Refractory Hypotension During Propofol/Fentanyl Anesthesia. A Report of Two Cases

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ABSTRACT. Although serious hypotension or cardiovascular collapse during anesthesia induction with propofol is not rare, refractory hypotension during propofol anesthesia has not been reported. We describe two cases of refractory hypotension during propofol/fentanyl anesthesia which were refractory to lowering infusion rate of propofol and administration of vasopressors. We speculate that long-term hemodialysis and aortic regurgitation may be related to the refractoriness of hypotension in these cases, respectively. We emphasize the importance of discontinuation of propofol infusion and switching to an inhalational aneshetic technique in such cases.

Key words : pharmacology-anesthetics-intravenous-propofol — hypotension-ephedrine-norepinephrine.

Propofol has become popular as an intravenous anesthetic for both induction and maintenance because of it's fast onset, rapid recovery and lower incidence of postoperative side-effects, such as nausea and vomiting in recent years.[1] Although hypotension and bradycardia are considered to be the major hemodynamic effects of propofol, they can be usually managed with ephedrine, atropine or preloading with crystalloid solution.[2,3] This case report describes two cases of severe hypotension during propofol/fentanyl anesthesia which were refractory to those measures. We emphasized the importance of discontinuation of propofol infusion and switching to an inhalational anesthetic technique in such cases.

Case reports (Table 1)

Case 1

A 67-year-old man was scheduled for intravascular surgery because of an unruptured aneurysm of the right posterior cerebral artery. He had been on haemodialysis three times a week for five years. He had undergone repair for an abdominal aortic aneurysm four years before. He had no cardiac symptoms or disease. He was taking several drugs including an calcium channel blocker for hypertension. Hemodialysis was performed on two consecutive days before operation. His preoperative electrocardiogram (ECG) and echocardiography showed no abnormal findings. He was not premedicated. Routine monitors (ECG, pulse oximeter and noninvasive blood pressure) were applied during

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TABLE 1. Summary of two patients with refractory hypotension during propofol/fentanyl anesthesia.

Case	Age gender	Diagnosis /operation	Anesthetic technique	Preoperative therapy or medications/ vasopressors
1	67 y/o, male	Unruptured cerebral aneurysm/ Intravascular surgery	Propofol/fentanyl Laryngeal Mask Airway Ventilation with O2-air (FIO2=50%)	Long-term dialysis,/ multiple drug intake: calcium channel blocker and H2-blocker ephedrine, norepinephrine
2	56 y/o, male	Cerebropontile tumor/ Extirpation	Propofol/fentanyl +N2O (FIO2=50%) Tracheal intubation	Aortic regurgitation/ dopamine

operation. Anesthesia was induced with Intravenous propofol 100 mg, fentanyl 0.1 mg and vecuronium 4 mg. A size 4 laryngeal mask airway was inserted and the lungs were mechanically ventilated with oxygen-air (FIO2=0.50). Anesthesia was maintained with a continuous infusion of propofol at 4 mg/kg/hr after induction of anesthesia, arterial pressure was monitored via a catheter placed in the right dorsalis pedis artery. Ten minutes after induction of anesthesia, arterial pressure gradually decreased from the preinduction value of 160/70 mmHg to 75/40 mmHg, with an unchanged heart rate of 110 bpm. Decrease in the propofol infusion rate to 2.5 mg/kg/hr and administeration of ephedrine 8 mg, twice were ineffective for restoring arterial blood pressure. His arterial blood pressure and heart rate remained around 70/40 mmHg and 110 bpm, respectively, although noradrenaline was continuously infused (5-10 μg/min) for 15 min. Propofol infusion was then turned off and sevoflurane was inhaled at 1.0%. His arterial blood pressure was gradually normalized to 125/60 mmHg over 10 min and the infusion of noradrenaline was stopped. Anesthesia was maintained thereafter with sevoflurane 1-2%. The surgery lasted for 100 min and the recovery from anesthesia was complete.

Case 2

A 56-year-old man was scheduled to undergo surgical resection of a cerebropontile tumor. He had aortic regurgitation: New York Heart Association class II without a history of heart failure. Echocardiography revealed left ventricular hypertrophy with almost normal wall motion (AR II, ejection fraction=0.58, left ventricular and-diastolic dimension=55 mm). The patient was received no medication preoperatively. After routine monitors were applied, anesthesia was induced with propofol 100 mg and fentanyl 0.1 mg, administered intravenouly, followed by vecuronium 10 mg, and endotracheal intubation. The lungs were mechanically ventilated with N2O (FIO2=0.50) in oxygen. Propofol was being infused at a rate of 4 mg/kg/min following the induction of anesthesia. Ten minutes after endotracheal intubation, his arterial blood pressure decreased to 70/40 mmHg with a heart rate of 60 bpm before skin incision. The infusion rate of propofol was decreased to 2.5 mg/kg/hr

and 5-10 μg/kg/min dopamin was infused. Since hypotension still continued for another 15 min after skin incision, infusion of propofol was discontinued and isoflurane was administered via a vaporizer for the maintenance of anesthesia. Within five min, his arterial blood pressure increased to 135/65 mmHg, and the infusion rate of dopamine was rapidly reduced and then discontinued. He became hemodynamically stable with arterial blood pressure of 120-140/45-60 mmHg and a heart rate of 60-70 bpm during surgery without vasopressors.

Discussion

Although several reports of incidences of serious propofol-induced hypotension or cardiovascular collapse[4-6] have described previously, most of them have reported to be observed during anesthesia induction. In contrast, in our cases a profound hypotension developed after anesthesia induction and persisted despite a minimum infusion rate of propofol, with adequate dose of ephedrine, dopamine or even noradrenaline administration.

Since a low dose fentanyl (0.1 mg) and nitrous oxide have only a minimal hemodynamic effects,[7] the hypotension could be attributed to the propofol infusion. Moreover, the fact that the arterial pressure returned to normal within 10 min after switching from propofol infusion to the inhalation of the volatile anesthetics, and that it stabilized thereafter without any need for vasopressors suggests that propofol was responsible for the refractory hypotension in these cases.

Earlier studies in humans and animals have shown that propofol-induced hypotension is due to a decrease in afterload,[2] ventricular preloads[6] or myocardial contractility.[8,9] An axperimental study using in situ normally working hearts showed that propofol has no direct negative inotropic effects at clinically relevant blood concentrations.[10] Similarly, a recent study by Robinson *et al*[11] demonstrated that propofol has no direct action on arterial or venous vasodilation in humans. In addition, they showed that inhibition of ssympathetic vasoconstrictor activity is responsible for propofol-induced vescular relaxation. Potent inhibition of sympathetic nerve activity and a decrease in baroreflex sensitivity have been demonstrated in propofol anesthetized humans[12] while volatile anesthetics have had no such effects.[13] Based on these findings, it is speculated that propofol causes hypotension by inhibiting centrally mediated sympathetic nerve activity, but it has no direct effects on myocardial contractility or peripheral vessels at clinical concentrations. Treatment with ephedrine; i.e., weak, sympathomimetic administration, or crystalloid loading for propofol-induced hypotension thus seem theoretically rational in most cases.

Why was the hypotension refractory to vasopressors in our cases? Several possible factors may be considered. First, pharmacokinetics may have been altered in our patients and the propofol concentration may have been unexpectedly high. However, we believe, this possibility is unlikely, because the hypotension persisted more than 15 min after the infusion rate of propofol was lowered, and because propofol pharmacokinetic profiles are similar in renal failure and healthy patients.[14] Second, the aortic regurgitation in case 2 may have played a role in his unresponsiveness to vasopressors. Matsuyama et al. demonstrated that with aortic regurgitation beta 1-down-regulation develops

and cardiac dilation per se blunts cardiac response to sympathetic stimulation.[15] Third, long-term hemodialysis may have been responsible for the refractoriness to vasopressors in case 1, because patients with chronic renal failure have reduced end-organ responsiveness to alpha agonists, whereas autonomic function is preserved.[16] In addition, hypovolemia resultiong from preoperative dialysis for two consecutive days may have led to enhanced hypotension and refractoriness to the vasopressors in case 1. Although the exact mechanism for the refractoriness remains unclear, the fact that it was reversed with discontinuation of propofol infusion suggests that the effect of propofol on sympathetic activity is closely related to it. Therefore, from the viewpoint of anesthetic management, it is very important to change the anesthetic technique with one using volatile anesthetics in such a situation.

In conclusion, we experienced severe hypotension refractory to vasopressor drugs during propofol/fentanyl anesthesia. We considered that long-term dialysis and aortic regurgitation might be responsible for the refractoriness of this propofol-induced hypotension. Therefore, in such cases, it is advisable to switch to inhalational techniques using volatile anesthetics.

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