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Case Report Open Access

# Profound Hypotension during Kidney Transplantation for a Patient with a Depressive Disorder

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## Introduction

The perioperative management of patients with depressive disorder is largely based on the individual's clinical condition. Patients with long-term antipsychotic treatment are challenging for anesthesiologists because of its psychiatric condition, interactions of psychotropics and anesthetics, and the problems requiring surgery. Although antipsychotics and antidepressants are generally safe to continue perioperatively [1,2], evidence-based guidelines for the perioperative management of psychotropics are lacking [3]. We treated a patient taking chlorpromazine, phenobarbital, paroxetine and mianserin who experienced refractory hypotension during general anesthesia.

## Case Report

A 63-year-old male (weight: 105 kg, height: 170 cm, body mass index (BMI): 36.3) presented to our hospital for elective living donor kidney transplantation for end-stage hyperuricemic nephropathy. He had a major depressive disorder which was treated with multiple medications, including benzodiazepines, a selective serotonin reuptake inhibitor (SSRI), and antipsychotics, for about ten years. He had an episode of temporary loss of consciousness eleven years before; epileptic seizure was suspected, and sodium valproate at a dose of 800 mg/day was prescribed. In preoperative evaluation, the psychiatrist determined that the patient's mental condition was stable. He recommended to decrease the dose of benzodiazepines because of the potential danger of postoperative delirium. The patient was given haloperidol (3 mg/day) and mianserin (20 mg/day) for delirium prophylaxis three days before surgery. Immunosuppressive therapy was also started simultaneously. Although the patient took angiotensin-converting enzyme (ACE) inhibitor, it was discontinued six days before surgery. The list of preoperative medications is shown in Table 1.

| Drug | Dosage (mg/day) |
|---|---|
| Cyclosporine | 600 |
| Mycophenolate | 1500 |
| Alprazolam | 0.4 |
| Chlorpromazine | 25 |
| Cloxazolam | 2 |
| Estazolam | 2 |
| Etizolam | 3 |
| Haloperidol | 3 |
| Mianserin | 10 |
| Nitrazepam | 10 |
| Paroxetine | 20 |
| Phenobarbital | 40 |
| Promethazine | 12.5 |
| Cilnidipine | 10 |
| Furosemide | 30 |

**Table 1:** Patient's preoperative medications

Electrocardiography showed normal sinus rhythm and transthoracic echocardiography revealed normal left ventricular function. Chest radiography was unremarkable. Serum chemistry revealed elevated serum creatinine (5.13 mg/dL) and hyperkalemia (5.5 mmol/L) associated with chronic renal insufficiency. He had mild anemia (hemoglobin level of 10.4 g/dL). His preoperative blood pressure (BP) was 121/65 mmHg, and the heart rate (HR) was 75 beats/minute. On arrival, the patient was slightly drowsy. General anesthesia was induced with 200 μg of fentanyl and 180 mg of propofol, and the trachea was intubated with 80 mg of rocuronium. High peak airway pressure (30–40 mm $H_2O$) was needed to obtain an adequate tidal volume during volume-controlled mechanical ventilation. A right radial arterial catheter and right internal jugular venous catheter were inserted. The anesthesia was maintained with 1.5% sevoflurane and continuous infusion of remifentanil at 0.2 μg/kg/min and rocuronium at 25 mg/h. Immediately after the beginning of the operation, the BP decreased to 60/30 mmHg, and HR increased to 100 beats/min. Arterial blood gas analysis revealed: $FiO_2$ 0.4 pH 7.303, $PCO_2$ 38.6, $PO_2$ 104, BE -6.7, $HCO_3$ 18.6, Hb 9.3, Ht 28.9. There was no rash and wheezing. Rapid infusion of 1000 ml of normal saline over 40 min was performed. The sevoflurane concentration was reduced to 1%, and the dose of remifentanil was reduced to 0.05 μg /kg/min. Although dopamine infusion was initiated at a rate of 3 μg/kg/min, which was subsequently increased to 12 μg/kg/min, the hypotension persisted (BP: 80/40 mmHg). A norepinephrine infusion (0.02 μg/kg/min) with incremental boluses of ephedrine (total dose: 15 mg) and norepinephrine (10-30 μg at a time, total dose: 180 μg) was also given. Additionally, vasopressin (0.96 units) and methylprednisolone (500 mg) were administered.

To evaluate the patient's hemodynamic status, a transesophageal echocardiography (TEE) probe was inserted. TEE revealed decreased ventricular volumes with normal to hyperactive left ventricular contraction. After arterial anastomosis of the graft was completed, transfusion of 5% albumin and packed red blood cells were initiated to maintain adequate perfusion of the graft. Infusion of 20% mannitol (200 ml) was administered according to a standard protocol.

Hemodynamic stability was finally achieved after administration of vasopressors and massive volume expansion. The patient's systolic BP increased to 100 mmHg, and HR became 80 beats/min.The cardiac output measured with the Doppler method was 10–15 L/min, and the central venous pressure was 7–10 cm $H_2O$.

Arterial blood gas analysis revealed mixed acidosis (pH 7.17, $PCO_2$ 55.1, BE -8.9, $HCO_3$ 19.3), which was corrected with 8.4% sodium bicarbonate. Intravenous carperitide infusion at 0.03–0.2 μg/kg/min was started with a bolus dose of furosemide (20 mg) for delayed diuresis. We administered fentanyl (total 300 μg) until the end of surgery for postoperative analgesia.

At the end of the surgery, the patient developed massive generalized edema especially noticeable in the face accompanied by palpebral edema (Figure1) and severe hypothermia with the pharyngeal temperature of 34.4 . Arterial blood gas analysis revealed: $FiO_2$ 1.0, pH 7.395, $PCO_2$ 38.6, $PO_2$83.6, BE -0.9, $HCO_3$ 23.2, Hb 11.8, Ht 36.5, Na138, K2.9, Glu 184. He remained unresponsive for >1 h after the discontinuation of the sevoflurane and remifentanil administration. The low bispectral index (BIS) value (<15) was obtained. He was also unresponsive to post-tetanic stimulation for >2 h after the cessation of rocuronium infusion. The chest radiogram was unremarkable. The duration of the anesthesia was 9 h, during which he received a total of 1680 ml of blood and 4700 ml of infusions including both crystalloid and colloid solutions. The estimated total urine volume was 230 ml, and the estimated blood loss was 650 ml.

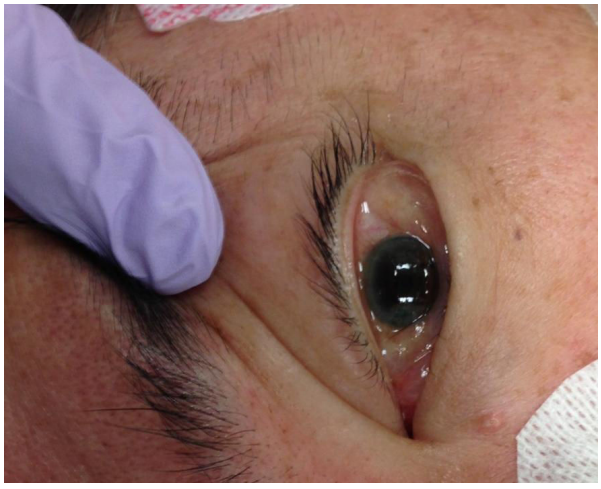

**Figure 1:** Generalized edema especially noticeable in the face accompanied by palpebral edema.

The patient was transferred to the intensive care unit (ICU) where hypothermia was treated with forced air warming. He was given a continuous dopamine and carperitide infusion to maintain hemodynamic stability and urine output. About 2 h after arriving in the ICU, he gradually emerged from anesthesia and became agitated, with unstable respiratory condition.

Dexmedetomidine infusion was started at 0.1 μg/kg/h to achieve adequate sedation for mechanical ventilation. The generalized edema was improved after the overnight intensive treatment. The patient's trachea was extubated the next morning, and he was transferred to a general ward. He was discharged one month after the surgery with a well-functioning graft.

## Discussion

This case report described a profound and sustained hypotension after induction of general anesthesia in a depressive patient who had been treated with multiple medications including a tetracyclic antidepressant, SSRI and antipsychotics (Table 1). Although there were many potential causes of the hypotension including hypovolemia and ACE inhibitor [4], we considered that α1-adrenoreceptor antagonism of psychoactive drugs are the main reason for the profound hypotension [5]. Antipsychotics are generally safe to continue in the perioperative period [1] and the incidence of intraoperative hypotension was low in patients on chronic antidepressant therapy [2], but in chronic kidney disease( CKD) patients the elimination half-lives of these agents could be prolonged , which could lead to accumulation of the drugs and their metabolites, causing unpredictably prolonged duration of action [6] . There is a report that haloperidol, which was added preoperatively for delirium prophylaxis [7] for our patient,could cause severe hypotension during anesthesia [8] .

If discontinuation of psychoactive drugs is planned, we should consider patient's renal function and be aware of the risk of withdrawal symptoms and psychiatric recurrence or relapse [3]. Differential diagnosis of hypotension during general anesthesia includes cardiovascular depression, myocardial ischemia, anaphylaxis, hypovolemia, and deep anesthesia. In our case, intraoperative electrocardiography and TEE revealed no evidence of ischemic heart disease. Considering the severe hypotension and generalized edema, anaphylaxis was undeniable, although its typical signs were not present. We did not administer epinephrine for hypotension because epinephrine is contraindicated in our country for patients treated with phenothiazine-and buthyrophenon-containing antipsychotics owing to paradoxical hypotension [9]. Although estimated blood loss which reported by nursing staff was 650 ml, we suspected that it had been underestimated. Considering intraoperative hemoglobin value and hemodynamic instability, the measurement of intraoperative blood loss seemed inaccurate. In addition, obesity with BMI 36.3 may have contributed to the hypotension via compression of the vena cava and reduction of venous return in the supine position [10]. There was little possibility that ACE inhibitor caused this hypotension because of its discontinuation prior to the operation.

Donnelly et al. reported a case in which high-dose norepinephrine in conjunction with epinephrine and dopamine was successful in treating hypotension in a patient who was treated with clozapine [11]. There were several cases in which ephedrine and phenylephrine were not effective, but vasopressin was most beneficial to restore hemodynamic stability in patients receiving α-adrenergic antagonists [10,12]. The treatment of hypotension in patients receiving antipsychotics will vary based on the level of -adrenergic blockade and anesthesia [12]. In our case, the high-dose norepinephrine infusion and low-dose vasopressin were effective for treating the severe

hypotension. If we had used more dose of vasopressin, we could have obtained hemodynamic stability more quickly.

Generally, intraoperative fluid management in kidney transplantation is intended to maintain an adequate intravascular volume and mean arterial pressure in order to maximize the graft function [6]. Traditional aggressive volume loading would cause volume overload, leading to pulmonary and systematic edema in patients with impaired cardiac function [6]. Although our patient's cardiac function was normal and the intraoperative TEE findings suggested normal to hyperactive left ventricular contraction, massive fluid administration and blood transfusion with delayed diuresis could lead to volume overload and generalized edema. We should administer more vasopressor and less transfusion to avoid volume overload.

Delayed emergence from general anesthesia could be attributed to multiple clinical factors, including residual anesthetics, hypothermia, and brain edema [13]. In our case, hypothermia and the sedative effect of benzodiazepines and antipsychotics could be the main causes of the delayed emergence. Core temperature regulation during general anesthesia may be impaired by dopamine blockade of antipsychotic drugs [14]. Sedation is a common dose-related side effect of antipsychotics, which block the central histamine H1 receptors [5,15]. The additional haloperidol and mianserin could cause sedation and the delayed emergence in our patient.

In addition to that, the SSRIs have potential to cause delayed emergence through inhibition of cytochrome-P450 (CYP) isoforms, which metabolize many anesthetics [16]. We also consider prolonged duration of rocuronium contributed to delayed recovery. Rocuronium is not recommended for patients with renal failure [17], but benzylisoquinoline muscle relaxants are not available in our country. Neurotoxicity attributed to immunosuppressive drugs such as cyclosporine is known after organ transplantations [18]. Although our patient had history of suspected epileptic seizure, he had no seizure perioperatively.

To summarize, we presented a case of profound hypotension and generalized edema in a depressive patient with CKD. To minimize the perioperative adverse effects of the psychoactive drugs, dose reduction or discontinuation of these drugs are needed in CKD patient. Successful outcome in patients with psychiatric disorders and severe physical impairment can only be achieved with an appropriate preoperative assessment and cooperation between psychiatrists and anesthesiologists.

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