, compared with a second standard dose. There is some evidence that high-dose adrenaline may cause harm.

Implications for Practice: Protocols for the resuscitation of children in cardiac arrest who do not respond to an initial standard dose of adrenaline should recommend a repeat standard dose rather than a higher dose of adrenaline unless further evidence becomes available.

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Background

Differing protocols exist as to whether the dose of adrenaline should be increased in children in cardiac arrest who have not responded to an initial dose of adrenaline. Some medication cards from the Royal Children's Hospital Melbourne recommend that a second of adrenaline dose ten times greater than the initial dose. A variety of Paediatric Advanced Life Support guidelines exist, most of which are not directive and suggest use of either a higher dose or a repeated dose of the same value. There are no official protocols at Southern Health for use of adrenaline in resuscitation of children.

Clinical Question

In children in cardiac arrest who do not respond to an initial standard dose of adrenaline (0.01mg/kg), does an increased second dose improve survival rates when compared to a repeat of the same dose?

Methods

Study Selection Criteria

Patient	Children in cardiac arrest who do not respond to an initial dose of adrenaline (Studies including only neonates were excluded)
Intervention	An increased second dose of adrenaline
Comparison	A repeat of the same dose of adrenaline
Outcomes	Mortality
Study Type	Randomised controlled trials or systematic reviews
Publication Date	1980-2005
Language	English

Search Strategy

Evidence Source	Date of Search
The Cochrane Library *	5 th May 2005
Medline (Ovid)	5 th May 2005
Embase	5 th May 2005
APLS [†] sites	18 th April 2005

*(including The Cochrane Database of Systematic Reviews, DARE, CENTRAL and HTA)

[†] Advanced Paediatric Life Support

Search Terms in Medline

Patient	(Exp Child/ OR exp Infant/ OR (child\$ OR infant\$ OR teenage\$ OR adolescen\$)) AND (exp Heart Arrest/ or exp Resuscitation/ OR ((cardiac OR cardio-respiratory OR cardiorespiratory OR cardiopulmonary OR cardio-pulmonary) ADJ (arrest OR resuscitation)))
Intervention	Exp Epinephrine/ OR (adrenalin\$ OR epinephrine)
Comparison	-
Outcomes	-

Data Collection & Analysis

Studies were selected and appraised by one reviewer in consultation with colleagues, using inclusion, exclusion and appraisal criteria established a priori.

Results

Our initial search retrieved 305 potentially relevant studies. 295 of these studies were excluded on review of abstract. Full text was retrieved for ten studies and all but one of these studies were excluded. One study¹ met the inclusion criteria.

Characteristics of included studies:

Study	Study Type	N(total)	Patients	Intervention	Comparison	Outcomes
Perondi 2004 ¹	RCT	68	Children who remained in cardiac arrest despite CPR and an initial dose of 0.01 mg/kg adrenaline	Second high dose of 0.10 mg/kg adrenaline	Second standard dose of 0.01 mg/kg adrenaline	Survival at 24 hours

Quality of included studies:

Study: Perondi 2004 ¹		Comments
Specified inclusion/ exclusion criteria	Yes	Neonates, children with sustained trauma, or whose cardiac arrest had commenced outside the hospital, and those with do-not-resuscitate orders were excluded.
Adequate method of randomisation	Yes	Randomisation by random number generator. However, protocol violations occurred in 18 of the 68 cases (inadvertent dosing deviations).
Concealment of allocation	Yes	Only the study pharmacist was aware of the concentration of study drugs.
Groups similar at baseline	Mostly	More boys in the standard dose group (59% vs 38%), more white children in the high-dose group (59% vs 38%), more children with asphyxia in the standard dose group (53% vs 35%) and more children arresting on the ward (rather than in ICU or ED) in the high dose group (18% vs 3%).
Blinding - patients/ investigators/ assessors	Yes	Only the study pharmacist was aware of the concentration of study drugs. Identical treatment packages labelled with consecutive numbers were created containing either 1:10,000 or 1:1,000 adrenaline solutions, from which 0.1ml/kg of the experimental solution was drawn.
Duration of follow-up	Good	Children were followed up to six months after discharge from hospital.
Proportion lost to follow up	None	
Objective & independent assessment of outcomes	Yes	Primary outcome was survival.
Inclusion of all subjects in analysis	Yes	

Results of included studies:

- Survival at 24 hours was lower in the group who received a high dose of adrenaline (2.9%) than in the group who received a standard dose (20.6%). (unadjusted OR for death with the high dose, 8.6; 97.5%CI 1.0 to 397.0; P=0.05).
- After adjustment for differences between the two treatment groups at the time of arrest (in terms of sex, race, location of the arrest, and initial cardiac rhythm), the high-dose group still tended to have a lower 24-hour survival rate and had a substantial odds ratio for death, but the difference from the standard-dose group was not significant (OR 7.9; 97.5%CI 0.9 to 72.5; P=0.08).
- The two treatment groups did not differ significantly in terms of the rate of return of spontaneous circulation (59% in high dose group vs 62% in standard dose group)
- None of the 34 patients in the high-dose group survived to hospital discharge, as compared with 4 of the 34 in the standard-dose group (P=0.11).

Conclusions

In the one relevant study identified, there is no evidence to suggest that a second high dose of adrenaline improves outcomes in children in cardiac arrest who do not respond to an initial dose of adrenaline, compared with a second standard dose.

There is some evidence that a high second dose of adrenaline may lead to reduced survival rates. This evidence is limited by the small size of the study and resulting variations between the baseline characteristics of the two groups, as well as the substantial number of protocol violations.

Implications for Practice

Protocols for the resuscitation of children in cardiac arrest who do not respond to an initial standard dose of adrenaline should recommend a repeat standard dose rather than a higher dose of adrenaline unless further evidence becomes available.

References

1. Perondi, M. B., Reis, A. G., Paiva, E. F., Nadkarni, V. M. and Berg, R. A. (2004) A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. *New England Journal of Medicine*, **350**, 1722-30.

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