

# Esmolol administration during cardiopulmonary resuscitation reduces post cardiac arrest brain injury

Dott.ssa FRANCESCA NESPOLI (1)(2), Dott.ssa LAURA RUGGERI (1), Dott.ssa FRANCESCA FUMAGALLI (1), Dott. DAVIDE OLIVARI (1), Dott.ssa DARIA DE GIORGIO (1), Dott. GIOVANNI BABINI (1)(3), Dott.ssa ROBERTA AFFATTO (1), Dott.ssa DEBORAH NOVELLI (1), Dott.ssa LIDIA STASZEWSKY (1), Dott. ROBERTO LATINI (1), Prof. GIUSEPPE RISTAGNO (3)

(1) Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Italia.

(2) Università degli Studi di Milano Bicocca, Italia.

(3) Università degli Studi di Milano, Italia.

Argomento: Trauma e arresto cardiaco

Epinephrine is first-line therapy in the treatment of cardiac arrest (CA). However, epinephrine provokes  $\beta_1$ -mediated disproportionate increases in myocardial oxygen demand and consumption. The  $\beta_1$ -adrenoceptor antagonist esmolol has been shown to ameliorate the oxygen demand/consumption balance in animal models of CA. Therefore, we investigated the effects of the administration of esmolol in association with epinephrine on myocardial perfusion and neurologic resuscitation outcome in a porcine model of CA.

The left anterior descending coronary artery was occluded in 16 pigs, and CA was induced. After 12 minutes of untreated CA, cardiopulmonary resuscitation (CPR) was performed. After two minutes of CPR (PC2, figure), animals received epinephrine 30  $\mu\text{g}/\text{kg}$  (control group) or esmolol 0.5 mg/kg immediately followed by epinephrine 30  $\mu\text{g}/\text{kg}$  (treatment group). After resuscitation, hemodynamic parameters were monitored for 4 hours. Plasma biomarkers of myocardial and brain injury were measured at different time points. Ninety-six hours after ROSC animals were sacrificed and the brain was harvested for histological analysis.

Coronary perfusion pressure during CPR was significantly higher in the treatment group compared to control ( $p < 0.05$ ). Post resuscitation, systolic, mean, and diastolic arterial pressure (SAP, MAP, DAP) were also higher in treatment group compared to controls (two-way ANOVA, SAP  $p = 0.003$ ; MAP  $p = 0.0002$ ; DAP  $p < 0.0001$ ). Cardiac troponin release was consistently higher in animals in the control group than in those in the treatment group ( $p = 0.036$ ). Less brain injury was observed in treated animals compared to control group as assessed by a reduction in serum NSE at 96 hours post-resuscitation ( $p < 0.0001$ ) and by a significantly lower reactive microglia activation ( $p < 0.001$ ).

This experimental study shows better cardiac perfusion during CPR in animals treated with esmolol, resulting in better hemodynamic performance and less post-resuscitation neurological injury.

