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Case Report

# Fentanyl-Induced Respiratory Depression in an Intensive Care Unit Patient

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## ABSTRACT

**Background:** Fentanyl citrate, a potent opioid analgesic, is widely used for pain management in mechanically ventilated patients in WHO Adverse Drug Reaction Probability Scale (ICU). Its use, however, is associated with serious adverse reactions such as respiratory depression, particularly in patients with compromised respiratory systems. **Case Presentation:** We present a case of a 75-year-old male with Chronic Obstructive Respiratory Disease (COPD) and multifocal bronchopneumonia admitted to the ICU due to severe respiratory distress and hypoxia. Despite aggressive management including oxygen therapy, non-invasive ventilation, intubation, and mechanical ventilation, the patient's condition deteriorated. Fentanyl citrate infusion was initiated for analgesia during mechanical ventilation. Unfortunately, this led to a progressive decline in oxygen saturation from 90% to 40% within 24 hr, indicating severe respiratory depression. Laboratory investigations revealed infection markers, and despite escalation of ventilatory support, the patient succumbed to acute respiratory failure. **Discussion:** This case highlights the critical importance of balancing effective pain management with the risk of respiratory depression in high-risk patients. Opioids like fentanyl, although effective for analgesia, pose significant risks in patients with pre-existing respiratory compromise. Alternative sedatives such as dexmedetomidine, ketamine, or remifentanil may offer safer options for pain management in such populations. **Conclusion:** The fatal outcome in this case underscores the need for individualized sedation strategies, vigilant monitoring, and careful selection of pharmacological agents to optimize outcomes in critically ill patients with respiratory compromise.

**Keywords:** Respiratory Depression, Adverse Drug Reaction, Fentanyl, Mechanical Ventilation, Fentanyl Citrate.

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## INTRODUCTION

Fentanyl Citrate is a potent opioid with the action of analgesia and sedation. It initially accumulates in skeletal muscle and fat and is then slowly released into blood.[1] Fentanyl citrate was originally approved by the FDA for the purpose of anesthesia, however over the years. Its indication has gradually expanded through undergoing various regulatory updates including its use for pain management during the mechanical ventilation especially in Intensive Care Units (ICU).[2] The indication of using Fentanyl citrate as an adjunctive therapy during mechanical ventilation for those requiring analgesia and sedation is based on its long-term use. However, its initial approval document as an adjunctive therapy for pain management during mechanical ventilation is not readily available. The common serious adverse drug reactions include respiratory depression,[3] apnea,[4] rigidity,[5] and bradycardia[6] which if goes unnoticed results in respiratory arrest, circulatory depression, or cardiac arrest.[1] When it comes to administration in those patients whose respiratory system is already compromised, extra measures need to be taken as the fentanyl citrate is known to worsen the respiratory drive and increase airway resistance.[1]

## CLINICAL PRESENTATION

A 75-year-old male with a known case of Chronic Obstructive Respiratory Disease (COPD) was brought to the Emergency Department on 21/08/2024, presenting with severe breathlessness and a non-productive cough for two days. His initial clinical assessment revealed significant respiratory distress and declined vital signs, including tachycardia (Pulse: 110 bpm), hypertension (BP: 150/80 mmHg), tachypnoea (RR: 26 cpm), and severe hypoxia ($SpO_2$: 60% on room air). The patient was diagnosed with bronchopneumonia, prompting immediate admission for further evaluation and management.

Upon admission, routine examinations showed that serum sodium, potassium, chlorine, Renal Function Test (RFT), and Liver Function Test (LFT) levels were within normal ranges, but C-reactive protein levels were elevated to 4 mg/dL, indicating an

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inflammatory response. A chest X-ray revealed multiple areas of opacities in the lungs, leading to a diagnosis of multifocal bronchopneumonia.

By 22/08/2024, the patient's condition had deteriorated, necessitating admission to the Intensive Care Unit (ICU). Oxygen therapy was initiated at 6 L per minute, improving SpO2 to 92%. Despite oxygen therapy, persistent hypoxia was present, necessitating the initiation of Non-Invasive Ventilation (NIV), followed by intubation and mechanical ventilation due to worsening oxygenation. For pain management during intubation and mechanical ventilation, fentanyl citrate infusion was started on 22/08/2024 with careful monitoring due to the increased risk of respiratory depression in geriatric patients.

Upon the administration of fentanyl citrate, the patient's oxygen saturation progressively declined, despite escalating ventilatory support. $SpO_2$ dropped from 90% under NIV with $FiO_2$ at 100% on 22/08/2024 at 11:30 AM to 40% on 23/08/2024 at 6:15 AM under Pressure-Controlled (PC) ventilation with a Positive End-Expiratory Pressure (PEEP) of 9 and $FiO_2$ of 100%, indicating the occurrence of respiratory depression as a serious adverse reaction.

Additionally, laboratory investigations revealed lymphopenia (15.9%) on admission and progressive leucocytosis (WBC: $5.6\times10^3$/uL on 21/08/2024 to $9.9\times10^3$/uL on 22/08/2024) with neutrophilia (73.1%) and declining lymphocytes (15.9% on 21/08/2024 to 8.5% on 22/08/2024), indicating signs of infection, a marker of multifocal bronchopneumonia. Despite aggressive management and escalating ventilatory support, the patient was declared dead on 23/08/2024 at 8:05 AM, raising concerns over the cause of death and highlighting a critical presentation of acute respiratory failure with severe hypoxia. According to the Naranjo Adverse Drug Reaction (ADR) probability scale, the probability of fentanyl-induced respiratory depression in this case is classified as possible (Table 1).

## DISCUSSION

The clinical management of the patient in the described case was primarily guided by standard critical care and respiratory management protocols. Specifically, the following aspects were considered:

### Acute Respiratory Failure Management Guidelines

The patient was managed based on established guidelines for the management of acute respiratory failure, particularly in the context of COPD and multifocal bronchopneumonia. These guidelines emphasize the importance of oxygen therapy, Non-Invasive Ventilation (NIV), and mechanical ventilation to address severe hypoxia and respiratory distress.

### Pain Management and Sedation Protocols

The administration of fentanyl citrate for pain management during mechanical ventilation was conducted according to standard ICU sedation and analgesia guidelines. These protocols recommend the careful titration of opioids and vigilant monitoring to prevent adverse effects such as respiratory depression, especially in high-risk populations like geriatric patients with pre-existing respiratory conditions.

### Infection Management Guidelines

The patient's infection markers, including elevated C-reactive protein levels and progressive leucocytosis, were managed based on guidelines for the treatment of multifocal bronchopneumonia. These guidelines suggest the use of appropriate antibiotic therapy and supportive care to manage the underlying infection.

Sedation and analgesia are two important aspects of care in mechanically ventilated patients in ICU. Understanding commonly used medications is essential for sedation plan and pain management in individual patients. Pain is a symptom that is frequently experienced in critically ill patients[7] due to various reasons such as intubation, mechanical ventilation, or other routine clinical care like moving patients, adjusting tubes and so on.[8] Although addressing pain is undeniable it is also important to know that not all the individuals who are mechanically ventilated experiences pain. For example, Puntillo and colleagues studied the experiences of 171 ICU patients who were at grave risk of death up to 2 weeks of administration to the ICU among which only 40% of the patients reported pain when intervened.[7] The most commonly used analgesia is of opioid family that acts on μ-opioid receptors in the Central Nervous System (CNS) inhibiting respiratory drive by reducing the brainstem's response to Carbon Dioxide ($CO_2$) levels. This effect can exacerbate hypoxia, especially in those patients already hypoxic and require high levels of ventilatory support.[9,10] Therefore, detection and management of opioid induced serious adverse drug reaction and medication errors is essential for the proper use of controlled medicines.[11]

In this case, the patient was administered with fentanyl citrate, whose mechanism underlies with that of opioid.[1,9] The oxygen saturation declined progressively from 90% under NIV to 40% under Pressure-Controlled Ventilation (PCV) with $FiO_2$ at 100% within 24 hr, correlating with fentanyl administration.

To minimize the risk of respiratory depression alternative strategies for pain management during mechanical ventilation can include dexmedetomidine a selective alpha-2 adrenergic agonist with sedative and analgesic properties,[12] ketamine a dissociative anaesthetic providing both sedation and analgesia,[13] and remifentanil an ultra-short-acting opioid with a rapid clearance profile.[14]

**Table 1: Naranjo Adverse Drug Reaction Probability Scale.**

| Questions | Yes | No | Do Not Know | Score |
|---|---|---|---|---|
| 1. Are there previous conclusive reports on this reaction? | +1 | 0 | 0 | +1 |
| 2. Did the adverse event appear after the suspected drug was administered? | +2 | -1 | 0 | +2 |
| 3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered? | +1 | 0 | 0 | 0 |
| 4. Did the adverse event reappear when the drug was readministered? | +2 | -1 | 0 | 0 |
| 5. Are there alternative causes that could on their own have caused the reaction? | -1 | +2 | 0 | -1 |
| 6. Did the reaction reappear when a placebo was given? | -1 | +1 | 0 | 0 |
| 7. Was the drug detected in blood or other fluids in concentrations known to be toxic? | +1 | 0 | 0 | 0 |
| 8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased? | +1 | 0 | 0 | +1 |
| 9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure? | +1 | 0 | 0 | 0 |
| 10. Was the adverse event confirmed by any objective evidence? | +1 | 0 | 0 | +1 |
| | Total Score | | | +4 |

## CONCLUSION

This case illustrates the critical challenges in managing acute respiratory failure especially in geriatric patient with COPD and multifocal bronchopneumonia. While fentanyl being a principal analgesic in ICU sedation protocols, its potential for inducing respiratory depression must not be overlooked, particularly in high-risk populations. Alternative sedatives, like dexmedetomidine or ketamine, should be considered in patients with pre-existing respiratory compromise.

The fatal outcome in this case highlights the importance of balancing effective pain management with the risk of respiratory depression in critically ill patients. Individualized sedation strategies, vigilant monitoring, and the selection of pharmacological agents are crucial in optimizing outcomes.

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## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The patient has been informed before publishing this work and written informed consent has been obtained prior to the publication.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ABBREVIATIONS

**ICU:** Intensive Cre Unit; **COPD:** Chronic Obstructive Respiratory Disease; **BP:** Blood Pressure; **RR:** Respiratory Rate; **$SpO_2$:** Oxygen Saturation; **RFT:** Renal Function Test; **LFT:** Liver Function Test; **NIV:** Non-Invasive Ventilation; **PEEP:** Positive End-Expiratory Pressure; **PC:** Pressure Controlled; **ADR:** Adverse Drug Reaction; **CNS:** Central Nervous System; **$CO_2$:** Carbon Dioxide; **PCV:** Pressure-controlled ventilation.

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