Use of Nicardipine during Pheochromocytoma Removal

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Nicardipine is a short-acting calcium slow-channel blocker[1], which has recently been introduced for intravenous use to control acute hypertension during anesthesia in Japan. Since there is no satisfactory drug for controlling of blood pressure in patients with pheochromocytoma, nicardipine may be expected to be a candidate for a drug of choice in intraoperative managements of blood pressure in such patients during the removal of pheochromocytoma[2]. We used nicardipine during pheochromocytoma removal and report the hemodynamic and hormonal changes observed in a patient anesthetized with nitrous oxide, oxygen and thoracic epidural blockade.

Case Report

A 64-year-old woman with a 2 month history of the sudden onset of remarkable hypertension, angina pectoris, and hyperhydrosis, was diagnosed as having a left adrenal pheochromocytoma (paroxysmal type) and scheduled for its removal. On admission, her blood pressure (BP) was 270/120 mmHg and the heart rate (HR) 120 beats·min^{-1}, with the serum epinephrine level being 3,780 pg·ml^{-1} (normal, < 120 pg·ml^{-1}) and the norepinephrine level 9,710 pg·ml^{-1} (normal, 60 ~ 450 pg·ml^{-1}). She was treated medicinally with bunazosin (8 mg), nifedipine (20 mg), propranolol (5 mg), and methyldigoxin (0.05 mg) daily for the last six weeks. During this period, her BP fell to a stable level of 140/70 mmHg and her HR to 70 beats·min^{-1}, without any episodes of sudden change.

She was premedicated with 0.5 mg of atropine intramuscularly 30 min before the arrival for operating room where her radial artery was cannulated and a flow-tipped baloon pulmonary catheter was inserted via the right internal jugular vein under local anesthesia. Cardiovascular variables before the induction of anesthesia were then measured. Next, a continuous thoracic epidural anesthesia catheter was inserted between the 8th and 9th thoracic vertebrae. Before the induction of general anesthesia, her BP was 139/69 mmHg, HR 82 beats·min^{-1}, the pulmonary capillary wedge pressure (PCWP) 3 mmHg, the cardiac index (CI) 3.18 l·min^{-1}·m^{-2}, serum epinephrine 1,030 pg·ml^{-1} and serum norepinephrine 3,140 pg·ml^{-1}. Twelve ml of 1% lidocaine was used for epidural anesthesia. Then general anesthesia was induced with thiopental (200 mg), and tracheal intubation was performed with the facilitation of pancuronium (4 mg). Cardiovascular changes were not remarkable during and after tracheal intubation (BP of 132/69 mmHg, HR of 84 beats·min^{-1}), except for the increased PCWP from 3 to

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Table 1. The hemodynamic and hormonal changes during pheochromocytoma removal

	heart rate (beats·min^{-1})	arterial pressure (mmHg)	pulmonary wedge pressure (mmHg)	cardiac index (l·min^{-1}·m^{-2})	epi-nephrine (pg·ml^{-1})	norepi-nephrine (pg·ml^{-1})
preinduction	82	139/69	3	3.18	1030	3140
postintubation	84	132/69	10	2.83	440	970
nicardipine (5 μg·kg^{-1}·min^{-1})	79	98/54	7	3.33	470	990
after incision	79	109/60	11	2.71	440	840
manipulation of tumor	126	207/93	20	6.14	23030	16500
nicardipine (2 mg bolus)	105	111/55	14	3.80	(−)	(−)
tumor removal	90	96/56	9	2.92	1970	1710
after skin closure	112	154/67	13	6.54	440	1010
after extubation	93	153/68	11	5.42	430	1046

Normal epinephrine level: < 120 pg·ml^{-1}
Normal norepinephrine level: $60 \sim 450$ pg·ml^{-1}

10 mmHg and the decreased CI from 3.18 to 2.83 l·min^{-1}·m^{-2}. Serum concentration of catecholamine decreased; epinephrine from 1,030 to 440 pg·ml^{-1} and norepinephrine from 3,140 to 970 pg·ml^{-1}. Anesthesia was maintained with nitrous oxide (67%) and oxygen in addition to epidural anesthesia and intermittent doses of pancuronium was also given as required.

Nicardipine infusion was started at a rate of 5 μg·kg^{-1}·min^{-1} after the tracheal intubation. Nicardipine produced remarkable hemodynamic changes; decrease in BP (to 98/54 mmHg) and PCWP (to 7 mmHg), but HR remained constant, and increase in CI (to 3.33 l·min^{-1}·m^{-2}). But it produced little changes in epinephrine (470 pg·ml^{-1}) and norepinephrine (990 pg·ml^{-1}) levels. After the skin incision, BP was maintained at 110/60 mmHg and PCWP at 10 mmHg by a 2 μg·kg^{-1}·min^{-1} nicardipine infusion and intravenous fluid administration. Despite a 5 μg·kg^{-1}·min^{-1} nicardipine infusion, surgical manipulation of the pheochromocytoma initiated significant increase in BP (to 207/93 mmHg), HR (to 126 beats·min^{-1}), PCWP (to 20 mmHg), CI (to 6.14 l·min^{-1}·m^{-2}), serum epinephrine (to 23,030 pg·ml^{-1}) and serum norepinephrine (to 16,500 pg·ml^{-1}) (table 1). A 2 mg of nicardipine bolus injection subsequently returned the hemodynamic variables to normal and no futher elevation of BP and HR was seen until the removal of the tumor had been completed 15 min later. After its removal, the nicardipine infusion was discontinued. BP decreased to 96/55 mmHg, but was restored quickly by infusion of dopamine (20 μg·kg^{-1}·min^{-1}) and norepinephrine (0.1 μg·kg^{-1}·min^{-1}), the dosage of which were gradually tapered during the next 45 min. At the emergence from anesthesia, especially at removal of tracheal tube, BP increased slightly, but the hemodynamic condition was stable (BP of 153/68 mmHg, HR of 93 beats·min^{-1}, PCWP of 11 mmHg, CI of 5.42 l·min^{-1}·m^{-2}) with the administration of dopamine (10 μg·kg^{-1}·min^{-1}) and norepinephrine (0.02 μg·kg^{-1}·min^{-1}) (table 1). Her postoperative course was uneventful.

Discussion

Many drugs, such as phentolamine, sodium nitroprusside, nitroglycerine, and prostaglandin E_1, have been used for prevention of dangerous hypertensive crisis by catecholamine release from pheochromocytoma during the surgical manupulation in anesthetized patients[3,4]. However, phentolamine has a slow onset and a long duration of action for immediate use and also causes

reflex tachycardia and tachyphylaxis. Sodium nitroprusside is not available commercially in Japan. Nitroglycerine and prostaglandin E_1 may require large doses to achive the desired effects. Sodium nitroprusside and nitroglycerine also have the dangerous potencies of cyanide toxicity and methhemoglobinemia, respectively. In addition, all these drugs could cause reactive hypercatecholaminemia when such antihypertensive agents being effective[3,4].

Calcium slow-channel blockers have powerful antihypertensive and antitachyarrhythmic properties. In addition to these beneficial effects on cardiovascular system, they also inhibit catecholamine release from the adrenal medulla, because they prevent a transmembrane calcium influx which could be initiated by depolarization of the cell membrane is necessary for catecholamine release from the adrenal medulla[1].

In the present patient, nicardipine infusion (5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) produced a decrease of BP and PCWP, and an increase of CI before the initiation of surgical manipulation. The decrease of preload was easily treated by fluid infusion. Although hemodynamic changes associated with surgical stimulation seemed to be prevented by a 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of nicardipine, the manipulation of pheochromocytoma per se were unable to eliminate significant changes in hemodynamics as well as significant increases in plasma catecholamine levels despite of nicardipine infusion (5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). A bolus injection of nicardipine (2 mg) returned them to normal. BP decreased after the removal of the tumor, and probably the bolus injection of nicardipine might be related with this decrease in BP[1]. But we were able to restore BP easily by a dopamine and norepinephrine infusion.

In a previous report by Arai et al, the use of a continuous infusion of nicardipine were recommended for a pheochromocytoma patient under high dose fentanyl anesthesia[2]. They used a very high dose, 21 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of nicardipine, during manipulation of the tumor. A usual dosage of nicardipine is 2–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ for continuous infusion and 10–30 $\mu g \cdot kg^{-1}$ for a bolus. Therefore we used a bolus injection when BP elevated suddenly during the manipulation. The difference between our patient and theirs might be related to use of fentanyl, because fentanyl has been reported to have a postsynaptic alpha-adrenergic blocking action[5], but none of the drugs we used had a cardiovascular inhibitory action among the agents selected for our anesthetic regimen, such as epidural lidocaine, oxygen, nitrous oxide, and pancuronium. Although a different dose of nicardipine needed in the present patient would be related to different technique of anesthesia as well as patient's condition, we believe that nicardipine can be used safer and easier in bolus with a certain effect on hemodynamic stability than in a higher dose infusion when abrupt and extreme hypertension could occur during pheochromocytoma surgery.

In summary, the use of nicardipine can provide an alternative way for management of cardiovascular hemodynamic changes during pheochromocytoma surgery.

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