Epinephrine for Cardiac Resuscitation: Too Much Beta for Its Own Good?**

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The present study. Epinephrine is an established pharmacologic agent for use during resuscitation from ventricular fibrillation (1). Its value has been proven in experimental animals (2), and it has been accepted and used in the clinical setting for more than a decade. Its potent alpha-adrenergic vasoconstrictive effects, which maintain blood pressure and coronary perfusion pressure, have been demonstrated to be its primary mechanism for benefit (3). In this issue of the Journal, Midei et al. (4) present experimental data suggesting that the potent beta-adrenergic effects of epinephrine are potentially deleterious because they may result in increased oxygen consumption both by exerting a direct metabolic effect and by increasing wall tension during fibrillation. The increased contraction strength of fibrillation might also reduce myocardial perfusion. Overall, this study was designed to evaluate whether this increase in myocardial oxygen consumption at the low perfusion pressures characteristic of cardiopulmonary resuscitation was disadvantageous. Epinephrine was compared with phenylephrine, which is a more potent alpha-adrenergic agent for use during resuscitation from ventricular fibrillation (1). Its value has been proved in experimental animals (2), and it has been accepted and used in the clinical setting for more than a decade. Its potent alpha-adrenergic vasoconstrictive effects, which maintain blood pressure and coronary perfusion pressure, have been demonstrated to be its primary mechanism for benefit (3). In this issue of the Journal, Midei et al. (4) present experimental data suggesting that the potent beta-adrenergic effects of epinephrine are potentially deleterious because they may result in increased oxygen consumption both by exerting a direct metabolic effect and by increasing wall tension during fibrillation. The increased contraction strength of fibrillation might also reduce myocardial perfusion. Overall, this study was designed to evaluate whether this increase in myocardial oxygen consumption at the low perfusion pressures characteristic of cardiopulmonary resuscitation was disadvantageous. Epinephrine was compared with phenylephrine, which is a more pure alpha-vasoconstrictor, although there is some inotropic stimulation of alpha-receptors in the myocardium.

Epinephrine versus phenylephrine. Interpretation of the results was simplified by use of the isolated perfused canine ventricles in which perfusion pressure can be controlled. Unfortunately this preparation is also far removed from the intact circulation, and therefore the study findings must be interpreted accordingly. In this study coronary blood flow and oxygen consumption levels were highest for epinephrine, intermediate for phenylephrine and lowest for no infusion of drug. Left ventricular function was measured by the slope of the end-systolic pressure-volume relation. With epinephrine this slope was only 72% of the baseline value 10 min after restoration of sinus rhythm and 100 mm Hg perfusion pressure. In contrast, in the phenylephrine-treated group the slope increased to 143% of the baseline value and in the control group it was 82% of baseline. End-diastolic pressure was not different at 10 min after defibrillation in any of the groups.

Because this study was performed in the isolated perfused heart, the peripheral alpha-vasoconstrictive effects of these drug doses could not be compared. The doses of epinephrine (5 µg/min) and phenylephrine (50 µg/min), which were infused directly into the coronary perfusion circuit, are high doses. As indicated in the protocol, a 10-fold higher dose of phenylephrine was chosen for the study than the dose that usually produced a full vasoconstrictive response. The most striking finding of this study was the increase in ventricular function seen in the phenylephrine-treated group. This may well be related to the high dose used and the presence of some myocardial alpha-receptors. Because the dose of phenylephrine caused only a small increase in oxygen consumption, it was suggested that this agent could conceivably be better than epinephrine, which increased myocardial oxygen demand more. However, the reduction in contractility with epinephrine seen 10 min after defibrillation and restoration of blood flow was not statistically less than in the control group. Thus, although one could demonstrate a higher oxygen consumption with epinephrine, one could not demonstrate a statistically significant reduction in postresuscitation contractility in comparison with the control group.

Conclusions. Thus, this interesting study should not prompt us to eliminate epinephrine as a drug for the treatment of cardiopulmonary resuscitation; experience has suggested its efficacy in the clinical setting. This study does indicate, however, that phenylephrine has some attractive features that should be further investigated. These include the production of peripheral vasoconstriction (so essential to the resuscitation process), a lesser rise in oxygen consumption and a small but demonstrable increase in contractility, which was a statistically better outcome than that afforded by infusion of epinephrine or of no drug, both of which resulted in diminished contractility. Studies in intact animals must be carefully performed before one can confidently recommend phenylephrine as a better drug than epinephrine. It should be noted that Schlein et al. (5) compared epinephrine with phenylephrine during cardiopulmonary resuscitation in dogs and found no differences in coronary or cerebral flow or resuscitation. Overall, however, it is clear that phenylephrine has some theoretic advantages over epinephrine and does deserve additional study.

References

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