

FENTANYL OVERDOSE INCREASES RISK OF ACUTE LUNG INJURY AND MULTIORGAN DAMAGE

Andreanne V Sannajust¹, Mohamed Basiouny¹, Emily Overley¹, Kristian Van Slyke¹, Shukuru Rushanika¹, Keller Brogdon¹, Alexander Sosa², Julie Harral¹, Jacqueline Rioux¹, Bradford Smith², Joseph Hippensteel¹, Livia A Veress¹

¹University of Colorado School of Medicine Anschutz Medical Campus, Aurora, CO

²University of Colorado Denver, Denver, CO

PURPOSE: Survivors of opioid overdose often require intensive care treatment and have recently been shown to be at higher risk for developing acute lung injury (ALI). The precise pathogenesis of and importance of naloxone reversal in ALI risk in this population is unknown. This study aimed to develop a rat model of fentanyl overdose, with and without rescue naloxone use, to investigate fentanyl and naloxone's contribution to ALI.

METHODS: Rats (male, Sprague Dawley, 250–275 g) were given a single overdose of fentanyl (0.72 mg/kg, intraperitoneal, n=13), with or without naloxone (0.4 mg/kg, intramuscular, n=8) 15 minutes after fentanyl and then monitored for 4 hours. Continuous endpoints include oxygen saturation (SpO₂), heart rate (HR), respiratory rate (RR), as well as muscle rigidity, activity, and breathing scores. Laryngospasm and respiratory secretion amounts were recorded every 30 minutes via direct visualization. At 4 hours, animals were euthanized; blood was collected for clinical chemistry and arterial blood gas (ABG) analysis. Bronchoalveolar lavage fluid was obtained from the left lung, while the right lung, liver, kidney, and heart were fixed in 4% paraformaldehyde for histopathological evaluation

RESULTS: Fentanyl overdose caused significant abnormalities within 15 minutes of exposure, including: sustained decreases in SpO₂ to 40% and RR to 50 breaths per minute (bpm); whole-body rigidity (persistent tonic/tetanic contractions) with absence of activity; shallow breathing; laryngospasm (abduction tetany); and increased oral/nasal secretions. Naloxone treatment normalized all parameters within 60 seconds of injection, except for oral/nasal secretions that continued in 4 animals. Naloxone reversal effects were sustained for 4 hours. Clinical Chemistry showed elevated liver enzymes, impaired renal function, and creatinine kinase in all animals, without improvements after naloxone. Lung wet to dry ratio was mildly elevated in all animals, without benefit from naloxone, and lung histopathology confirmed presence of mild patchy alveolar proteinaceous exudate and/or alveolar interstitial edema in >40% of fentanyl-only animals, and >60% of fentanyl plus naloxone animals.

CONCLUSION: Fentanyl overdose resulted in a multitude of abnormal clinical signs, such as hypoxemia, bradypnea, laryngospasm and whole-body tetany, all of which were reversed with naloxone treatment. Multiorgan injury was seen in all animals after fentanyl, without any benefit from naloxone treatment. Signs of ALI at 4 hours were present in several animals after fentanyl overdose, with increased ALI prevalence and severity after naloxone.