

Preoperative Management of Pheochromocytoma/Paraganglioma

The main objective is to reduce the risk of hypertension, hypotension, arrhythmia, myocardial infarction and stroke during anaesthesia and particularly at the time of tumour manipulation.

Alpha blockade

Phenoxybenzamine is a non-competitive, non-selective alpha-adrenoceptor antagonist with a relatively long duration of action. Inhibition of alpha-adrenergic receptors by phenoxybenzamine is therefore maintained even in the event of additional catecholamine release during surgery, making phenoxybenzamine the preferred choice in many centres. However, irreversible binding may predispose to an increased risk of post-operative hypotension.

Doxazosin is a competitive, selective alpha-1 adrenoceptor blocker with a relatively short duration of action. Due to its competitive nature, the alpha blockade can potentially be overcome by extra catecholamine release intraoperatively, predisposing to a hypertensive crisis. However, current evidence suggests that doxazosin is less likely to cause post-operative hypotension compared with phenoxybenzamine.

At present, there is no conclusive evidence to favour the use of non-selective α -receptor blockers (e.g. phenoxybenzamine) over selective α -1 adrenergic receptor blockers (e.g. doxazosin), although many clinicians continue to advocate the former.

Beta blockade

Beta-blockers must **NOT** be started before alpha blockade has been established because of the risk of inducing a hypertensive crisis due to unopposed α -adrenergic receptor-mediated vasoconstriction. Preoperative use of β -blockers is generally reserved for prevention and treatment of cardiac arrhythmias and reflex tachycardia.

Preoperative Management

Patients require pre-operative therapy to 'normalise' blood pressure (BP) and restore volume status prior to elective surgery.

Clinical practice varies widely, but a commonly recommended approach is to treat for at least 10-14 days, although some patients (e.g. those with cardiac disease) may require a longer optimisation period. All patients should be discussed with an experienced anaesthetist and surgeon. It may be necessary to admit to hospital for several days prior to surgery to ensure satisfactory adrenoceptor blockade and restoration of euvolaemia.

In addition, all patients should have an ECG and an echocardiogram to screen for the presence of cardiomyopathy.

Start **phenoxybenzamine** with a 10 mg test dose and monitor for postural hypotension. Increase phenoxybenzamine by 10-20 mg per day every 4-7 days according to BP response and tolerance. Most patients can be maintained on 20-40 mg per day (in divided doses) until admitted for surgery, when the dose can be titrated up to a maximum of 1.0-1.5 mg/kg per day on the day before surgery. For **Doxazosin**, the starting dose is typically 1mg once a day and titrated usually by 1mg steps. In some centres, a slow-release preparation is preferred.

Warn patients about postural dizziness, nasal stuffiness, fatigue and retrograde ejaculation in men

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Target BP: seated systolic BP <130 mmHg and standing systolic BP >90 mmHg.

Target pulse rate: 60-80 bpm.

Volume expansion: on the second day of alpha-adrenergic blockade, start a high sodium intake (>5g daily) to correct catecholamine-induced blood volume contraction and prevent hypotension. UK average sodium intake is 3.2g per day, and therefore an additional 2g of sodium is typically required. Some patients may require intravenous 0.9% sodium chloride to correct hypovolaemia, such as those with significant postural hypotension. Caution should be exercised in patients with cardiac or renal impairment.

Calcium channel blockers (e.g. amlodipine 5-10 mg od) may be added if BP remains uncontrolled.

Start **propranolol** 10-20 mg tds in patients with adrenaline-secreting tumours or when pulse rate > 80 bpm despite correction of hypovolaemia. This can be titrated up to 40 mg tds. An alternative is to use atenolol (25-50 mg per day). In patients with significant cardiac dysfunction, consider admission for supervised administration of first dose.

Intravenous 0.9% sodium chloride (2-3 L over 24 hours) should be commenced on admission (typically 1-3 days pre-operatively) as the alpha blockade dose is titrated up. Again, caution should be exercised in patients with cardiac or renal failure.

The decision when to discontinue alpha blockers prior to surgery should be individualised depending on preoperative haemodynamic stability. In general, Phenoxybenzamine is discontinued 24 hours before surgery and **Doxazosin** the evening before or the morning of surgery.

Intravenous 0.9% sodium chloride should be continued in the early post-operative period, to mitigate the risk of hypotension due to residual effects of pre-operative alpha blockade.

Monitor BP, pulse rate and capillary blood glucose (to detect rebound hypoglycaemia) for 24 hours post-operatively.

Note: Dexamethasone administration is associated with a potential risk of catecholaminergic crisis and, when dexamethasone suppression testing is indicated, it should only be performed once adequate blockade has been established.

Authors: **Amir H Sam, Mark Gurnell**

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