

Preoperative Calcium Channel Blockade In An Atypical Case Of Bilateral Pheochromocytoma.

R Sebastian, A Keebler

Citation

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Abstract

We report a 27 year old patient with bilateral pheochromocytoma in the setting of a family history of von Hippel Lindau disease. Calcium channel blocker was used towards preoperative medical management. The perioperative period was uneventful with no untoward cardiovascular complications.

INTRODUCTION

Pheochromocytomas are rare neuroendocrine tumors characterised by increased secretion of catecholamines. The clinical presentation of these tumors are highly variable but commonly present with headaches, sweating, palpitations, uncontrolled hypertension or sometimes is an incidental finding. They are associated with certain familial syndromes including MEN 2A and 2B, von Hippel Lindau disease and neurofibromatosis (von Recklinghausen disease). The treatment of choice is surgical excision. Appropriate preoperative preparation and better understanding of the pathophysiology has resulted in significant reduction in perioperative morbidity and mortality associated with the condition.

CASE REPORT

We report a 27 year old male with bilateral pheochromocytoma in the setting of a family history of von Hippel Lindau disease (VHL). Patient's sister was diagnosed with VHL when she developed cavernous sinus hemangioma. Patient subsequently underwent genetic testing and was diagnosed to have VHL. He had a screening MRI which was negative for masses or tumors and the blood and urine catecholamine levels were normal. He exercised regularly and did not have any symptoms. Eight months after the initial diagnosis and screening he presented to his primary care physician with sweating and mild headache and on examination was found to be mildly hypertensive. Urine and plasma catecholamine levels showed elevated levels of plasma norepinephrine-1552pg/ml, elevated 24 hour urine

norepinephrine-462mcg, elevated 24 hour urine metanephrine- 3381mcg and an elevated 24 hour VMA. A MRI of the abdomen with and without contrast revealed a 3.3cm left adrenal mass and a 2cm right adrenal mass.

Patient was started on phenoxybenzamine 10mg TID towards preoperative preparation for bilateral adrenalectomy. Two days later developed adverse response to phenoxybenzamine consisting of nasal congestion, severe orthostatic symptoms and constipation. His BP was 138/80mm Hg- sitting and 72/44mm Hg- standing with heart rates 89 and 110 beats/ min, respectively. Hence phenoxybenzamine was discontinued and Diltiazem 180mg started two weeks prior to the surgery.

Patient underwent laparoscopic left radical adrenalectomy and right laparoscopic subtotal adrenalectomy under general anesthesia. Standard monitoring and an arterial line was placed prior to induction. Induction of anesthesia was achieved with propofol 200mg, fentanyl 250mcg and rocuronium 50mg and anesthesia was maintained with isoflurane. The intraoperative course was notable for a transient hypertensive response on manipulation of the left adrenal gland, which responded appropriately to 2 boluses of 5mg phentolamine, nitroglycerine 80mcg, followed by a 10mg bolus of labetalol. Surgery was uneventful otherwise with an intraoperative blood loss of 200mls and patient was extubated at the end of surgery. The hemodynamic parameters in the postoperative period were stable requiring no pharmacological support. He continued to be stable and was discharged home on the third post operative day.

DISCUSSION

Pheochromocytomas are rare neuroendocrine tumors with a highly variable clinical presentation but most commonly present with episodes of headaches, sweating, palpitations and hypertension [1]. The tumor arises from the chromaffin cells of the adrenal medulla or extra-adrenal paraganglia and they secrete catecholamines [2]. Both epinephrine and norepinephrine are secreted and the clinical presentations could be variable depending upon the predominance of the type of the catecholamine secreted. The catecholamine specific effects on the adrenoceptors explain the wide range of clinical presentation of patients and serve as the basis for appropriate preoperative adrenergic blockade. However the dose required is often a lot less compared to the circulating amount of catecholamines and this might be due to the 'desensitization' of the receptors and depends on the duration of exposure of the receptors to effects of catecholamines [1]. Preoperative management of patients with pheochromocytoma is paramount in the preparation of the patient for surgery to prevent life threatening catecholamine storm during surgery and minimize the associated cardiovascular morbidity and mortality.

Phenoxybenzamine is the most commonly used drug for preoperative blockade. It causes non-competitive alpha-adrenergic blockade which allows the expansion of intravascular volume and reduces the incidence of adverse intraoperative cardiovascular events particularly during induction of anesthesia and tumor manipulation. It is usually started at a small dose, increased incrementally up to a total daily dose of 1mg/kg. The duration of therapy is typically 7-14 days prior to surgery. Common side effects with phenoxybenzamine included orthostatic hypotension, tachycardia, nasal congestion and syncope. The long duration of action often causes significant hypotension in the post-operative period requiring pressor support.

Calcium channel blockers have been successfully used on its own preoperatively for pheochromocytoma. They block the norepinephrine mediated influx of calcium into vascular smooth muscles and thereby control tachyarrhythmia and hypertension. They are particularly used to supplement adrenoceptor blockers in patients with inadequate blood pressure control or to replace adrenoceptor blockers in patients with side effects or to prevent adrenoceptor induced sustained hypotension in patients with intermittent

hypertension [1]. They do not produce overshoot or orthostatic hypotension and can be safely used in patients who are normotensive with occasional episodes of paroxysmal hypertension. They can also prevent other cardiovascular complications such as coronary artery spasm or myocarditis [3]. The use of beta blockers is reserved for treatment of tachyarrhythmias induced by catecholamines or alpha-blockers and should never be used in the absence of alpha adrenergic blockade due to its ability to cause epinephrine induced vasoconstriction by blocking its vasodilator component.

Recent advances in anesthetic and monitoring techniques, along with newer, faster acting vasoactive agents, such as sodium nitroprusside, nitroglycerin and phentolamine, have improved the management of sudden changes in intraoperative hemodynamics. In the absence of preoperative hypertension, not using any drugs preoperative has been successfully instituted. In the study by Ulchaker et al [3] there was no significant difference in the cardiovascular events or the mean intra-operative blood pressure readings between the treated and untreated patients. In fact, patients receiving no treatment required significantly less fluids compared to the group that were treated with alpha blockers. The study also showed that calcium channel blockers are just as effective and safer when used as the primary mode of antihypertensive therapy.

Panel of experts at the International Symposium on Pheochromocytoma has recommended that all patients with a biochemically positive pheochromocytoma or paraganglioma should receive appropriate preoperative medical management to block the effects of released catecholamines. The high variability in the clinical presentation of pheochromocytoma makes it unlikely that any single medical management or treatment strategy will be optimal for every patient. Because of this and in light of varying practices and international differences in available or approved therapies, and without evidence-based studies comparing different therapies, there was no specific recommendation about preferred drugs for preoperative blockade. Nevertheless, it was recommended that preoperative administration of antihypertensive drugs was a prudent consideration for all patients with catecholamine-producing pheochromocytomas and paragangliomas.

References

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Author Information

Roby Sebastian, MD. FRCA

Anesthesiology Resident, Cleveland Clinic Foundation

Allen Keebler, DO

Anesthesiology Staff, Cleveland Clinic Foundation