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Case Report

Naloxone Induced Pulmonary edema in a patient operated for Laparoscopic Appendectomy- a case report.

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ABSTRACT:
Naloxone induced pulmonary edema is a rare entity that can occur when Naloxone is used for treatment of opioid-induced respiratory depression in a perioperative period. The proposed mechanism includes an adrenergic crisis secondary to catecholamine surge which causes more volume shift to pulmonary vasculature, subsequently leading to pulmonary edema. Higher doses of naloxone will most commonly present with such clinical scenario. We present a case who underwent Laparoscopic Appendectomy under General Anesthesia. During the procedure, he received total Injection Fentanyl 150 mcg (0.22 mcg/kg) intraoperative and was shifted to Postoperative recovery unit after extubation. As patient was unable to maintain oxygen saturation and we suspected Opioid overdose, Injection Naloxone 0.4 mg was given intravenously as antidote. One hour later, this patient developed non- cardiogenic pulmonary edema diagnosed with chest X-ray, managed with Injection Lasix, Nebulization and Noninvasive ventilation.

Keywords: Naloxone, Pulmonary edema, opioid overdose, General anesthesia

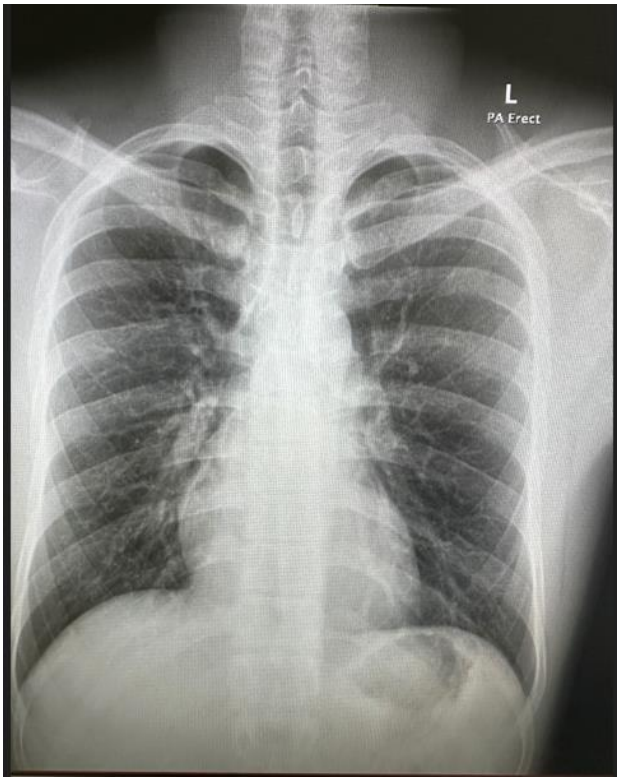
INTRODUCTION:

Naloxone is a competitive opioid receptor antagonist that is used for the reversal of opioid overdose. The adverse reactions of this drug include hypertension, ventricular arrhythmias, cardiac arrest, seizures, and rarely, pulmonary edema [1]. Naloxone-induced Pulmonary edema (NPE) is a rare but lethal complication of naloxone and has been reported scarcely in perioperative period. The pathophysiology of NPE is because of sudden increase in catecholamine release following opioid reversal, increased capillary permeability and changes in pressure gradients within pulmonary vasculature, leading to negative pressure pulmonary edema because of breathing against closed glottis. Here we report a case of NPE in a patient who underwent Laparoscopic appendectomy and developed pulmonary edema in a postoperative care unit and was given Injection Naloxone for opioid induced respiratory depression.

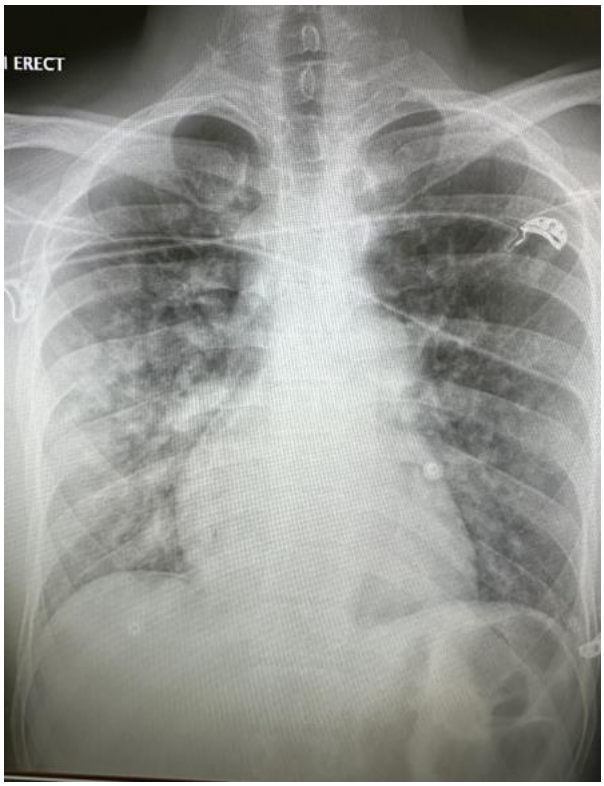
CASE REPORT:

A 23-year-old male patient, weight of 68 kg and BMI of 19.78 kg/m2 was diagnosed as acute appendicitis and was posted for laparoscopic appendectomy. Patient had no medical illness in the past, no allergies and no past surgical history. All laboratory values were within normal limits. Baseline Chest X-ray was also normal. Patient was given General anesthesia for which he received Injection Fentanyl 150 mcg, Propofol 200 mg and intubation was facilitated by Injection Rocuronium 70 mg intravenously. Patient was being continuously monitored as ASA standards including Neuromuscular monitoring and Bispectral Index (BIS) for depth of anesthesia. The duration of anesthesia starting from induction to extubation was around 2 hours. Patient was extubated with BIS above 85 and Train of four ratio of 0.9 after giving Injection Sugammadex 200 mg intravenously. Patient was shifted to recovery on oxygen by nasal prongs @2 litres per min. Modified Aldrete score (MAS) in Post Anesthesia care unit was 8. After 15 minutes, he was not maintaining oxygen saturation on pulse oximetry above 90% even with 40% venturi mask and was snoring. Suspecting respiratory depression

because of opioid overdose, Injection Naloxone 0.4 mg was given intravenously, after which the Modified Aldrete score was around 9. Within one hour of shifting to Post Anesthesia Care Unit (PACU) patient was having tachypnoea, pink frothy sputum and was restless with normal blood pressure. On physical examination, he was noted to have bilateral crackles at the lung bases. Chest X-ray showed development of multifocal pneumonitis in both lungs with increasing alveolar shadows, suggestive of cardiomegaly with pulmonary edema changes. An electrocardiogram was obtained that revealed normal sinus rhythm, and cardiac enzymes were noted to be within normal limits. The bedside echocardiogram was done by cardiologist which was normal. The patient was young, with no significant history of cardiac heart disease, and no prior history of exertional dyspnea or physical examination findings of a murmur, lower extremity edema, or jugular venous distension, giving heart failure a low probability as a cause of his clinical presentation with the preceding normal cardiac enzymes and electrocardiogram. He was given Injection furosemide 20 mg intravenous, which resulted in approximately 2 liters of urine output. He was maintained on mechanical Non-invasive Ventilation (NIV) Continuous positive airway pressure (CPAP) mode with Pressure Support of 10 and Positive End Expiratory Pressure-8, FiO2- 40%. After 2 hours, patient condition improved with no crackles in lungs on auscultation, good urine output and was able to maintain oxygen saturation above 95% on 2 liters oxygen supplementation with nasal prongs without any respiratory distress. Arterial Blood Gas (ABG) on nasal prongs @2 liters per min showed Partial Pressure of Oxygen (pO2)- 138 mm of Hg, Partial Pressure of Carbon dioxide (pCO2)- 42, pH-7.414. His Modified Aldrete score was 9 and hence discharged from Post anesthesia care unit to high dependency unit. The chest X-ray was repeated the next day which showed no signs of pulmonary edema and patient was maintaining Oxygen Saturation of 97% on room air, with no follow up from anesthesia side thereafter and discharged from hospital on 2nd postoperative day.



Preoperative Chest Xray - normal



Postoperative Chest X-ray showing Bilateral pulmonary edema

DISCUSSION:

Naloxone is a competitive opioid-receptor antagonist widely used to reverse the effects of opioid overdose by displacing opioids from their receptors. While it is highly effective, a rare but significant complication is Naloxone-induced Non-cardiogenic Pulmonary Edema (NCPE), which occurs in approximately 0.2% to 3.6% of cases [2,3]. The most common cause of pulmonary edema after naloxone administration is an adrenergic surge. This response is driven by a significant increase in

centrally mediated catecholamines triggered by naloxone [4]. The resulting catecholamine-mediated response manifests as hypertension, tachycardia, and diaphoresis [5], contributing to increased pulmonary capillary permeability and fluid accumulation in the lungs. Our patient exhibited tachypnea and tachycardia following naloxone administration, though their blood pressure remained within normal limits throughout the incident. Notably, oxygen desaturation occurred after naloxone was administered, with no evidence of hypoxia before its administration or during the preceding episode of respiratory depression. The clinical features observed are likely attributable to a catecholamine surge triggered by naloxone. This surge may have increased pulmonary capillary permeability, contributing to the development of pulmonary edema [6]. The sympathetic surge following naloxone administration involves the release of epinephrine, which antagonizes l-opioid receptors in the adrenal medulla. This increase in sympathetic outflow leads to a shift in blood volume toward the pulmonary vasculature, resulting in pulmonary vasoconstriction and pulmonary hypertension [7]. In our case, the patient showed no evidence of significant airway obstruction post-extubation, suggesting that the pulmonary edema was unlikely to have occurred independently of a triggering event. Notably, both patients with pre-existing heart disease and healthy individuals have been reported to develop this complication, even with standard naloxone dosages ranging from 0.2 to 0.4 mg or lower doses of 0.04–0.08 mg [8]. Our patient had no history of cardiac disease in the past or any other evidence of pulmonary edema or hypoxemia. The most probable diagnosis of his clinical presentation was Naloxone-induced pulmonary edema. Also, the patient was not taking any medication that could be identified as contributing to his clinical presentation. There have been many reports which suggest airway obstruction with administration of fentanyl. In a recent case report by Nasheena Jeeva et al, a 22-year-old without any comorbidities was operated on for shoulder surgery, 50 mcg of Fentanyl was administered intraoperative [9]. Naloxone 0.2 mg was given suspecting Narcotic induced respiratory depression which led to acute hypoxic respiratory failure. The patient was intubated postoperatively, and mechanical ventilation was initiated and was extubated after 6 hours. Naranjo assessment score of 6 indicates a probable relationship between the patient's symptoms and the suspect drug. Our patient received minimal fentanyl of 150 mcg at the initiation of the procedure, but he did not experience respiratory distress, or hypoxic respiratory failure until after the administration of naloxone at the end of the 2 hours procedure; therefore, fentanyl was unlikely the cause of our patient's respiratory distress. Most case reports suggest that non-cardiogenic pulmonary edema is best managed with the use of diuretics. For instance, Schwartz and Koenigsberg documented the successful resolution of naloxone-induced pulmonary edema with a combination of furosemide, nitroglycerin, and morphine sulfate [10]. Similarly, Lynn and Galinkin highlighted that this condition can often be treated with diuretics or, in some cases, the cautious administration of additional opioids to mitigate symptoms [11]. Bansal et al. reported a case where a patient experienced acute respiratory distress following naloxone administration for opioid overdose. The condition was effectively managed using intravenous furosemide, and the patient was extubated after eight hours with pulmonary infiltrates resolving [12]. To prevent such complications, securing the patient's airway prior to naloxone administration for opioid-induced respiratory depression is strongly recommended. This case underscores the potential for critical respiratory failure following naloxone use. While rare, naloxone-induced pulmonary edema is one of several adverse effects associated with the drug. Other complications include hyperalgesia, acute drug withdrawal, and circulatory instability, particularly in patients with underlying cardiac conditions [13]. Pulmonary edema, particularly when accompanied by hypoxemia and cardiac instability that is resistant to oxygen therapy, poses a significant challenge in patients unable to protect their airway in the context of opioid use. Despite this, naloxone remains the primary treatment for restoring and maintaining ventilation in patients with opioid-induced respiratory compromise [14]. The relationship between naloxone dosage and the occurrence of adverse effects such as pulmonary edema remains unclear. Therefore, the latest guidelines from the American Heart Association recommend administering the lowest effective dose of naloxone to achieve the desired therapeutic outcome [15].

Compliance with ethical standards:
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent may be requested for review from the corresponding author.

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Conflict of interest- none

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