CASE REPORT

Acute opioid withdrawal following the discontinuation of a short term epidural fentanyl infusion

Roland Kaddoum[1], Carine Foz[2], Muhammad Ibrahim[2], Doralina Anghelescu[3]

[1]Assistant Professor; [2]Resident
American University of Beirut, P. O. Box 11-0236, Riad el Solh1107,1107-2020 (Lebanon)

[3]Faculty Member, Division of Anesthesiology and Director of the Pain Management Service, St. Jude Children's research Hospital, Memphis, Tennessee (USA)

Correspondence: Dr. Roland Kaddoum, MD**,** American University of Beirut, PO Box 11-0236, Riad elSolh,1107,1107-2020; Phone: 961-1350000; FAX: 961-1745249; E-mail: rk16@aub.edu.lb.

ABSTRACT

Acute opioid withdrawal has been described after interruption of prolonged intrathecal opioids but has not been reported after discontinuation of epidural fentanyl. A 60 year old male underwent a Whipple procedure and T7 thoracic epidural was placed for postoperative pain management using bupivacaine 0.1% with fentanyl 2 μg/ml started at a rate of 6 ml/hr. On the third postoperative day the epidural was discontinued. The patient developed acute opioid withdrawal after four hours of discontinuation, to be relieved by intravenous tramadol and fentanyl. The epidural infusion was resumed and tapered down gradually over a period of 12 hrs with no recurrence of withdrawal symptoms.

Key words: Opioid withdrawal; Epidural; Fentanyl; Pain, Postoperative

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INTRODUCTION

Epidural analgesia is generally accepted as a superior modality to intravenous opioids and is the preferred method for management of postoperative pain after major surgeries.[1,2] The use of epidural fentanyl in addition to local anesthetic has been found to be associated with fewer side effects (postoperative nausea and vomiting and pruritus) than the use of morphine plus local anesthetics.[3] In our medical center, the use of a continuous infusion of 0.1% bupivacaine and fentanyl 2 μg/ml at a rate titrated to analgesic effect has become standard of care, as a safe and effective mean of providing analgesia while minimizing systemic opioids side effects.

Acute opioid withdrawal has been described in animals after reversal of intrathecal morphine with intrathecal naloxone.[4] Acute opioid withdrawal symptoms have been described after short term (3 weeks) intrathecal opioids[5]; and a protocol to prevent acute opioid withdrawal after interruption of intrathecal opioid has been described in patients with chronic pain.[6] Acute opioid withdrawal has been reported following administration of intravenous naloxone to treat pruritus after a single injection of epidural morphine.[7] To our knowledge the opioid withdrawal following discontinuation of fentanyl epidural infusion has not been reported in the literature. Here we report a case of acute opioid withdrawal following discontinuation of a short-term fentanyl epidural infusion in an opioid naïve patient. Written and verbal consents for publication were obtained from the patient.

CASE REPORT

A 60 year old male presented to our medical center with dull abdominal pain and jaundice. Extensive work up revealed a pancreatic head tumor and a Whipple procedure was performed for tumor resection. The patient weighed 83 Kg and was a known case of diabetes mellitus type II and hypertension. There was no history of cigarette smoking, alcohol consumption or opioid medications. A T7 thoracic epidural catheter was inserted before induction of general anesthesia and endotracheal intubation. Anesthetic maintenance

was achieved with intravenous and inhaled anesthetics and a continuous epidural infusion of lidocaine 1.5% at a rate of 6 ml/h, following a test dose of 3 ml lidocaine 1.5% with epinephrine 5 μg/ml. The total intraoperative fentanyl administration was limited to an induction dose of 150 μg. The surgery was uneventful and the patient was extubated fully awake and breathing spontaneously. A continuous epidural infusion of bupivacaine 0.1% with fentanyl 2 μg /ml was started at a rate of 6 ml/hr in the recovery room. Adequate pain control was achieved in the immediate postoperative period over 4 hrs with intermittent doses of intravenous fentanyl reaching a total dose of 200 μg and a gradual epidural rate increased to 12 ml/hr. During the first 3 postoperative days analgesia was provided with the epidural infusion. Pain intensity scores did not exceed 3/10 on a numeric rating scale and no intravenous opioids were necessary.

On third postoperative day, 4 hours after discontinuation of the epidural infusion, the patient experienced agitation, restlessness, profuse sweating, diffuse muscle aches, and lacrimation. The BP was 170/110 mmHg and the HR was 105/min. The patient received 75 mg of intravenous tramadol, after which the hemodynamic parameters and symptoms started to improve (BP 125/88 mmHg, HR 72/min), followed by two boluses of fentanyl 50 μg intravenously 3 minutes apart. Complete resolution of the symptoms resulted within a few minutes. A diagnosis of acute opioid withdrawal was made and the epidural infusion was resumed and tapered down gradually over a period of 12 hrs, by reducing the rate by 3 ml/hr every 3 hours, while providing additional analgesia with tramadol infusion 100 mg every 8 hours. There were no signs of recurrence of withdrawal symptoms so the epidural catheter was removed.

DISCUSSION

The opioid withdrawal syndrome is manifested by a constellation of signs and symptoms including lacrimation, mydriasis, rhinorrhea, tachycardia, nausea, vomiting, yawning, sweating, increased body temperature, tachypnea, piloerection, restlessness, muscle tremors and diarrhea.[6] Our patient experienced agitation, restlessness, profuse sweating, diffuse muscle aches, and lacrimation, all of which resolved upon administration of intravenous opioid, supporting the diagnosis of acute opioid withdrawal.

Opioid withdrawal is encountered usually after chronic systemic exposure. Tung et al described symptoms of agitation, hypertension, vomiting, tachycardia and pain in a patient after receiving a single intrathecal dose of morphine 15 hours after discontinuation of oral opioids. However, those symptoms were probably due to systemic rather than intrathecal withdrawal and resolved with administration of IV morphine.[9] Opioid withdrawal has also been described after naloxone administration for pruritus after a single epidural dose of 2 mg morphine.[7]

Stevens et al[10] showed that the continued administration of opioid agonists to experimental animals leads to the development of tolerance to the agonist effects and opioid dependence. Studies on acute opioid dependence in humans suggest that physiological adaptive changes begin even with the first exposure to opioids,[11,12] and that a short duration of opioid receptor occupancy by the agonist is necessary for the development of acute physical dependence. Our patient developed withdrawal signs after discontinuation of the epidural fentanyl that he received for only 3 days. Clinically, a short epidural infusion period is very unlikely to incur physical dependence; however, in our patient characteristics of opioid withdrawal appeared within 4 hours of discontinuation of the epidural infusion. In our medical center where epidural bupivacaine with fentanyl is the standard of care after major abdominal surgeries, withdrawal was never encountered after discontinuation. Although withdrawal symptoms have been reported to exhibit individual differences, both in intensity and patterns.[13]

It is a common practice in our center to discontinue the epidural infusion abruptly and provide supplemental analgesia by intravenous patient-controlled analgesia, if required. Our patient's epidural was running at 12 ml/h which total 24 μg/h of fentanyl. It would have been prudent to gradually decrease the epidural infusion rate over few hours before discontinuation. This could have prevented such incident.

Devulder et al reported signs of opioid withdrawal 5 days after intrathecal morphine due to catheter dislodgment and failure of continuous morphine administration via infusion pump.[5] Another study described withdrawal symptoms and loss of pain control due to intrathecal morphine pump failure in a patient with long standing failed back syndrome.[14] Taha et al also described symptoms of withdrawal in 24% of patients receiving intrathecal morphine through SynchroMed pumps at drug

residual volumes less than 4 ml.[15] Jackson et al described the first intentional intrathecal opioid withdrawal following a protocol using clonidine and IM buprenorphine. The symptom constellation was distinct in intrathecal from the systemic opioid withdrawal, as it lacked GI and other peripheral side effects.[6] Our patient lacked GI symptoms and only presented with lacrimation, muscle aches and diffuse sweating. The symptoms were easily controlled by restarting fentanyl infusion to be tapered off gradually.

CONCLUSION

Knowledge of the pathophysiology of neuraxial as well as systemic opioid withdrawal is still evolving, and future work needs to clarify the mechanism of opioid neuraxial withdrawal.

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