

# Respiratory arrest after low-dose fentanyl

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**A**ppropriate treatment of pain and anxiety is a major part of the routine practice of emergency medicine. This paper reports the first case of severe respiratory depression after administration of a subtherapeutic dose of fentanyl to an adult.

## Case report

A 31-year-old man with facial trauma was brought to the university-based hospital emergency department (ED). He reported that while working as a security guard 30 minutes prior, he was assaulted and struck in the left face with a monkey wrench. He complained of severe left facial pain, but denied any loss of consciousness, amnesia, vomiting, or neurologic deficit. He denied any alcohol or recreational substance use. His past medical history was unremarkable, and he was taking no medications.

The patient appeared awake, alert, and somewhat anxious, with normal vital signs. On examination, he had left malar flattening, left periorbital ecchymosis and edema, and a 3-cm laceration of the eyelid. His left malar area was markedly tender and step-off depressions were palpated over the orbital rims. Computed tomography of his head and face demonstrated a tripod fracture of the left zygomatic body, fracture of the orbital floor, fracture of the anterior, posterior, and medial walls of the maxillary sinus. No intracranial abnormality was noted.

An IV line was established to administer opioid analgesia per our department protocol for treating severe pain. The responsible physician elected to use fentanyl (total 200 µg/92 kg) because of its rapid onset, short duration, and titratability. The first dose consisted 50 µg, which was approximately equal to 0.5 µg/kg. Two minutes after the administration of the first dose of 50 µg of fentanyl, respiratory arrest with concomitant cyanosis ensued. Pulse oximetry revealed an oxygen saturation of 71% with no other changes in vital signs. The patient's respirations were immediately assisted with 100% oxygen and a bag-valve-mask device and he was given 0.4 mg of naloxone IV. Within two minutes, spontaneous respirations resumed. During his resuscitation, his chest wall movement appeared normal while being ventilated, oxygen saturation remained above 90%, and glucose level was 97 mg/dL. His blood alcohol level was reported to be 144 mg/dL and a toxicologic screen performed on a previously obtained urine was reported as negative for opioids, benzodiazepines and barbiturates. The patient was monitored for two hours and recovered uneventfully. His laceration was repaired and he was transferred to a nearby facility for definitive treatment.

## Discussion

Intravenous opioids are considered the drugs of choice for severe pain.<sup>1</sup> Respiratory depression is the most serious adverse effect of opioids. Adverse effects can be partly avoided by using opioids with shorter half-lives while concomitantly increasing the frequency of administration.<sup>2</sup>

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Fentanyl is the opioid most commonly used for analgesia during procedural sedation in the ED.<sup>3,4</sup> When given intravenously, analgesia can commence in 90 seconds.<sup>5</sup> The clinical effects of fentanyl in the acute setting last for approximately 30 minutes.<sup>5</sup> The recommended dose for both adults and children is 2 to 4 µg/kg titrated in IV doses of 0.5 to 1 µg/kg given slowly every 3 to 5 minutes.<sup>4,6</sup> Maximal respiratory depression after fentanyl administration occurs 5 minutes after administration, is dose dependent, and is most common when combined with a sedating agent, such as midazolam or propofol.<sup>3,4,6,7</sup> However, the present case experienced respiratory arrest within 2 minutes after administration of fentanyl unaccompanied by sedative agents.

Respiratory compromise and apnea have been associated with fentanyl use during procedural sedation in the ED, although these events are rare and usually transient.<sup>5</sup> In a study of 841 patients receiving fentanyl in the ED, only 6 experienced respiratory depression, 4 of whom had associated ethanol levels in excess of 160 mg/dL.<sup>5</sup>

Fentanyl does not reliably produce sedation or unconsciousness. It causes a dose-dependent effect on ventilation by decreasing the responsiveness to stimulatory effects of carbon dioxide.<sup>5</sup> Chest wall and glottic rigidity have been reported with high-dose fentanyl, resulting in an inability to ventilate the patient.<sup>5,6,8</sup> This complication occurs at much higher

doses than used in the ED and with rapid infusion, but has not been reported in the ED.<sup>4,6,8</sup> Maternal respiratory arrest associated with intravenous fentanyl use during labor has also been reported.<sup>9</sup> All documented cases with respiratory depression attributed to intravenous administration fentanyl are summarized in Table 1.

Recently, the potential for fentanyl to cause respiratory arrest received international attention after 118 Russian hostages and 51 Chechnyan terrorists were killed by an aerosolized agent alleged to be fentanyl during a rescue at a Moscow theatre in October 2002.<sup>10</sup> In the present case, respiratory arrest occurred after only 50 µg of fentanyl IV, an initial dose well within the range typically used in emergency care settings. This dose represents the least amount of the drug that was documented to have caused respiratory arrest. Although initially unsuspected, the patient's blood alcohol level of 144 mg/dL was likely to have been a contributing factor. The complete reversal of his respiratory arrest shortly after naloxone administration further supports the diagnosis of fentanyl-induced respiratory arrest. No other substances were identified on routine urine toxicologic screen.

A critical aspect of this case is the small dose of IV fentanyl that caused respiratory arrest in the ED. This serves to remind emergency physicians of the importance of titrating fentanyl in doses of 0.5 µg/kg IV in emergency patients. It also illus-

**Table 1.** Studies and reports indicating respiratory problems after fentanyl.

Author, year	Age (yrs)	Clinical setting	Dose in µg (Route)	Respiratory status	Other respiratory depressants
Chudnofsky, 1989	50	ED	100 (IV)	Shallow breathing	Ethanol (BAL=486 mg/dl)
Chudnofsky, 1989	Adult, N/A	ED	50 (IV)	Apnea (brief)	Ethanol (BAL>60 mg/dl)
Chudnofsky, 1989	Adult, N/A	ED	N/A (IV)	Apnea (brief)	Ethanol (BAL>160 mg/dl)
Chudnofsky, 1989	Adult, N/A	ED	N/A (IV)	Apnea	Ethanol (BAL>160 mg/dl)
Chudnofsky, 1989	Adult, N/A	ED	N/A (IV)	Apnea	N/A
Chudnofsky, 1989	Adult, N/A	ED	N/A (IV)	Apnea	N/A
Yaster, 1990	14 month	Ward	75 µg total dose, three times 25 µg (IV)	Respiratory arrest	Midazolam
Garner, 1994		Labor	N/A (IV)	Respiratory arrest	N/A
Kramer, 1998			N/A transdermal		Benzodiazepine, cocaine

N/A- Unknown or not reported

trates the importance of being prepared to provide respiratory support and naloxone reversal in any patient receiving IV fentanyl. The American Society of Anesthesiologists developed a guideline intended for provision of sedation and analgesia by nonanesthesiologists. This report mandates strict interactive and

mechanical monitoring throughout the procedure to preclude potential consequences.<sup>11</sup>

In conclusion, IV fentanyl should be administered with caution in the ED, since even subtherapeutic doses can cause respiratory arrest in patients with unsuspected mild alcohol intoxication.

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