Fentanyl and Duloxetine: You Give Me Fever

Heidi Chamula and Argun Can

**Introduction:** Fentanyl is a frequently used analgesic in the ICU setting given its rapid onset, short duration of action, and minimal cardiovascular effects. In addition to binding with mu receptors to provide analgesia, it also acts as a 5-HT1A agonist, causing serotonin release and inhibition of uptake, thereby increasing synaptic serotonin levels. Given in combination with other serotonergic agents, it can induce a serotonin syndrome, as demonstrated in our patient.

**Case Presentation:** A 40-year-old man with a history of opioid dependence and anxiety disorder presented with dyspnea due to suspected bacterial pneumonia which rapidly progressed to septic shock and respiratory failure requiring mechanical ventilation. Patient was started on broad spectrum antibiotics, with fentanyl and propofol infusions for analgesia and sedation. Sputum cultures grew methicillin-sensitive Staphylococcus aureus and antibiotics were de-escalated to nafcillin. Despite appropriate antibiotic therapy, patient remained febrile up to 103.1°F with up trending leukocytosis. Infectious disease consultation was sought and patient was re-cultured and transitioned back to broad spectrum antibiotics. It was noted that patient had been started on his home medication of duloxetine on admission, and given constellation of clinical findings including high-grade fevers, agitation, diaphoresis, and volatile blood pressures, concern for serotonin syndrome was raised. A thorough neurological exam revealed ocular clonus. Duloxetine was discontinued, and within 24 hours, temperature and blood pressure normalized, and diaphoresis and ocular clonus resolved.

**Discussion:** Serotonin syndrome is a potentially life threatening condition characterized by the triad of altered mental status, neuromuscular hyperactivity, and autonomic instability. Diagnosis can be made using the Hunter Criteria, which require the presence of one of the following features or groups of features: spontaneous clonus; inducible clonus with agitation or diaphoresis; ocular clonus with agitation or diaphoresis; tremor and hyperreflexia; or hypertonia, temperature above 100.4°F, and ocular or inducible clonus. A retrospective review examining the incidence of serotonin syndrome in patients treated with fentanyl on serotonergic agents showed an 18-fold increase in incidence of serotonin syndrome compared to patients that did not receive fentanyl while on a serotonergic agent. First-line management involves withdrawal of serotonergic agents and supportive care.

**Conclusions:** Serotonin syndrome can be a diagnostic challenge because of its variable and overlapping clinical presentation. Given the increasingly large proportion of patients on serotonergic agents in the community and the frequent use of fentanyl in intensive care units, clinicians need to be aware of the increased risk for serotonin syndrome, and maintain a high index of suspicion to accurately diagnose and treat it.

**Reference #1:** Katharine M. Koury BA, Becky Tsui MD, Padama Gulur MD 2015, 'Incidence of Serotonin Syndrome in Patients Treated with Fentanyl on Serotonergic Agents', Pain Physicians 18:E27-E30


**Disclosures:** No relevant relationships by Argun Can, source=Web Response

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