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ACTUALITIES IN THE ANAESTHETIC MANAGEMENT OF PHEOCHROMOCYTOMA/ PARAGANGLIOMA

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Abstract

The anaesthetic management of pheochromocytoma is complicated and challenging. However, preoperative pharmacologic preparation, modern anaesthetic techniques and drugs associated with advanced monitoring in conjunction with the evolution of surgical techniques (open laparotomy to laparoscopic surgery and robotic approaches in the present day) improved significantly perioperative outcome, and intraoperative and postoperative hemodynamic stability. Although there are not randomised clinical trials to suggest one approach over another and there is a high international variability amongst intraoperative anaesthetic techniques, most management principles are still universal.

Keywords: pheochromocytoma, anaesthesia, pharmacology, intraoperative management.

INTRODUCTION

Phaeochromocytomas are rare neuroendocrine, catecholamine-secreting tumours originating from chromaffin tissue of the adrenal medulla. Paragangliomas are related neuroendocrine tumours arising from extra-adrenal paraganglia. In 2004, the World Health Organization made more clearly comprehensible the terminology (1) when it described phaeochromocytoma as an intra-adrenal paraganglioma. The paragangliomas are derived from chromaffin cells too, such as tumours in juxta-aortic locations or carotid body tumours. These are defined as extra-adrenal paragangliomas.

In this article, we will describe current opinion of perioperative management of both phaeochromocytomas and extra-adrenal paragangliomas. The majority of tumours develop spontaneously, however the prevalence of familial and extra adrenal tumours in patients carrying specific gene mutations inherited in an autosomal-dominant fashion, may be up to 50% (2).The incidence rate of phaeochromocytomas in Europe is around 0.2 per 100 000 people per year, with a higher proportion of malignant (29%) extra-adrenal (24%) and/or familial (32%) tumours(3).

Surgical resection of a phaeochromocytoma is the only treatment and the peri-operative management of such patients can represent a serious challenge to the anaesthesiologist.

Haemodynamic instability is common with severe hypertensive episodes occurring frequently during manipulation of the tumour. In the past, perioperative mortality rates have been high, but in the present times they have dropped significantly due to the modern preoperative pharmacological approach and intraoperative management development. However, the anaesthetic management of patients with pheochromocytoma is still challenging and requires an understanding of tumour physiology and receptor pharmacology for appropriate intraoperative decisions.

Preoperative assessment

Although there is limited evidence reported from prospective randomized controlled trials. and majority of information on the surgical and anaesthetic approach to pheochromocytoma is reported from small case series or case reports, over the time there were developed consistent fundamental principles between countries and hospitals.

Due to their neural crest origin, almost all pheochromocytomas secrete an excess of catecholamines and/or catecholamine breakdown products. Also, up to 20% of head and neck paragangliomas secrete an excess of catecholamines too (4) and biochemical screening is mandatory for these tumours as well. Phaeochromocytomas produce

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a variable combination of norepinephrine, epinephrine, or rarely, dopamine and these lead to the hemodynamic instabilities at clinical presentation.

Patients with phaeochromocytomas have clinical presentation with classic symptoms of palpitations, diaphoresis, headache and sometimes fear of death. Hypertension is present in approximately 90% of cases with only 35–50% paroxysmal.

Other non-specific symptoms at presentation can be anxiety, nausea, weight loss, hyperglycaemia, tremor or abdominal pain resulting from bowel ischaemia due to excessive vasoconstriction. Malignant hypertension can lead to ocular papillo-edema with visual disturbances.

Although almost half of phaeochromocytomas are incidentally diagnosed on abdominal imaging for other indication, the literature still reports more complex and life-threatening presentations including shock, cardiomyopathy, orthostatic hypotension or even cardiovascular collapse.

Classical biochemical diagnosis of phaeochromocytomas is based upon 24h collections of urinary catecholamines and vanillylmandelic acid, and also blood sampling for plasma catecholamines. (5). Recommended diagnostic techniques include measurement of levels of metanephrine and normetanephrine which are breakdown products of epinephrine and norepinephrine, from blood (greater sensitivity) or urine (greater specificity) with nearly 100% sensitivity and no agreement which is superior. There is a current consensus that metanephrine analysis is a superior tool of diagnosis over classical methods (6). Dopamine-secreting tumours can be diagnosed by measuring plasma or urinary dopamine and homovanillic acid levels.

Many of the patient's daily medications can impact catecholamine release.

Tricyclic antidepressants, selective norepinephrine (NE) reuptake inhibitors (amitriptyline, olanzapine, venlafaxine), and monoamine oxidase inhibitors (moclobemide, phenelzine), all may decrease norepinephrine reuptake or influence its metabolism.

Recreational drugs (cocaine, amphetamine, caffeine) can have a direct effect on adrenal receptors or cause catecholamines release from storage vesicles. Haloperidol or droperidol are dopamine receptor antagonists and can lead to catecholamines release from the tumour.

Other drugs are:

- adrenergic receptor blockers (atenolol, phenoxybenzamine),
- sympathomimetics (salbutamol, terbutaline),
- paracetamol.

Preoperative investigations and treatment should focus on end-organ manifestations such as the paroxysmal or sustained hypertension. Renal function, and preoperative glucose levels should be determined. An ECG may reveal ventricular hypertrophy, tachyarrhythmias, myocardial ischaemia, ST changes, decreased QRS and QTc prolongation.

Echocardiography is considered mandatory and can show a diastolic dysfunction in the majority of patients, meanwhile left ventricular systolic dysfunction only in 10% of patients. Also many patients are found with hypertrophic cardiomyopathy, as a result of chronic hypertension and many cases of inverted (atypical) Takotsubo cardiomyopathy (7) were described.

After positive biochemical tests, the first investigation for localizing the tumour is either CT or MRI of the abdomen with further functional imaging such as scintigraphy with Meta-iodobenzylguanidine (MIBG-123) in patients with high probability of metastatic or multi-focal disease.

Although the anaesthesiologist is not commonly involved in preoperative diagnosis, he evaluates patients at preanesthetic examination requiring these results.

Preoperative pharmacologic preparation

The objectives of preoperative care include: management of hypertension and restoring the chronic depletion of circulating volume, management of arrhythmias with optimization of myocardial function, and treatment of glucose and electrolyte disturbances.

Historically, phaeochromocytoma surgery had high mortality rates of up to 45%, and associated severe intraoperative hypertension, arrhythmias, myocardial ischaemia, left ventricular failure or strokes, and refractory hypotension after tumour resection.

The safe perioperative care of the pheochromocytoma patient consists of appropriate preoperative blockade of the catecholamines effects (6).

The main goals of preoperative blockade are to control blood pressure and heart rate with restoring chronic volume depletion and final target to prevent catecholamine storm induced by surgery with its effects on the cardiovascular system (5). The standard for pre-operative blockade is provided usually at home for 10-14 days by blockade of catecholamine synthesis or blockade of downstream effect with the aim of

normalizing any cardiac changes. Until recently, the 1982 Roizen criteria (8) were cited: blood pressure < 160/90 mmHg for 24 hours prior to surgery, the presence of orthostatic hypotension with a decrease in systolic arterial pressure of at least 15% but not <80 mm Hg, an ECG which is free of ST or T wave changes for 2 weeks prior to surgery, and less than five premature ventricular contractions per minute (8). Although there is no consensus, actual arterial pressure targets are tighter (arterial pressure of <130/80mmHg) and orthostatic hypotension is not a necessity. ST or T wave changes may reflect inverted Takotsubo cardiomyopathy rather than ischaemia. Also an optimal duration of treatment is not universally agreed and shorter periods have been used successfully.

The most common drugs used in pre-operative stabilisation are described in Table 1.

PRESCRIPT trial (9) randomizes patients to receive either phenoxybenzamine or doxazosin and analyses the efficacity of doxazosin.

Phenoxybenzamine due to its long half-life should be stopped 24–48 h before surgery to prevent the postoperative catecholamine-resistant refractory hypotension. The pre-synaptic α2-blockade can interfere with the norepinephrine negative feedback loop that regulates norepinephrine release resulting in excess release of norepinephrine from cardiac sympathetic neurons and reflex tachycardia via β1stimulation. Symptoms such as headache, somnolence, and nasal congestion may result from central α2-blockade.

Beta-adrenoreceptor blockade is also commonly added to treat tachyarrhythmias accompanying alpha-blockade. Selective β1 antagonists (such as atenolol or metoprolol) are used to manage tachyarrhythmias resulting from epinephrine/dopamine secreting tumours or secondary to α-blockade and must be started after complete α-blockade.

Beta-adrenoreceptor blockade should not be used before or in the absence of alpha-blockade because the antagonism of β2-mediated vasodilation can induce α-mediated vasoconstriction associated with hypertensive crisis, while myocardial function can be compromised by the negative inotropic effect of β-blockade.

Calcium channel blockers inhibit norepinephrine-induced calcium influx and have been increasingly used in the recent years especially

Table 1. Mechanism of action and pharmacokinetics of medications used for pheochromocytoma control

Medication	Mechanism of action	Duration	Elimination t½	Dose
Phentolamine	Competitive inhibition of α adrenergic receptors	15 to 30 minutes	19 minutes	
Phenoxybenzamine	Noncompetitive blockade of α adrenergic receptors	Greater than 72 hours	24 hours	10 mg twice daily increased until symptoms resolve or appear side effects (postural hypotension, nasal congestion
Doxazosin (Cardura)	Competitive inhibition of a - 1 adrenergic receptors	Greater than 24 hours	22 hours	2-8 mg/day
Prazosin (Minipress)	Competitive inhibition of a - 1 adrenergic receptors	10 to 24 hours	2 to 3 hours	2-5 mg 2-3 times daily
Metoprolol	Competitive inhibition of β1adrenergic receptors	5 to 8 hours	3 to 8 hours	25-50 mg two or three times daily
Atenolol	Competitive inhibition of β1 adrenergic receptors			12.5-25 mg twice or three times daily
Labetalol	Competitive inhibition of a - 1 and β adrenergic receptors	2 to 18 hours	5 hours	
Nicardipine	Dihydropyridine calcium channel blockers	8 hours	2 to 4 hours	60-90 mg daily
Nifedipine	Dihydropyridine calcium channel blockers	Unknown	2 to 5 hours	30-90 mg daily
Clevidipine	Dihydropyridine calcium channel blockers	5 to 15 minutes	15 minutes	
Metyrosine	Inhibition of tyrosine hydroxylase inhibiting catecholamine synthesis	Unknown	3 to 4 hours	

in patients that do not tolerate phenoxybenzamine or in normotensive patients because they do not cause the hypotension generated by alpha-adrenoreceptor blockade.

Metyrosine is a tyrosine analogue that inhibits catecholamine synthesis and is associated with alpha blockade in patients with large or metastatic tumour or with hypertension even on high doses of phenoxybenzamine and in those with highly biochemically active tumours with the aim of decreasing the hypertension caused by tumour manipulation intraoperatively.

Octreotide can be used in addition to alpha blockade; it is thought that some phaeochromocytomas possess specific somatostatin binding sites, and octreotide may have some antisecretory potential.

In addition to pharmacological control, a high sodium diet and fluid intake are also recommended to help restore blood volume.

Monitoring

An arterial line should be placed before induction of anaesthesia aiming to avoid sympathetic nervous system stimulation by pain or stress. It is recommended placement by an experienced provider after administration of an anxiolytic (midazolam 2-4 mg IV) with small doses (25-100 mcg) of intravenous fentanyl and use of local anaesthetic (10,11).

Central venous access is necessary in expectation of the need for vasopressors to be administered by infusion after adrenal vein ligation and the sudden fall in endogenous catecholamines in the peri and postoperative period, and after the adrenal vein dissection and for measurement of central venous pressure. Usually it is inserted after induction.

Nevertheless there are no accurate predictors of which patients are likely to need central administration of vasopressors, and some patients require only low-moderate dose of alpha-agonist (e.g. phenylephrine) after tumour removal.

In phaeochromocytoma surgery there is no evidence base to support the routine use of cardiac output monitoring. However, there is a subgroup of patients with cardiomyopathy where the assessment of the circulatory volume based only on central venous pressure measurement is not reliable, so the cardiac output monitoring should be considered. Even if pulmonary artery catheters were the preferred cardiac output monitoring they are rarely used.

Oesophageal Doppler has been used in the paediatric population and a recent prospective study showed its efficacy in phaeochromocytoma to avoid volume overload and to visualize the variable intraoperative course (12) Devices relying on arterial pulse contour analysis PiCCO (Plus; Pulsion Medical Systems, Munich, Germany), Flotrac Vigileo™ (Edwards Lifesciences, Irvine, CA, USA) or VolumeView™/EV1000™ (Edwards Lifesciences, Irvine, CA, USA) neither have been formally evaluated in randomised trials for phaeochromocytoma surgery. More simple, pulse pressure variation is widely used as a valuable monitor of intravascular volume status. The alterations in blood flow and systemic blood pressure vary over the respiratory cycle allowing the anaesthesiologist to calculate the difference between the highest and lowest blood pressure. Systolic pressure variation is higher when hypovolemia occurs, because when the intravascular volume is lower the blood vessels are more susceptible to compression by positive pressure (13). The systolic blood pressure variation of 0-5 mmHg indicates hypervolemia, of 5-10 mmHg euvolemia, and > 10 mmHg hypovolemia. The limitations of this type of monitoring as a predictor of response to fluid challenge are the need for sinus rhythm and a closed chest and the advantages are the following: it is not expensive, is easy to use and does not require special equipment being assessed on most monitors.

Case reports describe the use of intraoperative transoesophageal echocardiography to guide fluid management and titration of vasodilators. Transoesophageal echocardiography is a modern mean of monitoring for volume status and myocardial ischemia, that can also diagnose and monitor valvular anomalies, and guide inotropic or vasopressor support in cardiomyopathy. However the equipment cost and need for advanced training by specialty providers lead to its limited application in pheochromocytoma intraoperative management to determine intravascular volume status except the cases of intracardiac pheochromocytoma, severe catecholamine-induced cardiomyopathy or cardiovascular shock.

Intraoperative management

Surgery is increasingly laparoscopic, reducing postoperative recovery times, but not haemodynamic instability. Open surgery is likely to be required for large or invasive adrenal masses and most paragangliomas.

A general anaesthetic is inevitably required for phaeochromocytoma resection using a wide variety of medications as part of a balanced anaesthetic (11).

The ideal anaesthetic technique should avoid catecholamine release induced by drugs, by anaesthetic

or surgical manoeuvres, should decrease haemodynamic responses to tumour handling and manage hypotension after tumour devascularization (14).

The risk factors for intraoperative haemodynamic instability are high plasma norepinephrine levels, large tumour size, frequent postural drop after starting of α-blockade, and a pre-anaesthetic mean arterial pressure (MAP) higher than 100 mm Hg(15).

Many frequently used drugs may increase catecholamine levels by stimulating their pre-synaptic release, inhibiting their reuptake or via increased catecholamine levels accompanying histamine release. For this reason it is best to avoid the following agents: desflurane, ketamine, morphine, pethidine, atracurium, ephedrine, droperidol, metoclopramide, and cocaine. Large boluses of morphine should be avoided due to histamine release that causes substantial catecholamine release and potential hypertensive crisis. In the past, histamine stimulation was used for the diagnosis of pheochromocytoma before modern biochemical assays were introduced.

Succinylcholine stimulates sympathetic ganglia and produces muscular fasciculation, that can increase intraabdominal pressure and thus may cause catecholamine release from pheochromocytoma. Yet succinylcholine has been used safely until now. Avoiding catecholamine release induced by anaesthetic or surgical manoeuvres

It is important to understand that patients with pheochromocytoma have multiple sources of catecholamine excess such as adrenal tumour stores or sympathetic neurons stores caused by the reuptake response to high circulating catecholamines levels. Consequently patients should be treated with adequate analgesia when awake and maintained at an enough deep level of anaesthesia during all anaesthetic and surgical manoeuvres (tracheal intubation, incision raised intra-abdominal pressure associated with pneumoperitoneum or coughing and surgical tumour handling) (16). Lower insufflations pressures have been associated with diminished hypertensive episodes during laparoscopic resection and mini-invasive approach is considered an important progress in pheochromocytoma surgery.

Propofol, thiopental, and etomidate have been used for induction of anaesthesia and all inhalational agents have been used during maintenance of anaesthesia for pheochromocytoma surgery (17). Nitrous oxide is not contraindicated and has been used in routine pheochromocytoma resection. Sevoflurane and isoflurane are commonly used in modern anaesthesia while desflurane is avoided due to its ability to cause significant sympathetic stimulation.

Fentanyl, sufentanyl and hydromorphone are commonly used for pain in pheochromocytoma surgery but remifentanil has the advantages of high potency, rapid titratability and very short half life, thus being very effective in blunting haemodynamic responses to intubation or pain.

Yet, several studies have detailed the use of remifentanil to control blood pressure during resection, but frequently very high doses have been reported without consistent effect (18). Due to remifentanil's very short half-life, adequate postoperative multimodal analgesia is required.

Magnesium sulphate is a potent alpha-adrenoreceptor antagonist, which inhibits adrenal catecholamine release and reduces α-adrenergic receptor sensitivity to catecholamines with main effect of arteriolar vasodilation and antiarrhythmic *via* antagonism of L-type calcium channels. It also reduces left ventricular afterload while maintaining preload.

A dose of 40–60 mg/kg of magnesium sulphate can be used prior induction of anaesthesia followed by an infusion of 1–2 g/h, providing good control of systolic arterial pressure before tumour handling (19).

Dexmedetomidine is a centrally acting selective α2-receptor agonist with sedative and analgesic properties. It has a slow onset and usually we need to use a loading dose of 1 μg/kg (over 10 min) followed by continuous infusion of 0.5 μg/kg h as an adjuvant to volatile or propofol intravenous anaesthesia. Dexmedetomidine has associated to its sedative and analgesic effects, the central sympatholytic effects resulting in decreasing of plasma norepinephrine levels, thus making it a very attractive agent for phaeochromocytoma surgery. However, only a few case reports describe dexmedetomidine use in this setting and all reported the use of additional vasodilators, especially during tumour handling (18).

Treatment of pre-excision hypotension

There are described short episodes of hypotension during the course of a pheochromocytoma resection before adrenal vein clamping. The treatment of hypertensive spikes may outlast the brief surgical stimulus such as tumour handling and catecholamine effect that is shorter and results in severe hypotension. The treatment in these instances is adequate volume repletion associated with small doses of direct-acting alpha-agonist (e.g. phenylephrine 50-100 mcg) but drugs with indirect or direct alpha and beta-agonist effect

(ephedrine or epinephrine) should be avoided (20).

Intraoperative Hypertension

Minimizing haemodynamic responses to tumour handling

During manipulation of the tumour there are released high amounts of catecholamines resulting in severe hypertension, bradycardia (with norepinephrine), and tachyarrhythmias (with epinephrine). This is one reason for the recommendation of early surgical ligation of the adrenal vein in order to attenuate intraoperative haemodynamic instability, but high increases in catecholamine levels may still occur, particularly in large tumours. However a recent randomized control trial found no difference in plasma catecholamine levels or episodes of haemodynamic instability between the early or late adrenal vein ligation groups (9).

Spikes in blood pressure are very common during pheochromocytoma resection even in well-prepared patients (21) because of tumour handling that can determine short but very high levels of circulating catecholamines. All the preventive measures were described above and include preoperative pharmacologic preparation, deep-plane anaesthesia and effective sympatholysis, short-acting opioid administration (fentanyl or remifentanil), dexmedetomidine, magnesium sulphate, but they cannot prevent entirely the spikes during tumour manipulation.

The best treatment of the hypertensive spikes should match with their expected duration. There are not randomized studies for the best treatment and many protocols or drugs have been used. The principles of treatment are the management of hypertensive crises with short acting vasodilator drugs, management of tachyarrhythmias with β-blockers, both minimizing the excessive inotropic effect of the epinephrine-secreting tumours.

Phentolamine is a reversible, non-selective α-receptor antagonist with short duration of action of vasodilation followed by reflex tachycardia. It can be administered as a bolus of 1–2 mg to control the blood pressure while establishing desired infusion rates of other drugs.

Sodium nitroprusside and glyceryl trinitrate (GTN) are both nitric oxide donors, which cause venular and arteriolar vasodilation with rapid onset and offset of action. Sodium nitroprusside mainly determines arteriolar dilation while GTN is a venodilator. Sodium nitroprusside leads to a more rapid reduction in arterial pressure and is preferred as the first-line vasodilator for phaeochromocytoma surgery, whilst GTN is preferred in patients with ischaemic heart disease because it increases coronary blood flow by dilating collateral vessels and inhibiting coronary vasospasm; on the other hand, sodium nitroprusside may reduce coronary perfusion through its greater effect on diastolic arterial pressure and potential to induce intracoronary steal. Sodium nitroprusside infusions can be started at 0.5–1.5 μg/kg min and increased up to 4 μg/kg min as required with very low risk of cyanide toxicity for intraoperative infusions of less than 12 h in patients with normal renal and hepatic function (22). GTN infusions are within the range of 10–200 μg/min. Some protocols recommend to administer a basic infusion of nitroprusside or NTG if baseline blood pressure allows.

Nicardipine is a calcium channel antagonist, with a potent action of arterial vasodilation and can be administered intraoperatively by infusion with a rate of 3–5 mg/h for 15 min and increased with 0.5 or 1 mg/h every 15 min if required.

When the target pressure is achieved, the infusion should be reduced to 2–4 mg/h. Also hypertensive crises can be treated with boluses of 1–2 mg. Nicardipine does not provoke reflex tachycardia seen when administering sodium nitroprusside or GTN and maintains cardiac output being the preferred drug for some authors. Nicardipine limitation is a half-life of 40–60 min with possible persistent hypotension.

Clevidipine is a novel alternative of calcium channel antagonist with a shorter half-life due to plasma and tissue esterase hydrolysis and has also been successfully used in phaeochromocytoma surgery with less disadvantage of hypotension (19).

Esmolol is a selective β1 antagonist with a rapid onset and short duration of action ideal in these cases. The loading dose is 500 μg/kg over 1 min, followed by a 4 min maintenance infusion of 50 μg/kg min, titrated to clinical effect.

Postresection Hypotension

Periods of hypotension during surgery are relatively frequent and may be caused by anaesthetic drugs especially if circulating volume is depleted or from the excessive treatment of the hypertensive spikes that are longer than catecholamines release. But the essential moment that marks the commencement of the hypotension is represented by adrenal vein ligation and removal of the catecholamines source from the circulation. Hypotension after ligation can be extremely severe and catecholamine-resistant.

Underlying mechanisms for postresection hypotension are: intravascular hypovolemia, residual

α-blockade particularly after the preoperative use of phenoxybenzamine, sudden catecholamine deficiency after tumour resection in combination with catecholamine receptor down-regulation caused by chronic elevation of catecholamine levels (23).

A good communication between the surgical and anaesthetic team is essential because after the ligation of adrenal vein the drug infusions that decrease the blood pressure should be immediately stopped. Also treatment of post-ligation hypotension should commence before adrenal vein ligation with fluid resuscitation (crystalloids), titration of vasodilators, and administration of vasopressors such as direct α-receptor agonists.

A pure alpha-agonist, such as phenylephrine is commonly used but norepinephrine or epinephrine may be required and should be administered centrally. Norepinephrine can initially be started to increase peripheral vascular resistance but vasopressin should be considered in refractory hypotension patients.

Vasopressin causes systemic vasoconstriction and pulmonary vasodilation with action on V1 receptors, but also increases depleted circulatory volume with action on V2 receptors in the distal convoluting tubule and collecting ducts of the kidney, thereby increasing water reabsorption (19).Vasopressin is useful in refractory hypotension because its effects are mediated through non-catecholamine receptors in cases of adrenal receptor down-regulation determined by chronic exposure to catecholamines. Another theory is that during hypotension after adrenal vein ligation, there is an inhibition of endogenous vasopressin release from the storage site in the posterior pituitary gland, because the chronic exposure to catecholamines may down-regulate hypothalamic vasopressin synthesis too. Literature comprises several case reports of the successful use of vasopressin after phaeochromocytoma resection (24) started with bolus dose administration of 0.4–20 units followed by an infusion of 1–3 mU/kg min that could be frequently weaned over the following 2-12 hours.

Postoperative Management

Most patients can be extubated at the end of surgery if the surgery is noncomplicated. All pheochromocytoma patients need intensive monitoring postoperative, for at least 24 h, usually in the intensive care unit. Patients who exhibit persistent hemodynamic instability may need postoperative ventilation (20, 21).

Postoperative issues are minimal in most of the patients who undergo laparoscopic surgery. Refractory or persistent hypotension may indicate hypovolemia due to bleeding or inadequate fluid resuscitation, or residual vasodilation. Persistent hypertension postoperatively leads to differential diagnosis between fluid overload, accidental ligation of the renal artery, or presence of residual tumour.

Hyperglycaemia as a result of catecholamine excess is managed with insulin infusion therapy ,but postoperative hypoglycaemia and hyponatremia are frequently encountered requiring appropriate blood glucose and electrolyte monitoring (10).

Rapid steroid replacement in the hypotensive patient after bilateral adrenalectomies should be considered followed by lifelong steroid replacement, otherwise steroid supplementation is rarely required for a short period of time.

In conclusion, patients with pheochromocytoma are at significant risk for major adverse cardiac complications in the perioperative period. Successful management requires careful preoperative optimization, mini-invasive surgical approach (laparoscopic or robotic), thoroughly intraoperative management with hemodynamic monitoring and treatment. Postoperatively all patients need careful monitoring in an intensive care unit for at least 24 hours due to the high-risk of complications as described above.

Conflict of interest

The authors declare that they have no conflict of interest.

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