**"Deciphering the Culprit: Origins of Non-Cardiogenic Acute Pulmonary Oedema in Opioid Toxicity – Opioid-Induced or Naloxone-Related?"**

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**Introduction:**
Non-cardiogenic Acute Pulmonary Oedema (APO) is a rare but potentially fatal complication of opioid toxicity with naloxone as its antidote. Despite its safe nature, naloxone administration can also cause APO. We report a case of high dose naloxone administration in a methadone toxicity causing worsening APO.

**Case Presentation:**
A 57-year-old gentleman was brought to our casualty after he was found unconscious after consuming 100mls of self-purchased Methadone. In ED, his GCS was 3 with bilateral pinpoint pupils. Respiratory rate was 6 with bi-basal crepitations and spo2 of 82%. Urine toxicology was positive for Methadone. IV Naloxone 2 mg was given twice. Subsequently, GCS improved to E3V4M6 with respiratory rate of 16. Patient required a 3rd dose of IV Naloxone 2 mg after 30 mins. Subsequently, he desaturated and developed worsening crepitation up to midzone. CXR showed congested lung field and bedside ultrasound showed worsening bilateral B-lines up to mid-zone with good cardiac contractility. Patient was started on Non-invasive Ventilation and given IV Furosemide 40mg. He was admitted to ICU and completed 12 hours of Naloxone infusion.  Oxygen supplement was able to be tapered down and he was discharged after 4 days.

**Discussion:**

Opioid overdose causes APO by inducing histamine release, hypoxia, and acidosis resulting in increased permeability of the pulmonary vasculature. APO secondary to naloxone is postulated to be due to unrestricted catecholamine surge causing pulmonary vasoconstriction and hypertension. Return of the respiratory drive resulting in inspiration against an obstructed glottis also precipitates negative pressure APO. The recommended dose of naloxone is 0.4-2 mg.  Incidence of naloxone induced APO is higher when a higher or repeated doses of naloxone is used. In this patient, repeated high doses of naloxone might have caused worsening APO. Infusion of Naloxone might have been better, it has been shown to prevent recurrence of opioid induced respiratory depression, with lower risk of side effects.

**Conclusion:**
Both opioid overdose and the administration of naloxone can trigger APO. Early initiation of naloxone infusion over repeated high doses of naloxone might be more beneficial especially in a long-acting opioid toxicity such as Methadone.

**Keywords:** Opioid, Naloxone, APO