

Fentanyl-Induced Chest Wall Rigidity in the Intensive Care Unit

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Abstract

Objective: To report a case of chest wall rigidity induced by low dose fentanyl infusion given for post-operative analgesia.

Data Sources: The data was gathered from medical record.

Study Selection: A 71-year-old woman developed severe postoperative ventilator dyssynchrony characterized by persistent hypercarbia, decreased pulmonary compliance, and episodic breath holding. Deepened levels of sedation with midazolam and fentanyl infusion at escalating doses were required to provide adequate ventilation; efforts at weaning the patient off sedation were met with worsened ventilator dyssynchrony. Ventilation improved only with neuromuscular relaxation and the cessation of fentanyl.

Data Extraction: The data were extracted from the medical record.

Data Synthesis: The data were synthesized from the patient's medical record.

Conclusions: Fentanyl is used frequently because of its modest side effect profile; however, our experience illustrates the need for continued appreciation of chest wall rigidity, a severe potential side effect.

Keywords: Fentanyl, Thoracic Diseases, Muscle rigidity, Intensive care units, Hypercapnia, Analgesics, Opioids

Introduction

Chest wall rigidity is a well-recognized side effect of fentanyl, characterized by asynchronous ventilation, hypercarbia and respiratory failure. Majority of the case-reports have been described in the setting of operation theatre when high doses of bolus fentanyl was used at the time of induction of anesthesia. However, chest wall rigidity has been rarely reported with low dose continuous fentanyl infusion given post-operatively for the purpose of analgesia.

We describe a case of post-operative hard ICU stay characterized by respiratory failure, prolonged intubation, early tracheostomy and morbidity. This was secondary to chest wall rigidity attributed to low dose continuous fentanyl infusion. We further discuss clinical presentation, mechanism of this side effect and enlist key recommendations.

Case Description

We report a case of a 71-year-old woman was admitted to our surgical Intensive Care Unit (ICU) immediately following an exploratory laparotomy with lysis of adhesions and resection of a serous borderline pelvic tumor. Approval for case report submission has been taken from the patient as a signed written informed consent. Her medical history included ovarian cancer, which had been treated with total abdominal hysterectomy and bilateral oophorectomy; morbid obesity (BMI 44.5 kg/m²); obstructive sleep apnea requiring nightly continuous positive airway pressure; coronary artery disease, which had been treated with a drug-eluting stent of the first obtuse marginal branch, angioplasty of the second obtuse marginal branch, and clopidogrel platelet inhibition therapy; Chronic Obstructive Pulmonary Disease (COPD); chronic renal insufficiency (preoperative creatinine level, 1.6 mg/dL); thyroid cancer, which had been treated with partial and completion thyroidectomies; bladder cancer, which had been treated with chemotherapy and was currently under observation; insulin-dependent diabetes mellitus; hypertension; and tobacco use, which had ceased 2 years prior to admission.

The patient underwent an uneventful induction of general anesthesia, which

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was maintained with desflurane. Intraoperative analgesia was provided with intermittent fentanyl boluses (250 mcg total, including induction), sufentanil boluses (40 mcg total), ketamine boluses and infusion (30 mg total), and hydromorphone (2 mg at the conclusion of her operation). One hour into her operation, she developed respiratory failure with respiratory acidosis (pH 7.19, PaCO₂ 81 mm Hg, PaO₂ 112 mm Hg on 100% FiO₂) and hypotension requiring significant vasopressor support (phenylephrine, ephedrine, and calcium chloride boluses and a norepinephrine infusion). Urgent intraoperative transesophageal echocardiography revealed no wall motion abnormalities to suggest ischemia as an etiology of her significant hypotension; the test revealed no gross valvular disease, no emboli, an estimated ejection fraction of 50%, and mild hypovolemia. Pulmonary compliance remained suboptimal, and high peak inspiratory pressures were required for ventilation throughout the remainder of the operation. Following conclusion of her operation, she was transferred to the surgical ICU, still intubated and sedated.

On arrival to the ICU, she received a 200-mcg fentanyl bolus and intermittent midazolam boluses (total 6 mg) to relieve agitation as she emerged from anesthesia. Upon emergence, her spontaneous breathing on the ventilator became more labored with a very prolonged expiratory phase. Lungs sounds remained vesicular. Chest radiography and electrocardiography revealed no abnormalities, and the patient's cardiac enzyme levels were within normal limits. On bi-level ventilation (high positive end-expiratory pressure [PEEP] 34 cm H₂O, low PEEP 10 cm H₂O, FiO₂ 0.6, respiratory rate 22), inhalations and exhalations were markedly asynchronous. Chest wall movements were noted to be discordant with the ventilator, and the chest wall rose minimally with ventilator breaths. Also noted were a decrease in lung compliance to 9 L/cm H₂O, a decrease in tidal volume to 2.5 mL/kg, an acute rise in airway resistance to 41 cm H₂O/L/s, and an increase in end-tidal CO₂ to 60 mm Hg. Arterial blood gas measurements indicated worsening respiratory failure (pH 7.14, pCO₂ 92 mm Hg). No endotracheal obstruction was noted on deep suctioning. The patient's sedation was increased with escalating fentanyl and midazolam infusions; she remained heavily sedated with gradual improvement in arterial blood gas measurements (pH 7.44 and pCO₂ 41 mm Hg) at FiO₂ of 1.0 and PEEP of 10 cmH₂O.

Over the next 2 days, the patient's postoperative course was complicated by acute-on-chronic kidney failure as well as presumed COPD exacerbation, which was evidenced by bilateral infiltrates noted on chest radiographs and for which she remained on ventilatory support and received antibiotics, ipratropium bromide, and levalbuterol.

Every attempt at weaning the patient off midazolam infusion while continued fentanyl infusion was met with periods of respiratory decompensation characterized by low minute ventilation, hypercarbia, and breath holding. Many of these intermittent episodes were associated with elevated blood pressure.

On the morning of postoperative day 3, the patient's breath holding episodes became resistant to sedation. A propofol infusion (12.5-25.0 mcg/kg/min) was added to the continuous fentanyl and midazolam infusions. Despite this treatment, her breathing remained labored; multiple ventilation modes were attempted with no significant improvement.

The propofol dose was increased incrementally; the patient's increased level of sedation finally ended her breath holding episodes and ventilator asynchrony. Consequently, the sedative doses were titrated, and she was weaned off midazolam and fentanyl infusions but remained on very low-dose propofol infusion. Later that day, agitation and ventilator asynchrony resumed and required increased sedation with fentanyl (100 mcg/min) and midazolam (10 mg/h); meanwhile propofol was discontinued. The patient continued to have substantial difficulty with ventilation, so a cisatracurium infusion was administered for neuromuscular relaxation. Meanwhile, computed tomography of the brain did not show any gross central cause of hypercapnia.

In light of the patient's ongoing ventilatory requirements and the difficulty in weaning her off sedation, an early tracheostomy was performed on postoperative day 6. On postoperative day 8, the possibility of fentanyl-induced Chest Wall Rigidity (CWR) was entertained owing to the continued episodes of ventilator asynchrony and hypoventilation when attempts were made to wean her off paralytics. Consequently, the patient's analgesic was switched to a hydromorphone infusion, and she continued to receive midazolam and cisatracurium infusions. Twenty-four hours after this change, the paralytics were withdrawn and no further episodes of respiratory acidosis, desaturations, or hypoventilation were noted. The patient was weaned off midazolam and hydromorphone soon thereafter, and she transitioned quickly to continuous positive airway pressure. She was subsequently transferred to a long-term acute care facility.

Discussion

CWR related to opiate administration was first described by Hamilton and Cullen in 1953 [1]. Following opiate administration, clinicians may observe significant difficulty with mask ventilation, respiratory arrest, and a rigid chest wall; this phenomenon has been noted with various opioid substances [2-17]. The majority of reported cases and physiologic studies focus on CWR occurring with high opioid doses—administered as part of anesthetic induction [2,4,6,7,11,18-21]. Though uncommon, significant chest wall rigidity has been reported with doses of fentanyl as low as 100 µg [3,8,14-16,22]. Anecdotal reports from anesthesiologists confirm the shared experience of difficult ventilation following small doses of fentanyl used during the induction of general anesthesia. Neonatal and pediatric patients are also susceptible to opioid-induced CWR [13,22-30]. Observation of CWR in the ICU has also been reported; the majority of these ICU cases occurred after surgery in patients who had received large intraoperative opioid doses [6,17,31]. In nearly all these patients, treatment with muscle relaxants or opioid receptor antagonists relieved CWR and eased ventilation immediately [3,6-8,11,12,14,15,17,19,20,31].

The Clinical Practice Guidelines for the Management of Pain, Agitation, and Delirium in Adult Patients in the Intensive Care Unit published by the Society of Critical Care Medicine recommend intravenous opioids as first-line therapy for non-neuropathic pain in critically ill patients [32]. Following an initial bolus dose, a low continuous infusion rate is set and subsequent adjustments made to achieve adequate analgesia. The range of fentanyl infusion rates recommended in these guidelines is 0.7-10.0 µg/kg/h; we rarely exceed 3 µg/kg/r in our unit. The elimination half-life of fentanyl is 2-4 hours; however, its context-sensitive half-life can

reach 12 hours or longer—prolonged further in patients with end organ dysfunction [32]. Fentanyl is predominantly metabolized in the liver and excreted largely via urine [33].

In our patient, fentanyl-induced CWR was diagnosed late in her ICU course and resulted in early tracheostomy and prolonged sedation and ventilation. The intraoperative events (hypotension, hypercarbia, respiratory failure) leading to her ICU admission were puzzling at the time but are most likely the initial signs of the development of chest wall rigidity. Examination of the anesthetic record does not reveal difficulty with anesthetic induction or mask ventilation; however, the possibility of a delayed reaction exists as the intraoperative setback occurred nearly 1 hour following induction. Furthermore, her ventilation and oxygenation parameters appeared to improve following the administration of a muscle relaxant; this may have been the only clue to the development of CWR in the operating room. In the presence of considerable comorbidities such as coronary artery disease, COPD, and morbid obesity, opioid-induced CWR was not the most likely condition among those considered in the differential diagnosis during our patient's anesthetic course.

Studies of high-dose fentanyl administration during anesthesia induction report some level of rigidity in the majority of patients [7,19,34]. The exact incidence of CWR in the setting of ICU analgesia or low-dose fentanyl use (as in sedation or anesthetic induction) is unknown. At our institution, fentanyl is commonly used in both the ICU and operating room, and we had not encountered CWR to the extreme seen in this patient—leading us to believe the incidence of clinically significant CWR in these settings is quite low. Therefore, clinical factors predisposing patients to develop chest wall rigidity have yet to be identified.

Investigations of CWR have noted generalized muscle rigidity and increased activity on electromyography following opioid administration [22,34-36]. Difficulty achieving adequate ventilation is the clinical hallmark of CWR and several studies report that glottic closure rather than the CWR itself is the root cause [2,4,19]. Conversely, other studies have noted open vocal cords on direct laryngoscopy in patients with CWR [14]. In efforts to understand the mechanisms of rigidity, early experiments examined the muscle reflex arc in humans and concluded that the origin was in the spine or pathways more proximal in the central nervous system [36]. Animal studies have suggested a role of various brainstem locations, including the substantia nigra and nucleus raphe pontis [37-39]. Intraventricular injections of opioid agonists specific to various opioid receptors suggest a role for central μ receptors in producing rigidity, whereas supraspinal κ -1 and δ -1 receptors may attenuate this effect [40].

We have reported a case of fentanyl-induced CWR diagnosed late in a patient's ICU treatment course and marked by significant morbidity that included prolonged intubation, prolonged sedation, and early tracheostomy. The patient's ICU course leading up to the diagnosis was notable for profound ventilator dyssynchrony, hypercarbia, and breath holding. Until her diagnosis, she received fentanyl infusion with only minor breaks; this near-continuous infusion lengthened her context-sensitive half-life of fentanyl, in the setting of decreased renal function and morbid obesity. Neuromuscular relaxation and fentanyl cessation (waiting more than 24 h prior to attempting to wean the patient from the ventilator) were the interventions ultimately responsible for her gradual improvement.

Conclusion

Fentanyl is used frequently because of its modest side effect profile; however, our experience illustrates the need for continued appreciation of CWR, a severe potential side effect of fentanyl and other opiates.

Conflicts of Interest and Source of Funding

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