Analysis of Anaesthetic Management of Excision of Phaeochromocytoma: Retrospective data of 51 operated cases in 15 Years

P Shroff, P Marghade, B Tendolkar, S Kamath

Citation

P Shroff, P Marghade, B Tendolkar, S Kamath. *Analysis of Anaesthetic Management of Excision of Phaeochromocytoma: Retrospective data of 51 operated cases in 15 Years*. The Internet Journal of Anesthesiology. 2006 Volume 14 Number 1.

Abstract

Background and Objective: Perioperative good control of blood pressure, invasive monitoring and cascade of drugs to manipulate haemodynamic changes remain the key to the successful management of excision of phaeochromocytoma. Laparoscopic excision has reduced perioperative problems.

Methods: The aim of our retrospective study in a teaching hospital was to analyze the demographic details, glands involved, clinical features, investigations and anaesthetic management for the management of the patients who underwent excision of phaeochromocytoma. All the perioperative sheets of patients who underwent phaeochromocytoma excision in our institute were carried out. Percentages were calculated.

Results: 29% of the patients with phaeochromocytoma were from the third decade. 94% of the patients had the tumour in the adrenal gland. 8% were detected to have bilateral tumours. All of them had hyper-adrenergic symptoms. One patient presented during pregnancy and one case was diagnosed on the table. 8% had associated diabetes mellitus, 4% had ischaemic heart disease and 2% patient each had neurofibromatosis, pemphigus and thyroid involvement. Levels of urinary vanillyl mandelic acid (VMA) and metanephrine were raised in 92% of the patients. Laparoscopic excision of pheochromocytoma was successful in six patients. 62% of the patients needed intravenous nitroglycerine infusion to control the hypertension intraoperatively. Hypotension following excision of the tumour was managed with intravenous fluids, colloids, dopamine, noradrenaline or ephedrine.

Conclusion: Successful management requires a team of experienced anaesthesiologists and surgeons.

INTRODUCTION

The term phaeochromocytoma was first used by Pick in 1912 which meant dusky coloured tumour. 1, 2 Phaeochromocytoma though uncommon is not rare. It has an incidence of 0.3 to 0.95% in the general population. It is diagnosed on investigating 0.5% of the patients having hypertension. The perioperative management of patients with pheochromocytoma is usually surrounded by aura and hype. Despite advances made in the field of anaesthesiology, no single technique for anaesthetic management of excision of phaeochromocytoma has gained universal acceptance. Anaesthetic management should be used carefully directed with the aims of minimizing the indirect release of catecholamines and prevention of stress and also to support therapy of haemodynamic crisis.3

Aim: To analyze the demographic details, glands involved, clinical features, investigations and anaesthetic management for the management of the patients who underwent excision of pheochromocytoma.

METHODS

A retrospective analysis of all the patients who underwent phaeochromocytoma excision from 1992 to 2004 in our institute were studied with reference to clinical features, biochemical investigations, methods of localization, drug therapy, associated diseases, preoperative preparation, intraoperative management, complications encountered and postoperative outcome were analyzed. Our protocol for management is also discussed. The endocrinology department primarily evaluated these patients. Iodine 131

meta-iodobenzyl-guanidine (MIBG) scan was done in patients with pheochromocytoma to rule out multiple and ectopic sites of overproduction. All these patients were admitted well in advance, till optimum control of blood pressure and blood sugars were achieved. Electrolyte abnormalities were corrected. Patients of pheochromocytoma were maintained on alpha-blockers prior to surgical intervention.

RESULTS

Table 1 show that there was a slight predominance of females over males. A majority of them belonged to the second decade. The youngest in our series was 13 year old male and the eldest was 66 year old male. Mean age in our series was 31.73 14.25 years.

Figure 1

Table 1: Demographic Data

		Number	Percentage
Gender	Males	23	45
	Females	28	55
Weight (Kg)	Mean ± SD	47.06 ± 10.27	
Age (years)	Mean ± SD	31.73 ± 14.25	
Age Distribution (years)	10-20	14	28
	21-30	15	29
	31-40	10	19
	41-50	6	12
	51-60	3	6
	61-70	3	6

As in table 2, of the 51 patients 50 had hyper-adrenergic symptoms. One patient was asymptomatic. 51% of the patients presented with hypertension. 49% presented with paroxysmal crisis that were subsequently diagnosed to have hypertension. 61% of the patients presented with palpitations, 51% with associated headache, 41% with sweating and 39% with giddiness. Anorexia was seen in 4% and convulsions in 16% patients.

Figure 2

Table 2: Clinical Features

Symptoms	Number	%
Palpitation	31	61
Headache	27	53
Hypertension	26	51
Sweating	21	41
Giddiness	20	39
Abdominal pain	13	26
Angina	11	22
Convulsions	8	16
Anorexia	2	4
Visual disturbances	1	2
Cardiomyopathy	1	2
Pregnancy	1	2
Asymptomatic	1	2

Four patients out of the 26 patients who had hypertension also had associated diabetes mellitus while 4% of them also had ischaemic heart disease. Neurofibromatosis, pemphigus and thyroid involvement were seen in one patient each. One patient was incidentally diagnosed to have phaeochromocytoma when explored for retroperitoneal abscess drainage.

Levels of urinary vanillyl mandelic acid (VMA) and metanephrine were raised in 92% of the patients. Ultrasonography and CT scan were done routinely in all patients. MRI scan was done in four patients. Meta iodo benzyl guanidine (MIBG) scan was needed to confirm the site of the tumour in 22%. Significant ECG changes like ST-T changes, left ventricular hypertrophy, left bundle branch block and myocardial infarction were seen in 25 patients.

Table 3 shows that, 94% of the patients had the tumour in the adrenal gland while only three patients had extra adrenal location. Of which, two patients had it in urinary bladder and one in mediastinum. 53% of the phaeochromocytoma were on the right side, while four cases had bilateral tumours that were excised simultaneously. Since 2001 laparoscopic excision of pheochromocytoma were attempted in eight patients, of which two had to be converted to open because of excessive bleeding.

Figure 3

Table 3: Localization of tumour

	Number	%
Right	27	53
Left	17	33
Bilateral	4	8
Extra adrenal	2	4
Bilateral + Extra adrenal	1	2

78% of the patients received alpha blockers along with beta blockers while eight patients received calcium channel blockers also as in table 4.

Figure 4

Table 4: Preoperative antihypertensive drug therapy

	Number	%
Alpha + Beta blockers	40	78
Alpha + Calcium channel blockers	4	8
Beta blockers + Calcium channel blockers	2	4
Calcium channel blockers	2	4
Beta blockers	1	2

62% of the patients needed nitroglycerine (NTG) to control the hypertension intraoperatively. In 21% patients, sodium nitroprusside (SNP) and propofol were also needed (table 5).

As in table 6, Intravenous lignocaine sufficed in 11 patients who needed dysrrhythmic agents to control tachycardia.

Figure 5

Table 5: Intraoperative management of hypertension

	Number	%
NTG	21	41
NTG +SNP	11	21
Propofol + NTG	10	20

Figure 6

Table 6: Intraoperative management of tachycardia

	Number	%
Lignocaine	11	21
Metoprolol	4	8
Esmolol	1	2

Hypotension following excision of the tumour was managed by giving intravenous crystalloids and colloids. In 29% of the patients inotropic agents like dopamine, noradrenalin or ephedrine were also needed. Postoperative analgesia was achieved using intravenous agents or via epidural route in 65% patients.

OUR PROTOCOL

Patients were operated within a month of diagnosis. Once the decision to operate is taken anaesthesiologist thoroughly evaluates the patient and establishes a good rapport with the patient with multiple visits. Preoperative optimization was done with initial control of hypertension with alpha blockers like phenoxybenzamine or doxazocine or prazosin depending on availability and affordability. Beta blockers were then added to control tachycardia. Few patients also needed calcium channel blockers. Anxiolytic agents were given for few nights previous to surgery. The antihypertensive agents were continued till the morning on the day of the surgery. A central venous access was established and at least one litre of normal saline was given intravenously overnight with monitoring of central venous pressure. Two peripheral wide bore veins were cannulated after prilocaine gel application. On the day of surgery, they were premedicated with buprenorphine 3µg/kg i.v., glycopyrrolate 4µg/kg i.v., midazolam 0.03mg/kg i.v. and ondansetron 0.2mg/kg i.v. one hour prior to the scheduled time of surgery. In the operating room, monitoring included ECG, blood pressure monitoring through the radial artery cannulation under local anaesthesia, oxygen saturation, capnography and central venous pressure monitoring. The patients were anaesthetized with thiopentone sodium or propofol. Lignocaine was used intravenously to attenuate the pressor response to intubation. Vecuronium was the muscle relaxant of choice for both intubation and maintenance. Surgery began after achieving a central venous pressure of at least six to eight cm of water. Maintenance of anaesthesia was done using oxygen, nitrous oxide, inhalational agent like isoflurane4, recently sevoflurane5 and propofol was used as and when needed. Glucose containing intravenous replacement fluids was started at the time of tumour removal with blood sugar monitoring. Intraoperative haemodynamic changes were maintained with fluids, nitroglycerine, sodium nitroprusside, metoprolol, esmolol, dopamine and noradrenaline. After the surgery patients were reversed with neostigmine and mechanically ventilated for six hours till the haemodynamic parameters stabilized. Analgesia was given postoperatively in the form of systemic agents in 35% and epidural analgesia in 65% patients. An epidural catheter was passed after giving general anaesthesia. The patients were observed in the intensive care unit for at least 48 hours. The three most important complications in the immediate

postoperative period were hypertension in 45% patients, hypotension in 28% and hypoglycaemia in 5% patients. These were nondiabetic patients. Therefore appropriate measures were taken such as, alleviation of pain with parenteral opioids and / or epidural analgesia and continuation or re-institution of anti-hypertensive medication. Hypotension although uncommon requires volume replacement with a high index of suspicion for intra-abdominal bleeding. Hypoglycaemia with associated encephalopathy may occur and the residual adrenergic blockade may mask valuable symptoms and signs. Therefore the blood glucose level was monitored closely in the early postoperative period.

DISCUSSION

The adrenal glands are organs, seated deep in the retroperitoneum amidst important structures. Phaeochromocytoma arises from the chromaffin tissues of the sympathetic nervous system. Few of them may be associated with familial pathological conditions. More than 90% of them occur below the diaphragm. 85% to 95% of them occur with equal frequency in the left and right adrenal gland. 10% of sporadic and 50% of familial adrenal tumours is bilateral in origin. We found 94% in the adrenal gland. Four patients had bilateral tumours and in two patients it was detected to be originating from the urinary bladder. In one case each mass was also found in mediastinum and gland of Zukerkandl. A similar incidence was found in the study by AM Lucon etal6.

50 patients had classical triad of hyper-adrenergic symptoms and presented with hypertension, headache, palpitations and sweating all due to paroxysmal release of catecholamines. The hypertension is usually episodic and often provoked by some activity or movement. A patient with bladder wall phaeochromocytoma classically gives history of these symptoms during micturition.7 However in the two cases of bladder involvement in our study, such symptoms were not seen. Anorexia, pallor, cold hands and feet are seen in many patients. In advanced cases with poor skin circulation, marbling or even gangrene can occur. There may even be mood swings. Beta adrenergic effects predominate in some tumours that are largely adrenaline secreting. In these patients, palpitations and tachyarrhythmia may be associated with normal or even decreased blood pressure. Rarely phaeochromocytoma present during pregnancy. In our series one patient presented during pregnancy.

Clinical presentation depends upon the catecholamine output of the tumour which may be either episodic or sustained and consists of adrenaline and noradrenaline. When noradrenaline is predominant, long periods of vasoconstriction leads to contraction of the venous pool and marked reduction in circulating volume occurs. Hence they are often advised to eat lot of salt in their diet and drink lot of fluids prior to surgery. However, if adrenaline is excessive, tachyarrhythmia with fewer changes in blood pressure and peripheral circulation occur.

High plasma catecholamine concentration leads to glycogenolysis and inhibition of release of insulin by islet cells. Though beta adrenergic stimulation promotes insulin release, alpha effect being more powerful, abnormal glucose tolerance is often seen. Also lipolysis increases free fatty acids which provides alternative energy substrates and impairs sensitivity to insulin. Thus patients develop signs of diabetes mellitus which are controlled with insulin therapy.

Sustained release of catecholamines may lead to cardiomyopathy. One patient in our review developed cardiac failure after beta blockers. This patient was diagnosed to have beta blocker induced cardiac failure and the patient was thus maintained only on alpha blockers.

If the effects of the release of catecholamines remain uncontrolled, the patient will ultimately suffer a life threatening crisis because of predominantly pressor effects. Hypertensive encephalopathy with neurological deficits, blindness or unconsciousness may occur. Eight patients in our study presented with episodes of convulsions.

Severe arterial spasm causes widespread under-perfusion and impalpable peripheral pulses leading to metabolic acidosis and even death. Alternatively, hypotension may also be seen following prolonged hypo-perfusion with multiple organ failure or when adrenaline is the predominant catecholamine and the patient may present with high output cardiac failure. Intense vasoconstriction may make indirect sphygmomanometry impossible despite normal or increased central arterial pressure.

The more advanced case may present as a diffusely hyper-metabolic state like thyrotoxicosis, diabetes mellitus, malignant hypertension, carcinoid syndrome or septicaemia. When phaeochromocytoma occurs during pregnancy, it may resemble toxaemia.

As soon as diagnosis is established, the patient must be protected from the hazards of uncontrolled catecholamine

release followed by imaging and surgical planning. Emergency surgery to remove a phaeochromocytoma from an unprepared patient must never be contemplated. One such patient in our series, who had a history of hypertension, was on beta blockers only when explored for a retroperitoneal mass had sudden increases in blood pressure during handling of the mass. The mass was not removed at that time. On further evaluation the patient gave a history of headache. The patient behaved intraoperatively as if having a phaeochromocytoma and the diagnosis was confirmed by the histopathology report after the mass was subsequently excised. Preoperatively, a surgeon is primarily interested in the size of the gland, its vascularity and proximity or involvement of surrounding important structures. CT scan and ultrasonography remain the predominant evaluation tools. MIBG may be needed to diagnose extra adrenal tumour. Urinary metanephrine level is more sensitive than urinary VMA level. In our study 6% patients had raised urinary metanephrine levels with normal urinary VMA levels.

The principal step in the pharmacological control is to prevent the pressor effects of catecholamines and this is best achieved by alpha blockers. Phenoxybenzamine is useful as it has long duration of action permitting twice- daily administration. It also causes a non-competitive adrenergic blockade, thus surges of catecholamine release cannot override the inhibition that may occur with a competitive agent. However it is comparatively costly. Hence other selective alpha blockers like doxazocin or prazosin have also been used successfully. It minimizes secondary beta adrenergic effects. Whichever alpha blocker is used it must be introduced with caution beginning with small doses and increased gradually. Alpha blockade is adequate if postural hypotension is controlled. 8

After establishing alpha blockade, tachycardia may be controlled with beta blockers. Earlier atenolol in a single daily dose was used. Now there are few reports recommending propranol in four doses daily. Calcium channel blockers who suppress catecholamine synthesis may have a useful role in patients who develop resistance to alpha blockers. 78% of our patients were maintained on both alpha and beta blockade. Four patients were on alpha blockers and calcium channel blockers, two on beta blockers and calcium channel blockers and two on calcium channel blockers.

Adrenal vein, being more constant in location, is the most important structure requiring early interruption during adrenalectomy. Hence during its dissection one must be extremely vigilant. Inadvertent handling of the gland can release hormones into the circulation, causing abrupt changes in physiology. Intraoperative haemodynamic changes occur during induction, intubation, and tumour manipulation and after adrenal vein ligation. Pharmacological control of catecholamine release during surgery can be achieved using nitroglycerine, sodium nitroprusside, metoprolol or esmolol. We used nitroglycerine in 41% of cases. Epidural blockade may also help. In thirty patients in whom epidural was also used along with general anaesthesia haemodynamic changes were same as found in patients in whom only general anaesthesia was used. Earlier the need for pharmacological intervention intraoperatively was more and was done with sodium nitroprusside.

In more recent times, nitroglycerine is being used and the intraoperative fluctuations are much less. Hypotension following removal of the tumour is managed using fluids and if needed dopamine or noradrenaline.2 Recently, angiotensin II analogs have been used to manage post excision hypotension.

Auto transfusion can be used to control hypotension following removal of phaeochromocytoma. This avoids the side effects of blood transfusion and minimizes the change in intravascular volume after removal of the tumour as most of the blood, which is lost, is reinfused. Furthermore the circulating catecholamine present in blood will help to maintain the blood pressure.5, 9 It may also lead to a significant elevation of the blood pressure because the catecholamine levels present may still be 3 to 20 times that of the normal range. Hypertension may be due to the patient recovering from anaesthesia or pain or due to some residual tumour or persistence of high plasma catecholamine levels, which may take a few days to return to normal values. Platelets are known to actively concentrate catecholamine during their life span and their destruction by suction or centrifugation may probably be responsible for the elevated levels of catecholamine in the collected blood.5 Two weeks following complete excision of phaeochromocytoma, urinary VMA levels return to normal.

Until 2001, adrenalectomy was performed by a long abdominal incision. Since 2001, laparoscopic adrenalectomy is been done with intra-abdominal pressure maintained at 12 mm Hg. The tip of the telescope becoming the eye of the operating surgeon, gives the surgeon accurate details of the anatomy. However two patients needed conversion to open

adrenalectomy due to excessive bleeding. With technological advancement and experience tumours up to 10 cm size are excised laparoscopically, as it leads to decreased incidence of haemorrhage, early recovery, decreased incidence of incisional hernia and better cosmesis.

CONCLUSION

Successful management requires a team of experienced anaesthesiologists and surgeons. Perioperative good control of blood pressure, invasive monitoring and cascade of drugs to manipulate remain the key in the success. Laparoscopic excision is becoming popular due to magnification and better dissection with decreased haemodynamic variations in the perioperative period. Reliable pharmacologic principles need to be utilized in the management of patients with this interesting and challenging neuroendocrine neoplasm.

CORRESPONDENCE TO

Dr Prerana Shroff Address: 126/5, Peaceland CHS Ltd, Prabhat Colony, 7th Road, Santacruz East, Mumbai 400055, Maharashtra, India. Tel No: 91-22-26114150, 0-9869117027 Email: preranaps@rediffmail.com

References

1. Samaan NA, Hicky RC, Shutts PE. Diagnosis, localization and management of pheochromocytoma. Pitfalls and follow-up in 41 patients. Cancer 1988; 62: 4251-4260.
2. Werbel SS, Ober P. Pheochromocytoma: Update on diagnosis, localization and management. Med Clin North Am 1995; 79:131-153.
3. Strecker U, Lipp M: Anaesthetic Management for phaeochromocytoma .Zentralbl Chir 1997, 122(6): 460-4.
4. Desmonts JM, Le Houeller J, Remond P, Duvaldestin P. Anaesthetic management of patients with phaeochromocytoma. Br. J. Anaesth 1977; 49 (10): 991-8.
5. Singh G, Kam P: An overview of anesthetic issues on Phaeochromocytoma. Ann. Acad. Med. Singapore 1998; 27: 843-8.
6. Lucon AM, Periera MA, Mendonca BB, Halpem A, Wajchenbeg BL, and Arap S. Phaeochromocytoma: Study of 50 cases. J. of Urology 1997; 157 (4): 1208-1212.
7. Zimmerman IJ, Biron RE, MacMohan HE Phaeochromocytoma of the urinary bladder. N. Engl. J. Med. 1953 2; 249 (1): 25-6.
8. Abdalla Saad Abdalla: Management of Phaeochromocytoma, Report on 30 cases Kuwait Medical Journal 2002, 34 (4): 276-280.
9. Breivik H. Perianaesthetic management of patients with endocrine disease. Acta Anaesthesiol Scand. 1996; 40(8 Pt 2): 1004-15.
10. Barvo EL, Gifford RW. Current concepts in Phaeochromocytoma: diagnosis, localization and management. N. Engl. J. Med 1984, 15; 311 (20): 1298-303.
11. Fay ML, Holsman RS. Isoflurane for resection of phaeochromocytoma. Anesth Analg, 1983; 62 (10): 955.
12. Stamenkoviv L, Spiderdijk J. Anaesthesia in patients with phaeochromocytoma. Anaesthesia 1976; 31 (7): 941-5.

Author Information

Prerana P. Shroff, M.D.
Associate Professor, Department of Anaesthesiology, Seth GSMC & KEMH

Pallavi Marghade, M.D., D.A.
Lecturer, Department of Anaesthesiology, Seth GSMC & KEMH

Bharati Tendolkar, M.D.
Professor, Department of Anaesthesiology, Seth GSMC & KEMH

Surekha K. Kamath, M.D.
Ex-Professor, Department of Anaesthesiology, Seth GSMC & KEMH