Postoperative Sudden Hypotension Due to Relative Adrenal Insufficiency

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Systemic blood pressure is regulated by three mechanisms: the sympathetic nervous system, the renin-angiotensin system, and the arginine-vasopressin system. Hypotension is a condition that can occur at any stage of management of general anaesthesia, including induction, extubation, and maintenance. Many of the medications used for anaesthesia produce a mild to moderate decrease in systemic vascular resistance (SVR) with a subsequent decrease in arterial blood pressure. Profound and sustained hypotension, however, can have a global impact, resulting in a failure to adequately perfuse systemic capillary networks. The following report describes the case of a 69-year-old man undergoing surgery for total hip replacement who had hypotension that was refractory to fluid administration and inotropic agents at the end of the surgery. In this case study, the role of methylprednisolone therapy in catecholamine-resistant hypotension is also discussed.

Key Words: Blood pressure, hypotension, catecholamine, fluid therapy, adrenal insufficiency

Introduction

Low blood pressure or hypotension is the heart's pumping less blood to the periphery than it normally does in each beat, and it leads to decreased perfusion of organs. Normal blood pressure values are 130/80-90/60 mmHg. Hypotension is a condition that can be associated with alcohol, and certain drugs such as antidepressants, anxiolytics, diuretics, and analgesics. Other factors that lead to hypotension can be listed as severe diabetes mellitus, dehydration, anaphylaxis, arrhythmia, shock, bleeding, and heart failure. It causes symptoms such as sleepiness, nausea, confusion, weakness and syncope, and may progress to shock and cardiac arrest unless treated promptly (1).

Hypotension is a condition that may be encountered in any phase of general anaesthesia including induction, maintenance and extubation. Drugs that are used for the induction of anaesthesia may cause substantial decrease both in systemic vascular resistance (SVR) and arterial blood pressure. At the same time, severe and persistent hypotension results in impaired perfusion in systemic capillary network (2, 3).

Inadequate cortisol response in stress conditions such as critical diseases despite normal serum cortisol concentrations is defined as relative adrenal insufficiency. Conditions that require mechanical and pharmacological support for preserving vital functions are called as critical disease conditions (4).

Glucocorticoids have an important role in adaptation to stress and provide haemodynamic stability. Normal adrenocortical functioning has an important role in survival. Adrenal insufficiency has an important place in the pathogenesis of septic shock. Inadequate blood flow to the adrenal glands and secretion of mediators that suppress adrenal and pituitary functions play an important role in the pathogenesis. Aetiology, signs and symptoms are the same with those in adrenal insufficiency (4).

In this paper, a case with hypotension, which developed in the two consecutive surgical procedures performed for coxarthrosis and was resistant to catecholamines and fluid replacement therapy, was presented and the place of steroid therapy in the treatment of hypotension that has not improved despite fluid replacement and catecholamine support was discussed.

Case Presentation

A 69-year-old male patient was scheduled to undergo hip prosthesis revision surgery as his complaints were not relieved after right total hip prosthesis surgery that he had undergone after being diagnosed with coxarthrosis. Although medical history

Figure 1. Perioperative hemodynamic monitoring of the case

Min: minute; SAP: systolic arterial pressure; DAP: diastolic arterial pressure; MAP: mean arterial pressure. Blood pressure values are given at 15 min. intervals

of the patient revealed no coexisting disease except for benign prostate hyperplasia, left ventricular diastolic dysfunction was determined on echocardiography. His electrocardiographic (ECG) findings were unremarkable and ejection fraction (EF) was 60%. He had had three anaesthesia experiences in two total hip replacement procedures and one transurethral resection of the prostate (TUR-P) procedure. Moreover, it was learned that he had a history of resistant hypotension that developed during extubation at the end of surgery, which he underwent a month ago. Preoperative anaesthesia evaluation performed before the surgery revealed normal blood chemistry and complete blood count. The patient expressed that in his previous anaesthesia experience, his heart arrested at the end of the surgery, immediate intervention was performed and he stayed in the intensive care unit. After obtaining patient consent for combined spinal-epidural anaesthesia, premedication was performed using 2 mg of midazolam, 20 mg of famotidine and 10 mg of metoclopramide via intravenous (IV) route. After intravenous access was established on the dorsum of the hand using an 18 Gauge (G) needle and 0.9% NaCl at a dose of 10 mL kg⁻¹ was administered intravenously, the patient was admitted to the operating room and routine monitoring was performed. The patient, who had left ventricular diastolic dysfunction and encountered a problem during previous anaesthesia experience, underwent right internal jugular vein catheterization for central venous pressure (CVP) monitoring and right brachial artery catheterization for invasive blood pressure monitoring. Combined spinal-epidural anaesthesia was administered at L₄₋₅ space under local anaesthesia by a single, blood-free intervention using 18 G epidural needle with the patient in decubitus position; the catheter was inserted 6 cm into the epidural space, spinal space was accessed through the needle using a 27 G spinal needle, and spinal anaesthesia was performed using 3 mL of 0.5% bupivacaine. After spinal anaesthesia was performed, the epidural catheter was placed. Following the anaesthetic procedure, the patient was placed in supine position and he was held in that position over the course of the surgery. A T₆ (thoracic) block level was achieved and the surgical procedure was started 15 minutes after anaesthesia induction.

The patient's blood pressure at admission was 143/90 mmHg, and systolic blood pressure values were between 143 and 87 mmHg and diastolic blood pressure values were between 90 and 47 mmHg during the perioperative period. The changes in systolic, diastolic and mean arterial blood pressure levels of the patient over the course of anaesthesia are demonstrated in Figure 1. The mean blood loss of the patient, who was haemodynamically stable in the perioperative period, was 1000 mL, and he received two units of erythrocyte suspension, 1000 mL of colloid and 3000 mL of crystalloid infusion. Blood gas samples obtained over the course of the surgery revealed no abnormality. No additional local anaesthetic was injected through the epidural catheter. Following the completion of surgery, 4.5 hours after anaesthesia application, the patient developed hypotension and he was given 50 mg ephedrine at certain intervals; and meanwhile, the level of block was at T₁₀. As the blood pressure did not increase despite ephedrine injections, first dopamine infusion at a rate of 3 mcg kg⁻¹ min⁻¹ and then noradrenaline infusion at a rate of 5 mcg kg⁻¹ min⁻¹ were commenced. Meanwhile, no tachycardia or desaturation was observed. Blood glucose level was 226 mg dL⁻¹, CVP was 3 cmH₂O, haemoglobin was 11 gr dL⁻¹ and the level of block was at L₁. Total duration of surgery was four hours and thirty minutes. ECG of the patient showed normal sinus rhythm, and his cardiac enzymes were within normal ranges. In arterial blood gas analysis, pH was 7.28, pO₂ was 87 mmHg, pCO₂ was 16 mmHg, sPO₂ was 96%, and HCO₃ was 18 meq L⁻¹. Since hypotension could not be corrected although dopamine dose was increased up to 20 mcg kg⁻¹ min⁻¹ and noradrenalin dose was increased up to 29 mcg kg⁻¹ min⁻¹, adrenal insufficiency was considered and 250 mg of methylprednisolone was administered. The patient was transferred to the postoperative intensive care unit, and in addition to dopamine and noradrenaline infusion methylprednisolone infusion treatment was commenced for 5 days considering adrenal insufficiency. The patient's cortisol level was 21.9 ng dL⁻¹ (N: 5-23 ng dL⁻¹) on the postoperative fifth day and 16 ng dL⁻¹ on the postoperative sixth day. As his blood pressure reached normal levels at 4 hours of intensive care unit stay, dopamine and noradrenaline infusions were gradually decreased and discontinued within eight hours. Methylprednisolone therapy was discontinued five days after by gradually decreasing the dosage. The patient was discharged after his blood pressure and general condition were improved.

Approximately one month later, the patient was consulted to us for femoral revision hip surgery. Preoperative Addison protocol was recommended for the patient, who was evaluated by the endocrinology department for adrenal insufficiency. His preoperative adrenocorticotrophic hormone (ACTH), cortisol, insulin-like growth factor 1 (IGF-1), somatomedin C levels, and thyroid function tests were normal. Addison protocol was commenced and the patient was admitted to the operating room following 2 mg of midazolam premedication and 10 mL kg⁻¹ of crystalloid infusion and he was

monitored. He underwent right jugular vein and left radial artery catheterizations under local anaesthesia. After disinfection of the surgical site, the area was covered using a sterile cover, spinal space was accessed at L₄₋₅ space with a single, bloodless intervention performed using 25 G spinal needle under local anaesthesia with the patient in lateral position and spinal anaesthesia was performed using 2.5 mL of 0.5% bupivacaine. Blood pressure and haemodynamic measurements of the patient were normal at admission to the operating room and over the course of the surgery; his CVP was 7-10 cmH₂O, systolic blood pressure was 121-138 mmHg, diastolic blood pressure was 66-72 mmHg, pulse pressure was 72-61 min⁻¹ and oxygen saturation values were between 96% and 100%. Total duration of the surgery was one hour and no problem such as arrhythmia, hypotension, respiratory distress or bradycardia was encountered during surgery. Cortisol levels of the patient were normal in the preoperative period (2.77 ng dL⁻¹), after induction (11.24 ng dL⁻¹) and in the postoperative period (8.23 ng dL⁻¹). Preoperative arterial blood gas values were as follows: pH: 7.46, pO₂: 68.9 mmHg, pCO₂: 29, sPO₂: 96.5%, and HCO₃: 23.1 mEq L⁻¹; whereas postoperative arterial blood gas values were as follows: pH: 7.41, pO₂: 112 mmHg, pCO₂: 32 mmHg, sPO₂: 98.8%, and HCO₃: 21.5 mEq L⁻¹. Steroid therapy was given for six days in the postoperative period, and then discontinued by gradually decreasing the dosage. The patient who did not develop hypotension during his follow-up in the intensive care unit, he was transferred to the ward after 24 hours. In addition, consent of the patient was obtained to share his clinical situation in a scientific journal.

Addison Protocol (5)

- 1) Administer 100 mg of hydrocortisone (or 40 mg of methylprednisolone) by intramuscular (IM) route on the day before surgery at 20:00 pm;
- 2) Administer 100 mg of hydrocortisone (or 40 mg methylprednisolone) by IM route two hours prior to surgery;
- 3) Administer 50 mg of hydrocortisone (or 20 mg of methylprednisolone) in 5% 500 mL dextrose at 6 hours intervals and replace dextrose with normal saline at every three administrations on the day of surgery; on condition to be started together with surgery. Attentively monitor the blood pressure;
- 4) Administer 50 mg of hydrocortisone (or 20 mg of methylprednisolone) on the postoperative Days 1 and 2 at 08.00 in the morning; and as was described above add 25 mg of hydrocortisone (or 10 mg of methylprednisolone) into the serum and infuse; monitor diuresis, serum electrolytes, BUN (blood urea nitrogen), and blood pressure levels;
- 5) Administer 50 mg of hydrocortisone (or 20 mg of methylprednisolone) by IM route in the morning on the Days 3 and 4; monitor blood pressure; give 15 mg hydrocortisone tablet (or 5 mg prednisolone tablet) in the morning,

10 mg hydrocortisone tablet (or 2.5 mg prednisolone tablet) at noon, and 10 mg hydrocortisone tablet (or 2.5 mg prednisolone tablet) in the evening;

- 6) It would be convenient to gradually decrease hydrocortisone or prednisolone that are given by oral route and shift to maintenance doses with monitoring blood pressure and general status on Day 6.

Discussion

While the mean arterial pressure is calculated by multiplying cardiac output (CO) by SVR; CO is defined as the multiplication of heart rate by stroke volume. Various drugs and anaesthesia influence blood pressure control mechanisms of the body and the need for inotropic agents. Neurohumoral pathways that are activated in response to hypotension during anaesthesia include sympathetic nervous system, renin-angiotensin-aldosterone system (RAAS) and arginine-vasopressin system (6, 7). The present case, which had undergone hip prosthesis surgery by means of different anaesthesia techniques, developed hypotension with an unidentified aetiology and resistant to catecholamine, at the end of the surgery. Blood pressure values of the patient began to increase and inotropic support was not required after steroid therapy, which was given in addition to inotropic and fluid replacement therapies.

Synthetic analogues such as vasopressin or terlipressin are recommended as alternative agents in the treatment of catecholamine-resistant hypotension (8-10). Vasopressin is a peptide hormone that is synthesized in the hypothalamus and stored in the posterior pituitary gland and primarily regulates serum osmolality and enables cardiovascular stability (8). It is released in conditions such as high serum osmolality, decreased arterial pressure and hypovolemia. Synthetic analogues such as vasopressin or terlipressin cause vasoconstriction by stimulating V1 receptors in smooth muscles (6, 10). Vasopressin has been associated with circulatory collapse and septic shock treatment (8). It is stated that vasopressin improves arterial blood pressure when sympathetic nervous system or RAAS is inhibited. Lindner et al. (11) reported that vasopressin used in cardioversion-induced ventricular fibrillation, enhances coronary perfusion pressure and myocardial blood supply better than norepinephrine. In the case we presented herein, we could not administer vasopressin as its IV form was not available in the acute period.

Cortisol is a hormone that plays a role in the improvement of impaired vasomotor tone in the vascular system, in the sensitivity of catecholamine receptors, and in the regulation of the distribution of body fluids (12). Adrenocortical insufficiency is an acute or chronic life-threatening condition that is developed due to hereditary or acquired lesions of hypothalamus, pituitary gland or adrenal cortex. Deficiency may involve one, two or all of glucocorticoid, mineralocorticoid and androgen hormones of adrenal cortex (13, 14).

Acute adrenal insufficiency or adrenal crisis is the development of catecholamine-resistant hypotension and shock and develops in patients without a prior diagnosis of adrenal insufficiency or in those that have a diagnosis but have not increased the dose of glucocorticoids, as well as in patients that have encountered a great physiological stress. Nevertheless, relative adrenal insufficiency is defined as insufficient cortisol response to stress in individuals with normal serum cortisol levels, with no known adrenal insufficiency in the past (4).

Nausea, vomiting, abdominal pain, weakness, fatigue, lethargy, confusion and coma may develop in stress conditions such as infection, trauma, and gastroenteritis. Abdominal tenderness and presence of fever may be confused with acute surgical abdomen. Hypoglycaemia may rarely be the first symptom particularly in secondary insufficiency. Normal plasma cortisol levels ($5\text{--}25\text{ ng dL}^{-1}$) do not exclude diagnosis in the presence of acute disease. A cortisol concentration of $<3\text{ ng dL}^{-1}$ indicates the diagnosis of adrenal insufficiency; however, a plasma cortisol concentration of 25 ng dL^{-1} in the presence of acute stress excludes the diagnosis of adrenal crisis. A cortisol concentration of $<20\text{ ng dL}^{-1}$ after ACTH stimulation test also indicates the diagnosis of adrenal insufficiency. In the case presented here, hypotension was improved after using steroids for both unexplainable hypotension and coexisting bronchospasm in the initial surgery. Combined spinal-epidural anaesthesia was applied in the second surgery; sudden hypotension that developed with the disappearance of sympathetic block, i.e. sympathetic activity, unresponsiveness to fluid and inotropic therapy, and history of hypotension in the previous surgical intervention suggested probable adrenal insufficiency and steroid therapy was commenced in the patient with worsened critical status and he responded to the treatment. Serum cortisol concentration, which has to be analysed at the time of stress to make the definitive diagnosis, could not be measured as he progressively worsened. However, the absence of perioperative hypotension due to Addison protocol implemented in the patient before the third surgical procedure supported the diagnosis of relative adrenal insufficiency.

For the treatment, physiological glucocorticoid replacement therapy should be given in patients with adrenal insufficiency. Mineralocorticoid replacement is frequently necessary. Parental glucocorticoids at pharmacological doses should be given in case of circulatory collapse in acute adrenal insufficiency. Treatment of adrenal insufficiency consists of three phases; fluid replacement (100 cc h^{-1} 10% dextrose or 0.9% NaCl $1000\text{--}1200\text{ cc h}^{-1}$), 20 mg methylprednisolone via IV route x for 4 days, and elimination of predisposing factors. Acute adrenal crisis may result in shock, coma and death unless diagnosed and treated.

Conclusion

We should keep in mind that it is quite difficult to make the diagnosis of corticosteroid-resistant hypotension. Therefore,

critical disease-related adrenocortical insufficiency should be suspected in the event of hypotension that does not respond to fluid replacement and vasopressor agents.

Informed Consent: Written informed consent was obtained from the patient who participated in this case.

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