

Remifentanil in the Management of Laparoscopic Resection of Pheochromocytoma – Case Reports[†]

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Abstract

Introduction: The laparoscopic adrenalectomy approach to pheochromocytoma surgery offers the opportunity to use new short-acting drugs to facilitate rapid recovery. **Clinical Picture:** We report on 2 cases who underwent laparoscopic resection of pheochromocytoma. The first was a 40-year-old lady who had been started on phenoxybenzamine 20 mg bd, but developed a recurrence of bronchial asthma after starting atenolol which was subsequently stopped. The second was a 51-year-old lady with neurofibromatosis who was taking phenoxybenzamine 20 mg bd and propranolol 20 mg tds. **Treatment:** The intraoperative management was facilitated by the stress suppressive effects of remifentanil infusion combined with nitroprusside as a vasodilator, and desflurane as an anaesthetic. **Outcome:** Both patients were extubated at the end of surgery and made uneventful recovery. **Conclusion:** Remifentanil possesses several useful properties, which deserve serious consideration in pheochromocytoma surgery, particularly in the instance where β -blockade is contraindicated. In combination with other titratable short-acting agents, it potentially facilitates rapid recovery especially following the laparoscopic approach to adrenalectomy.

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Introduction

The perioperative management of surgery for laparoscopic resection of pheochromocytoma presents a significant challenge.¹ Many different anaesthetic techniques and drugs have been used to control the haemodynamic fluctuations during pheochromocytoma resection.^{2,3} We report on our initial experience in the use of remifentanil, whose properties appear ideally suited to manage such cases. To our knowledge, this is the first case report in which remifentanil was used for this purpose.⁴

Case Reports

Patient 1

A 40-year-old Indian woman presented with a 3 months' history of accelerated hypertension and paroxysmal headaches. She had a past medical history of bronchial asthma from which she had been asymptomatic for the past

5 years. Biochemical 24-h urine analysis revealed vanillylmandelic acid (VMA) 120 $\mu\text{mol}\cdot\text{day}^{-1}$ (normal range, 0 to 34.3 $\mu\text{mol}\cdot\text{day}^{-1}$), epinephrine 178 $\text{nmol}\cdot\text{day}^{-1}$ (normal range, 0 to 109 $\text{nmol}\cdot\text{day}^{-1}$), norepinephrine 4480 $\text{nmol}\cdot\text{day}^{-1}$ (normal range, 89 to 473 $\text{nmol}\cdot\text{day}^{-1}$), metanephrine 2908 $\text{nmol}\cdot\text{day}^{-1}$ (normal range, 400 to 1600 $\text{nmol}\cdot\text{day}^{-1}$) and normetanephrine 47,899 $\text{nmol}\cdot\text{day}^{-1}$ (normal range, 600 to 1900 $\text{nmol}\cdot\text{day}^{-1}$). A computed tomography (CT) scan of the abdomen showed a 4.4 x 3.4 cm right adrenal tumour consistent with pheochromocytoma. She was started on phenoxybenzamine 10 mg OM increasing to 20 mg bd. Unfortunately, she developed dyspnoea and wheezes after starting atenolol 50 mg OM which was subsequently stopped. An echocardiogram showed no ventricular hypertrophy and normal ejection fraction.

On preoperative assessment, her heart rate was 90 beats per minute and blood pressure was 158/90 mm Hg without

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any postural drop. She was premedicated with lorazepam 1 mg and diazepam 7.5 mg, respectively, on the evening and morning before surgery. A total of 3L of intravenous crystalloids was administered in the 24 h prior to surgery. On arrival in the operating room, standard monitors were applied and a 20-g cannula inserted into the left radial artery under local analgesia. A remifentanyl infusion at $1 \mu\text{g kg}^{-1} \text{min}^{-1}$ was started and anaesthesia induced with propofol 120 mg, lignocaine 50 mg and maintained using desflurane in nitrous oxide and oxygen. Muscle relaxation was achieved with vecuronium 6 mg to facilitate tracheal intubation and artificial ventilation. A triple lumen catheter was sited in the right internal jugular vein for IV access and monitoring of central venous pressure.

Following induction and intubation, heart rate and blood pressure fell transiently (Fig. 1) requiring atropine 0.3 mg and a reduction in remifentanyl infusion rate for correction.

A combination of nitroprusside (0 to $10 \mu\text{g kg}^{-1} \text{min}^{-1}$) and remifentanyl infusions were used to control the blood pressure fluctuations resulting from tumour manipulation. 1.5L crystalloids and 1L colloid were administered during the 3½-hour procedure, with a resulting haematocrit of 31%. Epinephrine infusion $0.05 \mu\text{g kg}^{-1} \text{min}^{-1}$ was used to maintain blood pressure following adrenal vein ligation and was subsequently tailed off. Morphine 6 mg was administered 30 minutes before reversal of muscle relaxation, emergence and extubation. The patient was monitored in the surgical intensive care unit overnight using intravenous morphine for patient-controlled analgesia. She has since made an uneventful recovery.

Patient 2

A 51-year-old Chinese woman with neurofibromatosis was found to be hypertensive on perioperative assessment for myomectomy of uterine fibroids. She was asymptomatic apart from a history of occasional palpitations. Urinary epinephrine, norepinephrine, metanephrine and normetanephrine levels were $103 \text{ nmol.day}^{-1}$ (normal range, 0 to $109 \text{ nmol.day}^{-1}$), $252 \text{ nmol.day}^{-1}$ (normal range, 89 to $473 \text{ nmol.day}^{-1}$), $1988 \text{ nmol.day}^{-1}$ (normal range, 400 to $1600 \text{ nmol.day}^{-1}$) and $2300 \text{ nmol.day}^{-1}$ (normal range, 600 to $2000 \text{ nmol.day}^{-1}$). Magnetic resonance imaging (MRI) showed a $2 \times 1.8 \times 1.5 \text{ cm}$ tumour in the right adrenal gland. She was started on phenoxybenzamine 20 mg bd and propranolol 20 mg tds and scheduled for laparoscopic adrenalectomy.

On preoperative assessment, her blood pressure was 145/75 mm Hg and pulse rate 65 beats per minute. She was premedicated with oral midazolam 7.5 mg and given 3L crystalloids intravenously. A remifentanyl infusion at $0.5 \mu\text{g kg}^{-1} \text{min}^{-1}$ was started before anaesthesia was induced with propofol 120 mg, lignocaine 50 mg and the trachea

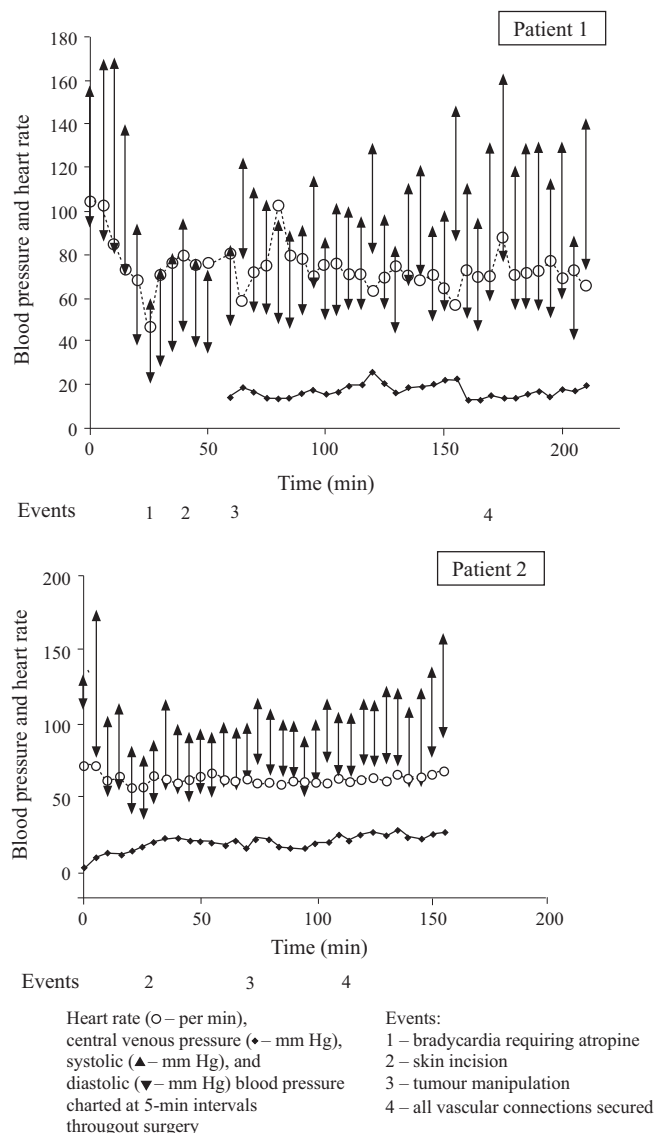


Fig. 1. Heart rate and blood pressure readings of patients 1 and 2 following induction and intubation.

intubated following muscle relaxation with vecuronium 6 mg. Anaesthesia was maintained using 70% nitrous oxide in oxygen supplemented by 3% to 4% desflurane. Remifentanyl (0.5 to $4 \mu\text{g kg}^{-1} \text{min}^{-1}$) combined with nitroprusside (0 to $3 \mu\text{g kg}^{-1} \text{min}^{-1}$) infusions were used to control haemodynamics during the procedure (Fig. 2). Two litres of crystalloids and 500 mL of colloids were administered. There were remarkably few untoward changes in heart rate and blood pressure during surgery. The trachea was extubated on the table following the administration of morphine 6 mg for postoperative analgesia. The patient was monitored on the intensive care unit overnight using patient-controlled analgesia with intravenous morphine.

Discussion

It is our usual practice to use β -blockers in combination

with vasodilators, such as nitroprusside, to control the effects of catecholamine release during tumour manipulation.

This was contraindicated by the history of bronchospasm in the first case hence leading to the use of remifentanyl. This agent has a number of properties, which make it eminently suitable for this purpose. In doses of up to 2 $\mu\text{g}\cdot\text{kg}^{-1}$, there are minimum alterations of systemic blood pressure and heart rate.⁵ Dose dependent reduction in blood pressure and heart rate have been reported^{6,7} with occasional marked bradycardia responsive to anticholinergics as happened in this instance.⁸ In patients undergoing cardiopulmonary bypass, remifentanyl based anaesthesia provided highly effective suppression of sympathetic haemodynamic responses to sternotomy.⁹ In a multicentre study, epinephrine and norepinephrine blood levels, from cardiac patients receiving an infusion of remifentanyl at 1 of 3 dose rates (1 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), were significantly lower than preanaesthesia levels at sternotomy.¹⁰ Hence, the role of remifentanyl in providing intense analgesia and obtunding surgical stress may reduce intraoperative catecholamine release from the pheochromocytoma, thereby contributing to haemodynamic stability.

Remifentanyl has pharmacodynamic properties similar to other potent μ -opioid receptor agonists with additional unique characteristics of rapid onset and offset of effect, regardless of duration of administration.¹¹ Rapid offset of action as demonstrated by a context-sensitive half-time of the order of 3 to 5 min^{5,11} is ideal in the management of pheochromocytoma, specially when catecholamine outflow is cut-off at adrenal vein ligation. Hence, remifentanyl was discontinued at the end of the case and postoperative analgesia provided by bolus (30 min before last suture) and patient-controlled morphine infusion.¹² It may be argued that the benefits of narcotics may be similarly provided by other μ -agonists such as morphine, alfentanil and sufentanil. However, none of these agents offer the ability for dose-effect titration afforded by unique pharmacokinetics of remifentanyl. In addition, the high dose of narcotics required to obtain the same degree of stress suppression would result in prolonged duration of action.

Many agents have been used to facilitate the perioperative management of pheochromocytoma surgery. Magnesium sulfate in combination with epidural anaesthesia has been described in a patient with coronary artery disease although esmolol was required postoperatively.¹³ Calcium channel blockade alone or in combination have been used with mixed results.^{14,15} It is generally agreed that the preoperative use of alpha-adrenergic blocking drugs benefit patients, although this and the optimal duration of treatment have

not been tested in a randomised study.¹⁶ This must be accompanied by intravascular volume expansion, as with intravenous crystalloids in this case. With adequate preparation, intraoperative haemodynamic changes are minimised and intraoperative management greatly facilitated. Desflurane has been useful in controlling hypertension during resection of pheochromocytoma, although labetalol and nitroprusside were required in the postoperative period.³ It must be emphasised that due to the rarity of the condition, there is unlikely to be any randomised trial to determine the optimum mode of management.⁴ Hence, existing literature continues to rely on case reports based on sound pathophysiological principles.

Our choice of remifentanyl is indicated by the desirable properties we have described. The lack of histamine release reported⁸ is useful in the first asthmatic patient with potential airway hyperactivity when β -blockers are contraindicated. Encouraged by the favourable results obtained in the first instance, we decided to use remifentanyl in the second patient who remained on propranolol. We were impressed by the haemodynamic stability, which is likely to be due to continued β -blockade although catecholamine levels were lower. The doses of remifentanyl and nitroprusside required were less than in the first case and there was no need to start epinephrine infusion following tumour excision.

A recent development is the use of the laparoscopic transperitoneal approach. Open surgery is usually quicker, but the patient may require longer postoperative hospitalisation. In the absence of complications resulting from persistent adrenergic blockade, patients may be ready to leave hospital 48 h after laparoscopic surgery. Laparoscopic excision of pheochromocytoma requires persistent tissue traction and diathermy which may cause sustained haemodynamic consequences of at least the same severity as during open surgery, but for possibly a longer duration. In combination with nitroprusside as a vasodilator and desflurane as an anaesthetic, the titratable analgesic and stress suppressive effects of remifentanyl have been found to be safe and effective in these 2 patients. The use of short-acting agents is particularly suited to the minimally invasive approach of this type of surgery.¹

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