

# CASE REPORT

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## ANESTHETIC MANAGEMENT OF A PATIENT WITH IMPLANTED PERMANENT PACEMAKER FOR EXCISION OF PHEOCHROMOCYTOMA

Gunjan Badwaik<sup>1</sup>, Charuta Gadkari<sup>2</sup>, Anjali Bhure<sup>3</sup>, Nitin Chopde<sup>4</sup>

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**INTRODUCTION:** Pheochromocytoma is a potentially lethal catecholamine secreting tumor of chromaffin tissues of the adrenal medulla and sympathetic chain.<sup>[1]</sup> Incidence across the globe is around 1 to 2 per million population.<sup>[2]</sup> Reported incidence in the United States is 1.55 to 2.1 per million populations per year.<sup>[3]</sup> This tumour is also rare in Indian population n but its actual incidence is not yet reported. The perioperative management of pheochromocytoma remains a complicated anaesthesia challenge requiring intensive preoperative preparation and vigilant intraoperative and postoperative care.

The provision of implantable pacemakers and implantable cardioverter defibrillators (ICDs) to treat abnormal heart rhythms is increasing and as a consequence more patients with these devices are likely to present for elective or emergency surgery. Currently more than 5,00,000 patients in the United States have pacemakers and nearly 1,15,000 new devices are implanted each year.<sup>[4]</sup> Although, no definite figures are available the number is also increasing in India. Both the above conditions individually present great problems in perioperative period.

We are presenting a case of anaesthetic management of a patient of both these co morbidities i.e. pheochromocytoma in a patient of implanted permanent pacemaker.

**CASE REPORT:** 77 years old male was taking treatment from a primary care centre for generalized weakness, easy fatigability, anemia and abdominal pain. As a routine battery of investigation, he was advised to undergo ultrasound examination on his third visit to that hospital. On ultrasound examination, he was diagnosed to have left sided adrenal mass which was later on confirmed by CT scan. He gave history of hypertension since last seven yrs. He was taking tab Nicardepin 10 mg daily. His history and previous documentations confirmed that he had permanent pacemaker implanted 3yr back for complaints of repeated syncope. Indication of permanent pacemaker implantation was complete RBBB, LAHB, high grade 2:1 block with intermittent complete heart block as revealed by old documents.

On preoperative visit, his blood pressure was 140/84 mmHg and other vitals and all route in biochemical investigations were within normal limit. ECG showed paced beats whereas ECHO was normal with ejection fraction of 58%. He denied any history suggestive of pheochromocytoma but urinary VMA was 26 ng/24 Hr (normal range 0-13.6) Sr Cortisol was 9.08 mcg/dl (normal range 4.3-22.4) and urinary Cortisol was 227.8 mcg/24 Hr (normal range 28.5-213.7). So diagnosis of pheochromocytoma was made. He was started on Tab. Phenoxybenzamine 5 mg TDS for 3 days and increased to 10 mg BD on fourth day. On fourth day

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he developed orthostatic hypotension and giddiness so Phenoxybenzamine was stopped and Surgery was planned after 2 days considering sufficient  $\alpha$  blockade. Meanwhile pacemaker evaluation was done by the manufacturer (Medtronic) which revealed that it's a bipolar VDD mode pacemaker with a lower sensing rate of 50 bpm and upper sensing rate of 120bpm and has an expected battery life of 2.5 to 3 years.

On Prior night of surgery, informed high risk consent was obtained and tab. alprazolam was given for anxiolysis. Provision of temporary pacing and cardio active drugs were kept ready. On the day of surgery, NBM status was confirmed and ECG, pulse rate, SPO<sub>2</sub>, NIBP and temperature monitoring started. Thoracic epidural inserted at T9-T10 level. Test dose with 3 ml of plain lignocaine 1.5% (without Adrenaline) given and found to be negative. Pt sedated with inj midazolam and Inj fentanyl. Rt internal jugular vein and Lt radial artery were cannulated under local anaesthesia. General anaesthesia induced with inj Propofol, inj. Vecuronium and inj Fentanyl. Pt was intubated by doing gentle and quick laryngoscopy following lignocaine spray. Maintenance of anaesthesia done with Isoflurane, Fentanyl and epidural infusion of 0.25% Bupivacaine. Use of cautery was limited and wherever required, only Harmonic cautery was used. Intraoperative hypertensive surge (max. BP=194/120mmHg) responded well to Nitroglycerin infusion for a short period whereas tachycardia (max 114 bpm) responded well to 0.5mg of inj. propranolol. Profound hypotension after tumor resection (min.64/44 mmHg) responded to fast infusion of crystalloids and inj. Mephenteramine 3mg. Perioperative blood sugar levels were within normal limits. Extubation was uneventful.

Pt was kept in SICU for 3 days of monitoring. No vasoactive drug support was required. Epidural analgesia was continued for 5 days. Pacemaker functioned well. Histopathology report proved it to be pheochromocytoma grade II. Pt was discharged on day 10. He was advised pacemaker assessment postoperatively.

**DISCUSSION:** With advancement in the field of cardiology and availability of good and affordable health care centres in developing countries like India, we are bound to get increasing number of patients with implanted pacemakers and ICDs (Implanted Cardioverter and Defibrillator). Pacemakers are being used with greater frequency for both conduction and arrhythmia problems in such patients.<sup>[5,6]</sup> These patients may require one or more surgical procedures after receiving the pacemaker.<sup>[7]</sup> Though the protocol for anaesthetic management of these patients is well established, the problem arise when these patients come for high risk surgeries with anticipated haemo dynamic instability. Our patient with pacemaker was diagnosed to have pheochromocytoma, a condition in which we obviously anticipated huge haemo dynamic surges in intra op and post-operative period to be managed pharmacologically keeping pacemaker in mind.

Pre anaesthetic checkup of patient with pacemaker includes evaluation of the patient and the pacemaker. It should include not only detailed evaluation of the underlying cardiovascular disease responsible for the insertion of pacemaker, but also other associated medical problems. Since substantial number of these patients suffers from coronary artery disease (50%), hypertension (20%) and diabetes (10%),<sup>[8]</sup> one should know the severity of the cardiac disease, the current functional status, effort tolerance and medications of the patient. The patient should

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also be questioned about the initial indication for the pacemaker and pre implantation symptoms such as lightheadedness, dizziness or fainting. If these symptoms are still present, cardiology consultation should be obtained.<sup>[9]</sup>

MHRA (Medicine and Healthcare product Regulatory Agency) London in March 2006 gave guidelines for the perioperative management of patients with implantable pacemakers or implantable cardioverter defibrillators, where the use of surgical diathermy/electrocautery is anticipated.<sup>[10]</sup> On preoperative visit, following information is to be obtained about pacemaker:

- Device manufacturer, model.
- Implanting hospital, follow-up hospital.
- Date of implant.
- Reason for implant (e.g. heart block etc.)
- Battery life.
- Lead position.
- Is device approaching replacement phase.
- Programme an ICD prior to surgery to a 'monitor only' mode to prevent inappropriate therapy/shock delivery.

Ten percent decrease in the rate from the time of implantation indicates power source depletion.<sup>[10]</sup>

In our patient, we assessed the pacemaker from the manufacturing company and assured that the pacemaker has a good battery life. The indication of pacemaker implantation in our patient was intermittent complete heart block which made us infer that our patient is definitely pacemaker dependent and we kept temporary pacing ready to tide over any untoward event.

**PACEMAKER AND EMI (ELECTROMAGNETIC INTERFERENCE):** When the surgical procedure is remote from the pacemaker/ICD and the device has been checked and verified within the last three months (especially battery condition), risk of malfunction will be minimal. However, where the procedure is close to the implant, risk of malfunction is increased.<sup>[10]</sup>

AHA guidelines advise that all antitachycardia therapy should be disabled before anaesthesia. If the risk of electromagnetic interference (EMI) is high, such as, when the electricity is in close proximity to the generator, alternative temporary cardiac pacing device should be available. The use of magnet may also be necessary.<sup>[5]</sup> Magnets can be used to protect the pacemaker dependent patient during EMI, such as diathermy or electrocautery. However, not all pacemakers switch to asynchronous mode on application of magnet. The response varies with the model and the manufacturer and may be in the form of no apparent change in rate or rhythm, brief asynchronous pacing, continuous or transient loss of pacing, or asynchronous pacing without rate response. It is advisable to consult the manufacturer to know the magnet response before use.<sup>[5]</sup> The new generation pacemakers are relatively immune to magnet application and may not convert pacemaker to asynchronous mode.<sup>[11]</sup> Thus, the use of magnet may be safe in nonprogrammable pacemaker, however, the most current devices should be considered programmable unless known otherwise.<sup>[9,12]</sup>

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In our patient, we have not used magnet and allowed paced beats in intraoperative period. We took adequate precautions to prevent EMI. Surgeons minimized the use of cautery and if required, only harmonic cautery was used which does not allow current to dissipate to surrounding tissues. Patients ECG was continuously monitored and facilities for temporary pacing and CPR were readily available. Asynchronous pacing and mode resetting are the most common outcomes of EMI and should be considered if pacing modes appear to change suddenly or intermittently on ECG monitors.<sup>[13]</sup>

## **Measures to decrease the possibility of adverse effects due to electrocautery:**

- Bipolar cautery should be used as much as possible as it has less EMI.
- If unipolar cautery is to be used during operation, the grounding plate should be placed close to the operative site and as far away as possible from the site of pacemaker and should have good skin contact.
- Electrocautery should not be used within 15 cm of pacemaker. Frequency of electrocautery should be limited to 1-second bursts in every 10 seconds to prevent repeated asystolic periods. Short bursts with long pauses of cautery are preferred.<sup>[9, 10, 14]</sup>
- Provision of alternative temporary pacing (transvenous, noninvasive transcutaneous) should be ready in the OT.<sup>[7]</sup>
- Drugs such as isoproterenol and atropine should be available.
- If defibrillation is required in a patient with pacemaker, paddles should be positioned as far away as possible from the pacemaker generator. If possible, anterior to posterior positioning of paddles should be used.
- Careful monitoring of pulse, pulse oximetry and arterial pressure is necessary during electrocautery, as ECG monitoring can also be affected by interference.
- The device should always be rechecked after operation.

Where it is not possible for the pacemaker/ICD to be checked before surgery, as in emergency situations, then device function should be checked as soon as feasible post-operatively. Ensure that cardio-pulmonary resuscitation, temporary external or transvenous pacing, and external defibrillation equipment are available.<sup>[10]</sup>

Intraoperative monitoring should be based on the patient's underlying disease and the type of surgery. Continuous ECG monitoring is however, essential to monitor pacemaker functioning. In addition, both electrical and mechanical evidence of the heart function should be monitored by manual palpation of the pulse, pulse oximetry, precordial stethoscope and arterial line, if indicated<sup>[11,15]</sup> Presence of pacemaker is not an indication for insertion of pulmonary artery (PA) or central venous catheter.<sup>[8]</sup> If these are indicated, care should be taken during insertion of the guide wire or central venous catheter as they are potentially arrhythmogenic. In our patient, we inserted both CVP catheter and Arterial line as we expected many haemodynamic fluctuations due to pheochromocytoma. Preop x-ray of chest revealed lead position from it subclavian vein to rt atrium. So accordingly we selected Rt internal jugular vein for CVP cannulation with gradual and gentle insertion of guide wire to avoid any displacement of electrodes.

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Inhalational anaesthetic agents do not alter current and voltage thresholds of the pacemaker.<sup>[16]</sup> Skeletal myopotentials, succinylcholine fasciculation, myoclonic movements, or direct muscle stimulation can inappropriately inhibit or trigger stimulation, depending on the programmed pacing modes.<sup>[17]</sup> Etomidate and ketamine should be avoided as these cause myoclonic movements.<sup>[18]</sup> Pacemaker function should be verified, before and after initiating mechanical ventilation, as there may be dislodgement of pacemaker leads by positive pressure ventilation,<sup>[19]</sup> or nitrous oxide entrapment in the pacemaker pocket.<sup>[20]</sup> The Task Force of ASA believes that anesthetic techniques do not influence pacemaker/ ICD function. However, anesthetic-induced physiologic changes (i.e., cardiac rate, rhythm, or ischemia) in the patient may induce unexpected responses or adversely affect the pacemaker/ICD-patient interaction. <sup>[21]</sup>

We avoided succinylcholine and used Vecuronium for intubation as fasciculations caused by succinylcholine would not only interfere with pacemaker function but also can also increase intra-abdominal pressure and increase release of catecholamines from pheochromocytoma. Pre-operative assessment of patients with pheochromocytoma is an essential part in management. The common problems arising from the over-production of epinephrine and nor epinephrine by pheochromocytoma are:

- Vasoconstriction, producing sustained or paroxysmal hypertension and the resulting cardiac failure, pulmonary oedema, renal failure, and cerebral haemorrhage.
- Vasodilatation, induced by  $\alpha$  blocker therapy in preoperative period and after resection of tumor post operatively, producing severe hypotension.
- Sensitization of the myocardium, producing severe and fatal arrhythmias.
- Stimulation of the production of epinephrine and norepinephrine by manipulation of the tumour, or by the pharmacological action of the anesthetic drugs.

Roizen et al recommended the following preoperative conditions prior to surgery for pheochromocytoma:

- Blood pressure < 160/90 mmHg for 24 hr before surgery,
- Postural hypotension > 80-45 mmHg,
- ECG should be free of any ST-T changes for a week and
- No PVCs more than 1 in five min 7.

In our case we strictly adhered to Roizen's criteria. Though the blood pressure was around 140-150 preoperatively, still we started on phenoxybenzamine to ensure  $\alpha$  blockade. Patient developed postural hypotension 4days after starting phenoxybenzamine which was an indirect indicator of sufficient  $\alpha$  blockade.<sup>[22]</sup> Newer generations of selective alpha-blocker have been used which carry several advantages compared to phenoxybenzamine: they do not produce reflex tachycardia, have shorter half-life, so dosage can be adjusted rapidly, such that preoperative and postoperative hypotension should be less.<sup>[23]</sup> Prazocin and terazocin may be considered although no specific guideline has been formulated to guide the choice of  $\alpha$  blocker. We gave a  $\alpha$  blocker free day between stopping phenoxybenzamine and surgery in order to avoid hypotension in post- operative period due to residual drug effect as phenoxybenzamine is a longer acting drug. We continued Nicardipine till morning of surgery. Preoperative beta-blockade is usually not necessary.

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Anxiolysis prior night of surgery is very important and we achieved it with 0.5 mg of tab Alprazolam. Patient was shifted to operating room on trolley with utmost care in handling so as to minimize catecholamine release from the tumor. After reassurance, Arterial line was inserted under local anaesthesia so that we can get beat to beat changes in BP during laryngoscopy and intubation. Similarly we inserted thoracic epidural catheter in T9-T10 space before induction of anaesthesia. We used Fentanyl and medazolam to sedate the patient. Thiopentone and Propofol are the commonly used drugs during induction of anesthesia. However, propofol is preferred as it produces vasodilatation and blunts to some extent the hypertensive response to laryngoscopy and intubation. Succinylcholine can be hazardous as it produces sympathetic activation and the raised pressure due to abdominal muscles contraction can be transmitted to the tumor mass that causes release of catecholamines. With pacemaker in our patient, succinylcholine was contraindicated due to reasons mentioned above. We preferred Vecuronium due to its cardiovascular stability and least histamine release. Tubocurarine, atracurium, and mivacurium releases histamine, while pancuronium is not preferred because of its indirect sympathetic stimulation profile. All these anesthetic agents may exhibit pharmacological merits in theoretical practice but their clinical efficacy and advantages have not been established by any clinically controlled study.

Based on 32 years of experience with this surgery, Prys-Roberts has suggested a practical rational anaesthesia technique consisting of a mid to low thoracic epidural combined with general anaesthesia and selective adrenergic antagonists to control haemodynamic surges in response to tumour manipulation.<sup>[24]</sup> Numerous anesthetic techniques have been used from time to time but among these the use of a combined epidural and general anesthesia is considered to be the most suitable and the preferred technique.<sup>[25,26,27]</sup> We also preferred thoracic epidural combined with general anaesthesia. The regional anesthetic technique though suppresses the stress response of surgical incision but cannot control the quantum of catecholamines released during the tumor handling, hence it has to be managed separately with hypotensive agents without realizing on high dose epidural for intra operative high BP surges. On the contrary, high dose epidural may add up to hypotension after resection of tumor.

Among the inhalational agents, Isoflurane and Sevoflurane are the preferable agents as they do not sensitize the myocardium to catecholamines as compared to halothane and enflurane which are potentially arrhythmogenic in the presence of catecholamines.

The drugs used for neuromuscular blockade reversal should be a combination of neostigmine and glycopyrrolate. Anti-muscarinic effects of glycopyrrolate coincide with the cholinergic effects of neostigmine and hence produce less tachycardia.<sup>[24]</sup>

Manipulation of the tumour causes a significant haemodynamic response and both systolic and diastolic blood pressures increase briskly. Sodium nitroprusside (SNP), phentolamine, prazosin, nitroglycerine and various other agents like magnesium sulphate, nicardipine, diltiazem, esmolol etc., have been used to control intraoperative rises in blood pressure.<sup>[24,28,29,30,31,32]</sup> Intraoperative use of beta adrenergic antagonists can help control tachycardia and tachyarrhythmias. Esmolol has haemodynamic effects that may be uniquely suited for the intraoperative management of pheochromocytoma.<sup>[33]</sup> Its rapid effect and short duration makes it easily titratable, both to control heart rate and blood pressure. It is difficult to comment on the

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best medication to be used for haemodynamic control during resection of pheochromocytoma as it is not possible to conduct properly designed randomized trials because of the rarity of the condition. It has been suggested for the anesthesiologists to rely on their familiarity of particular drugs or methods.<sup>[34]</sup> We used Nitroglycerin for hypertensive surge. Propranolol was used for tachycardia in a total dose of 0.5 mg only keeping pacemaker function in mind. After the adrenal veins are ligated, there is a sudden decrease in the circulating catecholamines which may lead to hypotension. At this point the vasodilators and blocker should be discontinued and a modest fluid bolus should be given. An eye must be kept on the blood loss and blood given if required. Infusion of a vasopressor such as norepinephrine or phenylephrine may be required temporarily.<sup>[28]</sup> Hypotension in our patient responded well to IV fluids and only 3mg of mephenteramine.

The three most important complications in the immediate postoperative period are hypertension, hypotension and hypoglycaemia.<sup>[35]</sup> After removal of the tumour, the pancreatic beta cell suppression is no longer present and insulin levels increase. The lipolysis and glycogenolysis is also absent due to removal of tumour and alpha blockade. This may lead to hypoglycaemia.<sup>[34]</sup> Therefore blood glucose levels should be monitored in the perioperative period and glucose containing intravenous fluids should be started after tumour removal.<sup>[29]</sup> Post-operative shivering can interfere with pacemaker function, measures to reduce shivering like warming blankets, warm IV fluids etc. should be instituted.

**CONCLUSION:** Two difficult to handle situations, pheochromocytoma and patient with pacemaker, demand us to apply our knowledge keeping in mind the altered physiology of the patient. Such situation demands that the guidelines to manage both situations to be clubbed together and then individualize according to patient.

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## **AUTHORS:**

1. Gunjan Badwaik
2. Charuta Gadkari
3. Anjali Bhure
4. Nitin Chopde

## **PARTICULARS OF CONTRIBUTORS:**

1. Assistant Professor, Department of Anaesthesia, NKP Salve Institute of Medical Science & Research Centre, Nagpur.
2. Associate Professor, Department of Anaesthesia, NKP Salve Institute of Medical Science & Research Centre, Nagpur.
3. Professor & HOD, Department of Anaesthesia, NKP Salve Institute of Medical Science & Research Centre, Nagpur.

4. Senior Resident, Department of Anaesthesia, NKP Salve Institute of Medical Science & Research Centre, Nagpur.

## **NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. Gunjan Badwaik,  
Plot No. 40,  
Shilpa Co. Op. Housing Soc-1,  
Behind UCO Bank, Narendra Nagar,  
Nagpur-440015.  
E-mail: painkiller\_gab@yahoo.co.in

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