JECT. 2012;44:66–68
The Journal of ExtraCorporeal Technology

Case Reports

High Flow and High Dose Neosynephrine are Effective to Maintain Perfusion Pressure for the Patient with Preoperative Angiotensin Converting Enzyme Inhibitor during Cardiopulmonary Bypass

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Abstract: Angiotensin converting enzyme inhibitors (ACEIs) are widely used in the treatment of hypertension, myocardial infarction, and congestive heart failure. They have a known adverse effect of unresponsiveness to vasoconstrictors resulting in hypotension for the patients undergoing cardiac surgery. We report a case of a 43-year-old female patient with preoperative lisinopril (2.5 mg per day for a week prior to cardiac surgery), who was diagnosed with severe mitral and tricuspid valve regurgitation. She underwent both a mitral and tricuspid valve replacement operation using cardiopulmonary bypass (CPB). To address her ACEI-associated hypotension on cardiopulmonary bypass, bypass flows were as high as cardiac index of greater than 3 (3.1 ± .2) L/min/m^2 to provide sufficient perfusion indicated by cerebral oxymetry monitoring and adequate urine on pump. In addition, due to unresponsiveness to regular concentration of neosynephrine (neo), boluses of higher concentrations up to 320 μg/mL of neo were administered to maintain the perfusion pressure on pump. The patient was weaned from CPB uneventfully and was discharged home on postoperative day 7. Additional therapeutic treatment to ACEI-associated hypotension and unresponsiveness to neo for the patients undergoing cardiac surgery using CPB is reviewed as well in this paper. **Keywords:** angiotensin converting enzyme inhibitor, cardiopulmonary bypass, mitral valve replacement, tricuspid valve replacement. *JECT. 2012;44:66–68*

Angiotensin converting enzyme inhibitors (ACEIs) are widely used in the treatment of patients with hypertension, congestive heart failure (CHF), and myocardial infarction. A study in 2011 showed that ACEIs decrease mortality and cardiovascular events and improve quality of life (1). More and more patients who are undergoing cardiac surgery receive these drugs preoperatively. ACEI-associated hypotension and vasoplegic syndrome are among the most adverse events in the perioperative period of cardiac surgery. ACEIs increase vasoconstrictor requirements to maintain systolic blood pressure at more than 85 mmHg despite a normal cardiac output after cardiopulmonary bypass (CPB), and long-term ACEIs treatment attenuates adrenergic responsiveness by more than 50% (2). In this paper, we present a case of a 43-year-old female patient on preoperative lisinopril who underwent double valve replacements using CPB. We also describe the strategy to maintain the sufficient perfusion pressure on CPB.

Received for publication July 10, 2011; accepted April 2, 2012.
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The senior author has stated that authors have reported no material, financial or other relationship with any healthcare-related business or other entity whose products or services are discussed in this paper.

DESCRIPTION

A 43-year-old woman with difficultly breathing and chest pain presented to the emergency room at Lakeland Medical Center; she was found to have both severe mitral regurgitation and tricuspid regurgitation by transesophageal echocardiogram (TEE) with an ejection fraction of 40–45%. She had an extensive history of pneumonia, chronic obstructive pulmonary disease, pulmonary hypertension, CHF, bipolar disease, cirrhosis, and drug addiction. Her medications included lisinopril 2.5 mg per day for a week,

which was discontinued 2 days prior to surgery. Chest x-ray showed an enlarged heart and the electrocardiogram indicated sinus tachycardia. The patient was 160 cm tall and weighed 64 kg, body surface area was 1.69, and body mass index was 24.9. The patient presented to the operating room with an initial blood pressure of 81/40 mmHg. Following induction of general anesthesia, a Swan-Ganz catheter was placed via the right internal jugular vein to monitor the cardiac output (and withdrawn into the right atrium before repair and eventual replacement of the tricuspid valve), a TEE probe was inserted, and TEE exam confirmed the previous findings. A cerebral oxymetry device INVOS system (model: 5100B, Somanetics, Troy, MI) was used to continuously monitor the cerebral regional O_2 saturation intraoperatively.

A routine CPB circuit was used for this patient. Our system consists of a hollow fiber oxygenator (Terumo CAPIOX RX25, Terumo, Ann Arbor, MI), Terumo Sarns System 1 heart-lung machine with roller-head arterial pump (Terumo), X-coated circuit with arterial line filter, and 4:1 blood cardioplegia system (Terumo). A hemoconcentrator (Terumo CAPIOX) was placed in the circuit, and an inline blood gas monitoring device, CDI 100 (Terumo), was used for continuous monitoring of venous O_2 saturation, hemoglobin, and hematocrit. Our circuit was initially primed with 2000 mL Normosol (Plasmalyte A) and continuously debubbled according to our standard protocol until the surgical incision started. After 900 mL of fluid was removed from the circuit, 25 g mannitol, 10 g Amicar, 100 mg lidocaine, 50 meq sodium bicarbonate, and 10k units heparin were added to the circuit and the system was continuously debubbled again until systemic heparinization started. Once the chest was opened and the heart was exposed, the patient was given 26k units heparin by anesthesia and the activated clotting time was 483. A 7-mm soft-flow aortic cannula (Terumo) was placed in the ascending aorta and two 36-Fr right angle venous cannulae (Edwards Life Science, Irving, CA) were used for bicaval cannulation due to patient's enlarged heart. A Cell Saver 5+ (Haemonetics, Braintree, MA) was used intraoperatively to process the sequestered blood from the surgical field and the remaining blood in the circuit after decannulation.

After the patient was placed on CPB, moderate hypothermia was used to cool her to a bladder temperature of 30°C. Initial antegrade and retrograde cardioplegia with 4:1 ratio (subsequent 16:1 ratio after initial dose) of blood over cardioplegia were applied to arrest the heart immediately after the X-clamp was placed on the aorta. The heart was completely arrested after 1000 mL of 4:1 cardioplegia (200 mL cardioplegia and 800 mL blood) was given to the patient. The initial blood pressure on pump stayed in the low 40s mmHg after the heart was arrested. To elevate the blood pressure to reasonable 50s or 60s mmHg, we increased the bypass flow to greater than 3.0 L/min/m^2 of cardiac index (Table 1) and gave initial boluses of 80 μg/mL neosynephrine (neo) through the manifold by syringe; however the patient was barely responsive. The higher concentration of neo was applied and we ended up using 320 μg/mL neo to maintain the average blood pressure at 58 (58.6 ± 3.9) mmHg during CPB (Table 1). The average hemoglobin and hematocrit on pump were 8 gm/dL and 23.4%, respectively with a total of 2400 mL fluid filtered by the hemoconcentrator during CPB. No packed red blood cells were used during CPB. The mitral valve replacement and tricuspid valve annuloplasty were initially performed on the patient. After completion, the patient was weaned off CPB successfully, but TEE exam found the repaired tricuspid valve was still severely regurgitant. The surgeon decided to go back on CPB and replace the tricuspid valve. When the tricuspid valve replacement was done, the patient was weaned from CPB uneventfully. The total CPB time was 268 minutes and X-clamp time was 109 minutes. After the surgery, the patient was transferred to critical care unit and was extubated next morning. The patient was progressing daily and discharged home on postoperative day 7.

COMMENT

Since the first ACEI was produced in the late 1970s, this type of drug has been widely used in treatment of the patients with hypertension, CHF, and myocardial infarction. ACEIs will likely attenuate adrenergic responsiveness and increase vasoconstrictor requirement for the cardiac patients. ACEIs, especially lisinopril, have the known adverse effects of hypotension and unresponsiveness to vasoconstrictors. The ATLAS trial study reported 7–11% occurrence of lisinopril-induced severe hypotension in the treatment of chronic heart failure (3).

Table 1. The patient's intraoperative parameters.

	MAP (mmHg)	PAP (mmHg)	rSO_2 (%)	Blood flow (L/min)	CI (L/min/m^2)	Sweep Flow (L/min)	sVO_2 (%)
Pre-CPB (post-intubation)	81/40	44/35	41	—	1.8	—	41
Post-CPB	76/42	—	43	—	—	—	80
On CPB	58.6 ± 3.9	—	$47.3 \pm .9$	$5.2 \pm .4$	$3.1 \pm .2$	$1.5 \pm .4$	90.5 ± 4.7

MAP, mean arterial pressure; PAP, pulmonary arterial pressure; rSO_2, cerebral regional oxygen saturation; CI, cardiac index; sVO_2, mixed venous oxygen saturation.

In this case study we present a patient with preoperative lisinopril-induced hypotension on CPB for mitral valve replacement and tricuspid valve replacement operation. To maintain the reasonable bypass pressure and adequate bypass perfusion during CPB, we increased bypass flow to average cardiac index of 3.1 L/min/m^2 with help of substantial venous drainage, the sufficient cerebral perfusion was confirmed by cerebral oximeter monitoring (Table 1) and 800 mL urine was achieved during CPB. Meanwhile, due to the fact that the patient was less responsive to neo on CPB, we increased the neo concentration from 80 μg/mL to ultimately 320 μg/mL to maintain the pump blood pressure at upper 50s (58.6 ± 3.9) mmHg. George et al. reported that 90% effective dose of neo was 147 μg (95% confidence interval 98–222 μg) on healthy female patients with a cesarean delivery (4). In this case, the bolus of 320 μg/mL dose was demonstrated a safe and effective dosage on CPB. The mechanism of unresponsiveness to neo for the patients on the preoperative ACEIs is unclear to date. ACEIs inhibit the production of angiotensin II, which is the most potent endogenous vasoconstrictor (40 times more potent than norepinephrine) and potentiate the effects of bradykinin, an endogenous potent vasodilator. The reduced angiotensin II and increased bradykinin effects are likely among the reasons for ACEI-induced unresponsiveness to neo. Vasoplegic syndrome is generally defined as an arterial pressure less than 50 mmHg, cardiac index greater than 2.5 L/min/m^2, right atrial pressure less than 5 mmHg, left atrial pressure less than 10 mmHg, and low systemic vascular resistance during intravenous norepinephrine infusion. The incidence of vasoplegic syndrome associated with the pre-operative use of ACEIs was reported as high as 44.4% in the patients using CPB (5). Use of methylene blue (MB) (6) and vasopressin, such as terlipressin (7), were reported to have beneficial effects to attenuate unresponsiveness to neo, and were used to treat ACEI-induced hypotension in patients using CPB. MB is believed to act through competition with nitric oxide, in binding to guanylate cyclase resulting in enzyme activation. A dose of intravenous MB (2 or 3 mg/kg) was recommended as a rescue treatment, and continuous infusion was optional for patients not responding to single dose of MB (8,9). Methylene blue should not be administered to patients that take antidepressant medications with selective serotonin re-uptake inhibition (SSRI) properties such as fluoxeine. The monoamine oxidase inhibitor properties of MB could cause a serotonin storm when combined with SSRIs (10). Terlipressin is a synthetic analogue of arginine vasopressin; it binds specifically to v1 receptor and produces a strong vasopressor effect. Administration of a bolus of 1 mg demonstrated a useful alternative in treatment of refractory hypotension post CPB (7). Therefore application of MB and vasopressin should be considered if high bypass flow and high dose neo fail to maintain the reasonable perfusion pressure during CPB.

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