Respiratory arrest after low-dose fentanyl

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Intravenous opioids are considered the drugs of choice for severe pain. 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.
Fentanyl is the opioid most commonly used for analgesia during procedural sedation in the ED.\(^3\,4\) When given intravenously, analgesia can commence in 90 seconds.\(^5\) The clinical effects of fentanyl in the acute setting last for approximately 30 minutes.\(^5\) 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.\(^4\,6\) 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.\(^3\,4\,6\,7\) 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.\(^5\) 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.\(^5\)

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.\(^5\) Chest wall and glottic rigidity have been reported with high-dose fentanyl, resulting in an inability to ventilate the patient.\(^5\,6\,8\) This complication occurs at much higher doses than used in the ED and with rapid infusion, but has not been reported in the ED.\(^4\,6\,8\) Maternal respiratory arrest associated with intravenous fentanyl use during labor has also been reported.\(^9\) 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.\(^10\) 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 | 14 month | Labor | N/A (IV) | Respiratory arrest | N/A |
| Kramer, 1998 | N/A transdermal | | | | Benzodiazepine, cocaine |

N/A: Unknown or not reported
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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. 11

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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