

Case Report

Opioid Withdrawal Presenting as Delirium and Role of Buprenorphine: A Case Series

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ABSTRACT

Opioid withdrawal is very rarely characterized by delirium unlike alcohol or benzodiazepine withdrawal. PubMed search through October 2016 reveals only two case series on delirium as feature of withdrawal in opioid dependence syndrome. We report two cases of opioid withdrawal (heroin) presenting with delirium when low-dose buprenorphine (2 mg/day) was added. Both the cases had no other substance abuse history and nil contributory past and family history. Both of them were improved after increasing the buprenorphine dosage to 6–8 mg/day. The possibility of delirium as a part of withdrawal symptom or as a phenomenon induced by buprenorphine or due to impurities in the heroin used is discussed.

Key words: *Buprenorphine, delirium, heroin withdrawal, opioid withdrawal, opioid withdrawal delirium*

INTRODUCTION

Opioids withdrawal is characterized by pupillary dilatation, severe muscle cramps, profuse diarrhea, abdominal cramps, yawning, piloerection, rhinorrhea, lacrimation, hypertension, tachycardia, and temperature dysregulation.^[1] Rarely, delirium has been reported as a feature of opioid withdrawal. PubMed search through October 2016 reveals only two case series on delirium as feature of withdrawal in opioid dependence syndrome.^[1,2] Here, we present two cases of opioid withdrawal that went into delirium after low-dose buprenorphine was added.

CASE REPORTS

Case 1

A 26-year-old married male Muslim from lower socioeconomic background, working as a rickshaw puller till 3 years back, presented to us with an 8-year history of regular use of heroin (smack).

The patient started working as a rickshaw puller at the age of 17 and was introduced to heroin at the age of 18 years by his fellow rickshaw pullers. Initially, he used to take it for pleasure and for increasing his working

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capacity. He used to take the street heroin, popularly called “Brown Sugar (BS),” by chasing method. Initially, he used 100–400 rupees worth of heroin per day and developed dependence pattern of use over next 1 year or so. Gradually over next 3–4 years, his use increased to 1000–2500 rupees worth BS per day. To meet with his rising expenditure for heroin, he started stealing from his household, which gradually progressed to stealing from neighbors. Since last 4 years, stealing from others was his main livelihood. He was brought to us by his wife and brothers for treatment forcefully. At the time of admission, he was abstinent from heroin for 3 days. At the time of admission, his Clinical Opiate Withdrawal Scale (COWS) score was 8. On the 2nd day of admission (i.e., day 4 of withdrawal), his withdrawals increased (COWS score becoming 26). He was started on sublingual buprenorphine and naloxone combination (2 mg + 0.5 mg) (since the combination rather than plain buprenorphine was hospital supply) once daily. By day 3 of admission (day 5 of withdrawal), he exhibited delirium like picture as he became agitated, restless, confused, disoriented to time, place, and person, and fearful with altered sleep-wake pattern and irrelevant speech.

Case 2

A 29-year-old unmarried male Hindu patient working as a driver presented with a 6-year history of regular heroin (smack) use by chasing method. He started using it under peer pressure and became dependent within a few months of use. Average daily consumption was between 1000 and 2000 rupees per day. For the past 2–3 years, he was irregular at work, found lying on streets in an intoxicated state, and often became aggressive and abusive toward family members after intoxication. He often threatened his family members and pressurized them into giving money for his drug abuse. He was forcibly taken for treatment by the family members after 4 days of abstinence when he started showing symptoms of withdrawal such as myalgia, lacrimation, rhinorrhea, and diarrhea. The treating psychiatrist prescribed him 2 mg of buprenorphine per day sublingually following which he presented with symptoms of delirium. On the 2nd day of delirium (5th day of withdrawal), he was brought to our hospital. At the time of admission, he was disoriented to time, place, and person, agitated, confused, and fearful.

In both the cases, the family members corroborated that there was no history of any other substance of abuse except the regular use of tobacco in the form of gutka. There was no history of injectable drug use, head injury, seizure disorder, high fever, or altered sensorium in the past. There was no past or family history suggestive of any psychiatric or neurological illness in either of them.

The routine investigations including a complete hemogram, random blood sugar, liver function test, renal function test, thyroid function test, serum electrolytes, urine analysis, chest X-ray, and electrocardiogram were within normal limits in both cases.

A diagnosis of mental and behavioral disorders due to the use of opioids; acute withdrawal with delirium was made. Since no other substance of abuse was suspected for causing the delirium, the dose of buprenorphine was increased from 2 mg/day to 6 mg/day sublingually over 24 h after the appearance of delirium apart from supportive management in the form of intravenous fluids and analgesics (ibuprofen 400 mg twice daily). The symptoms started showing response to therapy in both cases within 24 h of 6 mg buprenorphine per day. It was further increased to 8 mg per day and maintained at the same level. The delirium subsided after 48–72 h of initiating buprenorphine at 6–8 mg/day.

The opioid replacement therapy with buprenorphine-naloxone combination was continued along with motivation enhancement therapy, cognitive behavior therapy, problem-solving skill training, and supportive psychotherapy for 3 weeks after which the patients were discharged in a stable condition with a maintenance dose of 6–8 mg buprenorphine-naloxone combination per day. Both of them are currently on follow-up with us for past 3–5 months and are abstinent since discharge from the hospital.

DISCUSSION

In both the cases, the clinical picture was suggestive of delirium (The International Classification of Diseases, Tenth Edition). The absence of any head injury, loss of consciousness, and high fever along with no history of any other substance abuse pointed toward delirium precipitated by opioid withdrawal. The negative laboratory investigations were also supportive of the above. Moreover, the response of the symptoms to buprenorphine alone confirmed the diagnosis.

Complicated withdrawal with seizures and delirium are common in alcohol and benzodiazepine withdrawal. Neonatal abstinence syndrome in infants of opioid-dependent mothers is known to cause epileptiform activity with seizures due to opioid withdrawal.^[3] Seizures during opioid withdrawal in opioid dependence syndrome patients have also been reported.^[4] A high incidence of delirium (20% over a period of 1 year) following rapid opioid detoxification with naltrexone and clonidine has been reported in methadone-dependent patients.^[5] Delirium has been reported as adverse events in terminal patients treated with opioids.^[6] An imbalance in

the cholinergic/dopaminergic systems in the central nervous system is thought to be the mechanism by which opioids induce delirium. Electrophysiological and behavioral studies show that morphine and other opioids inhibit central cholinergic activity in various cortical and subcortical brain areas.^[7] Whether opioid withdrawal leads to a complex shift in receptor dynamics precipitating delirium and seizures is a matter of speculation at this point.

The incidence and prevalence of opioid withdrawal delirium are unknown worldwide, with very few case reports available for the same.^[1,2]

Curiously, in both our cases, delirium was precipitated after low-dose buprenorphine was started in an opioid withdrawal state. Buprenorphine has been rarely reported to induce delirium, which subsided after withdrawing buprenorphine.^[8,9] It has been speculated to cause such an effect by possible excitatory or disinhibitory effect on limbic and extrapyramidal systems or an increase in beta-endorphin in corpus striatum or by altering serotonergic or cholinergic pathways.^[9]

Since both the cases were already in significant opioid withdrawal, the buprenorphine acting as an antagonist thereby precipitating withdrawal and delirium appears remote.

An alternative explanation may be the presence of impurities in the heroin used may give rise to the withdrawal delirium, but unfortunately, since urine toxicology screening was not available at our hospital, we could not confirm the same.

However, since both the cases responded to increase in buprenorphine dose, used alone without any benzodiazepine or other medications, it can be speculated that the delirium was caused by opioid withdrawal.

The idea behind reporting the same is to increase awareness about an atypical manifestation of a very common clinical condition (opioid withdrawal).

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Conflicts of interest

There are no conflicts of interest.

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