DOI: 10.35975/apic.v28i3.2044

# CORRESPONDENCE

# **PERIOPERATIVE MEDICINE**

# Fentanyl infusion in a multi-organ failure patient on adaptive support ventilation: a conundrum

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# **SUMMARY**

The authors present a case of an 85-year-old male patient with multiple co-morbidities. He underwent laparotomy for carcinoma rectum, recovered from anesthesia, and was shifted to the ward. On sixth day his condition deteriorated, so was shifted to ICU. In ICU, he was put on ventilator in ASV mode, and fentanyl infusion started. The next morning a high  $V_T$  of 900-1000 mL was noticed to be delivered, while the respiratory rate was 8-10/min. Naloxone administration eased the respiratory parameters. Careful monitoring of sedation levels and respiratory drive becomes crucial for preventing volutrauma in ASV mode of ventilation.

**Abbreviations**: ASV - Adaptive support ventilation, FiO<sub>2</sub> - Fraction of inspired Oxygen, MV - minute ventilation, PEEP - positive end expiratory pressure, RASS - Richmond Agitation Sedation Scale, RR - respiratory rate, Vt - tidal volume

Keywords: Closed loop ventilation, Complication, Opioids, Volutrauma

**Citation:** Kukanti C, Karim HMR, Panda CK, Jain A. Fentanyl infusion in a multi-organ failure patient on adaptive support ventilation: a conundrum. Anaesth. pain intensive care 2024;28(3):608–610; **DOI:** 10.35975/apic.v28i3.2044

Received: February 20, 2024; Accepted: March 31, 2024

Decreased work of breathing and achieving a regular, spontaneous breathing pattern, whenever possible is one of the prime mottos while choosing a ventilation mode. ASV is a newer and advanced mode, having closed-loop controlled ventilation, designed to optimize the patient's work breathing.<sup>1</sup> Sedation is often required in ventilated patients for providing patient comfort, pain control, and mechanical ventilation facilitation; fentanyl is one of the agents used owing to its analgo-sedative property.<sup>2</sup> Despite frequent adjustments of fentanyl infusion rate, the pharmacokinetic and pharmacodynamic can cause trouble in such patients, especially when the patient also has a multi-organ failure.

An 85-year-old male patient presented with abdominal distension and constipation for six days associated with pain for three days and vomiting for one day. He has been a known case of diabetes mellitus and hypertension for the past 15 y on tab. teneligliptin 20 mg and tab. telmisartan 40 mg. He is also a known case of chronic kidney disease stage-V on medical management. Radiological evaluation showed a growth in the sigmoid colon extending up to the rectum with pericolic lymph nodes causing luminal compression, multiple liver

nodules, and a small bilateral kidney with loss of corticomedullary differentiation. He was anemic, afebrile, having vitals; pulse rate 62/min, blood pressure 116/78mmHg, SpO<sub>2</sub> 97% on room air, with a respiratory rate of 20/min. 12-lead resting electrocardiogram was unremarkable.

Exploratory laparotomy under general anesthesia revealed the mass as non-resectable, and the abdomen was closed with an ileostomy. Intraoperatively, the patient had episodes of hypotension managed with boluses of inj. phenylephrine. The patient was extubated on the table, and immediate postoperative his heart rate was 93/min, blood pressure 90/50 mmHg, SpO<sub>2</sub>- 90% at room air (kept on  $O_2$  by facemask to maintain near 94%), and RR 24/min.

He was shifted to the critical care unit on the sixth postoperative day because of his deteriorating mental status and intractable hyperkalemia (K<sup>+</sup> = 6.83 meq/L). On arrival, his GCS score was E3V2M5 and had acute respiratory failure; consciousness further deteriorated over the next hours, and the trachea was intubated, and he was put on ventilator. Inj. fentanyl 20  $\mu$ g/h (0.33  $\mu$ g/kg/h). Inj. noradrenaline infusion at the rate of 0.02

µg/kg/min was started and titrated to maintain mean arterial pressure 65-70 mmHg and RASS -2. Patient was on ASV mode with settings of FiO<sub>2</sub> 40%, PEEP 5 cmH<sub>2</sub>0, minute volume 80% with backup. Fentanyl infusion was continued at the same rate for 18 h when the Richmond Agitation-Sedation Scale (RASS) score was noted as -4; the infusion rate was reduced to 10 µg/h. However, in the night, his sedation level, although maintained at -1, was trying to move his hands and head inappropriately. Therefore. fentanvl infusion was escalated by 10 µg/h. The next morning,

he was deeply sedated; the RR was regular but 8-10/min with Vt of 900-1000 ml even after reducing min volume to 30% (Figure 1A). Opioid overdose was suspected, and the fentanyl infusion was discontinued. Intravenous naloxone 0.4 mg stat was administered, the RR increased to 17-20/min, and Vt decreased to nearly 400 ml (Figure 1B). However, the response was not sustained much, so naloxone 0.4 mg was repeated after 5 minutes, and the RR, Vt, sedation level and pupil size became acceptable per the patient's condition (Table 1).

As the patient was having advanced stage of carcinoma, multiple organ failure and was elderly with high frailty, end-of-life care was initiated after discussing with the family members; no escalation of therapy was done, and supportive management for comfort was provided in his journey towards eternity.

Critically ill patients are at risk of opioid overdose even if they receive lower dosages. For fentanyl infusion, the

Parameters	Post intubation	Naloxone administration	
		Before	After
pН	7.328	7.30	7.33
pCO2	22.4	23	20.3
pO2	104.8	141.9	179.5
HCO3 <sup>-</sup>	11.8	11.6	10.9
RASS	Titrated to -2	-5	-1
Pupil	Normal, reactive	Miosis +, reactive	Normal, reactive

 Table 1: Blood acid-base values, sedation and pupillary sizes

 before and after naloxone administration.

infusion duration is crucial due to context-sensitive halftime. Our patient had sepsis, and chronic renal failure, which also contributed to the retention of the drug.

The development of respiratory depression with a deteriorating RAAS score indicated opioid overdose. In the ASV mode, with decreasing RR, Vt delivered increased to achieve the target MV. After administration of naloxone, the RR increased eventually, and Vt delivered decreased up to 500 ml. Vt of nearly 1000 ml can lead to lung overdistension resulting in volutrauma. As there is no fail-safe mechanism to cap Vt or set it,<sup>1</sup> careful monitoring of sedation levels and respiratory drive becomes crucial for preventing volutrauma, as suggested in our case.

A significant advancement in technology and its application in the medical field has led to significant developments in mechanical ventilation. ASV is one such advanced mode in which the algorithm employed



Figure 1: Showing the ASV ventilatory settings and delivered values before (A), and after (B) the administration of naloxone

aims to provide a pre-set level of alveolar ventilation while minimizing the total work of breathing performed by the ventilator and patient. The ASV mode is supposed to prevent pressure and volume-related complication as its working principle is based on the Radford nomogram and Otis equation, which takes airway resistance, compliance, and predicted bodyweight-based MV into account for calculating the respiratory rate and optimal point of work of breathing.<sup>3</sup> However, clinical evaluation has shown that it delivers an unwanted RR-Vt combination, especially a tendency towards lower RR.<sup>4</sup> Decreased RR leads to increased delivery of Vt to maintain MV. This phenomenon had a significant implication for our patient, who had an opioid overdose leading to significant sedation and lower RR, ultimately culminating in very high-volume delivery to the patient. Pressure or volume-related complication is scarcely reported with ASV. We could find only a case of pneumothorax using ASV for weaning.<sup>5</sup>

#### **Conflict of interest**

The authors report no conflicts of interest.

#### **Ethical considerations**

Written consent of a close relative of the patient was obtained to publish this manuscript for academic interest.

### **Authors' contribution**

All authors took active part in the management of this patient as well as preparation of the manuscript.

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