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Early Epinephrine Administration for Cardiac Arrest

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Okubo et al[1] observed a time-dependent association between epinephrine administration and survival to hospital discharge and a favorable funtional outcome at discharge in adults with out-of-hospital cardiac arrest (OHCA) with an initial shockable (ventricular fibrillation/pulseless ventricular tachycardia) or nonshockable cardiac rhythm (pulseless electrical activity and asystole). Findings of the study suggest that if epinephrine is used during cardiopulmonary resuscitation (CPR) it is more likely to be beneficial if given early in the resuscitation attempt. The authors used a large data set (>40 000 patients from North America) and time-dependent propensity score–matching to limit resuscitation time bias.[2] During CPR, epinephrine treatment is more likely to occur as the duration of CPR increases, but the need for a longer CPR attempt is also associated with a worse outcome and can bias observations toward a harmful treatment effect from epinephrine. This risk of bias can be decreased by comparing patients who received epinephrine after a given number of minutes of resuscitation with similar patients who were at risk of receiving epinephrine in the same minute during their resuscitation (ie, ongoing CPR but not given epinephrine).

Most of our recent understanding of the role of epinephrine during CPR comes from the PARAMEDIC-2 randomized clinical trial[3] that compared epinephrine with placebo in 8014 patients with OHCA in the UK and showed that epinephrine increased return of spontaneous circulation (ROSC) (36% vs 12%) and survival to hospital discharge (3.2% vs 2.4%) compared with placebo (unadjusted odds ratio, 1.39 [95% CI, 1.06-1.82]; $P = .02$). The low overall survival was attributed to a median time of 21 minutes between the emergency call and study drug administration. The main concerns raised by the study were regarding secondary end points, such as whether epinephrine increases brain injury in survivors or helps achieve ROSC at a late stage of cardiac arrest when severe brain damage is more likely. Specifically, there was an increase in the proportion of survivors with poor neurological function in the epinephrine group vs the placebo group (39 of 126 patients [31.0%] vs 16 of 90 patients [17.8%] had a poor neurological outcome, 39 of 4015 patients [1.0%] vs 16 of 3999 patients [0.4%] of the patients in each group). Another concern was that epinephrine use increased intensive care admissions in patients who subsequently died. A secondary cost-analysis of PARAMEDIC-2 suggested that epinephrine use was associated with an increase in the number of organs donated by nonsurvivors and the number of organ transplant recipients.[4] When organ donation and transplants were taken into account, administration of epinephrine changed from not being a cost-effective option to being a cost-effective intervention.

The study by Okuda et al[1] corroborates another secondary finding of the PARAMEDIC-2 study in that any beneficial treatment effect of epinephrine on ROSC, survival to discharge, and favorable functional outcome declined with increasing time to drug administration compared with placebo, and any beneficial treatment effect was greater for initial nonshockable cardiac rhythms.[5] There are no randomized clinical trials of epinephrine for in-hospital cardiac arrest (IHCA). For IHCA, the time to drug administration for cardiac arrest is much shorter than for OHCA. The importance of early administration in the IHCA population is supported, however, by an observational study using data from the American Heart Association Get With The Guidelines Resuscitation registry. In that study of patients with initial nonshockable cardiac rhythm, survival decreased in a stepwise fashion for every 3 minutes of delay to administration of the first epinephrine dose.[6] For shockable rhythms, however, propensity score–matched data from the same IHCA registry that accounted for resuscitation time bias found that epinephrine given within the first 2 minutes of CPR was associated with decreased ROSC, survival to hospital discharge, and favorable neurological outcome at discharge.[7]

Epinephrine, 1 mg, is used as a blunt instrument during CPR to increase the rate of ROSC and survival to discharge. Epinephrine has a more pronounced treatment effect when given early in the resuscitation attempt, especially for a nonshockable cardiac arrest. In addition, this drug probably increases the number of survivors with both a good and poor neurological outcome, the number of organs donated by nonsurvivors, and the number of transplant recipients. The study by Okuda et al[1] supports current guidelines for the use of epinephrine during CPR. Current guidelines for both OHCA and IHCA recommend that epinephrine be given as soon as feasible when the initial cardiac arrest rhythm is nonshockable and after initial defibrillation attempts have failed when the initial cardiac rhythm is shockable.

ARTICLE INFORMATION

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