

Case Report

Acute Opioid-Induced Myoclonic Reaction after Use of Fentanyl as an Anesthetic Drug for an Emergency Cesarean Section

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Keywords

Fentanyl · Myoclonus · Opioids · Toxicity

Abstract

Myoclonus is an abnormal involuntary movement that has been previously reported with administration of high doses of opioids for prolonged periods of time. In this case, however, we report an acute myoclonic reaction and review the literature on the possible causative pathophysiology. We report the case of a 24-year-old woman who was admitted for postdated cesarean section. She started to have abnormal involuntary movements after administration of an epidural anesthesia containing 700 µg of fentanyl with 115 mL (0.5) bupivacaine and 40 mL (2%) lidocaine. Upon examination, the patient was conscious, alert, and oriented. Her vital signs were stable. Her movements can be described as generalized, sudden, involuntary, jerking movements, involving the upper limbs, head, torso as well as the lower limbs. The frequency of these jerks was about every 1–2 min lasting for 10 s. There was no change in level of consciousness during these abnormal movements. The rest of the neurological examination was normal. Laboratory values showed normoglycemia and normal serum biochemistry. A routine electroencephalogram showed no epileptiform activity. Brain imaging was normal. Based on

history, examination, and laboratory findings, we made the diagnosis of drug-induced myoclonus, which in this clinical scenario was secondary to fentanyl. We discontinued fentanyl and, gradually, the intensity and frequency of the abnormal movements decreased and disappeared after a few hours. A clear definitive explanation of the acute effect of opioids is still to be reached. It involves an interaction of complex neuroanatomical pathways and neurophysiological receptors. Nonetheless, a unanimous effort is needed to raise awareness about the role of opioids in the development of abnormal movements and their clinical management, to insure that they do not go unnoticed in the clinical scenarios, and to further add more scientific content that could help in reaching an explanatory theory.

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Introduction

Myoclonus is an abnormal involuntary movement with a shock-like character that has been previously reported with administration of high doses of opioids for prolonged periods of time. Especially in the setting of palliative care, myoclonus is usually encountered as a neuroexcitatory side effect of opioids. Previous studies have linked subsequent metabolites with the neuroexcitatory effect, resulting in the abnormal manifestation of movements. In this case, however, myoclonus developed in an acute setting: fentanyl was used for operative anesthesia for an emergency cesarean section, thus suggesting that the abnormal movements were probably due to the drug itself and not its metabolites. The pathophysiology behind such an acute reaction is still unclear but is worth exploring. In this study, we report a case of acute fentanyl-induced myoclonus and discuss the possible etiology.

Case Presentation

A 24-year-old woman, not known to have any medical illness, was admitted to King Fahd Hospital of the University, as a case of postdated pregnancy for caesarian section. Her pregnancy was going smoothly with no complications. The patient received prostaglandin (PGE2) for induction of labor, completed 3 cycles of PGE2 1 mg, and progressed to a 4-cm dilated cervix. She was put on epidural analgesia for pain management containing a total dose of 700 µg fentanyl with 115 mL (0.5) bupivacaine and 40 mL (2%) lidocaine divided interally over 4 cycles of infusion. She then progressed to an 8-cm dilated cervix, with no further progression for 2 h, so the decision was made to perform an emergency cesarean section due to failure to progress. Her operation went smoothly and was successful. After approximately 5 h of epidural insertion, the patient started to have abnormal, involuntary movements. The anesthesiologist on duty was informed immediately, evaluated the patient, and witnessed the abnormal movements. He then consulted the neurology team.

Upon examination by the neurology team, the patient was conscious, alert, and oriented. Her vital signs were stable. Her movements can be described as generalized, sudden, involuntary, jerking movements, involving the upper limbs, head, torso as well as the lower limbs. The frequency of these jerks was about every 1–2 min lasting for 10 s. There was no change in level of consciousness during these abnormal movements. The rest of the neurological examination was normal.

Laboratory values showed normoglycemia and normal serum biochemistry, including renal and liver function. A routine electroencephalogram showed no epileptiform activity. Brain

imaging was normal. Based on history, examination, and laboratory findings, we made the diagnosis of drug-induced myoclonus, which in the clinical context was secondary to fentanyl. We discontinued fentanyl and, gradually, the intensity and frequency of the abnormal movements decreased and disappeared after a few hours. Thus, no measurements of fentanyl concentration in the blood were obtained.

On follow-up examination days later, no spontaneous or stimulus-induced myoclonus was observed. The decision was made to admit the patient and she received the following medications for postoperative pain: morphine 5 mg every 8 h for 1 day, tramadol 50 mg every 12 h for 2 days, and lornoxicame 16 mg every 12 h for 2 days.

Discussion

Fentanyl is a potent opioid analgesic. In the literature, abnormal fentanyl-induced movements have rarely been encountered with the use of the drug. The manifestations of fentanyl use include but are not limited to: chest wall rigidity, seizure-like activity with normal electroencephalograms, tremors, ataxia, choreoathetosis, opisthotonus, and torticollis [1–7]. Exemplary reactions were observed exclusively with high doses of opioids, one of them being fentanyl, for prolonged periods of use [8–10]. Thus, it is not striking to find more scarcity in reports denoting such abnormal movements, to the acute administration of opioids. In the present study, we report an acute myoclonic reaction and review the literature on the possible causative pathophysiology.

It is only reasonable for us to first present the more established theory that associates the abnormal induced movements with the prolonged use of opioids to understand how the acute movements result. Several reports and *in vitro* experimental studies agreed that the neuroexcitatory effect, hence the opioid-induced myoclonus, is secondary to the build-up of several opioid metabolites such as morphine-3-glucuronide or hydromorphone-3-glucuronid in the plasma and the cerebrospinal fluid (CSF) and is not due to the direct effect of the drug itself [11, 12]. Therefore, the treatment of choice is usually through the periodic rotation of agents that reduce the individual metabolite levels in the cerebrospinal fluid [11].

The previously discussed theory resonates with the long-term effect, but not in the setting of our patient as well as a subset of cases reporting the development of opioid-induced myoclonus within a brief interval after acute administration of fentanyl. The nature of these reactions strongly suggests that the neuroexcitatory effects are not only a reaction to opioid metabolites but are induced by opioids themselves [12–14].

Emerging theories in the literature propose the involvement of opiate, serotonergic, dopaminergic, and other mechanisms, but a definitive cause is yet to be reached [15]. Thus, further scientific evidence is needed to explain the acute effect. In an attempt to reach a definitive explanation, it is also worth noting that myoclonus is not a single clinical entity, but rather a complex syndrome of diverse cause, neuroanatomic localization, and pathogenesis [16, 17].

Neuroanatomical pathways at the pontine level have been linked experimentally with the abnormal movements resulting from the central effects of opioids [18]: mainly the reticular formation with its distinct nuclei, the raphe magnus nucleus, and the locus coeruleus. The raphe magnus nucleus inhibits the neuronal activity at the posterior horn of the spinal cord upon application of small doses of opioids through the disinhibition of serotonergic neurons from inhibitory interneurons located at the nucleus.

On the other hand, the locus coeruleus has been correlated with opioid-induced rigidity, through its descending projections to the ventral horn of the spinal cord. The structures have

been believed to play a role in the manifestation of the movements seen upon opioid administration, but further work is needed to establish any theories. Thus, the final hypothesis is that the net effect of inhibition of opioids on neuronal firing results in activation of the ventral horn motor neurons and electromyographic activation in animals and thus could explain the abnormal movements [18].

Other researchers attributed the reaction to opioid antagonistic effects to the postsynaptic inhibitory glycine and gamma-amino-butyric acid (GABA) activity in the spinal cord, which further leads to depolarization of the spinal cord neurons and myoclonus [19]. Some also referred to opioid antagonistic activity of dopamine as well as the correlation between endogenous opioids and the basal ganglia disorders, which could contribute to movement disorders through extrapyramidal pathways [4, 19].

In conclusion, a clear definitive explanation of the acute effect of opioids is still to be reached. Admitting that the neuroexcitatory effects probably involve multiple neuroanatomical pathways and neurophysiological receptors, it is imposed as a rising challenge to find a clear explanation. Nonetheless, a unanimous effort is needed to raise awareness about the role of opioids in the development of abnormal movements and their clinical management, to insure that they do not go unnoticed in the clinical scenarios, and to further add more scientific content that could help in reaching an explanatory theory.

Our patient experienced an acute and uncommonly encountered neurological reaction. The abnormal reaction improved spontaneously after cessation of epidural fentanyl, suggesting it to be the cause after excluding other diagnoses. Early recognition of the syndrome and adequate treatment are crucial. If treated adequately, opioid-induced movement disorders are self-limited with few complications.

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Statement of Ethics

The authors state that informed consent has been obtained from the patient and that the study protocol has been approved by the institute's committee on human research

Disclosure Statement

No authors have any financial/conflicting interests to disclose.

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