

# Epidural Anesthesia Combined with Remifentanil-Propofol (TIVA) for

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## Abstract

We describe a patient with pheochromocytoma under the successfully combination of epidural anesthesia and TIVA based remifentanil-propofol for tumour removal surgery. After preparing the patient with the use of  $\alpha$  and  $\beta$  blockers effectively, this anesthetic combination was administered without any complications perioperatively. Excessive epidural anesthesia leading to extensive sympathetic blockade facilitated the effectiveness of remifentanilpropofol and also prevented the cardiovascular responses to surgical stimuli and tumor manipulations.

Implications: Although most techniques often combine with many different drugs to minimize acute blood pressure fluctuations and prevent dysrhythmias in pheochromocytoma surgery, the combination of remifentanil-based TIVA and extensive epidural anesthesia (EA) which is first used for pheochromocytoma resection may hamper the hypertensive and dysrhythmic attacks during surgery of pheochromocytoma.

## INTRODUCTION

Numerous anesthetic techniques and agents have been used for anesthetizing pheochromocytoma patients (1,2). However, a comparison based on literature reports is difficult, since most describe only isolated cases. Most techniques often combine with many different drugs to minimize acute blood pressure fluctuations and prevent dysrhythmias in pheochromocytoma surgery (3,4). The combination of remifentanil-based TIVA and extensive epidural anesthesia (EA) may hamper the hypertensive and dysrhythmic attacks during surgery of pheochromocytoma. This is the first report with the combination of EA and TIVA for pheochromocytoma resection.

## CASE REPORT

A 38-year-old female patient with a symptomatic, solitary pheochromocytoma in the left adrenal gland was prepared for 4 weeks with the use of  $\alpha$  and  $\beta$  blockade pre-operatively (phenoxybenzamine 40 mg BID and atenolol 100 mg daily). She had a history of hypertension and tachycardia with headache, sweating and palpitation. The diagnosis of pheochromocytoma in adrenal gland was made by computerised tomography and was confirmed with a 24-h urinary catecholamine measurement. Pre-operative

hematological and biochemical evaluations and liver function tests were normal. The blood pressure (BP) stabilized at 130/90 mmHg supine and standing, with a regular heart rate (HR) of 75 beats min<sup>-1</sup>. Electrocardiogram showed normal sinus rhythm, with non-specific T wave changes in V1-V4 leads. Hematocrit was 43% and blood sugar level normal.

The patient was intravenously premedicated with 3 mg of midazolam and 50  $\mu$ g of remifentanil in the holding area, and 1.5 L of isotonic crystalloid was infused before entry into the operating room. Her BP and HR were 150/100 (mean BP:110) mmHg, and 95 bpm, respectively. The epidural anesthesia was performed at the L1-2 interspace with 35 ml of bupivacaine 0.5% and epidural catheter was advanced in a cephalad direction 3 cm into the epidural space for postoperative analgesia. Twenty minutes later BP and HR were 130/70 (mean BP:95) mmHg, and HR 80 bpm, respectively. The sensory block level was T2 on both sides. The induction of anesthesia was performed with propofol 200 mg and remifentanil 100  $\mu$ g. Intubation was uneventfully facilitated with vecuronium 10 mg. Monitoring consisted of a radial artery cannula and a catheter in the right internal jugular vein for continual pressure monitorization and an hourly monitorization of blood sugar and urine

output.

Anesthesia was maintained by titrating propofol (125-250  $\mu\text{g kg}^{-1} \text{ min}^{-1}$ ) and remifentanil (0.25-3  $\mu\text{g kg}^{-1} \text{ min}^{-1}$ ) infusions. Mean BP was aimed to maintain between 60 and 100 mmHg by titrating of the sodium nitroprusside (0.5-10  $\mu\text{g kg}^{-1} \text{ min}^{-1}$ ) and noradrenaline (0.1-1  $\mu\text{g kg}^{-1} \text{ min}^{-1}$ ) infusions, if needed. Fluid transfusion was maintained throughout the surgery to keep central venous pressure between 5 and 10 mmHg. Neither hypertensive attack nor dysrhythmia was seen until removal of tumor and thus, the need for use of antihypertensive agents was not required. Ligation of the efferent vein of the tumour immediately resulted in a fall in BP which reached 60/40 (Mean BP 50) mmHg. This hypotension treated by volume loading of 1 L lactated Ringer's solution, decreasing the rate of propofol-remifentanil infusions gradually and starting noradrenaline infusion that required for 10 min. Thereafter, BP returned to normal without further treatment. The surgery lasted an hour and the patient was kept sedated, intubated and transferred to the intensive care unit (ICU) with a BP of 120/70 mmHg and a 85 beats  $\text{min}^{-1}$  and fentanyl (20  $\mu\text{g h}^{-1}$ ) infusion via epidural catheter for postoperative analgesia was administered. Two hours later, the sedation was discontinued, and the patient was extubated. Her pain was controlled by epidural patient-controlled analgesia in addition to basal infusion. Her postoperative course was uneventful and she was discharged to the ward on the 2nd and home on the 8th postoperative day. Histology confirmed the tumour as pheochromocytoma.

### **DISCUSSION**

Close monitoring and regulation of cardiovascular parameters is probably more important than actual anesthetic technique when removing active pheochromocytomas (3,4,7,10). The peri-operative mortality of the removal of tumors has been greatly reduced by careful preoperative  $\alpha$  and  $\beta$  blockade and with various strategies for the control of blood pressure intraoperatively.

In the anesthesia of the pheochromocytoma surgery, hypertensive crisis and attacks of dysrhythmia should be avoided until the removal of tumor. The use of suitable anesthetic technique to prevent hypertensive attacks is very important. High and extensive sympathetic blockade formed with epidural anaesthesia (EA) may enhance the efficacy of both  $\alpha$  blockers and  $\beta$  blockers, and also reduce to requirement of these drugs. We used the combination of extensive EA and TIVA with remifentanil-propofol in this

case without using any additional antihypertensive drug. Mean BP ranged from 60 to 100 mmHg was stable throughout the surgery including during manipulation of the tumour until the removal of tumour. In this case, excessive hypotension occurred after ligation of the efferent vein and excision of the tumour.

Hypotension as much as 40 mmHg of mean BP developed at the both situations was successfully treated by the use of incremental rate of norepinephrine infusion and decreasing rate of the propofol and remifentanil infusions, and also by aggressive fluid infusions.

Although the management of pheochromocytoma has been reviewed recently (4), there is little published information on the use of remifentanil in the anesthetic management of these patients. The rapid onset and short duration of action of remifentanil makes it easy to titrate to ensure adequate depth of anesthesia and to avoid significant increases in blood pressure and heart rate (5,6). It has also been shown to cause minimal histamine release, making it a suitable agent for use in patients with cardiovascular disease (7).

In addition to pre-operative  $\alpha$  blockade and intra-operative vasodilators, increasing anesthetic depth is an important measure in the prevention of hypertensive crises (3). Opioids in high dosage are known to blunt the sympathetic response to surgical stimuli. We used remifentanil with propofol underwent extensive epidural anesthesia during pheochromocytoma resection. Its even high infusion rate can be used intraoperatively without delaying the onset of spontaneous respiration (6). Remifentanil with the pharmacokinetics facilitated rapid alterations in anesthetic depth, suiting it to situations where catecholamine surges are anticipated (5,6).

The use of remifentanil has been recommended because of its ability to minimize the hypertensive response to tracheal intubation and surgical stimulation in various types surgery, especially in the removal of pheochromocytoma (8,9). The use of potent vasodilators was required previously cases although remifentanil was infused (10,11). In this case, however, we prevented the hypertensive responses to manipulating tumour by using the extensive EA in addition to remifentanil-propofol based TIVA.

The use of EA with TIVA has not been yet reported for pheochromocytoma surgery. The technique we reported in this case has the potential advantage over traditional methods of blood pressure control in that it might be thought

to inhibit the release of catecholamines from the pheochromocytoma as well as producing vasodilatation. The adrenal gland is innervated by sympathetic nerves from T5 to T12. Thus epidural sympathetic blockade across these levels would obtund the neurogenic stimulation of a possible adrenal tumour. An epidural also provides optimal analgesia, thus reducing catecholamine concentrations further. Moreover, when extended epidural sympathetic blockade combines remifentanil-propofol based TIVA the more sympathetic blockade is obtained. This combination may be effective for anesthetic management of pheochromocytoma surgery as in our case that we succeeded

With the exception of a drop in blood pressure immediately after tumour removal, significant intraoperative hemodynamic stability was observed. There was no need for the intraoperative administration of hypotensive or anti-arrhythmic drugs, nor was any prolonged postoperative anesthetic effect noted. In this case, the combination of propofol and remifentanil with EA was successful in maintaining cardiovascular stability until the tumour was removed. The consequent drop in blood pressure responded to fluid and noradrenaline infusions, a not uncommon event in pheochromocytoma surgery. Although a prospective randomized study for resection of pheochromocytoma showed that the choice of the anesthetic technique is not a crucial factor in determining the patient outcome, we feel this technique of propofol-remifentanil with EA is a worthy alternative to previously used techniques. The lack of significant myocardial depressive effect of the two drugs, coupled with its simple administration, makes it a useful technique in the anesthetic management of pheochromocytoma resection.

The combination of extensive EA and TIVA with propofol-remifentanil reported here, produced a simple and elegant solution to the thorny problem of anesthesia for pheochromocytoma. There are no previous reports on both the use of remifentanil-propofol anesthesia and combination of TIVA and EA for this surgery. However, we need more cases to decide the effectiveness and safety of the combination we used in this case without using hypotensive drugs for pheochromocytoma surgery.

In summary, this case highlights successful intraoperative hemodynamic management of a patient with pheochromocytoma using the combination of extensive EA and TIVA with remifentanil-propofol. This first report of combining epidural anesthesia with TIVA in pheochromocytoma surgery suggests that the combined technique of EA and TIVA is an efficacious approach.

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