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Comparison of epinephrine and dopamine during cardiopulmonary resuscitation

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Abstract. The effectiveness of epinephrine and dopamine for restoring spontaneous circulation after asphyxial or fibrillatory cardiac arrest was compared using a porcine model. Asphyxial arrest: 7 animals received 45 μg/kg epinephrine, 7 animals 2.5 mg/kg dopamine, the remaining 7 animals received no drug treatment. All 7 animals given epinephrine could be resuscitated after 174±53 s, spontaneous circulation could be restored in only 3 of 7 animals given dopamine after 487±63 s and in none of the control animals could spontaneous circulation be established. Ventricular fibrillation: 7 animals were defibrillated without either mechanical measures or drug therapy. The following doses were given before defibrillation and after starting mechanical measures to separate groups of 7 animals each: 45 μg/kg epinephrine, 2.5 mg/kg dopmaine, or no drug therapy. In the absence of either drug or mechanical measures and with mechanical measures only, spontaneous circulation could not be established in any of the cases. After administration of epinephrine, defibrillation and restoration of spontaneous circulation was achieved in 6 of 7 animals in 667±216 s, with dopamine, all the animals could be successfully resuscitated in the shorther time of 174±85 s. Epinephrine was found to be superior to dopamine in the treatment of asphyxial arrest whereas dopamine was found to be better in the management of ventricular fibrillation, probably by improving the balance between myocardial oxygen supply and demand.

Key words: Cardiopulmonary resuscitation – Asphyxial and fibrillatory cardiac arrest – Epinephrine – Dopamine – Porcine model

One of the most important factors which determine whether spontaneous circulation can be restored during cardiopulmonary resuscitation (CPR) is adequate myocardial perfusion. Myocardial blood flow is increased when epinephrine is given [1]. Experimental studies have shown that the actions of epinephrine important for restoration of spontaneous circulation are mediated by its alpha-adrenergic properties [16, 18]. The beta-adrenergic stimulation is probably also of importance during CPR, firstly, because beta-stimulation can lead to an increase in oxygen requirements during ventricular fibrillation (VF) [11, 12], and secondly, because the use of a pure alpha-agonist has not been found to cause as large an increase in myocardial blood flow as epinephrine after prolonged arrest [2].

The effects of dopamine as an endogenous precursor of norepinephrine are due to the combination of its action on alpha, beta and dopamine receptors and the release of endogenous norepinephrine. It is well documented that higher doses than 10 μg/kg/min cause both stimulation of alpha-1-adrenergic receptors and release of norepinephrine from nerve endings resulting in increased systemic and venous pressures [22].

We have compared the efficacy of epinephrine with that of dopamine in the management of asphyxial and electrically induced cardiac arrest and monitored the hemodynamic changes over a period of 2 h in the immediate post-resuscitation phase using a porcine model.

Methods

In 49 pigs weighing 18–27 kg (age 10–12 weeks) anaesthesia was induced by injecting metomidate (Hypnodil® 12.5 mg/kg i.v.). The animals were endotracheally intubated during spontaneous respiration. Muscular relaxation was carried out with pancuronium bromide (Pancuronium, Organon® 0.2 mg/kg, i.v.). The animals were subsequently ventilated with a Servo ventilator 900 (Siemens, FRG) using O_2/N_2O 35/65%. In order to maintain anaesthesia, ketamine (Ketavet® 10 mg/kg) was given i.v., followed by an infusion of

7.5 mg/kg/h. On completion of the preparatory phase, the ketamine infusion was stopped and the animals were ventilated for 10 min with 100% oxygen before arrest was induced. The infusion of ketamine was only resumed following successful resuscitation at the same dose as previously mentioned. Repeated doses of pancuronium 0.2 mg/kg were given as necessary.

Monitoring of cardiac rhythm was performed using a standard lead II ECG. Fluid-filled catheters were advanced via femoral cutdowns into the right atrium and abdominal aorta. A 7F quadruple-lumen flow-directed thermistor-tipped pulmonary artery catheter (Model SP5107, American Edwards Laboratories, Santa Ana California) was inserted via right external jugular vein cutdown. Cardiac output was measured in triplicate by thermodilution technique with 10 ml iced saline using the Edwards Laboratories Cardiac Output Computer 9520 A.

Intravascular pressures were recorded from the intraabdominal aorta, right atrium and pulmonary artery by using Statham P23Db transducers, which were aligned at the level of the right atrium and zeroed to atmospheric pressure and calibrated against a mercury column. Catheter position was confirmed at postmortem examination. All pressures were recorded on a four-channel recorder (Model LRS 4 R Penless, Linseis, FRG). An electronic subtraction circuit was used to record end-diastolic arteriovenous pressure differences (aortic minus right atrial pressure differences). The highest arteriovenous pressure difference, which was measured between 30 and 120 s after drug injection, was noted in the protocol.

Asphyxial arrest In 21 pigs asphyxial cardiac arrest was induced by clamping the endotracheal tube at the end of a normal exhalation. Arrest was defined as that point at which the aortic pulse pressure decreased to zero. In most cases the ECG showed a slow idioventricular rhythm (< 30 beats/min) or ventricular asystole. Cardiac arrest was allowed to continue for 3 min. During CPR the animals were ventilated at a respiratory rate of 20/min and with that tidal volume which, prior to induction of cardiac arrest, had been shown to result in normal blood gas values. Cardiac massage was carried out using a pneumatically driven chest compressor (Thumper®, Modell 1004, Michigan Instruments, Grand Rapids, Michigan) set to a compression rate of 80/min. The sternum was depressed by 5 cm, for which a compression force of 80–100 pounds had to be applied. The compression to relaxation phase was 1:1.

Thirty seconds after mechanical CPR had been initiated a bolus of epinephrine 45 μg/kg in 10 ml isotonic NaCl was given intravenously to 7 pigs. Another 7 animals were treated with 2.5 mg/kg dopamine in 10 ml saline. A control group of 7 animals was given 10 ml of saline. When this dose did not meet with success within 3 min, a repeat injection of the same amount was given. Mechanical resuscitation was continued using the parameters described above until spontaneous circulation was resumed or for a maximum of 30 min from the beginning of resuscitation. A spontaneous circulation was considered to be present when the ECG showed coordinated electrical activity, the systolic blood pressure was more than 90 mmHg and the diastolic blood pressure more than 40 mmHg for at least 30 min during which neither mechanical measures nor drug therapy were necessary.

Fibrillatory arrest. Ventricular fibrillation (VF) was induced in 28 animals by applying an alternating current of 50 Hertz and 60 volts via two subcutaneously placed needle electrodes. Ventilation was stopped at the same point in time at which the electric shock was applied. Cardiac arrest was allowed to continue for a period of 4 min before mechanical measures were applied and epinephrine, dopamine or saline were given intravenously in the same dose and timing as in the asphyxial studies mentioned above. Sixty seconds after drug application, the animals received external countershocks of 4 J/kg (Life-Pak 4, Physio-Control, Redmond, Washington). Two further groups of 7 animals received countershocks without either CPR or drugs. When the initial countershock failed to convert the VF, the animal received another countershock of 4 J/kg 30 s later. Ventilation and chest compressions were continued during and between attempts at defibrillation. When this second countershock was also unsuccessful, a third and further countershocks were administered at intervals of 90 s using 8 J/kg. After the sixth countershock the energy level was increased to 16 J/kg. Defibrillation was considered to be successful when VF was replaced by sinus rhythm, electromechanical dissociation or asystole.

Blood gases were measured using a blood gas analyser (IL 1302, Instrumentation Laboratories, Bornheim, FRG). Aortic blood samples were used to measure hematocrit, plasma lactate, sodium, potassium, glucose, colloid osmotic pressure and osmolality by standard techniques.

Statistical analysis of the differences between individual groups during the period of asphyxia and before and after resumption of spontaneous circulation were calculated using an analysis of variance. A p-value of < 0.05 was considered significant. Success of resuscitation was analyzed using a chi-square table analysis ($p < 0.05$).

Results

Asphyxial arrest

Period of asphyxia (Table 1). 4 min after clamping the endotracheal tube the heart rate, mean arterial blood pressure and mean pulmonary artery pressure were higher in all groups than pre-arrest values. A hemodynamic depression was observed after 6 min of asphyxia. The duration of asphyxia up to the point at which cardiac arrest was registered was 9.4 ± 1.3 min in the control group, 9.2 ± 0.8 min in the epinephrine group and 9.4 ± 1.2 in the dopamine group.

The hypoxemia led to a severe metabolic and respiratory acidosis. Hematocrit levels increased during the first 6 min of the asphyxial phase, but there was no further increase during the period of arrest. Plasma sodium concentrations remained unchanged in the physiological range. The highest plasma potassium values were measured 6 min after inducing asphyxia. In accordance with the changes in glucose, lactate and potassium concentrations there was a significant increase in plasma osmolality up to 10 to 15 mosmol/l. There were no major changes in plasma colloid osmotic pressure in any of the groups. Pre-arrest and during the period of asphyxia no significant differences between the groups were found.

CPR phase. Under external cardiac compression the mean peak value of end-diastolic arteriovenous pressure difference after saline was 10 ± 3 mmHg, after epinephrine was 32 ± 8 mmHg, and after dopamine was 29 ± 5 mmHg. None of those animals which were given neither epinephrine nor dopamine survived despite continuing the mechanical measures for a period of 30 min. When epinephrine was applied all 7 animals could be resuscitated after a mean duration of 174 ± 53 s. When dopamine was used a spontaneous circulation could only be achieved in 3 of the 7 ani-

Table 1. Hemodynamic, blood and plasma measurements pre-arrest and during the period of asphyxia[a,b]

		Pre-arrest	2A	4A	6A	S
Hemodynamic parameters						
HR (min^{-1})	MECH	116±14	126±12	152±14	58±6	–
	EPI	114±11	120±10	150±18	63±14	–
	DOP	113±13	123±15	147±8	53±9	–
MAP (mmHg)	MECH	88±16	116±10	134±10	52±8	–
	EPI	83±15	101±17	130±7	50±10	–
	DOP	95±14	111±16	130±18	57±6	–
MPAP (mmHg)	MECH	17±3	24±7	35±4	24±4	–
	EPI	16±6	22±6	32±3	21±3	–
	DOP	16±2	23±6	36±6	26±5	–
		Pre-arrest	2A	5A	S	
Arterial blood gas analysis						
PaO_2 (mmHg)	MECH	428±36	28±14	10±6	4±1	
	EPI	417±26	23±10	8±3	6±2	
	DOP	402±86	30±11	9±7	6±2	
$PaCO_2$ (mmHg)	MECH	38±5	66±6	92±24	108±26	
	EPI	37±4	64±6	82±21	96±31	
	DOP	39±4	67±5	88±7	117±19	
pH	MECH	7.44±0.04	7.26±0.06	7.11±0.08	7.00±0.16	
	EPI	7.48±0.06	7.29±0.06	7.16±0.10	7.08±0.15	
	DOP	7.43±0.06	7.24±0.05	7.09±0.06	6.95±0.09	
BEa (mmol/l)	MECH	2.4±2.6	1.9±2.0	−2.6±2.5	−6.8±5.0	
	EPI	4.4±2.6	3.4±2.7	−0.8±2.6	−4.1±4.3	
	DOP	2.3±3.0	1.4±2.5	−3.7±3.0	−8.1±3.0	
		Pre-arrest	2A	4A	6A	S
Laboratory parameters						
Lactate (mmol/l)	MECH	3.0±2.4	3.2±2.0	7.4±2.6	10.1±3.2	10.4±2.9
	EPI	2.3±1.1	2.1±1.2	5.7±2.2	7.5±3.6	10.1±1.7
	DOP	3.1±1.6	3.0±1.5	7.0±2.2	10.6±2.6	11.2±2.1
Hematocrit (l/l)	MECH	0.29±0.04	0.32±0.04	0.36±0.02	0.37±0.03	0.37±0.04
	EPI	0.30±0.03	0.33±0.03	0.39±0.03	0.38±0.03	0.36±0.02
	DOP	0.32±0.07	0.33±0.07	0.38±0.06	0.39±0.06	0.37±0.07
Sodium (mmol/l)	MECH	138±2	139±2	138±3	137±2	137±3
	EPI	138±2	139±2	139±1	139±2	135±2
	DOP	139±3	140±2	139±3	136±7	136±7
Potassium (mmol/l)	MECH	3.9±0.4	4.3±0.9	6.7±2.0	8.6±2.4	8.6±1.2
	EPI	3.7±0.5	4.2±1.1	6.8±1.9	7.4±2.5	7.2±1.0
	DOP	4.1±0.6	4.2±0.7	7.9±1.9	9.5±2.0	9.1±0.9
Glucose (mmol/l)	MECH	7.1±1.4	7.0±1.4	7.9±1.6	10.4±3.0	12.2±4.7
	EPI	7.0±1.2	6.8±1.3	7.6±1.5	9.5±2.7	16.5±3.0
	DOP	6.9±1.6	6.6±1.7	7.5±1.0	10.8±3.9	11.0±5.7
Osmolality (mosmol/l)	MECH	287±7	292±4	299±5	307±6	303±8
	EPI	290±4	292±3	300±10	303±10	308±5
	DOP	290±8	290±7	299±8	304±9	300±10
Colloid osmotic pressure (mmHg)	MECH	13.6±2.0	13.4±1.8	13.6±1.6	12.4±2.0	12.0±1.8
	EPI	13.8±1.3	13.7±1.1	13.8±1.1	13.3±1.1	12.2±1.0
	DOP	13.9±1.7	13.6±1.7	13.6±1.7	13.2±1.7	11.8±2.2

[a] Values are mean ± standard deviation

[b] Abbreviations: 2A, 4A, 5A, 6A = 2, 4, 5 and 6 min of asphyxia, S = stillstand (cardiac arrest), HR = heart rate, MAP = mean arterial pressure, MPAP = mean pulmonary artery pressure, MECH = mechanical measures only, no drug control, EPI = epinephrine, DOP = dopamine

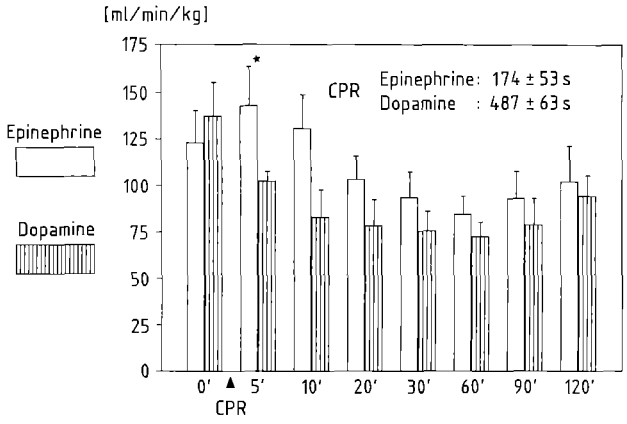

Fig. 1. Cardiac index pre-arrest and during a 2 h post-resuscitation period in the epinephrine and dopamine group (asphyxial arrest). CPR time is shown in the *right upper corner.* Values are mean ± sd. *$p < 0.05$ between groups

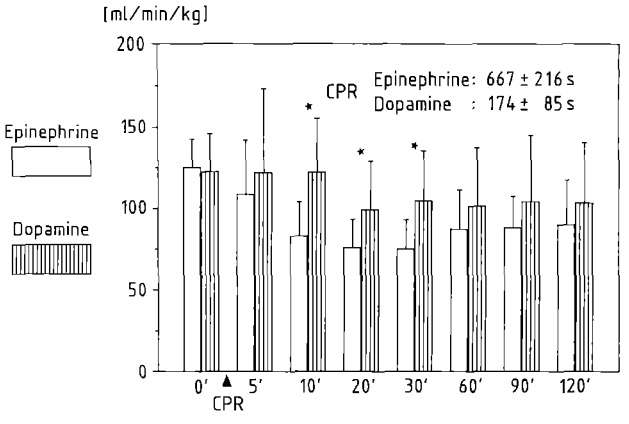

Fig. 2. Cardiac index pre-arrest and during a 2 h post-resuscitation period in the epinephrine and dopamine group (fibrillatory arrest). CPR time is shown in the *right upper corner.* Values are mean ± sd. *$p < 0.05$ between groups

mals after an average duration of 487 ± 63 s. After epinephrine, 3 animals and after dopamine 2 animals developed VF, which was converted with a 4 J/kg countershock to electromechanical dissociation and then to a normal sinus rhythm during the further course of CPR. The observed frequency of successful resuscitation between the group receiving no drug and those receiving epinephrine or dopamine was significantly different. There was also a significant difference in success of resuscitation between the epinephrine and dopamine group. All the animals which could be successfully resuscitated survived during the following 2 hour period of observation without having to be given any further drug therapy.

Post-CPR phase. When spontaneous circulation had been resumed for a period of 5 min the mean heart rate of the epinephrine group was 287 ± 19 compared to the significantly lower rate of 242 ± 8 beats/min in the dopamine group. The heart rates of both groups returned to normal during the further period of observation, during which no further significant difference between the groups could be found. The mean arterial blood pressure was similar in both groups, rising to a value of 130 mmHg during the first minutes after resuscitation and then slowly decreasing in both groups between the 20th and 60th min to a value of about 10 – 30 mmHg below pre-arrest levels. During the second 60 min period of observation, values tended to return towards pre-arrest levels. The values of cardiac index were significantly higher in the epinephrine group immediately after restoration of spontaneous circulation (Fig. 1).

The changes in arterial blood gases, hematocrit, plasma lactate, electrolytes, glucose, osmolality and colloid osmotic pressure pre-arrest and after restoration of spontaneous circulation are shown in Table 2.

Fibrillatory arrest

CPR phase. There was no significant difference in hemodynamic and laboratory parameters measured before induction of arrest between the 4 groups.

There was a marked difference between the frequency with which VF could be successfully defibrillated and the number of cases in which spontaneous circulation was resumed. Despite successful defibrillation in all animals, spontaneous circulation was not resumed in a single animal without drug therapy having to be given. The mean peak value of end-diastolic arteriovenous pressure difference after saline was 12 ± 4 mmHg, after epinephrine 32 ± 8 mmHg, and after dopamine 34 ± 6 mmHg. Because VF tended to recur when epinephrine was used, only 6 of the 7 animals could be resuscitated after 667 ± 216 s, whereas when dopamine was applied, all the animals could be resuscitated within the significantly shorter time of 174 ± 85 s. Success of resuscitation was not significantly different between the epinephrine and dopamine groups.

Post-CPR phase. In the epinephrine group, the mean heart rate increased immediately after successful resuscitation to 295 ± 26, while it rose to only 202 ± 21 beats/min in those animals treated with dopamine. The changes in mean arterial pressure were much the same in both groups. In the post-resuscitation period the cardiac index was higher in the dopamine group (Fig. 2). Laboratory measurements pre-arrest and after the resumption of spontaneous circula-

Table 2. Blood and plasma measurements pre-arrest and after resumption of spontaneous circulation in the asphyxial arrest model[a,b]

		Pre-arrest	Min after restoration of spontaneous circulation						
			5	10	20	30	60	90	120
PaO_2	EPI	417±26	264±130	255±130	256±148	315±155	371±89	300±114	308±105
(mmHg)	DOP	402±86	292±149	349±41	370±89	369±68	411±105	390±32	390±128
$PaCO_2$	EPI	37±4	51±12	48±7	46±9	44±10	42±8	44±8	43±9
(mmHg)	DOP	39±4	49±4	47±0	43±4	43±2	44±1	48±1	45±3
pH	EPI	7.48±0.06	7.19±0.12	7.23±0.10	7.26±0.11	7.29±0.11	7.36±0.12	7.38±0.11	7.39±0.12
	DOP	7.43±0.06	7.14±0.10	7.21±0.04	7.28±0.03	7.30±0.02	7.34±0.03	7.35±0.03	7.38±0.04
BEa	EPI	4.4±2.6	−8.0±4.5	−6.5±4.4	−5.1±4.0	−4.0±3.7	−0.6±4.5	1.0±4.2	1.4±0.1
(mmol/l)	DOP	2.3±3.0	−11.3±5.5	−7.8±2.7	−5.8±2.3	−4.4±1.7	−1.6±1.1	1.4±1.3	1.7±1.4
Lactate	EPI	2.3±1.1	8.4±2.4	7.3±2.2	6.7±2.0	6.2±1.8	4.0±2.1	3.0±1.9	2.7±1.7
(mmol/l)	DOP	3.1±1.6	10.7±3.3	7.7±1.6	6.8±1.1	6.1±0.5	3.9±0.7	2.5±0.6	1.9±0.3
Hematocrit	EPI	0.30±0.03	0.37±0.01	0.35±0.01	0.31±0.02	0.30±0.02	0.29±0.02	0.29±0.02	0.30±0.02
(l/l)	DOP	0.32±0.07	0.38±0.03	0.37±0.04	0.34±0.05	0.30±0.03	0.27±0.02	0.27±0.01	0.27±0.01
Sodium	EPI	138±2	137±2	139±3	139±2	140±2	139±2	139±1	140±2
(mmol/l)	DOP	139±3	137±3	138±0	139±1	138±1	139±1	140±1	140±1
Potassium	EPI	3.7±0.5	6.4±1.2	3.9±0.9	3.8±0.5	3.7±0.6	3.9±0.6	4.1±0.6	4.1±0.5
(mmol/l)	DOP	4.1±0.6	6.5±2.2	4.4±0.9	3.8±0.3	3.6±0.2	3.9±0.1	4.1±0.1	4.2±0.1
Glucose	EPI	7.0±1.2	13.8±1.8	14.1±2.5	13.7±2.7	11.8±2.8	7.7±1.6	5.7±1.7	5.4±1.7
(mmol/l)	DOP	6.9±1.6	12.5±5.4	16.2±2.6	16.3±3.1	15.3±3.5	10.4±2.1	7.1±1.6	6.6±1.1
Osmolality	EPI	290±4	301±5	302±6	300±5	296±5	294±5	292±6	294±6
(mosmol/l)	DOP	290±8	305±3	304±5	300±5	298±9	294±4	294±4	293±4
COP	EPI	13.8±1.3	14.1±1.0	13.3±1.0	12.1±0.9	11.7±1.3	11.6±1.3	11.5±1.3	11.7±1.2
(mmHg)	DOP	13.9±1.7	14.7±3.1	15.7±0.8	14.0±0.6	12.7±0.1	11.7±0.7	11.6±0.7	11.7±0.5

[a] Values are mean±standard deviation
[b] Abbreviations: COP = colloid osmotic pressure

tion in the epinephrine and dopamine groups are summarised in Table 3.

Discussion

The asphyxial cardiac arrest model was chosen, because in children cardiac arrest is often caused by this mechanism [15]. A possible explanation for the rapid fall in arterial partial pressure of oxygen after clamping the endotracheal tube could be a high oxygen consumption and a low functional residual capacity of the animals when in the supine position. The hypoxemia and hypercapnia led to an initial increase in heart rate, and in mean arterial and pulmonary artery pressure. The decrease in tissue oxygenation causes a lactic acidosis. Protein is probably lost into the interstitial space, since the colloid osmotic pressure does not increase with simultaneous hemoconcentration. During the period of asphyxia and arrest, VF did not occur. Plasma potassium levels rise during the asphyxial phase and hypoxia leads to a fall in intracellular ATP concentration. The subsequent disturbance in cellular homeostasis allows potassium to pass down its concentration gradient, i.e. out of the cell. The period from circulatory arrest to initiation of treatment was different between the two arrest groups, because an oxygen deficit was already present at the beginning of the arrest period in the asphyxial model.

After successful resuscitation a metabolic and a respiratory acidosis at unchanged respirator settings was observed in both models. The hypercapnia might have been caused by an accumulation of carbon dioxide in the underperfused tissues during CPR, in combination with impaired pulmonary function (interstitial lung edema) [4, 5, 14]. An increase in hematocrit compared to baseline control was seen immediately after resuscitation in both forms of cardiac arrest, whereas the colloid osmotic pressure did not rise. Pre-arrest hematocrit values were restored at between 20 and 30 min and were subsequently lower than pre-arrest values. The following interpretation of the pathophysiological changes is possible [9]: During asphyxia and resuscitation plasma water and protein are lost into the interstitial space and hematocrit is increased, whereas colloid osmotic pressure is unchanged. Approximately 30 min post-CPR plasma water is probably redistributed and the hematocrit falls

Table 3. Blood and plasma measurements pre-arrest and after resumption of spontaneous circulation in the fibrillatory arrest model[a,b]

		Pre-arrest	Min after restoration of spontaneous circulation						
			5	10	20	30	60	90	120
PaO_2	EPI	425±50	349±74	365±76	390±97	403±92	429±63	419±70	429±50
(mmHg)	DOP	422±66	340±75	397±66	402±58	421±55	403±49	403±83	423±51
$PaCO_2$	EPI	36±3	49±9	44±6	40±4	41±4	42±5	40±5	39±6
(mmHg)	DOP	38±4	51±10	46±6	45±8	43±6	44±7	44±5	43±5
pH	EPI	7.47±0.05	7.23±0.13	7.27±0.10	7.30±0.09	7.31±0.08	7.32±0.06	7.38±0.06	7.42±0.06
	DOP	7.46±0.05	7.23±0.08	7.27±0.06	7.29±0.07	7.31±0.05	7.33±0.06	7.33±0.05	7.35±0.04
BEa	EPI	3.5±2.7	−5.9±5.2	−5.4±4.7	−5.0±4.8	−4.2±4.3	−1.7±3.2	−0.3±3.6	1.1±4.2
(mmol/l)	DOP	3.3±1.6	−5.3±3.0	−4.7±2.8	−4.1±2.8	−3.6±2.4	−2.1±2.4	−1.4±3.1	1.3±3.3
Lactate	EPI	2.8±1.2	8.6±3.4	8.1±3.5	7.7±3.0	7.5±2.7	6.5±2.8	5.5±2.5	4.7±2.4
(mmol/l)	DOP	2.6±1.5	7.4±2.6	6.6±2.5	6.8±3.0	5.6±2.4	4.9±2.9	4.5±3.0	3.9±3.4
Hematocrit	EPI	0.28±0.04	0.36±0.03	0.33±0.03	0.30±0.03	0.29±0.03	0.28±0.02	0.28±0.02	0.29±0.02
(l/l)	DOP	0.32±0.03	0.40±0.04	0.37±0.04	0.34±0.05	0.32±0.05	0.30±0.04	0.30±0.04	0.30±0.04
Sodium	EPI	138±3	138±4	140±3	139±3	140±4	140±4	140±3	139±4
	DOP	139±2	139±3	140±3	140±2	140±2	140±2	141±2	141±2
Potassium	EPI	4.2±0.5	6.7±0.7	4.2±1.0	4.2±1.0	4.2±1.1	4.2±0.7	4.2±0.6	4.1±0.5
(mmol/l)	DOP	4.0±0.3	6.4±1.3	4.2±1.0	4.0±0.5	3.9±0.6	3.9±0.4	4.0±0.3	4.1±0.3
Glucose	EPI	7.0±1.6	11.9±3.4	12.1±3.6	12.2±3.9	11.2±4.1	8.8±2.6	8.3±2.7	7.1±1.3
(mmol/l)	DOP	7.5±1.7	11.3±2.4	11.6±2.7	11.2±3.3	11.7±4.4	9.3±2.9	7.1±2.2	6.0±1.5
Osmolality	EPI	290±5	299±7	298±6	2196±5	296±6	297±4	294±7	292±7
(mosmol/l)	DOP	288±10	299±5	299±4	297±3	295±4	294±5	293±5	291±5
COP	EPI	14.7±1.2	15.6±0.8	15.1±1.3	13.5±1.3	13.0±1.3	12.8±1.3	12.8±0.9	12.8±0.9
(mmHg)	DOP	14.8±1.0	16.4±0.8	15.4±0.8	13.9±1.3	13.2±1.7	12.7±1.5	12.3±1.5	12.1±1.6

[a] Values are mean ± standard deviation
[b] Abbreviations: COP = colloid osmotic pressure

to pre-arrest levels while colloid osmotic pressure is than lower than baseline controls.

In the animal model used in this study, epinephrine was found to be superior to dopamine for the management of asphyxial cardiac arrest as assessed by the time to successful resuscitation and the number of successful resuscitated animals. On the other hand, dopamine resulted in a more rapid restoration of circulation after fibrillatory arrest than epinephrine.

As previously shown by Kern et al., resuscitation was never successful when the diastolic arteriovenous pressure difference, which reflects myocardial perfusion pressure, was around 10 mmHg, as seen in our control group [7]. The diastolic arteriovenous pressure differences measured in our study indicate that the administered dose of epinephrine was adequate for restoration of spontaneous circulation [21]. We presume that approximately the same degree of vasoconstriction was caused by epinephrine and dopamine, because coronary perfusion pressure was practically the same in both groups.

In the setting of CPR epinephrine and dopamine may not only cause vasoconstriction in the peripheral circulation and hence an increase in coronary perfusion pressure, but also may alter the coronary blood flow by direct stimulation of alpha- and beta-receptors on coronary blood vessels.

Both beta-adrenoceptor-mediated and metabolically induced coronary artery vasodilation can antagonize alpha-adrenoceptor vasoconstriction [13]. This hypothesis is supported by the fact that the use of a pure alpha-agonist does not lead to as large an increase in myocardial blood flow as does epinephrine when given after prolonged arrest [8]. Epinephrine and dopamine thus appear to have the same effects. Dopamine is also an indirect sympathomimetic amine and leads to the release of norepinephrine. The beta-2-sympathomimetic activity of dopamine is weaker than that of epinephrine. In an investigation using the same model, we found that restoration of spontaneous circulation was possible in a significantly shorter time with epinephrine as compared to norepinephrine [10]. Epinephrine is assumed to markedly increase both the inotropy and chronotropy of the heart via beta-2-receptors [19]. Beta-2-receptor stimulation probably facilitates restarting of the arrested heart. Furthermore, for the restoration of asphyxial arrest, dopamine is even less effective than norepinephrine, be-

cause it increases the cholinergic tone of the heart [6]. This in turn may play a role in the treatment of asystole, for there are also some data to suggest that atropine is effective in the management of ventricular asystole [3, 20].

Using dogs weighing 12–20 kg, Otto et al. found no difference in resuscitation success between dopamine 40 mg and epinephrine 1 mg in asphyxial arrest [17]. These differing results compared to those in our study are perhaps due to the different species used. When faced with the question of which animal model to use there are undoubtedly a number of factors for and against the use of both models. We are concerned that myocardial and cerebral recovery is possible in the canine model after very much longer cardiac arrest times than in the human being and the pig.

It is assumed that during VF beta-2-stimulation is detrimental to the balance of myocardial oxygen delivery and consumption [11]. This may be the reason why reanimation could be achieved within a shorter period of time when dopamine and norepinephrine were used in comparison to epinephrine. Further studies are necessary to determine whether the advantages observed during the use of dopamine and norepinephrine for the treatment of experimental fibrillatory arrest also apply to VF in humans.

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