Adrenaline dosage and buffers in cardiac arrest

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Immediate survival among patients in cardiac arrest after three attempted direct current (DC) defibrillations for ventricular fibrillation (VF) or who are in asystole and receiving adequate cardiopulmonary resuscitation is less than 10%—the hospital discharge rate is less than 2%. Adrenaline is advocated to improve survival. The recommended dose of adrenaline is 1 mg bolus administered intravenously repeated every three minutes as necessary. A prospective placebo controlled trial of “standard dose” adrenaline (0.01–0.02 mg/kg), however, has not been performed in patients with cardiac arrest. The effects of standard dose adrenaline have been analysed in a large retrospective study of 1360 patients with witnessed out-of-hospital VF. Some emergency medical staff were authorised to give standard doses of adrenaline during the observational period. Adrenaline was given to 35% of patients and was associated with a significantly greater rate of restoration of spontaneous circulation and hospital admission. However, there was no significant difference in hospital discharge rates between the two groups. Thus adrenaline and its dosage during cardiac arrest remain controversial.

High dose adrenaline

Administration of high dose adrenaline (0.1 or 0.2 mg/kg) compared with that of a standard dose in experimental animals after cardiac arrest causes an increase in aortic diastolic pressure, coronary perfusion pressure, resuscitation rates, and neurological outcome. However, the fibrillating heart rapidly consumes oxygen. High dose adrenaline may increase myocardial oxygen demand without increasing oxygen availability, and may cause contraction brand necrosis in the myocardium. In addition, ventricular arrhythmias and ventilation perfusion defects are associated with high dose adrenaline. Four large randomised studies have compared high dose and standard dose adrenaline in adults with cardiac arrest. 1–4 A further study included a placebo group. 1

The first study reported by Stiell et al in 1992 2 was performed in-hospital and out-of-hospital. High dose adrenaline (7 mg) was compared with a standard dose (1 mg), each administered at five minute intervals to a maximum of five doses. There were 650 patients (mean age of 66 years for patients given high dose adrenaline and 67 years for those given a standard dose). Fifty per cent and more of these patients were managed initially out-of-hospital, 69% had a witnessed cardiac arrest, and a cardiac cause was found in over 70%. VF or ventricular tachycardia was the initial rhythm in more than 25% of patients. The average dosage was 0.1 mg/kg in the high dose group and 0.015 mg/kg in the standard dose group. Survival at one hour (18% for the high dose group and 23% for the standard dose) or to discharge did not differ between the groups (3% in the high dose and 5% in the standard group).

Brown et al 5 also in 1992, reported 1280 patients (mean age 66 years) with out-of-hospital cardiac arrest who were randomised to receive either high (0.2 mg/kg) or standard dose (0.02 mg/kg) adrenaline. Cardiac arrest was witnessed in 36% of patients in the high dose group and in 39% of those in the standard dose group. The initial rhythm was VF or ventricular tachycardia in 46% of patients given high dose adrenaline and in 50% of those given a standard dose. Resuscitation was initially successful in 23% of patients in the high dose group and in 22% in the standard dose group: 5% in the high dose group survived to discharge and 4% in the standard dose group (p = NS). Callaham et al 6 also in 1992, reported results from three groups of patients (n = 816) with out-of-hospital cardiac arrest who received high dose adrenaline (15 mg), high dose noradrenaline (11 mg) or standard dose adrenaline (1 mg) up to three doses each. Mean age was comparable between the groups (more than 60 years). More than 60% of cardiac events were witnessed and more than 20% of patients had VF at the time of treatment. More patients given high dose adrenaline (18%) survived to be admitted to hospital than those given standard dose adrenaline (10%) and high dose noradrenaline (13%) (p = 0.02). Hospital discharge, however, was only 1.7%, 1.2%, and 2.6% for high dose adrenaline, standard dose adrenaline, and high dose noradrenaline, respectively (p > 0.05).

In the study by Choux et al, repeated high doses of adrenaline were compared with standard doses administered to 536 patients with out-of-hospital cardiac arrest 3. Patients randomly received either high dose (5 mg) or standard dose (1 mg) adrenaline at five minute intervals to a maximum of 15 doses. Mean age was 59 for patients given high dose adrenaline and 61.5 for those given a standard dose. Initially, 18% in the high dose group and 16% in the standard dose group had VF. Twenty...
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four per cent of patients in the high dose group and 20% in the standard dose group were admitted to hospital. Fifteen day survival rates were 4% in the high dose group and 2% in the standard dose group (p = NS).

Woodhouse et al compared high dose adrenaline (10 mg) and standard dose (1 mg) with placebo in patients with cardiac arrest in hospital and out-of-hospital. Mean ages were 70, 68, and 67 years in the high dose, standard dose, and placebo groups, respectively. Cardiac arrest occurred out-of-hospital in 44%, 46%, and 44% of patients in the high dose, standard dose, and placebo groups, respectively. VF was initially present in 39%, 37%, and 39% of patients in the respective groups. The immediate survival rate was 9.6%, 9.7%, and 7%. The only survivors to leave hospital were from the standard dose group (2%).

These randomised and non-randomised studies show that high dose adrenaline has no advantage over low dose. The relevant question is: does even low dose adrenaline improve survival to leave hospital?

The difference between the encouraging results with high dose adrenaline in animals compared with those in human studies may arise from time delays to treatment and the presence of significant coronary artery disease. The interval from arrest to treatment with adrenaline in humans is likely to be much longer than in the experimental laboratory, and the balance between oxygen delivery and demand may deteriorate with high dose adrenaline in the presence of fixed atherosclerotic plaques.

**VASOPRESSIN**

One of the newer areas with potential for improving survival is the administration of vasopressin to patients with out-of-hospital VF resistant to DC shocks. Lindner et al compared administration of 1 mg adrenaline in 20 such patients with 40 units vasopressin in a further 20 patients. Thirty five per cent of patients in the adrenaline treated group and 70% in the vasopressin treated group were admitted to hospital: 15% and 40%, respectively, survived to leave hospital. While this study is encouraging, the numbers are very small. These patients cannot be equated to those in the five high dose adrenaline trials for cardiac arrest reported here.

**Buffers in cardiac arrest**

**RESPIRATORY OR METABOLIC ACIDOSIS**

Respiratory or metabolic acidosis is associated with decreased myocardial contractility, with impaired cardiovascular response to catecholamines. Metabolic acidosis reduces the VF threshold. Lactic acidosis is usually defined as an arterial pH of 7.2 or less. This condition is caused by hypoxia or has a metabolic aetiology. Treatment includes identification and correction of the cause.

Administration of buffers (sodium bicarbonate) to overcome metabolic acidosis during cardiac arrest has given rise to significant controversy. Sodium bicarbonate can increase intracellular acidosis, reduce cardiac output, cause hypernatraemia and hyperosmolarity with the oxygen dissociation curve shifted to the left, increasing the affinity of haemoglobin for oxygen and thereby reducing oxygen release in the tissues.

**BUFFERS**

Bar-Joseph et al reported improved resuscitability in dogs with VF for 10 minutes given sodium bicarbonate compared with animals given sodium chloride, carbicarb and Tham, or saline. Spontaneous circulation was restored in seven of nine animals given sodium bicarbonate (p = 0.003), six of 10 given carbicarb (p = 0.04), but only two of 10 given saline. Unfortunately, there are no controlled trials of sodium bicarbonate in human cardiac arrest. Limited information can be gained from a retrospective study of 619 out-of-hospital cardiac arrests with 273 successful resuscitations. Blood gases and electrolytes were recorded on admission to the accident and emergency department. A total of 215 patients received an average of 79 mEq sodium bicarbonate during arrest (58 patients were not given bicarbonate). There was no difference in mean age between the groups. Cardiopulmonary resuscitation time was much longer in patients treated with sodium bicarbonate—usually more than three times longer than those who were not treated with bicarbonate. Most patients were intubated. VF was the initial cardiac arrest rhythm in 89.7% of patients who were not given bicarbonate and in 63.7% of those who were given bicarbonate. There was no significant difference in survival for either group presenting in VF irrespective of the length of time of cardiopulmonary resuscitation. There were no differences in blood gases in either group. A definite conclusion cannot be drawn as this study was only a subset of prehospital cardiac arrest victims who survived to hospital.

In 1995, Dybvik et al carried out a prospective, randomised, double blind, controlled trial of the buffer Tribonat in patients with out-of-hospital cardiac arrest (asystole or VF with failure of first DC shock). A total of 502 patients were randomised to receive either Tribonat (250 ml) or 0.9% saline (250 ml). The mean dispatch response interval for both groups was identical together with the percentage of patients admitted to hospital. Ten per cent of those who received Tribonat were discharged from hospital versus 14% who received saline.

**Recommendations**

Adequate alveolar ventilation is the mainstay of control in patients with cardiac arrest, to maintain acid base balance.

Until further studies become available, patients treated with sodium bicarbonate should fall into one of four groups:

- **severe acidosis** (arterial pH < 7.1, base excess ≤ 10)
- **blind administration only after prolonged cardiac arrest** (10–20 minutes)
- **cardiac arrest associated with hyperkalaemia**
- **cardiac arrest associated with tricyclic anti-depressant overdose.**
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