A 52-year-old man with fentanyl-induced muscle rigidity

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A 52-year-old man injected a mixture of opioids intravenously at Insite, a supervised consumption facility in Vancouver. Shortly after injection, he was found by nursing staff seated with elbows flexed, fists clenched, and neck flexed and stiff; his eyes were open, but he was unresponsive to verbal stimuli or sternal rub. He was cyanotic, had a rigid chest and was not spontaneously breathing. Artificial respirations were initiated with a bag valve mask on 25 L/min of oxygen, providing partial ventilation, and 0.4 mg of naloxone was administered subcutaneously. His oxygen saturation was 84%, and his heart rate was 92 beats/min with a strong carotid pulse. Two minutes following naloxone administration, it became easier to ventilate the patient and to position his airway. His saturation had improved to 100%, and he began to take respirations with stimulation. Within six minutes, his rigidity had fully subsided, with relaxed arms and neck, he opened his eyes when spoken to and he was breathing spontaneously at a rate of eight breaths/min. The patient fully recovered without any apparent sequelae. He reported that he had injected a mixture of heroin and methadone from a new supplier.

The cooker the patient had used to prepare his drugs was transported to Health Canada's Drug Analysis Service by a member of the Vancouver Police Department. The analyzed sample was found to contain fentanyl (N-(1-phenethyl-4-piperidyl) propionanilide), but cocaine, methamphetamine, other opioids or fentanyl analogues were not detected. (In a supervised consumption setting where there are limited resources and the client has responded to the intervention, further details and toxicology are not usually obtained and hence were not available for this case report.)

Fentanyl-induced muscle rigidity was diagnosed. Although the differential diagnosis includes seizure (toxicologic, hypoxemic or hypoglycemic), dystonia caused by antidopaminergic medication, anticholinergic overdose and hemorrhagic stroke, the acute onset of symptoms following fentanyl injection, the prompt reversal with naloxone and apparent complete recovery make other diagnoses unlikely.

Discussion

The recent opioid overdose crisis in British Columbia has caused substantial morbidity and mortality. Provisional data for 2017 show that fentanyl was detected in more than 1150 deaths (81%)

KEY POINTS

- Injection of illicit fentanyl can cause fentanyl-induced muscle rigidity.
- Signs of fentanyl-induced muscle rigidity include jaw clenching and chest rigidity, which can interfere with ventilation.
- Fentanyl-induced muscle rigidity requires immediate intervention, while taking care not to induce withdrawal symptoms, which may include vomiting.
- In the community, naloxone 0.4 mg intramuscularly should be administered immediately; if no response occurs, additional doses of intramuscular naloxone should be given at two-minute intervals.

from illicit drug overdose in BC, which was more than seven times the number in 2015.[1] Although the increased potency of fentanyl relative to other opioids is likely contributory to the increased deaths, fentanyl-induced muscle rigidity, also known as "wooden chest syndrome," is a complication of intravenous injection of fentanyl and has been postulated to play a role in the increased mortality.[2] Current published literature is limited to clinical case reports in hospitals.

Fentanyl-induced muscle rigidity in the drug-injecting community in BC has been reported by paramedics attending overdoses in Vancouver and bystanders who have witnessed overdoses in the community, and documented by staff at Insite. Reports included descriptions of jaw and fist clenching, inability to insert an oral airway, chest or torso rigidity interfering with ventilation, and finger stiffness interfering with oxygen saturation monitors.

Fentanyl-induced muscle rigidity is well documented in the context of anesthesia induction in both adult and pediatric hospital settings,[3] and has also been reported during bronchoscopic procedures.[4,5] The pattern of rigidity described in the literature closely mirrors what has been observed at Insite. It is characterized by rigidity of the trunk, neck and jaw muscles after the injection of fentanyl or other synthetic, lipid-soluble opioids like acetylfentanyl, alfentanil and sufentanil.[2,5] Laryngeal spasms occur in 50%–100% of cases of fentanyl-induced muscle rigidity, depending on the dose and injection rate.[3] Decreased chest compliance and inability to open the mouth to insert an oral airway owing to masseter muscle spasm have been reported.[3] These

clinical signs lead to difficulty ventilating the patient (using a bag valve mask or otherwise) and may hasten respiratory failure independently from the central respiratory depressant effect of opioids. Hand clenching[5] and upper limb flexion with lower limb extension[3] without signs of lateralization have also been observed. These manifestations may interfere with effective resuscitation procedures for first responders in the field. Symptom onset most commonly occurs within seconds[3,4] to minutes[5] after fentanyl administration, but can take longer (hours).[6]

Management

Fentanyl-induced muscle rigidity requires immediate intervention. In the hospital setting, management of fentanyl-induced muscle rigidity has comprised treatment with short-acting neuromuscular blockade and/or naloxone to supplement assisted ventilation efforts. Several case reports describe achieving successful reversal of the syndrome with a short-acting neuromuscular blocking agent in conjunction with subsequent endotracheal intubation.[3] Some case reports describe almost immediate reversal of clinical signs with naloxone administration.[4,5,7] The effective naloxone doses given to adults in case reports varied from 0.2 mg[5] to 0.4 mg.[4] Overdose response guidelines at Insite are to administer naloxone intramuscularly; however, the subcutaneous route is sometimes used while the trained nursing staff monitor oxygen saturation and perform bag-valve-mask ventilation. In a community environment, we suggest that naloxone be given by the intramuscular route for ease of rapid administration and more consistent absorption. The dose of intramuscular naloxone needed to reverse the syndrome is unknown, as patients could be exposed to doses of fentanyl or derivatives that far exceed those therapeutically administered.

Given the lack of specialized medical resources in the community, administering intramuscular naloxone is the most important intervention to reverse the fentanyl-induced muscle rigidity, and the administration should occur as soon as possible to allow progress in resuscitation efforts. If trained first responders encounter this problem in the community, or more than one responder is available, then standard ventilation supportive measures should be initiated, even if they may only be partially effective. Although the optimal initial dose of intramuscular naloxone continues to be a matter of contention, a starting dose of 0.4 mg may be sufficient to reverse the clinical signs; additional doses of intramuscular naloxone should be given at two-minute intervals if no response occurs or until paramedics arrive.[6] The intramuscular route of administration is recommended by the BC community take-home naloxone program and the overdose prevention services guidelines.[8] It is crucial to reverse the syndrome quickly to prevent asphyxiation while taking care not to induce withdrawal symptoms, which may include vomiting, potentially complicating airway management. The patient should ideally be observed for a minimum of six hours as recommended by BC's Opioid Overdose Best Practices Guidelines for the management of symptomatic patients at high risk (see "Risk factors and prevention" below) to monitor for recurrence of overdose and muscle rigidity.[6]

If the rigidity is not reversed with naloxone, the patient may need to be intubated and neuromuscular blocking agents administered in a hospital setting as a last resort. In nonmedical settings, where there is often a lack of airway-management equipment, expertise or advanced monitoring methods, it is essential to have naloxone readily available for bystanders, first responders and other care providers in the community. Jurisdictions should ensure provision and evaluation of effective programs that provide overdose-response training and free naloxone to those who use opioids, to family and friends at risk of witnessing an overdose, and to organizations providing services to people at risk of an overdose, as well as addressing barriers to access.

Risk factors and prevention

In addition to immediate management considerations, awareness among medical professionals and the drug-injection community about risk factors for fentanyl-induced rigidity can inform safer injection practices and mitigate the chance of developing this complication. This syndrome is known to be precipitated by rapid injection and high doses of fentanyl.[2,4,5] Hospital-based case reports suggest that people over the age of 60 years may be at increased risk for fentanyl-induced muscle rigidity.[3–5] In addition, underlying neurologic (e.g., essential tremor) or metabolic illness, conditions or medications that cause a deficiency of dopamine levels, such as Parkinson disease, and use of medications that increase norepinephrine and serotonin levels, such as certain antidepressants, are associated with an increased risk.[3,4,7,9]

Prevention measures for fentanyl-induced muscle rigidity include counselling regarding risk factors. People who inject drugs should be made aware of the risk of muscle rigidity with fentanyl injection. General harm-reduction messaging should be reinforced, that is, advice to inject a small amount of a drug first, as a test, and to inject slowly. People who inject drugs are encouraged to inject where they can be observed and immediate intervention with naloxone and oxygen is available, for example, at a supervised injection site or an overdose prevention site.[10] These services should be accessible for people who inject drugs. This is especially advisable for those who are at higher risk of the complication owing to their age, medications or underlying medical comorbidities. After a traumatic event, an individual may be willing to consider treatment; opioid agonist therapy and rapid referral should be available.

Conclusion

The treatment of fentanyl-induced muscle rigidity is challenging, especially in a community setting where the fentanyl analogues and doses taken are unknown, and resources and expertise may be limited. We recommend risk-reduction measures by people who inject drugs, including access to supervised injection facilities and rapid access to treatment and opioid agonist therapy. Questions that warrant further investigation include whether fentanyl-induced muscle rigidity can occur after smoking fentanyl, whether it can recur after naloxone wears off and whether there are any genetic factors that predispose an individual to the syndrome.

References

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The section Cases presents brief case reports that convey clear, practical lessons. Preference is given to common presentations of important rare conditions, and important unusual presentations of common problems. Articles start with a case presentation (500 words maximum), and a discussion of the underlying condition follows (1000 words maximum). Visual elements (e.g., tables of the differential diagnosis, clinical features or diagnostic approach) are encouraged. Consent from patients for publication of their story is a necessity. See information for authors at www.cmaj.ca.

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