

Commentary

Vasopressin combined with epinephrine during cardiac resuscitation: a solution for the future?

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See related research by Grmec and Mally in this issue [<http://ccforum.com/content/10/1/R13>]

Abstract

Epinephrine given during cardiopulmonary resuscitation (CPR) may cause beta-mimetic complications in the postresuscitation phase. Vasopressin may be an alternative vasopressor drug during CPR. A subgroup analysis of a large prospective CPR investigation and of retrospective CPR studies suggests that vasopressin may be especially beneficial when combined with epinephrine. Beneficial effects of adding vasopressin were observed in other catecholamine-refractory shock states as well, such as vasodilatory shock and haemorrhagic shock. In order to maximize effects of any vasopressor during CPR, rapid aggressive chest compressions must be ensured to maximize blood flow and to enable advanced cardiac life support drugs to reach the arterial vasculature. We suggest alternating injections of 1 mg epinephrine i.v. and 40 IU vasopressin i.v. every 3–5 minutes during CPR until spontaneous circulation can be achieved or CPR efforts are terminated.

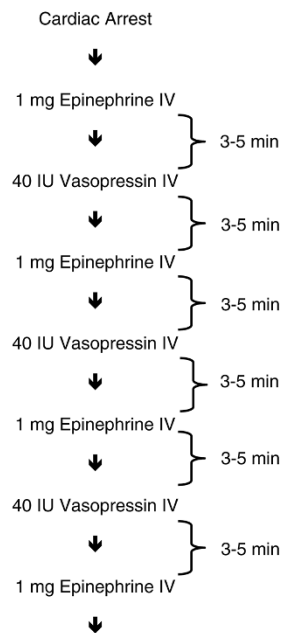
Epinephrine has been employed for cardiac resuscitation for approximately 100 years [1], although it is known that this drug increases myocardial oxygen consumption during cardiopulmonary resuscitation (CPR) and increases the likelihood of cardiac failure after restoration of spontaneous circulation [2]. In contrast, vasopressin proved to be beneficial over epinephrine as regards improving coronary perfusion pressure during CPR and as regards improving neurological recovery in the CPR laboratory [3,4]. It was then hoped that vasopressin may also be better than epinephrine in large prospective clinical CPR trials [5], but these assumptions could not be proven in an in-hospital CPR trial in Canada [6] and in an out-of-hospital CPR trial in Europe [7]. A large subgroup ($n = 732$) in the European vasopressin trial [7] and a retrospective analysis of CPR patients from Pittsburgh, PA, USA [8], however, suggested possible beneficial effects of a combination of vasopressin and epinephrine when given during CPR. This strategy is currently being studied in an ongoing, very large ($>2,000$ patients), out-of-hospital prospective CPR trial in France.

The exciting retrospective study of Grmec and Mally from Slovenia adds further support to the hypothesis that a combination of vasopressin and epinephrine given during CPR may be more effective than epinephrine alone [9]. While the authors acknowledge limitations of their investigation, such as a lack of randomizing and subgroup analysis of myocardial infarction patients, it is very impressive that 530 patients were studied in a very difficult setting without any funding. This investigation is in full agreement with studies showing that adding vasopressin in catecholamine-refractory shock states was beneficial during CPR [10], vasodilatory shock [11], and hemorrhagic shock [12]. Similar to balanced anaesthesia, it may be valuable to combine two drugs during CPR instead of increasing the dose of one drug. Accordingly, the Slovenian data confirm that the cumulative epinephrine dosage was significantly lower when additional vasopressin was employed. If the authors had used 2×40 IU vasopressin i.v. instead of only 1×40 IU vasopressin i.v., as in the present study, this effect would most probably have been even greater.

Disappointment about advanced cardiac life support drugs is probably due to both complex effects of global ischaemia during CPR [13] and our own lack of understanding about CPR treatment effects. While we know in the laboratory that only continuous, aggressive chest compressions are able to improve vital organ perfusion to levels that render successful defibrillation likely, we failed to enforce laboratory CPR quality on the streets and on the wards [14,15]. Insufficient CPR is unfortunately occurring very often in hospitals and in the emergency medical service [16]; for example, chest compressions were performed less than 50% of the available time, therefore greatly underutilizing CPR possibilities. If blood does not flow during CPR, a given vasopressor is less likely to reach the target organ arterial vasculature, rendering beneficial effects of advanced cardiac life support drugs less likely. In one study of ventricular fibrillation victims, 75% of the

CPR = cardiopulmonary resuscitation.

Figure 1



Continue until spontaneous circulation is achieved, or CPR efforts are terminated depending on individual judgment of the CPR team leader

Innsbruck vasopressor strategy during cardiopulmonary resuscitation. If basic life support does not result in spontaneous circulation, our strategy is to alternate between an initial injection of 1 mg epinephrine i.v. and a subsequent injection of 40 IU vasopressin i.v. every 3–5 minutes if return of spontaneous circulation does not occur, independently of the initial electrocardiographic (ECG) rhythm. In one study, not a single patient with asystole or pulseless electrical activity as the initial ECG rhythm survived to hospital discharge if ≥ 3 mg epinephrine were injected; ventricular fibrillation patients tolerated higher epinephrine dosages [7]. There is no clear evidence how many times a vasopressor should be given until cardiopulmonary resuscitation (CPR) efforts should be terminated if return of spontaneous circulation does not occur.

surviving patients had a return of spontaneous circulation without injection of a vasopressor [17]; the remaining 25% of patients who required a vasopressor indicated that, if basic life support does not restore spontaneous circulation, the general outcome is most probably poor. Accordingly, once advanced cardiac life support drugs are necessary, rescuers need to understand that the chance the patient will be discharged from the hospital is $<10\%$ [7].

The recently published European Resuscitation Council CPR Guidelines state that ‘current evidence is insufficient to support or refute the routine use of any particular drug or sequence of drugs’; the respective CPR algorithm primarily recommends injection of 1 mg epinephrine every 3–5 minutes, while vasopressin may also be injected [16]. In contrast, the approach of the American Heart Association CPR guidelines is more liberal, stating that ‘one dose of vasopressin may

replace either the first or second dose of epinephrine’ [18]. A question arises: should vasopressin be injected during CPR based on results from a subgroup analysis and retrospective studies? The pragmatic answer is yes. As already described, basic life support saves the ‘best’ cardiac arrest patients; any subsequent advanced cardiac life support intervention has a decreasing likelihood to restore spontaneous circulation over time. Vasopressin should therefore be employed rapidly if initial epinephrine does not restore spontaneous circulation. Our strategy is to alternate between an initial injection of 1 mg epinephrine i.v. and a subsequent injection of 40 IU vasopressin i.v. every 3–5 minutes during CPR (Figure 1), since it may combine both beneficial effects of combining two drugs and avoiding complications of injecting excessive dosages of one drug alone. Similar to most CPR strategies, this approach is not yet backed up by a randomized controlled trial, but the next CPR attempt may be just moments away.

Competing interests

Data from a previous study [7] is being used for a vasopressin registration application process by Aguetant (Lyon, France) in Europe. Aguetant supported our working group in 2002 with grant support. No author has a financial interest in drugs being discussed in this manuscript.

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