

Altered Hemodynamic Response To Epinephrine Before and During Cardiopulmonary Bypass in Man

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Abstract

The hemodynamic response to epinephrine was investigated in 10 patients undergoing aorto-coronary bypass surgery. Prior to bypass, the intravenous injections of epinephrine 10 µg increased the mean arterial pressure by $32.6 \pm 5.1\%$ associated, with a significant increase of the cardiac output, while the systemic vascular resistance did not show a significant change. In contrast, injection of the same dose of epinephrine during cardiopulmonary bypass and aortic cross-clamp only produced $17.9 \pm 8.9\%$ increase of mean arterial pressure associated with a corresponding increase of systemic vascular resistance. The results suggest that the pressor response to epinephrine is significantly lower during bypass as compared to the pre-bypass period.

Introduction

The vasopressor effect of phenylephrine (PH), a selective alpha-adrenergic agonist, is significantly greater during cardiopulmonary bypass and aortic cross-clamp (CPB + AXC) as compared to the pre-bypass period (1, 2).

In contrast to PH, epinephrine (EP) is a mixed alpha-and beta-adrenergic agonist (3). The present report compares the pressor response to EP during the pre-bypass period to that achieved during CPB + AXC.

Materials and Methods

Investigation was carried out in 10 patients having coronary artery disease, scheduled for elective aorto-coronary bypass grafting. Their age was 53-71 years, and their weight was 64-90 kg. All patients had good left ventricular function; none of the patients had congestive heart failure or LVEF < 0.4. All patients were maintained preoperatively until the day of surgery, on oral propranolol (10 mg tid), nifedipine (10 mg tid) and isordil (10 mg tid). The investigation was approved by the Institution Research Committee and an informed consent was obtained.

Patients were premedicated with morphine 10 mg, scopolamine 0.4 mg, and promethazine 25 mg im. Anesthesia

was induced with midazolam, 0.1 - 0.2 mg/kg, fentanyl 40 µg/kg and a mixture of alcuronium 0.25 mg/kg and pancuronium 0.1 mg/kg. Following tracheal intubation, the patients were ventilated with 100 percent oxygen without any inhalation anesthetic supplementation.

The patients were continuously monitored by EKG (V5), a radial artery catheter and a Swan-Ganz thermodilution PA catheter, which was introduced via an internal jugular vein introducer cannula (Arrow). The cardiac output was measured in duplicate using 9520 A cardiac output computer (a), while the pressures were measured by Gould Statham Medical Pressure Transducers attached to a calibrated display (b). Hemodynamic monitoring included mean arterial pressure (MAP), cardiac output (CO), and pulmonary capillary wedge pressure (PCWP). Also, the systemic vascular resistance was computed as $\frac{MAP-CVP}{CO} \times 80$ dyne-sec-cm⁻⁵. Hemodynamic

parameters prior to CPB were recorded 10-20 minutes following induction of anesthesia before skin incision. A bolus of EP 10 µg was then injected via the side-port of the internal jugular vein introducer cannula. A single small bolus of EP was investigated to minimize any potential increase of myocardial wall stress and myocardial oxygen consumption. When the peak MAP following EP was reached, the other hemodynamic parameters were measured.

During CPB, a Bentley-10 adult bubble oxygenator (c) was primed with 1500 ml lactated Ringer's solution. The patient was perfused by a roller pump (d) at a constant flow of 2.3 l/m²/min, and the oxygenator was bubbled by an equal flow of 100% oxygen. The mean hematocrit was lowered to $22.8 \pm 0.45\%$ during CPB from a pre-bypass level of $43 \pm 2.8\%$. As soon as CPB was instituted, the patients were cooled to a central venous temperature of $27.4 \pm 2.8^\circ\text{C}$, and the heart was arrested after aortic cross-clamping by cardioplegic solution (K⁺ 30 mEq/l and 4°C). Approximately 20-30 minutes following CPB + AXC, a steady MAP was achieved. A bolus of EP 10 µg was then injected into the venous line of the oxygenator, and its peak

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- a. American Edwards Laboratories
 - b. Hellige-Servomed
 - c. American Bentley, Irvine, CA
 - d. Sarns 5000, Ann Arbor, MI

effect on MAP and reservoir volume (RV) was recorded. Also, SVR was calculated. The percentage changes of MAP and SVR following the injection of EP during CPB were calculated and compared to those achieved when EP was injected prior to CPB. Each patient served as his own control.

All data were expressed as mean \pm SD. The paired t-test was used to compare the different hemodynamic parameters. $P < 0.05$ was considered significant.

Results

Hemodynamic Changes Before CPB (Table 1)

The injection of EP 10 μ g prior to CPB significantly increased MAP from 80 ± 13.3 mmHg to 106 ± 18.4 mmHg ($P < 0.001$), amounting to a mean percentage increase of $32.6 \pm 15.1\%$. The increase of MAP was associated by a significant increase of CO from 4.0 ± 0.8 l/min to 4.9 ± 0.95 l/min ($P < 0.01$), amounting to a mean percentage increase of $25.4 \pm 18.6\%$. The mean SVR did not show a significant change.

Hemodynamic Changes During CPB + AXC (Table 2)

The mean pump flow during CPB was 5.0 ± 0.6 l/min. After 20-30 minutes, the MAP stabilized at 67.5 ± 17.5 mmHg, which was not significantly different from the control MAP prior to bypass. Injection of EP 10 μ g during CPB + AXC significantly increased MAP from 67.5 ± 17.5 mmHg to 79.0 ± 18.4 mmHg ($P < 0.001$), amounting to a mean percentage increase of $17.9 \pm 8.9\%$. The mean percentage increase of MAP was significantly lower than the percentage increase prior to CPB.

Control SVR during CPB before the injection of EP was

Table 1

	CONTROL	EPINEPHRINE	%CHANGE	P
MAP (mmHg)	80 ± 13.3	106 ± 18.4	$32.6 \pm 15.1\%$	<0.001
CO l/min	4.0 ± 0.85	4.98 ± 0.95	$25.4 \pm 18.6\%$	<0.01
PCWP mmHg	12.0 ± 4.1	15.3 ± 6.29	28.3 ± 38.1	<0.05
SVR dyne.sec.cm ⁻⁵	1480.9 ± 429.3	1549.4 ± 412.1	$6.5 \pm 16.8\%$	NS
HR / min	69.5 ± 10.5	66.6 ± 12.2		NS

The effect of epinephrine 10 μ g on the different hemodynamic parameters prior to CPB.

calculated as 1118 ± 416 dyne-sec-cm⁻⁵, which was not significantly different from control SVR prior to bypass. Injection of EP during CPB increased SVR from 1118 ± 416 dyne-sec-cm⁻⁵ to 1292.5 ± 469 dyne-sec-cm⁻⁵ ($P < 0.001$), amounting to a mean percentage increase of $16.5 \pm 8.1\%$.

Discussion

The present report shows that EP 10 μ g results in a significantly greater pressor response when administered prior to CPB, as compared to that achieved during CPB + AXC. In contrast, Massagee, et al. (1) and Schwinn, et al. (2) have shown that less pH is required during CPB + AXC than before bypass to produce the same pressor effect. Such difference between EP and pH may be attributed to the different mechanisms by which these drugs increase the blood pressure (4, 5, 6).

Blood pressure is the product of CO x SVR. Prior to CPB, the response to a vasopressor is determined by its effect on both CO and SVR. During CPB + AXC, the heart is excluded from the circulation and the pump flow is maintained at a constant level; hence, SVR becomes the main determinant of the pressor response. Vasopressors, which increase the blood pressure by a predominant increase of SVR, may be more effective during CPB, while those acting by a predominant increase of CO may be more effective during the pre-bypass period (4).

pH is a selective alpha-adrenergic agonist (1, 6, 7), which increases the blood pressure by increasing SVR. Prior to CPB, the vasopressor response to pH is associated with an increased afterload and by reflex, vagotonic discharge via the baroreceptors. This will result in bradycardia and decreased

Table 2

	CONTROL	EPINEPHRINE	%CHANGE	P
MAP (mmHg)	67.5 ± 17.5	79.0 ± 18.4	$17.95 \pm 8.9\%$	<0.001
SVR dyne.sec.cm ⁻⁵	1118 ± 416	1292.5 ± 469.0	$16.5 \pm 8.1\%$	<0.001
RV (ml)	2100 ± 950	2160 ± 1000		NS

The effect of epinephrine 10 μ g on MAP and SVR and reservoir volume (RV) during CPB + AXC.

cardiac output (1, 8). Since the blood pressure is the product of CO x SVR, the decreased CO can partially counteract the vasopressor response of pH, and hence, a higher dose of pH may be required before bypass than during CPB + AXC to produce the same pressor effect (1, 2).

In contrast with pH, epinephrine is a mixed alpha- and beta-adrenergic agonist (3). The present report shows that the injection of EP 10 µg prior to CPB is followed by a significant increase of CO and MAP without a significant change of SVR, denoting that the pressor response to this dose of EP is predominantly due to its beta-adrenergic inotropic action on the heart. Injection of the same dose of EP during CPB + AXC only produced $17.9 \pm 8.9\%$ increase of MAP as compared to the $32.6 \pm 5.1\%$ increase that was achieved when the same dose of EP was injected before bypass.

The decreased pressor response to EP during CPB + AXC may be attributed to exclusion of the heart from the circulation; hence, the pressor response can be only achieved by increasing SVR. The altered response may be also attributed to other events which follow the initiation of bypass, such as hypothermia (9) and hemodilution secondary to the use of crystalloid prime (10). Hemodilution will not only decrease the blood viscosity, but can also dilute the circulating catecholamines (10, 11), and may even blunt their alpha-adrenergic vasopressor response (12).

In conclusion, the intravenous injection of EP 10 µg prior to CPB produces a significant increase of MAP and CO, without a significant change of SVR. Injection of the same dose of EP during CPB + AXC, when the heart is excluded from circulation, results in a lower pressor response.

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