Postoperative sore throat, dysphonia, or aphonia following endotracheal intubation should resolve rapidly in 2 to 3 days.[6] Patients with symptoms of longer duration or atypical presentation probably warrant indirect laryngoscopic evaluation. With the current trend toward outpatient procedures and shorter hospital stays, increased vigilance and evaluation of this rare occurrence may be needed to prevent long-term sequelae.

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Sevoflurane Anesthesia with Adenosine Triphosphate for Resection of Pheochromocytoma

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Sevoflurane is a potent inhaled anesthetic. Its low blood gas partition coefficient of 0.60[1] allows rapid changes in alveolar anesthetic concentrations, and therefore arterial blood pressure can be altered promptly. In addition, its arrythmogenicity with epinephrine is lower than that of halothane and equal to that of isoflurane.[2] Adenosine triphosphate (ATP) is a potent vasodilator with rapid onset time and recovery.[3,4] ATP also has an antiarrythmic action on epinephrine-induced ventricular arrhythmias[5] and on supraventricular tachycardia.[6] These characteristics of sevoflurane and ATP seem to be suitable for anesthesia during pheochromocytoma resection. We describe our experience of sevoflurane anesthesia with ATP for five cases of pheochromocytoma resection.

Report of Five Cases

Five patients with clinical and laboratory diagnosis of pheochromocytoma were studied. After operation, the diagnosis of pheochromocytoma was confirmed histologically in all patients. Informed consent was granted by each patient. Pertinent patient information is listed in table 1. Although, in all patients preoperative plasma catecholamine levels were significantly elevated (table 2), arterial blood pressure had been well controlled with oral antihypertensive drugs (table 1). Both plasma volume and total blood volume estimated with ^{125}I-human serum albumin and hematocrit, measured in four of five patients, were adjusted to the normal range with blood transfusions. No patient had any significant alterations in the function of the brain, heart, liver, and other organs.

The patients were given 10 mg diazepam orally with 0.5 mg scopolamine and 50 mg hydroxyzine im, 120 min and 30 min before arrival in operating rooms, respectively. During anesthesia, ECG was monitored with the CS5 lead. A radial artery catheter was inserted with the patients under local anesthesia before induction of anesthesia. A pulmonary artery catheter was also inserted into patients 1, 2, and 3 when they were under local anesthesia before induction of anesthesia; however, in patients 4 and 5 the catheter was inserted after induction of anesthesia.

Then anesthesia was induced with 150–200 mg of thiopental iv and 4–5% of sevoflurane. Intubation of the trachea was facilitated with 20 mg of alcuronium iv. The induction of anesthesia was smoothly performed in four of five cases. In patient 4, circulation was severely changed during the induction of anesthesia. After infusion of 200 mg of thiopental, arterial blood pressure increased to 200/124 mmHg and heart rate increased to above 100 beats/min. Arterial blood pressure and heart rate could not be controlled with 5% sevoflurane and 60% nitrous oxide inhalation. Then ATP was infused up to 0.6 $mg \cdot kg^{-1} \cdot min^{-1}$. Arterial blood pressure then decreased rapidly, however, heart rate remained above 100 beats/min. Therefore, 0.4 mg of propranolol iv successfully decreased heart rate. Orotracheal intubation was then performed without any complication.

During operation, anesthesia was maintained with inspired concentrations of 1.6–4.9% sevoflurane, 35–50% oxygen, and 50–65% nitrogen for patients 1, 2, and 3; and with inspired concentrations of 1–5% sevoflurane, 50–65% nitrous oxide, and 35–50% oxygen for patients 4 and 5. Inspired and end-tidal sevoflurane concentrations were monitored with a mass spectrometer in patients 1, 2, and 3. In patients 4 and 5, inspired sevoflurane concentration was estimated from the dial of the precalibrated vaporizer.

During tumor manipulation, 0.1–1.2 $mg \cdot kg^{-1} \cdot min^{-1}$ of ATP was used as a vasodilator in all patients. Although surgical maneuver made plasma catecholamine concentrations significantly high (table 2), hypertension was controlled promptly, and tachycardias were prevented with increasing inhaled sevoflurane concentrations and ATP infusion rates in patients 1, 3, and 5. In patients 2 and 4, because plasma norepinephrine concentrations were extremely high, heart rate could not

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TABLE 1. Patient Data

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (yr)	31	53	55	51	45
Sex	F	F	M	M	F
Weight (kg)	55	37	62	50	48
Height (cm)	169	152	170	170	148
Plasma volume (ml)	3,116	2,932	3,409	/	2,650
Total blood volume (ml)	5,038	4,165	6,643	/	4,020
Preoperative antihypertensive drugs ($mg \cdot day^{-1}$)	Labetalol 450 Nifedipine 30	Prazosin 1	Labetalol 450 Prazosin 3	Prazosin 1.5	Prazosin 6 Propranolol 15
Surgical time (min)					
Total	123	427	321	270	180
Until tumor removal	80	268	167	95	106
Total blood loss (g)	129	6,000	1,100	4,415	100
Tumor weight (g)	75	820	70	370	165
Adenosine triphosphate					
Time used (min)	33	214	141	146	98
Maximum dose ($mg \cdot kg^{-1} \cdot min^{-1}$)	0.6	1.0	0.6	1.0	1.2
Norepinephrine					
Time used (min)	44	50	—	1,454	—
Maximum dose ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	0.5	0.3	—	2.0	—
Other drugs used for cardiovascular control	—	Propranolol	—	Propanolol Phentolamine	—

/ = not measured; — = not used.

be controlled completely with sevoflurane and ATP, so propranolol, 0.4 mg (patient 2) and 3.2 mg (patient 4), was given iv.

After pheochromocytoma removal, norepinephrine was required to manage hypotension in patients 1, 2, and 4 (table 1).

Throughout the anesthesia, no ventricular arrhythmia was noted in four of the patients, and only a single ventricular arrhythmia appeared during tumor manipulation in patient 4. All five patients had uneventful postoperative courses.

In all five cases the origin of the pheochromocytoma was in an adrenal gland. Three of five cases, patients 1, 2, and 4, were of the norepinephrine-predominant type, and the other two cases were of the epinephrine-predominant type pheochromocytoma (table 2).

DISCUSSION

The difficulty of anesthetic management during resection of pheochromocytoma varies from case to case. As shown in table 2, plasma catecholamine concentration changes were variable. In addition, the amount of blood loss, weight of the tumor, time required for the tumor resection, and surgical time differed among cases (table 1). In three of our patients (patients 1, 3, and 5), the small tumor was easily removed without massive blood loss and plasma catecholamine increases were modest. Management in these patients consisted mainly of sevoflurane and ATP, with no norepinephrine or only slight support with norepinephrine. For our patients 2 and 4, who had large pheochromocytomas and lost large amounts of blood, several drugs (phentolamine, propranolol, norepinephrine) were required to control arterial blood pressure and heart rate. Nevertheless, anesthesia management was completed with the use of sevoflurane and ATP without any severe complications in these difficult cases.

TABLE 2. Catecholamine Concentrations in Plasma

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
	NE	E	NE	E	NE	E	NE	E	NE	E
Preoperative	10.40	0.18	5.52	0.30	1.00	1.20	6.71	0.30	0.75	0.53
After induction	19.10	0.15	3.79	0.23	0.93	0.83	17.82	0.67	0.32	0.55
After incision	18.20	0.21	3.74	0.47	0.71	1.08	22.51	0.72	0.87	2.00
During exploration	62.30	0.80	121.00	5.95	21.90	54.80	606.60	14.50	18.26	124.05
After resection	5.25	0.19	4.92	0.21	0.53	0.46	44.03	0.19	0.56	2.31
Recovery room	1.59	0.44	0.87	0.14	0.26	0.22	17.27	0.93	0.44	0.75

NE = norepinephrine ($ng \cdot ml^{-1}$); E = epinephrine ($ng \cdot ml^{-1}$). Normal values: NE < 0.35 $ng \cdot ml^{-1}$; E < 0.12 $ng \cdot ml^{-1}$.

TABLE 3. Hemodynamic Status during Pheochromocytoma Removal

	n	HR	SBP	DBP	CI	SVRI
Patient 1						
Preoperative	1	62	136	89	3.27	2,538
After induction	1	85	117	85	2.61	2,657
After incision	4	75 ± 2 (72–78)*	120 ± 3 (116–124)	91 ± 3 (87–95)	2.71 ± 0.09 (2.59–2.82)	2,713 ± 137 (2,495–2,844)
During exploration	6	78 ± 3 (73–82)	99 ± 12 (82–120)	63 ± 10 (51–83)	3.95 ± 0.57 (2.78–4.45)	1,428 ± 497 (1,001–2,515)
After resection	8	74 ± 6 (67–86)	91 ± 15 (70–120)	57 ± 12 (44–83)	3.92 ± 0.92 (2.92–5.52)	1,334 ± 406 (708–2,019)
Recovery room	6	78 ± 8 (66–87)	126 ± 12 (114–148)	69 ± 5 (63–78)	4.64 ± 0.97 (3.31–5.80)	1,385 ± 275 (1,010–1,886)
Patient 2						
Preoperative	1	76	160	70	5.47	1,416
After induction	1	100	116	71	4.96	1,240
After incision	1	83	82	65	3.91	1,344
During exploration	9	74 ± 8 (60–84)	143 ± 30 (103–190)	76 ± 14 (59–106)	4.10 ± 0.48 (3.52–5.25)	1,960 ± 436 (1,536–2,623)
After resection	7	93 ± 24 (71–127)	115 ± 11 (100–129)	79 ± 9 (65–89)	2.55 ± 0.48 (1.86–3.19)	2,921 ± 716 (1,902–4,028)
Recovery room	1	96	132	83	2.92	2,736
Patient 3						
Preoperative	1	55	131	69	2.83	2,333
After induction	1	82	86	50	3.79	1,988
After incision	5	79 ± 11 (70–100)	84 ± 12 (71–101)	48 ± 13 (37–71)	3.79 ± 0.52 (2.99–4.32)	1,235 ± 249 (864–1,514)
During exploration	4	84 ± 19 (63–110)	145 ± 26 (108–179)	63 ± 10 (50–78)	5.18 ± 0.66 (4.38–6.03)	1,354 ± 130 (1,145–1,467)
After resection	7	89 ± 7 (83–104)	88 ± 13 (63–111)	45 ± 7 (32–58)	4.22 ± 0.49 (3.56–4.97)	1,039 ± 124 (853–1,293)
Recovery room	1	82	92	47	4.69	954
Patient 4						
Preoperative	1	60	182	92	—	—
After induction	1	101	117	62	5.80	1,052
After incision	1	99	133	76	5.39	1,291
During exploration	2	123 ± 18 (105–141)	171 ± 13 (158–183)	91 ± 4 (87–95)	4.92 ± 0.87 (4.05–5.79)	1,909 ± 507 (1,402–2,415)
After resection	4	109 ± 9 (94–117)	98 ± 18 (69–114)	62 ± 12 (41–72)	4.35 ± 1.37 (3.23–6.69)	1,406 ± 438 (919–1,857)
Recovery room	1	89	111	79	3.48	2,057
Patient 5						
Preoperative	1	96	154	90	—	—
After induction	1	69	106	68	2.27	2,835
After incision	1	74	94	61	2.25	2,412
During exploration	4	82 ± 9 (69–95)	118 ± 39 (93–185)	64 ± 17 (55–93)	3.46 ± 0.69 (2.85–4.59)	1,709 ± 654 (969–2,739)
After resection	2	89 ± 1 (88–89)	88 ± 5 (83–93)	52 ± 4 (48–56)	3.89 ± 0.02 (3.87–3.90)	1,163 ± 83 (1,080–1,246)
Recovery room	1	88	118	67	3.92	1,611

HR = heart rate (beats/min); SBP = systolic blood pressure (mmHg); DBP = diastolic blood pressure (mmHg); CI = cardiac index ($l \cdot min^{-1} \cdot m^{-2}$); SVRI = systemic vascular resistance index ($dyn \cdot s \cdot m^{-5} \cdot cm^2$) mean ± SD* (range).

Prevention of life-threatening ventricular arrythmias is an important component of anesthesia for resection of pheochromocytoma. Isoflurane[7,8] and enflurane[9,10] have been recommended for pheochromocytoma resection because they do not sensitize the heart to the arrythmogenic effects of epinephrine. In animals, Imamura *et al.* reported that the arrhythmogenic dose of epinephrine during anesthesia with sevoflurane is much larger than that during anesthesia with halothane and is as large as that with isoflurane.[2] ATP is not only a potent vasodilator but is also an antiarrythmic drug that strongly suppresses ventricular ectopy associated with epinephrine.[5] Although ECG has not been recorded on tape or disk so that dysrhythmias could have been missed, we could prevent dangerous ventricular arrythmias completely during the five cases of pheochromocytoma resection with the use of sevoflurane and ATP.

In many cases of pheochromocytoma resection, patients have tachycardia. ATP slows heart rate with significant atrioventricular conduction delay.[6] This effect may antagonize epinephrine-induced tachycardias during pheochromocytoma resection. Murata *et al.* have reported that 0.4 $mg \cdot kg^{-1} \cdot min^{-1}$ of ATP with halothane or enflurane anesthesia controls arterial blood pressure and heart rate without atrioventricular block during five cases of pheochromocytoma resection.[11] In three of our patients, heart rate could be maintained at less than 100 beats/min with ATP and sevoflurane. In another two patients (patients 2 and 4), however, 1.0 $mg \cdot kg^{-1} \cdot min^{-1}$ of ATP did not decrease heart rate sufficiently so that propranolol was required. ATP (1.0 $mg \cdot kg^{-1} \cdot min^{-1}$) induced atrioventricular block in patient 5 was eliminated by decreasing the infusion. Therefore, the maximum dose of ATP infusion seems to be 1.0 $mg \cdot kg^{-1} \cdot min^{-1}$. For heart rate control, 0.4 $mg \cdot kg^{-1} \cdot min^{-1}$ of ATP was enough in the Murata *et al.* study[11] and 1.0 $mg \cdot kg^{-1} \cdot min^{-1}$ was not enough in this study. This difference possibly depends on the plasma catecholamine concentrations. In patients 2 and 4, plasma norepinephrine concentrations were higher than the maximum norepinephrine value (91.3 $ng \cdot ml^{-1}$) in the Murata *et al.* study (table 2).[11] It seems impossible for sevoflurane and ATP alone to prevent tachycardia completely when plasma catecholamine concentrations are so high.

During anesthesia for pheochromocytoma resection, hemodynamic changes may occur rapidly. Thus, it is desirable to use an anesthetic with which anesthetic level may be rapidly altered and controlled. The low solubility of sevoflurane in blood and fat indicates that it is such an anesthetic.[12] In our five cases, rapid control of anesthetic depth was useful for smooth induction of anesthesia and prevention of extreme decreases of arterial blood pressure after tumor removal. Thus, sevoflurane is a suitable inhaled anesthetic for pheochromocytoma resection. The rapid onset and disappearance of the effect of ATP makes it similarly useful in the management of these patients. Although anesthesia was maintained with sevoflurane and ATP, three of our patients required norepinephrine infusion after tumor removal. Hemodynamic profiles suggest that the cause of hypotension was the significant decrease of systemic vascular resistance induced by norepinephrine withdrawal in patients 1 and 4 and was the decrease of blood volume with massive blood loss in patient 2 (table 3).

Because we have no control group, we cannot definitively compare the advantages of sevoflurane or ATP with other anesthetics or vasodilators. Nevertheless, our five cases suggest that sevoflurane and ATP are useful for patients with pheochromocytoma.

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