# Intravenous Phenoxybenzamine for Acute Hypertension of Phaeochromocytoma
## A Case Report

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## ABSTRACT

**Objective:** To illustrate the use of IV phenoxybenzamine (not commercially available in Australia) in a patient presenting with acute phaeochromocytoma which was unsatisfactorily controlled with other agents, including IV phentolamine.

**Clinical features:** The patient was a 52-year-old female who presented for an elective total abdominal hysterectomy and bilateral salpingo-oophorectomy. During the operation her blood pressure rose precipitously and she had an episode of myocardial ischaemia. A presumptive diagnosis of phaeochromocytoma was made and subsequently proven. Postoperatively she was admitted to ICU on infusions of phentolamine and glyceryl trinitrate.

**Case progress and outcome:** By day 4 her phentolamine infusion had increased to 80 mg/h with frequent boluses required. When a phenoxybenzamine infusion was substituted for the phentolamine the blood pressure rapidly came under control and the patient could be transferred to the medical ward. She was discharged with her symptoms well controlled on oral medication to await surgical removal of the phaeochromocytoma.

**Conclusion:** IV phenoxybenzamine may successfully treat acutely ill patients with phaeochromocytoma unresponsive to other agents.


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## INTRODUCTION

Phaeochromocytoma is a rare tumour of chromaffin cells that secrete catecholamines, often in massive quantities. Unsuspected phaeochromocytoma can be unmasked when anaesthetising cases for surgical procedures,[1] or during surgery itself if the tumour is manipulated. These cases can lead to a life-threatening hypertensive crisis. Sodium nitroprusside and phentolamine are the agents most commonly used intra-operatively to control blood pressure when a phaeochromocytoma is suspected. Phenoxybenzamine is a longer acting α-adrenergic blocking agent than phentolamine and is used orally to control the symptoms of phaeochromocytoma before surgical removal of the tumour. An IV preparation of phenoxybenzamine was previously marketed in Australia by SmithKline Beecham but was discontinued in August 1993.

## CASE REPORT

A 52-year-old female was admitted for an elective total abdominal hysterectomy and bilateral salpingo-oophorectomy. Her anaesthetic record noted a past history of migraines and palpitations when stressed and pre-operatively her blood pressure was 160/104 mm Hg. During surgery her systolic blood pressure rose to 220 mm Hg. This hypertension did not respond to increased isoflurane, β-blockers and hydralazine, but there was 'some response' to phentolamine.

A phaeochromocytoma was suspected and this was later confirmed by plasma catecholamines, serial urinary excretion of metabolites and a CT scan showing a 6.5 cm mass in the right suprarenal region.

She was sent to ICU on infusions of both glyceryl trinitrate and phentolamine. The phentolamine was infused at 20-40 mg/h with 5 mg boluses when the systolic blood pressure rose above 155 mm Hg. Metoprolol was prescribed to counter the tachycardia induced by phentolamine and was given at a dose of 2 mg every four hours and 2 mg when the heart rate exceeded 140 bpm.

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On the first and second days after the operation her blood pressure was controlled at this phentolamine dose when the patient was left undisturbed but was extremely labile when the patient was touched. This responded quickly to 5 mg bolus doses of phentolamine. On day 2, oral phenoxybenzamine was started at a low dose.

By day 4 the hypertension was still not controlled well and the phentolamine infusion had been gradually increased to 80 mg/h. The patient had severe diarrhoea (a common side effect of α-adrenergic blocking agents) and it was felt she was not absorbing any oral medications. At this stage the patient was using 200 ampoules per day of phentolamine 10 mg/mL (i.e. 2 g/d) and we had exhausted supply of the drug from both local sources and from a large interstate wholesaler. It was a weekend and attempts to find other large scale suppliers were unsuccessful.

We became aware that IV phenoxybenzamine was being supplied to cardiac paediatric hospitals and determined that it was being manufactured by the Western Australian Hospitals Central Pharmaceutical Manufacturing Facility (at the Princess Margaret Hospital for Children in Perth). We subsequently borrowed some stock from The Prince Charles Hospital pharmacy and an infusion of phenoxybenzamine was substituted for the phentolamine late on day 4.

Phenoxybenzamine at a relatively low infusion rate of 4 to 8 mg/h controlled the systolic blood pressure to greater extent than phentolamine at 80 mg/h and the diarrhoea ceased, allowing oral medications to be absorbed.

By day 6 the patient was well controlled on oral phenoxybenzamine 30 mg three times a day, atenolol 50 mg once daily, lisinopril 5 mg once daily and a glyceryl trinitrate patch 5 mg once daily. The phenoxybenzamine infusion had been weaned down to zero and no further boluses of phentolamine had been required.

On day 7 the patient was transferred from ICU to the medical ward and the rest of her stay was unremarkable. She was discharged on oral medications with the plan to surgically remove the phaeochromocytoma after a period of stable management of the condition.

## DISCUSSION

Phentolamine is a quick acting α-adrenergic inhibitor and is routinely used for the intra-operative control of phaeochromocytoma. It would be expected that this drug would be effective for postoperative control when the tumour remained in situ. There are few effective parenteral alternatives available for the acutely sick patient for whom oral medications are inappropriate.

Phenoxybenzamine is a longer acting agent and in its oral form is commonly used for hypertensive episodes of phaechromocytoma. It is the agent of choice for initial control and for maintenance or preoperative therapy.[1] An IV preparation of phenoxybenzamine was formerly available in Australia (marketed by SmithKline Beecham under the brand name of Dibenyline Injection) but was not licensed for use in phaeochromocytoma.

A possible explanation for phenoxybenzamine's success in this instance is that it is an irreversible blocker of $\alpha_1$ and $\alpha_2$-adrenergic receptors. Thus restoration of receptor responsiveness to α-adrenergic agonists, including catecholamines, probably requires synthesis of new receptors. In contrast, phentolamine is a competive α-adrenergic antagonist and could be 'overcome' by the quantity of catecholamines available in phaeochromocytoma.[2] Hull stated that the non-competitive adrenergic blockade produced by phenoxybenzamine means that surges of catecholamine release cannot override the inhibition as may occur with a competitive blocker.[1]

It is important that pharmacists are aware that specialised, non-commercially available pharmaceuticals may be manufactured and supplied by Therapeutic Goods Administration licensed units such as the WA Hospitals Central Pharmaceutical Manufacturing Facility. These products, for which there is usually only a limited demand, may have a significant beneficial impact on patient outcome.

**References**

1. Hull CJ. Phaeochromocytoma: diagnosis, preoperative preparation and anaesthetic management. Br J Anaesth 1986; 58: 1453-68.
2. Hoffman BB, Lefkowitz RJ. Catecholamines, sympathomimetic drugs, and adrenergic receptor antagonists. In: Hardman JG, Limbird LE, editors. Goodman & Gilman's the pharmacological basis of therapeutics. 9th ed (international). New York: McGraw-Hill, 1996: 227-9.

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