Dexmedetomidine Infusion to Facilitate Opioid Detoxification and Withdrawal in a Patient with Chronic Opioid Abuse

Surjya Prasad Upadhyay, Piyush Narayan Mallick, Waleed Mohamed Elmatite, Manish Jagia, Salah Taqi

Department of Anaesthesiology and Critical Care, Al Jahra Hospital, Ministry of Health, Kuwait City, Kuwait

Address for correspondence: Dr. Surjya Prasad Upadhyay; E-mail: usurjya@rediffmail.com

ABSTRACT

Many patients are admitted to the intensive care unit (ICU) for acute intoxication, serious complication of overdose, or withdrawal symptoms of illicit drugs. An acute withdrawal of drugs with addiction potential is associated with a sympathetic overactivity leading to marked psychomimetic disturbances. Acute intoxication or withdrawal of such drugs is often associated with life-threatening complications which require ICU admission and necessitate prolonged sedative analgesic medications, weaning from which is often complicated by withdrawal and other psychomimetic symptoms. Dexmedetomidine, an alpha-2 (α_2) agonist, has been used successfully to facilitate withdrawal and detoxification of various drugs and also to control delirium in ICU patients. Herein, we report a case of a chronic opioid abuse (heroin) patient admitted with acute overdose complications leading to a prolonged ICU course requiring sedative–analgesic medication; the drug withdrawal-related symptoms further complicated the weaning process. Dexmedetomidine infusion was successfully used as a sedative–analgesic to control the withdrawal-related psychomimetic symptoms and to facilitate smooth detoxification and weaning from opioid and other sedatives.

Key words: Dexmedetomedine, Facilitate, Opioid dependence, Substance abuse, Withdrawal symptoms

INTRODUCTION

Substance abuse often leads to emergency hospital admission for various life-threatening symptoms. The presenting symptoms are often multiple, misdiagnosed, and often inconsistent because of variable dosage and adulteration of drugs, a mixed intoxication–withdrawal state, and sometimes adverse or idiosyncratic reactions. An acute withdrawal of these illicit drugs is associated with agitation, restlessness, insomnia, generalized muscle and joint pain anxiety, dysphoria, and various psychomimetic disturbances,[1] and most of these symptoms are caused by central nervous system (CNS) hyperactivity and are very distressing which frequently lead to relapse to drug use.[2,3] Acute intoxication and withdrawal of some illicit drugs are often associated with severe and life-threatening complications such as rhabdomyolysis,[4] acute renal failure,[4,5] neurological complication,[5] acute pulmonary edema,[6] ARDS,[6,7] etc., which not only prolonged the intensive care unit (ICU) stay but also made the withdrawal and detoxification process complex. In addition, critically ill patients who received long-term sedative–analgesic therapy in ICU developed functional tolerance and experienced withdrawal symptoms similar to those patients addicted to narcotics, alcohol, or other stimulant drugs.[8-10] So far we do not have standard guidelines or recommendations on the use of sedation–analgesia in patients with drug addiction problems or who are prone to have addiction potential.

Access this article online

Quick Response Code:

Website: www.jpalliativecare.com

DOI: 10.4103/0973-1075.92353

Dexmedetomidine has been gaining popularity in controlling withdrawal symptoms associated with varieties of substance abuse and dependences and has been successfully used to facilitate withdrawal of prolonged sedation in ICU.[1,2,10-14]

We are reporting a case of an acute, severe overdose of an opioid (heroin) in an opioid addict complicated by rhabdomyolysis leading to acute renal failure and later development of adult respiratory distress syndrome (ARDS) which leads to a prolonged ICU stay in which prolonged dexmedetomidine was used to facilitate the withdrawal process.

CASE REPORT

A 32-year-old male, addicted to heroin for 3 years, was found in a semiconscious, unresponsive state in his room and brought in a state of shock with gasping respiration by family members to the emergency room. He was hypothermic, hypotensive with blood pressure 70/45 mmHg, a heart rate of 128 per min, shallow respiration with a rate of 12/min, and hypoxemic with oxygen saturation 88% on 10 liter per min oxygen. Initial evaluation was suggestive of an acute opioid overdose as the patient was a known heroin addict; there were pinpoint pupils with hypoventilation and hypothermia. A blood sample was sent to the toxicology laboratory. After 0.4 mg of intravenous naloxone in increments of 0.1 mg boluses, patient's sensorium level improved and respiration became more normal with an improvement in oxygen saturation, but he remained hypotensive. Fluid resuscitation was continued, vasopressor (noradrenaline infusion) added, and an infusion of naloxone was started. The patient was shifted to the ICU for further observation and treatment. Blood gas analysis showed persistent metabolic acidosis. Hematological parameters were normal but biochemistry revealed signs of acute rhabdomyolysis with a marked rise in the creatinine kinase level, hyperkalemia, and high blood urea nitrogen (BUN) and creatinine. Aggressive hydration with alkalinazation and forced diuresis was started. Despite the aggressive therapy for about 3 h, the patient went into anuria with a marked rise in creatinine. The patient started to agitate, and become restless with a complaint of generalized body and joint pain and his respiration became labored; auscultation revealed bilateral diffuse crepitation. The patient was intubated and connected to a mechanical ventilator with propofol and remifentanil infusion as sedative-analgesic. An urgent chest X ray confirmed acute pulmonary edema. Nephrology consultation was sought for urgent dialysis; naloxone infusion was stopped. Although the metabolic parameters improved after urgent dialysis, the ventilatory parameters worsened requiring higher amounts of oxygen and a higher level of positive end expiratory pressure (PEEP). Echocardiographic evaluation revealed a normal cardiac function. The lung condition worsened further over the next couple of days with severe hypoxemia consistent with ARDS. The patient was managed with a lung protective ventilatory strategy with the infusion of methyl prednisolone 1 mg/kg/day along with other supportive care in the form of regular dialysis, antibiotics, nutritional support, chest physiotherapy, etc. In view of the prolonged ventilatory support, the sedation–analgesia regime was changed into midazolam and morphine. After about 10 days, respiratory parameters were gradually improved, and the kidney function started to recover. The patient was successfully extubated and liberated from the ventilator when he passed the spontaneous breathing trial (SBT) on day 15. Few hours after extubation, the patient started to show signs of opioid withdrawal with agitation, generalized aches and pain all over the body, lacrymation, increasing restlessness, tachypnea, tachycardia, and hypertension. The trial of intravenous haloperidol failed to control his agitation. He was reloaded with a short-acting opioid, remifentanil, to which he responded; psychomimetic and other physical symptoms were modestly controlled with 400 μg/h of remifentanil, but he required increasing doses of remifentanil and was restless and agitated on the slightest reduction of remifentanil infusion. The trial of midazolam and propofol infusion failed to reduce the remifentanil requirement. On day 18, dexmedetomedine infusion was added after a loading dose of 50 μg over 30 min, and remifentanil infusion was successfully tapered off over 4 h. The patient was managed with a continuous infusion of dexmedetomidine 0.7 μg/kg/h, and lorazepam was added for night comfort. On day 5 of dexmedetomidine infusion, we gave oral clonidine 25 μg every 4 h to the patient and slowly tapered off dexmedetomidine over the next 2 days. He remained conscious, oriented, and calm throughout the dexmedetomidine treatment. Finally, he was shifted to a rehabilitation center on oral clonidine.

DISCUSSION

One of the problems encountered while treating critical illness in patients on ventilators who are already addicted to opioids or other drugs of abuse is the development of dependence and withdrawal process itself; these patients are prone to develop delirium in ICU. Unfortunately, the drugs of choice such as benzodiazepine and opioids are

similar to ones that are abused. Once patient's primary condition improved, a smooth withdrawal of the sedative–analgesic without psychomimetic symptoms became the limiting factor for the recovery of the patient. An alpha-2 (α_2) agonist has been successfully used to attenuate the hypertension, tachycardia, agitation, anxiety, and fever occurring during the withdrawal of benzodiazepine and the opioid.[14-18] Clonidine has been used to attenuate the symptoms of withdrawal from alcohol, narcotics, and naloxone-induced hypertension for more than 20 years. Dexmedetomidine, a selective α_2-adrenergic agonist with an affinity eight times more than that of clonidine, results in more selective α_2 activation and exerts the desired effects of sedation, analgesia, anxiolysis, and sympatholysis with less respiratory depression[13] and negligible effects on α_1 stimulation,[19] and it has been used to facilitate the withdrawal of various drug dependencies such as alcohol,[20,21] cocaine,[17,22] opioid,[11,12,19] and benzodiazepine.[12] It has also been used successfully even in infants to detoxify opioid and benzodiazepine sedation.[12]

The mechanism of dexmedetomidine in controlling the withdrawal of opioids is poorly understood but it is hypothesized that the withdrawal from narcotics is characterized by a hyperadrenergic state: the α_2 agonist decreases the sympathetic outflow and adrenergic activity counteracting the physiological effects of the withdrawal and these effects are largely mediated by postsynaptic α_{2A} subtype receptors in the locus ceruleus.[23-25] The α_2 agonist and opioid act synergistically on the central sympathetic outflow.[26] The mechanism of how dexmedetomidine enhances the opioid analgesia is not yet clear. The potentiating effects of the α_2 agonist on morphine reduce the amount of the opioid needed and a low dose of the opioid may be effective for a long period.[27] There are some evidences that the α_2 agonist induced antinociception results by the acetylcholine release inhibiting nociceptive neurons in the spinal cord.[27]

In summary, our observation suggests that dexmedetomidine infusion facilitated the opioid withdrawal and control of opioid withdrawal symptoms in an opioid-dependent patient without causing either significant neurological or respiratory depression. Dexmedetomidine may also be useful in the management of opioid-induced hyperalgesia and iatrogenic-induced tolerance seen in patients maintained on opioid therapy for chronic painful conditions. A further study with a larger sample size is needed to explore its potential in the management of opioid tolerance or dependence and also to facilitate opioid withdrawal.

REFERENCES

1. Maccioli GA. Dexmedetomidine to facilitate drug withdrawal. Anesthesiology 2003;98:575-7.
2. O'Connor PG, Kosten TR, Stine SM. Management of opioid intoxication and withdrawal. In: Graham AW, Schultz TK, Mayo-Smith MF, *et al*, editor. Principles of addiction medicine. 3rd ed. Chevy Chase (MD): American Society of Addiction Medicine; 2003. p. 651-68.
3. Jaffe JH. Drug addiction and drug abuse. In: Gilman AG, Rall TW, Nies AS, Taylor P editors. Goodman and Gilman's the pharmacological basis of therapeutics. 8th ed. New York: Pergamon Press; 1990. p. 522-73.
4. Deighan CJ, Wong KM, Mclaughlin KJ, Harden P. Rhabdomyolysis and acute renal failure resulting from alcohol and drug abuse. QJM 2000;93: 29-33.
5. Kumar R, West DM, Jingree M, Laurance AS. Unusual consequences of heroin overdose: rhabdomyolysis, acute renal failure, paraplegia and hypercalcemia. Br J Anaesth 1999;83:496-8.
6. Wilson KC, Saukkonen JJ. Acute respiratory failure from abused substances. J Intensive Care Med 2004;19:183-93.
7. Ridgway ZA, Pountney AJ. Acute respiratory distress syndrome induced by oral methadone managed with non-invasive ventilation. Emerg Med J 2007;24:681.
8. Jenkins DH. Substance abuse and withdrawal in the intensive care unit: Contemporary issues. Surg Clin North Am 2000;80:1033-53.
9. Tobias JD. Tolerance, withdrawal, and physical dependency after long-term sedation and analgesia of children in the pediatric intensive care unit. Crit Care Med 2000;28:2122-32.
10. Littler C, Scobie SD, Shelly MP. Withdrawal of sedation after long term ventilation on the intensive care unit. Clin Intensive Care 1995;6:83-5.
11. Belgrade M, Hall S. Dexmedetomidine infusion for the management of opioid induced hyperalgesia. Pain Med 2010;11:1819-26.
12. Finkel JC, Elrefai A. The use of dexmedetomidine to facilitate opioid and benzodiazepine detoxification in an infant. Anesth Analg 2004;98:1658-9, table of contents.
13. Rahman RA, Azmi MH, Ishak NH, Manap NA, Zain JM. The use of dexmedetomidine for refractory agitation in substance abuse patient. Crit Care Shock 2010;13:59-60.
14. Multz AS. Prolonged dexmedetomidine infusion as an adjunct in treating sedation-induced withdrawal. Anesth Analg 2003;96:1054-5, table of contents.
15. Shafer A. Complications of sedation with midazolam in the intensive care unit and a comparison with other sedative regimens. Crit Care Med 1998;26:947-56.
16. Ghignone M, Quintin L, Duke PC, Kehler CH, Calvillo O. Effects of clonidine on narcotic requirements and hemodynamic response during induction of fentanyl anesthesia and endotracheal intubation. Anesthesiology 1986;64:36-42.
17. Kersten JR, Pagel PS, Hettrick DA, Warltier DC. Dexmedetomidine partially attenuates the sympathetically mediated systemic and coronary hemodynamic effects of cocaine. Anesth Analg 1995;80:114-21.
18. Baddigam K, Russo P, Russo J, Tobias JD. Dexmedetomidine in the treatment of withdrawal syndrome in cardiothoracic surgery patients. J Intensive Care Med 2005;20:118-23.
19. Virtanen R, Savola JM, Saano V, Nyman L. Characterization of the selectivity, specificity and potency of medetomedine as an alpha 2-adrenoreceptor agonist. Eur J Pharmacol 1988;150:9-14.
20. Rovasalo A, Tohmo H, Aantaa R, Kettunen E, Palojoki R. Dexmedetomidine as an adjuvant in the treatment of alcohol withdrawal delirium: A case report. Gen Hosp Psychiatry 2006;28:362-3.
21. Darrouj J, Puri N, Prince E, Lomonaco A, Spevetz A, Gerber DR. Dexmedetomidine infusion as adjunctive therapy to benzodiazepines for acute alcohol withdrawal. Ann Pharmacother 2008;42:1703-5.
22. Kontak AC, Wang Z, Arbique D, Victor RG. Central sympatholysis with dexmedetomidine is an effective countermeasure for cocaine-induced sympathetic activation and peripheral vasoconstriction in chronic cocaine abusers. Circulation 2009;120:S1178.
23. Coupar IM. Effect of alpha-2 adrenoceptor agonists on the expression of morphine withdrawal in rats. Naunyn Schmiedebergs Arch Pharmacol

1992;345:553-7.
24. Lidbrink P. The effect of lesions of ascending noradrenaline pathways on sleep and waking in the rat. Brain Res 1974;74:19-40.
25. Glass MJ, Pickel VM. Alpha(2A)-adrenergic receptors are present in mu-opioid receptor containing neurons in rat medial nucleus tractus solitarius. Synapse 2002;43:208-18.
26. Maze M, Virtanen R, Daunt D, Banks SJ, Stover EP, Feldman D. Effects of dexmedetomidine, a novel imidazole sedative-anesthetic agent, on adrenal steroidogenesis: *In vivo* and *in vitro* studies. Anesth Analg 1991;73:204-8.
27. Meert TF, De Kock M. Potentiation of the analgesic properties of fentanyl-like opioids with alpha 2-adrenoceptor agonists in rats. Anesthesiology 1994;81:677-88.

How to cite this article: Upadhyay SP, Mallick PN, Elmatite WM, Jagia M, Taqi S. Dexmedetomidine infusion to facilitate opioid detoxification and withdrawal in a patient with chronic opioid abuse. Indian J Palliat Care 2011;17:251-4.

Source of Support: Nil. **Conflict of Interest:** None declared.