J Anesth (1994) 8:425–428

Journal of
Anesthesia

Influence of tumor size on anesthetic management for pheochromocytoma resection

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Abstract: The relationship between tumor size and the complexity of anesthetic management was studied using several values: plasma catecholamine concentrations, requirement of vasoactive agents, surgical time, blood loss, plasma glucose concentrations, and hemodynamic variables. Ten patients with clinical and laboratory diagnosis of pheochromocytoma were prospectively studied. Each anesthesia was maintained using inhalational anesthetic agents. Control of arterial blood pressure (ABP), heart rate (HR), and pulmonary artery blood pressure (PABP) was attempted with only titrating the inhalational anesthetics and adenosine triphosphate (ATP). If the titration of both the inhalational anesthetic and ATP failed to control ABP, HR, or PABP, then phentolamine, propranolol, trinitroglycerine, or norepinephrine was additionally used. Tumor weight was significantly correlated with amount of blood loss, surgical time, duration of ATP requirement, maximal dose of ATP infusion used, maximal plasma glucose concentration, and plasma total catecholamine concentration. However, the tumor weight was not correlated with hemodynamic variables. Patients who required propranolol generally had a significantly larger tumor than those who did not. In conclusion, surgical removal of large pheochromocytoma required more complicated anesthetic management than that of small pheochromocytoma.

Key words: Pheochromocytoma—Anesthesia management, Tumor weight—Plasma catecholamine—Adenosine triphosphate

Introduction

Anesthetic management for patients with pheochromocytoma has been improved by new aesthetic agents and advances in monitoring equipment. However, the risk of the management varies from case to case. Pheochromocytoma can vary markedly in size, ranging in weight from 1 to 4000 g [1]. Crout and Sjoerdsma reported that the turnover and metabolism of catecholamines were rapid in small tumors and slow in large tumors [2]. Except for their report, there have been no studies that revealed the influence of tumor size on anesthetic management for resection of pheochromocytoma. Therefore, the relationship between tumor size and the complexity of anesthetic management was studied using several parameters: plasma catecholamine concentrations, requirement of vasoactive agents, surgical time, blood loss, plasma glucose concentrations, and hemodynamic variables.

Materials and methods

Ten patients with clinical and laboratory diagnosis of pheochromocytoma were included in this study. The diagnosis of pheochromocytoma was confirmed in all patients postoperatively. This study was approved by our institutional human research committee. Informed consent was granted by each patient. The demographics of the patients are listed in Table 1. Although in all patients, preoperative catecholamine levels were significantly elevated, arterial blood pressure had been well controlled with oral antihypertensive drugs. Preoperative fluid infusion and blood transfusion were performed to normalize the blood volume. Following the treatment, both plasma volume and total blood volume were estimated in six of ten patients with ^{123}I-labeled human serum albumin and hematocrit, and were confirmed to be in the normal range. No patient had any significant alternations in the function of the brain, heart, liver, and other organs.

This study was arranged as a prospective study. Anesthesia for each patient was performed under similar protocols. The patients were given 5–10 mg diazepam

Address correspondence to: M. Doi
Received for publication on January 31, 1994; accepted on May 9, 1994

Table 1. Demographics of the patients

	Mean (SD)	Range
Age (years)	46.1 (17.4)	10–67
Sex (male/female)	4/6	
Weight (kg)	49.4 (10.1)	28.0–62.0
Height (cm)	156.5 (13.3)	128–170
Plasma volume ($ml \cdot kg^{-1}$)[a]	56.3 (12.5)	41.5–79.2
Total blood volume ($ml \cdot kg^{-1}$)[a]	95.7 (14.1)	76.4–112.6
Plasma levels		
Epinephrine ($ng \cdot ml^{-1}$)	0.69 (14.1)	0.11–2.47
Norepinephrine ($ng \cdot ml^{-1}$)	5.40 (4.15)	0.75–12.7

[a] $n = 6$

orally with 0.25–0.5 mg scopolamine and 25–50 mg hydroxyzine im, 120 min and 30 min before arrival in the operating rooms, respectively. During anesthesia, ECG was monitored with a CS5 lead. A radial artery catheter was inserted under local anesthesia before induction of anesthesia. A pulmonary artery catheter was also inserted into six of the ten patients under local anesthesia before induction of anesthesia; however, in the other patients the catheter was inserted after induction of anesthesia.

Anesthesia was then induced with 150–200 mg of thiopental intravenously and inhalational anesthetic agents: sevoflurane in seven patients and enflurane in three. Intubation of the trachea was facilitated with one of three neuromuscular blockades: vecuronium, pancuronium, or alcuronium. During anesthesia, control of arterial blood pressure (ABP), heart rate (HR), and pulmonary artery blood pressure (PABP) was attempted with the inhalational anesthetics and adenosine triphosphate (ATP) as a vasodilator. Until the resection of the pheochromocytoma, if the titration of both the inhalational anesthetic and ATP failed to control systolic arterial blood pressure (SABP) below 150 mmHg, HR below 100 $beat \cdot min^{-1}$ or diastolic PABP below 20 mmHg, then phentolamine, propranolol, or trinitroglycerine (TNG) was administered, respectively. After the resection of pheochromocytoma, if cessation of the inhalational anesthetic and ATP with infusion of lactated Ringer's solution failed to maintain systolic arterial blood pressure above 80 mmHg, then norepinephrine was infused. If ventricular arrhythmias appeared at any time during the anesthesia, lidocaine was injected. The amount of glucose infusion was controlled below 5 $g \cdot h^{-1}$ until the resection of pheochromocytoma, and 10–15 $g \cdot h^{-1}$ after the resection.

To evaluate the influence of tumor size on the complexity of anesthetic management, a linear regression analysis was performed between the logarithmic tumor weight and the following parameters during anesthesia: plasma total catecholamine concentration (total epinephrine and norepinephrine) during tumor manipulation, blood loss, requirement of ATP (maximal dose and duration), surgical time, maximal plasma glucose level, maximal SABP and diastolic arterial blood pressure (DABP), cardiac index (CI), and peripheral vascular resistance index (PVRI) during tumor manipulation, and differences between maximal and minimal values of SABP, HR, CI, and PVRI (ΔSABP, ΔHR, ΔCI, and ΔPVRI). Influence of the tumor weight on requirement of vasocative agents was also assessed. Differences of tumor weight in two groups, those who required the agents or those who did not, were analyzed using the Mann-Whitney U-test. A P value of less than 0.05 was regarded as statistically significant.

Results

The tumor weight correlated with amount of blood loss, surgical time, duration of ATP requirement, maximal dose of ATP infusion, maximal plasma glucose level, and plasma total catecholamine concentration (Table 2). However, the tumor weight did not correlate with the hemodynamic variables: maximal SABP and DABP, CI, and PVRI during tumor manipulation, ΔSABP, ΔHR, ΔCI, and ΔPVRI (Table 3). Figure 1 shows differences of tumor weight between the group that required vasoactive agents and the group that did not. Patients who required propranolol had significantly larger tumors than those who did not. However, there was no difference in tumor weight between the patients who required phentolamine, TNG, or norepinephrine

Table 2. Correlation coefficients and formulas of regression line between the tumor weight and the values during anesthesia

	r		Regression formula
Blood loss (g)	0.835	$P < 0.01$	3449 log tw – 5346
Surgical time (min)	0.793	$P < 0.01$	114.9 log tw – 87.6
ATP duration (min)	0.766	$P < 0.01$	94.7 log tw – 93.6
Max ATP ($mg \cdot kg^{-1} \cdot min^{-1}$)	0.706	$P < 0.05$	0.475 log tw – 0.210
Max plasma glucose ($mg \cdot dl^{-1}$)	0.706	$P < 0.05$	162.8 log tw – 17.9
Max plasma total catecholamine ($ng \cdot ml^{-1}$)	0.700	$P < 0.05$	206.4 log tw – 266.0

r = correlation coefficient; ATP, adenosine triphosphate; tw, tumor weight (g).

Table 3. Correlation coefficients of regression line between the tumor weight and the hemodynamic values during tumor manipulation

	r	
ΔPVRI (dynes·sec·cm^{-5}·m^2)	0.549	ns
ΔSABP (mmHg)	0.497	ns
ΔCI (l·min^{-1}·m^{-2})	0.442	ns
CI (l·min^{-1}·m^{-2})	0.338	ns
PVRI (dynes·sec·cm^{-5}·m^2)	0.300	ns
Max SABP (mmHg)	0.259	ns
Max DABP (mmHg)	0.095	ns
ΔHR (min^{-1})	0.003	ns

r, correlation coefficient; CI, cardiac index; PVRI, peripheral vascular resistance index; SABP, systolic arterial blood pressure; DABP, diastolic arterial blood pressure; HR, heart rate.

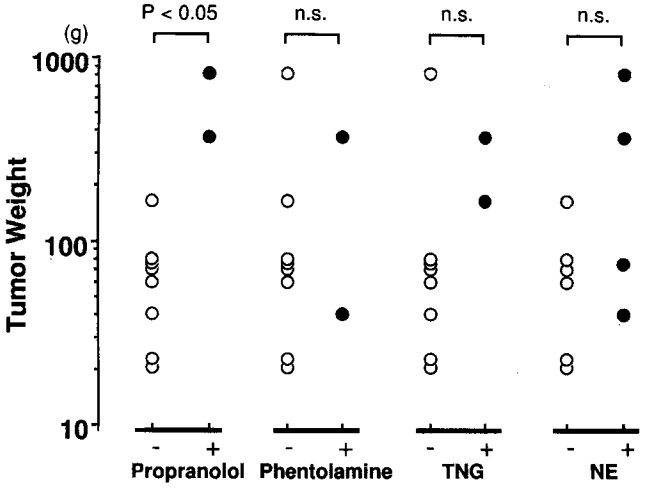

Fig. 1. Distribution of the tumor weight in patients who required or who did not require the agents. A *minus sign* indicates patients who did not require the agent; a *plus sign* indicates patients who required the agent. Patients who required propranolol had a significantly larger tumor than those who did not. There was no significant difference in tumor weight between the patients who required phentolamine, trinitroglycerine (*TNG*), or norepinephrine (*NE*) and those who did not

and those who did not. Throughout the anesthesia, no ventricular arrhythmia was noted in nine of the patients, and only a single ventricular arrhythmia appeared during tumor manipulation in one patient. None of the patients required lidocaine injection as an antiarrhythmic therapy.

Discussion

To evaluate the complexity of anesthetic management in pheochromocytoma resection, each anesthesia should be performed under a similar protocol. In the present study, each anesthesia was maintained using inhalational anesthetic agents, and control of hemodynamic variables was attempted with only titrating the inhalational anesthetics and ATP. Both of the inhalational anesthetics used, sevoflurane and enflurane, have a larger arrhythmogenic dose of epinephrine than halothane [3, 4], and have been recommended for pheochromocytoma resection [5–7]. Since ATP is a potent vasodilator with extremely rapid onset time and recovery [8, 9], and has an antiarrhythmic action [10, 11], ATP was reported to be suitable for cardiovascular control in pheochromocytoma resection [12]. Although this anesthesia protocol provided rapid and potent hemodynamic controllability, it was impossible in several patients to control hemodynamic variables. The need for additional vasoactive agents could be interpreted as complexity in the anesthetic management.

Under this protocol, it was revealed that in several respects, anesthetic management in patients with large pheochromocytoma was more complex than in patients with small tumors.

First, large pheochromocytoma increased plasma catecholamine levels more than did small pheochromocytoma. Extremely high levels of plasma catecholamine required a high dose of ATP infusion and additional propranolol injection to control hemodynamic status. Large amounts of catecholamine released from the tumors during the manipulation caused severe hypertensions and tachycardias that were difficult to treat. High plasma glucose concentrtion could result from high concentration of plasma catecholamines that inhibit insulin secretion and promote glycogenolysis. During anesthesia management for pheochromocytoma resection, occurrence of hyperglycemia should be taken into consideration, especially when the tumor is large.

Secondly, large pheochromocytoma required a long surgical time. The duration of ATP requirement reflected the interval between the start of tumor manipulation and tumor resection, and the time necessary for hypertension treatment. Combined with high plasma catecholamine levels, prolonged manipulation of the tumor could be a great risk for anesthesia management.

Thirdly, a large amount of blood was lost in patients with large pheochromocytomas. Combined with extreme fluctuations in the plasma catecholamine levels, the large amount of blood loss might cause a catastrophic disturbance in hemodynamic status

However, the tumor weight was not correlated with the hemodynamic variables during tumor manipulation. During the anesthesia, inhalational anesthetics, ATP, and other vasoactive agents were used to stabilize arterial blood pressure, heart rate, and pulmonary artery blood pressure. This management might diminish the fluctuation of hemodynamic variables induced by increase in plasma catecholamine levels.

As mentioned above, this study revealed the risks associated with large pheochromocytoma resection. In the preoperative evaluation of patients with pheochromocytoma, the size of the tumor may provide important information for the anesthesia management.

In conclusion, the anesthetic management during surgical removal of large pheochromocytoma was more complex than that of small pheochromocytoma.

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