



Severe Refractory Intraoperative Hypotension in a Patient with Major Depression under Long-Term Antidepressant Treatment: A Case of Left Nephrectomy Surgery

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According to the World Health Organization, about 450 million people suffer from mental and behavioral disorders worldwide,¹ whereas depression has a lifetime prevalence between 10% and 20%.² Many surgical patients may take antidepressants, and several studies have reported an increased incidence of sudden cardiac death in these patients. We here present a patient who had major depression under medication control for 20 years and underwent left nephrectomy. Severe hypotension, resistant to catecholamine (such as ephedrine, epinephrine, and dopamine) treatment, was developed after general anesthetic induction. A review of preoperative psychotropic medications on patient's hemodynamic changes and the management for the refractory hypotension after general anesthetic induction are presented and discussed in this case report.

Key words: Intraoperative hypotension, antidepressants, transesophageal echocardiography

INTRODUCTION

Many patients with psychiatric illnesses are prescribed with long-term drug therapy, and anesthesiologists should be aware of the interactions of psychotropic medications and anesthetic agents.¹ Tricyclic antidepressants (TCAs) are used in the treatment of depression. Intraoperative hypotension in patients with long-term TCA treatment is usually a result of peripheral vasodilatation (alpha-adrenergic blockade) or myocardial contractility decrease (quinidine-like myocardial suppressant effect).³ We present the case of an 87-year-old woman who has major depression under long-term TCA treatment and experienced severe intraoperative hypotension. This article aims to discuss the relationship between long-term TCA medication and intraoperative hypotension, which is associated with general anesthetic induction. Furthermore, this article discusses the drug of choice among norepinephrine, vasopressin, dopamine, and epinephrine in the management of intraoperative hypotension associated with long-term TCA treatment.

CASE REPORT

An 87-year-old woman (150.5 cm, 68.5 kg) was scheduled for elective left nephrectomy. The patient suffered from

symptoms of transient painless gross hematuria for 6 months; urological computed tomography examination revealed a 1.9 cm × 2 cm × 2.4 cm filling defect lesion over the left pelvic region and uroepithelial tumor was suspected. She has a medical history of major depression and panic disorder for 20 years and was under regular antidepressant (escitalopram initially then switched to imipramine 25 mg HS) and benzodiazepine (alprazolam 0.5 mg bid, estazolam 2 mg, and seroquel 50 mg HS) treatment, and hypertension is under control with propranolol 10 mg bid treatment for 10 years. Her past surgical history included cholecystectomy and bilateral total knee replacement. Her physical examination on admission showed a blood pressure (by cuff) of 110/58 mmHg, heart rate of 70 beats/min, and temperature of 36.4°C. Preoperative cardiac echo revealed normal left ventricular function with left ventricular ejection fraction of 65%, but a 48-mm ascending aorta aneurysm was noted. Electrocardiogram (ECG) showed sinus rhythm with first-degree atrioventricular (AV) block and borderline prolonged QT interval (QTc >485). Laboratory data were all within normal limits. In the operating room, before general anesthetic induction, her blood pressure was

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110/58 mmHg (by cuff), and ECG leads and pulse oximetry probe were applied. General anesthesia was induced by fentanyl 100 µg intravenously (IV), lidocaine 50 mg IV, and propofol 100 mg IV. Tracheal intubation was facilitated by cisatracurium 10 mg IV and anesthesia was maintained with desflurane (6%) with oxygen ($\text{FiO}_2 = 0.5$). Ventilation was controlled with a tidal volume of 600 ml at 10 breaths/min. Hypotension was noted 5 min after induction and, on Jackknife position placement, the blood pressure dropped to 100/50 mmHg and the heart rate was 70 beats/min. The patient was then placed back to supine position, and 8 mg of ephedrine and fluids was given; however, the blood pressure continued to decrease to 70/35 mmHg, and the heart rate was 65 beats/min. Arterial and central venous catheters (central venous pressure: 10 cmH_2O) were placed immediately; dopamine infusion was then started from 5 µg/kg/min and additional ephedrine 32 mg and Solu-Cortef 200 mg were given; however, bradycardia with borderline prolonged QT occurred accompanied by hypotension of 80/40 mmHg. Anesthetic maintenance was then shifted from desflurane to sevoflurane with oxygen ($\text{FiO}_2 = 0.5$), and the blood pressure was elevated to 100/50 mmHg after 20 µg of norepinephrine was given. However, the blood pressure dropped to 70/40 mmHg again and the heart rate was 60 beats/min even though dopamine infusion was increased to 7.5 µg/kg/min and an additional 10 µg of norepinephrine was given. Meanwhile, transesophageal echocardiography (TEE) examination was arranged which revealed a dilated aortic root with diameter 44 mm, and aortic dissection was highly suspected [Figure 1]. Therefore, explorative sternotomy was performed by cardiovascular surgeon to manage the aortic dissection. The schedule nephrectomy for the left kidney neoplasm was cancelled. Crystalloid and colloid solutions and blood transfusion with packed red blood cell were applied. Dopamine infusion was increased to 10 µg/kg/min, and epinephrine infusion up to 4 mg/h and intravenous norepinephrine boluses (30 µg) were started to maintain the blood pressure; however, she remained in the hypotensive state with 75/45 mmHg and the heart rate was 60 beats/min in the next 4 h. Surprisingly, the intrathoracic examination only revealed dilated aortic root without any aortic dissection.

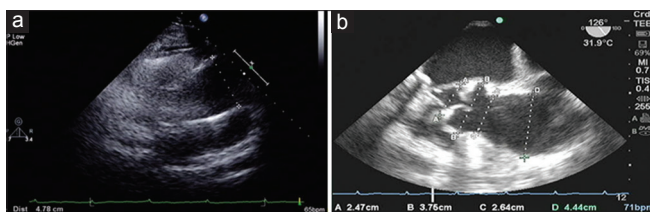


Figure 1: (a) Heart echo: Ascending aortic aneurysm (48 mm). (b) Transesophageal echocardiography: Dilated aortic root with ascending aorta of diameter 44 mm

The estimated blood loss was 50 ml and volume replacement consisted of 2050 ml of crystalloid and colloid solutions. After the patient recovered from the anesthetic effect, the infusion of the two drugs, dopamine and epinephrine, were not withdrawn in order to maintain her blood pressure to a desirable level. However, her blood pressure was around 90/50 mmHg and her heart rate was 70 beats/min. Then, she was transported to the Intensive Care Unit (ICU) for recovery and, on arrival to ICU, the blood pressure was 106/64 mmHg and heart rate was 80 beats/min. Fortunately, the patient was recovered and discharged without any sequel.

DISCUSSION

Our patient is an 87-year-old woman who has major depression under long-term TCA treatment. A severe refractory intraoperative hypotension and bradycardia were noted after general anesthetic induction. Age-related changes in the central and peripheral nervous systems may affect the response to anesthetics; increased vagal tone and decreased sensitivity to adrenergic receptors lead to a decline in heart function. Diminished cardiac reserve in many elderly patients may be manifested as exaggerated drop in blood pressure during general anesthetic induction.³

Antidepressants are divided into four main groups: TCAs, selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, and atypical agents. TCAs act by blocking presynaptic reuptake of norepinephrine or serotonin; they theoretically increase the effects of direct- or indirect-acting agonists at these synapses.⁴ TCAs may also block alpha-adrenergic receptors, which causes hypotension resulting from reduction of myocardial contractility and systemic vascular resistance.^{4,5} TCAs inhibit Na/K-ATPase and act like quinidine-like antiarrhythmics by stabilizing excitable membranes and delaying His bundle conduction. Therefore, TCAs resulting in AV block.⁵ Electrocardiography changes include prolongation of the PR interval, QRS complex, QT interval which can be observed at therapeutic or overdose of TCAs;⁶ uncommon bradyarrhythmias may occur due to AV block.⁷ Psychiatric patients receiving antipsychotics usually associate with an increasing risk of sudden cardiac death and the risk may elevate during long-term use.⁸ QTc-interval prolongation is often observed in psychiatric patients receiving TCAs or antipsychotics.⁹

Our patient under long-term TCA treatment experienced severe intraoperative hypotension and bradycardia after general anesthesia. There are several differential diagnoses which we should put into consideration. With TCA treatment, hypotension may occur due to bradycardia or vasodilation secondary to alpha-adrenergic receptor blockers.¹⁰ In our

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patient, hypovolemia was ruled out since her low blood pressure did not elevate after continuous IV fluid resuscitation. The blood gas data showed pH = 7.451 and K = 3.76 mEq/L and both were within the normal range. Although the patient had drug allergy history of piroxicam, no allergic reaction was observed. TEE plays a central role in the diagnosis of suspected dissection in clinical settings; it can determine whether the dissection extends into coronary artery and provides information about left ventricular function, wall motion abnormalities, and the presence or absence of pericardial effusion and tamponade.¹¹ However, false-positive findings may occur which are mainly caused by acoustic artifacts in the ascending aorta, where aortic dilatation, wall atherosclerosis, and calcifications may lead to erroneous interpretations.¹² TEE is also relative impaired visualization of the distal ascending aorta and aortic arch, which is caused by the interposition of the air-filled trachea. Experience with conventional TEE is a prerequisite and additional training should be considered.¹³

For the TCA-related hypotension, there is disagreement about the best way to treat it. Direct-acting vasopressor should be used instead of an indirect-acting agent. The duration of TCA treatment should also be considered.¹⁴ In short-term TCA treatment, patients can respond to indirect-acting sympathomimetics such as ephedrine due to increased presynaptic availability of norepinephrine. In contrast, in long-term treatment, TCAs induce adrenergic desensitization, and moreover, catecholamine depletion may further deteriorate response to sympathomimetics.⁵ The less potent sympathomimetics may not be effective for the hypotension in long-term TCA treatment patients because the adrenergic receptors are desensitized and catecholamine storage is depleted.¹⁵ The depletion of norepinephrine stores resulting from TCAs causes a peripheral adrenergic receptor blockade and they block the reuptake of norepinephrine and dopamine at presynaptic nerve terminals.¹⁶ This predisposes chronic TCA users to lower blood pressures during induction of anesthesia. The long-term TCA therapy was reported to deplete cardiac catecholamines, which potentiates the cardiac depression by anesthetics.³ If intraoperative hypotension occurs and vasopressors are needed, direct-acting drug such as norepinephrine is recommended. Dopamine acts indirectly through the release of norepinephrine. TCAs may block dopamine-induced norepinephrine release, thereby blunting the indirect pressor effect produced by dopamine.¹⁶ Due to the alpha-adrenergic blockade by TCAs, the beta 2 action of dopamine leads to more vasodilatation. One retrospective case series suggested that norepinephrine, a direct-acting catecholamine, appears advantageous over dopamine as the first-line vasopressor agent for those who require

vasopressor support of TCA-induced hypotension.¹⁷ A similar report described a patient on chronic TCA therapy who developed hypotension and was resistant to ephedrine, phenylephrine, and dopamine, but norepinephrine was eventually successful.¹⁴ Increasing the availability of norepinephrine is crucial for treating the exaggerated hemodynamic status during general anesthesia.⁴

During anesthesia and surgery, it is important to avoid stimulating the sympathetic nervous system. Sensitivity to the catecholamines is enhanced by TCAs, which may result in arrhythmias and hypertension when indirect- or direct-acting sympathomimetic drugs are used.¹ Similarly, anesthetics known to increase endogenous circulating catecholamines such as ketamine-, pancuronium-, and epinephrine-containing solution should be avoided.⁴ Vasopressin is a nonapeptide hormone synthesized in the magnocellular neurons of the paraventricular and supraoptic nuclei of the hypothalamus.⁵ The vasoconstrictive effect of vasopressin is independent of catecholamine and angiotensin receptors. For patients who respond poorly to catecholamines, vasopressin provides another therapeutic option.¹⁸ A single case report showed that vasopressin stabilized blood pressure in a patient with hypotension who failed to respond to norepinephrine.¹⁹ Vasopressin is not considered a first-line therapy of hypotension; however, it can be given as a bolus of 1–2 units to treat intraoperative hypotension, although the effects are short lived.⁵ The use of vasopressin for patients with severe hypotension and shock is controversial and further study will be required to identify the efficacy, dose, and potential side effects of vasopressin.¹⁸

Mood stabilizers should be continued during the perioperative period to prevent from worsening of depression or discontinuation syndrome such as disturbances in sleep, senses, movement, and mood.¹ Antipsychotic drugs also have potential dangerous effects during general anesthesia. For patients with complex psychiatric illness, the decision to discontinue psychoactive medication should be made by consulting their psychologist to ensure that the perioperative period is as smooth as possible.⁶ We anesthesiologists should be aware of the multiple interactions of psychotropic medications and anesthetic agents to ensure better patient outcome. The intraoperative safety and prevention of postoperative complications are important tasks for our anesthesiologists.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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