CASE REPORT

NALOXONE-INDUCED PULMONARY EDEMA: A POTENTIAL CAUSE OF POSTOPERATIVE MORBIDITY IN LAPAROSCOPIC DONOR NEPHRECTOMY

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ABSTRACT

A 28-year-old patient operated for laparoscopic donor nephrectomy (LDN) developed overdose effect of fentanyl leading to poor postoperative recovery. Naloxone (200 µg) treatment was used to reverse fentanyl effects, but it was associated with hypertension. The patient developed pulmonary edema after 2 hours and required overnight mechanical ventilation with positive end-expiratory pressure. Volume overload prescribed in the management of LDN to overcome the immediate poor renal graft functioning probably predisposed this healthy young patient to develop cardiac failure during sympathetic surge associated with naloxone administration. The authors feel that the reversal of overdose effect of opioid by naloxone after intravascular blood volume expansion puts the patient at risk to develop pulmonary edema.

Key words: Donor nephrectomy, fentanyl, laparoscopic nephrectomy, naloxone, pulmonary edema

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INTRODUCTION

Laparoscopic donor nephrectomy (LDN) is now routine with intent to reduce postoperative pain, to shorten convalescence and to improve cosmetic outcome of the kidney donor. However, impaired short-term function of transplanted nephrectomy kidney has been reported due to diminished intra-operative blood flow during pneumo-peritoneum, trauma to kidney graft removal through a small incision, and longer warm ischemia time.[1] To overcome this, vigorous hydration is practiced to promote diuresis during surgery,[2,3] and the advantages of maintaining urine output at approximately 300 mL/h during LDN have been stressed.[4] Variability in response to intravenous opioids may have a threefold to fivefold difference in the therapeutic or toxic effects of a given dose.[5] Naloxone, a standard medication for the treatment of opioid overdose, is associated with morbidity in emergency patients.[6] We wish to share our experience of naloxone-induced pulmonary edema in a young healthy patient during LDN.

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CASE REPORT

A 28-year-old ASA grade I male patient weighing 50 kg was posted for left laparoscopic donor nephrectomy under general anesthesia (GA). He was found to be a suitable tissue match for his sibling for renal transplantation. The patient was fasted overnight and he received oral premedication of lorazepam (1 mg) the night before surgery and in the morning.

General anesthesia was induced with midazolam (2 mg), fentanyl (150 μg) and propofol (100 mg) and vecuronium (6 mg) to facilitate oro-tracheal intubation. Anesthesia was maintained with propofol infusion (100 to 200 mg/h); and intermittent halothane in oxygen (40%) and air were used to control blood pressure. The patient's vitals were monitored using ECG lead II, noninvasive arterial pressure, SpO_2, capnography ($ETCO_2$) and body temperature. Intra-operatively he was given 3 L of crystalloid [Ringer's lactate, 2100 mL; and saline (0.9%), 900 mL] and colloid [Hetastarch (6%), 500 mL] to build up central venous pressure (CVP) to 10 to 12 mm Hg as per requirement of transplant unit protocol. He had blood loss of approximately 150 mL and urine output (1100 mL) during surgery lasting for 2.5 hours. At the end of surgery, propofol infusion was stopped and vecuronium effect was reversed by IV neostigmine (2.5 mg) with glycopyrrolate (0.2 mg). Trachea was extubated when the patient started breathing spontaneously (tidal volume, 300 mL), responded to verbal command and sustained head lift for 5 seconds.

In the postoperative ward after half an hour or so, his consciousness deteriorated, and he developed respiratory depression (RR, 6/min) with desaturation (SpO_2, 94%) on oxygen. His respiration was immediately assisted with bag-and-mask ventilation. On examination pupils were characteristically pin-pointed, with sluggish reaction to light, and suggested overt toxic effects of fentanyl. Naloxone (200 μg) IV was given slowly over 5 minutes. The patient responded immediately with increase in respiratory rate (from 6/min to 14/min), SpO_2 (from 75% to 99%) and alertness (obeying verbal command).

After 1 hour, again SpO_2 started decreasing; but this time, the patient had tachapnea (RR, 20/min) with excessive bilateral crepitations and diminished bilateral air entry. We also noticed sinus tachycardia (heart rate, 128 beats/min) and hypertension (arterial pressure, 176/98 mm Hg) and no signs of cardiac ischemia on ECG. The patient was restless; and arterial blood gas measured pH, 7.13; PaO_2, 78 mm Hg; $PaCO_2$, 48 mmHg; and base deficit, 9.8. Considering deterioration in consciousness and insignificant improvement in SpO_2 with the bag-and-mask ventilation, we decided to put him on respiratory support. Immediately the trachea was intubated and mechanical ventilation started on pressure support — 20 cm H_2O; PEEP, 10 cm H_2O; and FiO_2, 0.6. Pink, frothy secretions poured out of the endotracheal tube, which suggested pulmonary edema (PE). Intravenous furosemide (20 mg) was given to induce diuresis. Aminophylline infusion 0.5 mg/kg/h was started. Invasive arterial pressure monitoring and central venous access were secured. CVP measured 17 mm Hg. Nitroglycerin infusion (2 μg/kg/min) was started. Chest radiograph showed features

of PE. Oxygenation improved and after 6 hours of ventilation, as the patient improved in respiratory effort and regained consciousness, CPAP (12 cm H_2O) mode was started. The next day, when he was conscious, oriented, breathing normally (RR, 16/min) at adequate tidal volume (450 mL) and had an improved chest x-ray, endotracheal extubation was performed successfully. The patient was discharged after 3 days.

DISCUSSION

Our patient was a healthy young man who developed fentanyl toxicity (unconsciousness, pin-pointed pupils and low respiratory rate). This probably was related to his higher sensitivity towards fentanyl. He developed PE with hypertension after naloxone treatment, even without airway obstruction or laryngospasm in this period.

The various causes for postoperative PE include airway obstruction, laryngospasm, fluid overload, acute left ventricle failure. This young patient was without compromised cardiac function or respiratory predisposition. Since the patient neither had any evidence of ischemic cardiac illness nor had any ischemic episode, either of these was an unlikely cause for PE. The fluid overloading commonly practiced to avoid adverse effects of increased intra-abdominal pressure during LDN predisposes patients to acute pulmonary edema too.[7]

In our patient, although acceptable dose of fentanyl (3 μg/kg) was administered, its effect was unduly prolonged and the patient developed opioid toxicity. Naloxone is a pure antagonist of opioids and reverses the overdose effects of fentanyl, like respiratory depression and unconsciousness, but precipitates PE in immediate succession. Naloxone therapy is associated with significant morbidity in the form of cardiac arrhythmia,[8] hypertension,[8] agitation and convulsion.[6] PE following naloxone administration has been explained by excessive sympathetic surge leading to massive release of catecholamines in response to pain with displacement of blood from the systemic to the pulmonary bed.[9] Thus, our patient being volume-overloaded, this side effect of naloxone got more pronounced and precipitated PE.

He responded well to mechanical ventilation with PEEP; aminophylline infusion to reduce pulmonary vascular resistance; and nitroglycerine infusion to control blood pressure and to reduce preload. Furosemide-induced diuresis also helped to decrease volume overload, but complete recovery from PE required overnight mechanical ventilation with moderate PEEP. The unforeseen development of PE after naloxone reversal not only added to the morbidity in immediate postoperative recovery in an otherwise healthy voluntary organ donor but also added undue concern in the members of his family. Hence through this case report of a critical event, the authors wish to emphasize a word of caution in the use of naloxone in over-hydrated patients in terms of its benefits vis-à-vis the risks involved.

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