Calcium channel blockade and uncontrolled blood pressure during phaeochromocytoma surgery

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Phaeochromocytoma has traditionally been managed by preoperative adrenergic blockade followed by surgical devascularization and excision. Recently, various studies have reported the use of calcium channel blocking drug therapy, either as monotherapy or in combination with other non-adrenergic blocking antihypertensive medications for blood pressure control in the preoperative management of phaeochromocytoma. In this case report, diltiazem as monotherapy was used to establish adequate preoperative blood pressure control in a patient with metastatic phaeochromocytoma to the liver. During cryoablation therapy surgery of the liver metastasis, the patient demonstrated extreme blood pressure lability requiring nitroprusside and high end tidal concentrations of isoflurane for blood pressure control. This case report suggests that during resection of a phaeochromocytoma where tumour devascularization is not obtainable, calcium channel blocking drugs as monotherapy may be inadequate to control blood pressure extremes. The authors suggest that under clinical circumstances reported above strong consideration be given to the use of standard adrenergic blocking drug therapy pre- and intraoperatively.

Traditionnellement la thérapie du phéochromocytome exigeait un bloc adrénergique suivi de la dévascularisation et de l'excision de la tumeur. Récemment, plusieurs études ont rapporté l'utilisation d'inhibiteurs calciques seuls ou associés à d'autres anti-hypertenseurs sans propriété adrénergique inhibitrice pour contrôler la tension artérielle avant la chirurgie. Cette observation décrit l'utilisation du diltiazem seul pour contrôler la tension artérielle préopératoire chez un porteur de phéochromocytome avec une métastase hépatique. Pendant la cryoablation de la métastase, la tension artérielle est devenue extrèmement labile ce qui a nécessité l'administration de nitroprussiate et de concentrations téléexpiratoires élevées d'isoflurane. Cette observation porte à croire que, lorsqu'il est impossible pendant la résection du phéochromocytome d'effectuer une dévascularisation tumorale, les inhibiteurs calciques seuls peuvent être insuffisants pour contrôler des tensions artérielles extrêmes. Les auteurs suggèrent dans ces circonstances de considérer sérieusement l'usage de bloqueurs adrénergiques avant et pendant l'intervention.

Key words
PHARMACOLOGY: diltiazem; nitroprusside;
SURGERY: phaeochromocytoma;
SYMPATHETIC NERVOUS SYSTEM: pharmacology, labetolol.

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Traditional treatment of phaeochromocytoma has included preoperative alpha blockade, surgical venous devascularization, followed by excision of the tumour.[1] Recent reports have shown calcium channel blocking drugs to be useful in the preoperative management of these catecholamine secreting tumours, in combination with other antihypertensive therapy (non-selective alpha antagonists,[2,3] selective alpha$_1$ antagonists[3,4]) or as single monotherapy.[5-10] We report a case of a metastatic phaeo chromocytoma treated preoperatively only with calcium-channel blockade (diltiazem) that demonstrated extreme fluctuations of intraoperative blood pressure.

Case report

This 70-yr-old white man five years before admission underwent an uneventful right nephrectomy for a phaeochromocytoma under inhalational general anaesthesia with preoperative alpha and beta adrenergic blockade. Intraoperative blood pressure was well controlled at that time.

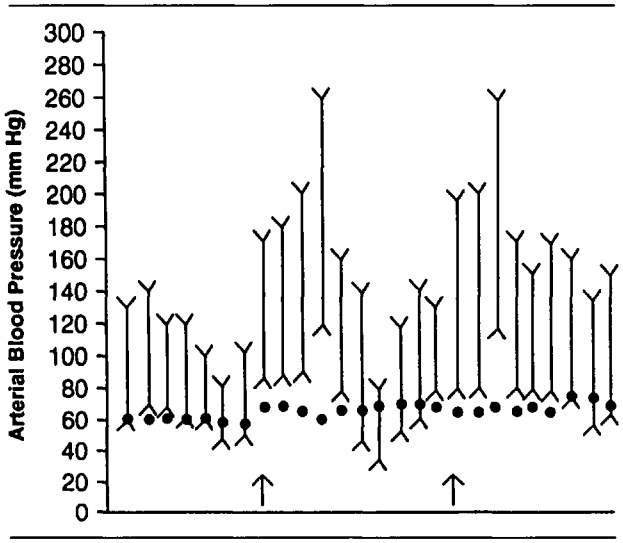

FIGURE Intraoperative blood pressure recordings during cryotherapy cycles (↑) during ablation of metastatic phaeochromocytoma of liver.

He presented at this time with an acute onset of left hemiparesis, and elevated blood pressure (200/110 mmHg by arm cuff), laboratory investigation demonstrated elevated values of serum catecholamines (plasma epinephrine 190 $pg \cdot ml^{-1}$ and norepinephrine 970 $pg \cdot ml^{-1}$, upper range of normal 110 and 750 $pg \cdot ml^{-1}$, respectively) and a single large metastatic lesion in the right lobe of the liver. Internal medicine consultation suggested treatment with oral diltiazem (240 $mg \cdot day^{-1}$) for ten days, this resulted in acceptable blood pressure control (140/90 mmHg by arm cuff). It was determined that this patient would be a poor candidate for liver resection because of the possibility of massive blood loss with a recent onset hemiparesis, so a cryosurgical ablation of his liver lesion was selected as the procedure of choice. On the day of surgery, lorazepam 4 mg *po* was given as preoperative sedation and, upon arrival in the operating room, a left radial arterial 20 ga catheter and a right internal jugular balloon-tipped flow-directed pulmonary artery catheter were placed, as well as standard monitors. Anaesthesia was induced with thiopentone 350 mg *iv*, fentanyl 25 $\mu g \cdot kg^{-1}$, vecuronium for facilitation of intubation and muscle relaxation, and isoflurane (1.0–1.5% inspired) in 50% N_2O in oxygen for maintenance was administered. At laparotomy, a 6 cm mass in the right lobe of the liver was found. A cryosurgical unit with a 12 mm cryoprobe was placed under ultrasound guidance and four cryosurgical cycles of five minutes each at −60°C were administered. During each cycle extreme lability of systemic arterial blood pressure was measured (Figure). Systemic blood pressures as high as 260/80 mmHg and pulmonary artery pressures up to 62/30 mmHg (baseline 140/60 mmHg and 30/18 mmHg, respectively) were recorded. In order to control these extreme fluctuations, sodium nitroprusside infusions (up to 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and isoflurane (up to 3% end expiratory concentrations) were given. Following the fourth and final cryotherapy cycle, the patient's blood pressure stabilized at 160/60 mmHg after 15 mg labetolol *iv* and continuation of nitroprusside at 2 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The remainder of the intra- and postoperative course was uneventful.

Discussion

The preoperative management of phaeochromocytoma has traditionally been with alpha-adrenergic blockade.[1] Originally, non-selective α_1 and α_2 antagonism with phenoxybenzamine was utilized[11] but, due to undesirable tachycardia, the selective α_1 antagonist, prazosin 1 mg *po* t.i.d. for two weeks before surgery[4] has been recommended. The reduction in intravascular blood volume known to occur with inadequately treated hypertension[12] is corrected with adequate alpha blockade therapy.[1]

Secondly, it has been taught traditionally that early venous devascularization followed by total excision of the tumour is the definitive curative procedure.[1]

Calcium-channel antagonists have been shown to reduce norepinephrine release in both human studies[13,14] and *in vitro*.[15] Others have reported that nifedipine 30 to 60 $mg \cdot day^{-1}$ *po* up to ten days prior to surgery induced good blood pressure control without reducing plasma or urinary catecholamine concentrations.[5] Because of these reports, internal medicine consultation suggested calcium-channel antagonist therapy, without an alpha adrenergic antagonist, which resulted in good preoperative blood pressure control.

This case report suggests that preoperative calcium-channel antagonist therapy without alpha antagonism is inadequate protection from extreme intraoperative blood pressure fluctuation during cyrosurgical ablation of phaeochromocytoma. By not removing venous drainage of this metastatic phaeochromocytoma before manipulation and subsequent cryotherapy, it appears that calcium channel antagonist therapy was unable to control blood pressure increases in response to the catechol release. This case serves as a warning that established therapy should not be ignored in the management of similar cases, and strong consideration for preoperative alpha adrenergic antagonism therapy, especially when the tumour is not devascularized, should be given.

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