Title: A COMPARISON OF EPINEPHRINE AND NOREPINEPHRINE ON MYOCARDIAL OXYGEN DELIVERY AND CONSUMPTION DURING CARDIOPULMONARY RESUSCITATION

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Introduction. While epinephrine improves myocardial blood flow (MBF) during cardiopulmonary resuscitation (CPR), its beta adrenergic effects may increase myocardial oxygen consumption (MVO_2) more than myocardial oxygen delivery (MDO_2). This study was carried out in order to compare the effects of epinephrine and norepinephrine, which are both mixed alpha and beta agonists, on MDO_2 and MVO_2 during open chest CPR in a ventricular fibrillation model, because the changes in these parameters have not as yet been investigated after treatment with norepinephrine in this setting.

Methods. 21 pigs weighing 20 - 22 kg (mean = 21 kg) were allocated to receive either placebo (controls) (N = 7), or 45 µg/kg epinephrine (N = 7), or 45 µg/kg norepinephrine (N = 7) following 5 min of electrically induced ventricular fibrillation and 3 min of open chest CPR. MBF (measured with radionuclide labeled microspheres) and arterial and coronary sinus oxygen contents (CaO_2 and CsO_2) were measured during normal sinus rhythm, and during open chest CPR before, and at 90 s after drug application. MDO_2 and MVO_2 were calculated using the formula: MBF x CaO_2 and MBF x (CaO_2 - CsO_2). Extraction ratios were calculated as MVO_2/MDO_2. Defibrillation was attempted 6 min after drug administration with a rapid sequence of 3 internal countershocks of 16, 16 and 32 J respectively. If restoration of spontaneous circulation was not achieved, the above doses of epinephrine, norepinephrine or placebo were again injected and mechanical measures continued between further attempts of defibrillation for 5 minutes. A spontaneous circulation was considered to be present when the systolic blood pressure was more than 80 mm Hg and the diastolic blood pressure more than 40 mm Hg for at least 5 min during which neither mechanical nor drug therapy were necessary. Statistical analysis of the differences between individual groups before and after drug therapy was performed using the Wilcoxon-Mann-Whitney-test for unpaired groups.

Results. The results following drug administration are shown in the table. CaO_2 was not significantly different between the groups before and after drug therapy. CsO_2 was significantly higher after norepinephrine than after epinephrine. MBF and MDO_2 were increased after epinephrine and norepinephrine injection. 90 s after epinephrine the MVO_2 was approximately 3 times higher, but after norepinephrine only 1.5 times higher as compared to the control group. Epinephrine did not influence O_2 extraction ratio, whereas norepinephrine diminished it. Restoration of spontaneous circulation was accomplished in 3 of 7 pigs in both the control and epinephrine groups, whereas all 7 animals of the norepinephrine group could be resuscitated.

Discussion. Epinephrine and norepinephrine are both strong alpha- and beta-1-receptor stimulators, but in contrast to epinephrine, norepinephrine does not influence beta-2-receptors. MBF during open chest CPR in a ventricular fibrillation arrest model is increased after both epinephrine and norepinephrine injection. Because epinephrine leads to a greater increase in MVO_2 than norepinephrine (perhaps via beta-2-stimulation), the myocardial oxygen extraction ratio and hence myocardial metabolism remains unchanged. In contrast to epinephrine, norepinephrine improves the O_2-extraction ratio and eases defibrillation and restoration of spontaneous circulation.

References.

1. Brown CG, Werman WA, Luu T, et al: Effect of epinephrine on myocardial oxygen delivery/utilization during CPR (abstract). Crit Care Med 15:419, 1987

		open chest CPR	
	group	before drug	90 s after therapy
CaO_2 ($cc O_2$/ml)	I	12.7 ± 1.2	12.7 ± 1.2
	II	13.7 ± 1.0	13.6 ± 0.9
	III	12.6 ± 1.6	12.7 ± 1.1
CsO_2 ($cc O_2$/ml)	I	7.0 ± 2.0	6.5 ± 2.1
	II	7.8 ± 1.8	6.7 ± 1.7
	III	6.8 ± 1.0	7.9 ± 1.4[C]
MBF (ml/min/100 g)	I	51 ± 23	54 ± 18
	II	71 ± 10	126 ± 18[B]
	III	74 ± 11	107 ± 30[A]
MDO_2 ($cc O_2$/min/100 g)	I	6.5 ± 3.0	6.8 ± 2.0
	II	9.6 ± 1.7	17.1 ± 3.2[B]
	III	9.4 ± 1.8	13.6 ± 4.2[B]
MVO_2 ($cc O_2$/min/100 g)	I	3.0 ± 1.8	3.3 ± 1.6
	II	4.0 ± 1.5	9.4 ± 3.0[B]
	III	4.2 ± 0.8	5.1 ± 2.0[C]
ER (%)	I	45 ± 12	51 ± 15
	II	43 ± 14	52 ± 13
	III	46 ± 5	37 ± 10[C]

group I, with placebo (controls);
group II, with epinephrine;
group III, with norepinephrine.

[A] $p < .05$ vs control group
[B] $p < .01$ vs control group
[C] $p < .05$ vs epinephrine group