

CASE REPORT

Naltrexone-Precipitated Delirium

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Abstract

Naltrexone is a long acting opioid antagonist, administration of which to opioid dependent patients within 12 hours of last intake results in an immediate 'withdrawal syndrome' often of considerable severity characterized by unremitting vomiting, diarrhoea, agitation, dysphoria and abdominal cramps lasting many hours. Rarely, delirium and psychotic episodes have also been reported. We report a case of opioid dependence, who developed delirium while receiving naltrexone (German J Psychiatry 2005;8:101-103).

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Introduction

Naltrexone is nonspecific, competitive, long acting opioid antagonist used in maintenance treatment of detoxified opioid dependent patients. Since 1984, it has been used as a pharmacoprophylactic agent for opioids. Since 1997, accelerated (or "rapid") detoxification has been vigorously promoted as part of a "cure" for opioid dependence⁴. In rapid detoxification the process of withdrawal is speeded up with an opioid antagonist such as naltrexone, which precipitates a more severe but relatively briefer withdrawal.

In India many of the patients receive pharmaco-prophylaxis with naltrexone, either on their own initiative or under the pressure of family. Patients, who are poorly motivated, frequently experiment with opioids and many of them undergo "accidental rapid detoxification" and develop complications like delirium. We report a case of opioid dependence, who developed delirium on receiving naltrexone, while he had already taken an opioid and discuss the associated issues.

Case Report

A 22 yr old, male, single, educated upto class VIII, driver by profession presented with a history of nicotine dependence for 7 years, opioid dependence (Heroin) for 1½ years, alcohol dependence for past 1 year, resulting in severe occupational dysfunction, in the form of absenteeism, unpunctuality, fights with colleagues, repeated risk taking behavior in the form of unprotected sexual intercourse with commercial sex workers, driving under the influence of both alcohol and heroin even after repeated accidents and warnings, resulting in frequent conflict with the law. The patient was brought by family members for de-addiction, had superficial motivation to quit heroin, underwent opioid detoxification as an outpatient and after counselling and negative urinalysis by Thin Layer Chromatography for opioids, was started on naltrexone 50 mg/day.

For initial 2 weeks, the patient took naltrexone under supervision of his mother and maintained abstinent /sober state, both in relation to heroin and alcohol. After this, the patient

relapsed and restarted using heroin, though irregularly. Initially, the patient did not perceive the pleasurable effect with heroin. As a result, he increased the dose of heroin. Gradually the patient became irregular with naltrexone and kept on taking heroin. Whenever he took naltrexone 24 hours after last dose of heroin, he would have mild withdrawal symptoms in the form of lacrimation, yawning, aches and pains. To overcome the same, he would take alcohol. During this period, while coming for follow-up, he denied use of any opioids, but his mother reported that she was not able to supervise the naltrexone regularly.

After about 5 weeks of starting naltrexone the patient was brought to follow-up with complaints of confusion, agitation, odd behavior of 2 days duration. Exploration revealed that the patient had chased an unspecified amount of heroin, about 14 hours prior to receiving naltrexone 50 mg from his sister. Within 2 hrs of receiving naltrexone, the patient was found to be restless, agitated, confused, disoriented to time, place and person, had hallucinatory behavior (visual, auditory and tactile) and was fearful. He also repeatedly visited the toilet for repeated loose motions. History did not reveal any evidence of head injury, seizures, fever, hypertension or diabetes mellitus. His last intake of alcohol was about 10 days prior to onset of the above symptoms.

On physical examination, the patient was afebrile, had BP-130/90 mm of Hg, pulse 100/ min regular, respiratory rate 24/min regular, pupils bilaterally mid dilated but reacting to light. Systemic examination did not reveal any abnormality. His Mini Mental Status Examination (MMSE) score was 15 out of 27 (had poor attention & concentration, poor registration and immediate memory, and was disoriented to time and place). On mental state examination, the patient was tidy but ill kempt, fearful, hypervigilant, had visual and tactile hallucinations. The patient was immediately admitted in the emergency and his investigations in the form of blood urea and creatinine, serum electrolytes, haemogram, liver function tests, arterial blood gas measurements, chest X-ray, ECG, computed tomography of brain were found to be normal. Provisional diagnosis of naltrexone-precipitated delirium was considered. Naltrexone was discontinued immediately, and the patient was started on risperidone 1mg per day and admitted to de-addiction centre. The patient was kept under supervision with regular monitoring of vital parameters and his cognitive functions were monitored using serial MMSEs. Over the next 7 days, his cognitive functions improved (MMSE score increased from 15 to 30). After complete recovery, patient disclosed that he had used heroin about 14 hours prior to receiving naltrexone as discussed earlier, and he had not protested to take naltrexone to hide his drug taking behavior.

While in the ward, the patient was psycho-educated, was explained about the course of the illness, lapse and relapse, underwent motivation enhancement therapy and relapse prevention counselling was done. Patient's family was also psychoeducated about the illness and early signs of lapse and relapse. Psychosocial intervention including a change of profession was planned in consultation with the family members. After ensuring proper supervision and being explained interaction of naltrexone with opioids, the patient was restarted on naltrexone 50 mg/day with weekly follow-

up along with regular toxicological analysis. The patient has been maintaining abstinence since discharge (7 months).

Discussion

Naltrexone is a nonspecific competitive opioid receptor antagonist, which binds to all the three types of receptors (μ, κ, δ) in a dose dependent manner. Naltrexone was approved by the U.S Food and Drug Administration in 1984 for providing blockade of effects of exogenously ingested opioids in detoxified opioid addicts. Administration of naltrexone to opioid dependent patient within 12 hours of last intake results in an immediate 'withdrawal syndrome' often of considerable severity characterized by unremitting vomiting, diarrhoea, abdominal cramps lasting many hours, agitation, dysphoria, delirium and rarely psychotic features. Delirium can last for up to 12 hours. The major factor associated with the severity of precipitated withdrawal is recency of opioid use – the greater the interval between opioid use and administration of naltrexone, the less severe is the precipitated withdrawal. This is because the severity of precipitated withdrawal is proportional to the amount of drug (heroin). The severity of precipitated withdrawal also depends upon the level of dependence; thus people with high opioid tolerance experience more severe precipitated withdrawal. Management of precipitated withdrawal is supportive, with sedation (benzodiazepines if there is no evidence of delirium), antiemetics (ondansetron), IV fluid in case of impending dehydration and non-opioid analgesia (non-steroidal preparations). Delirium is managed with low-dose antipsychotics (risperidone, haloperidol). Life threatening opioid intoxications can also result if the patient tries to surmount the blockade with excessive use of opioids leading to respiratory failure and cardiovascular collapse¹. Reports of acute opioid withdrawal precipitated by naltrexone are increasingly being reported in literature^{2,3,5}, which emphasizes the need for better patient selection, adequate counselling, awareness of family members regarding the need for supervision and regular follow up.

The need for pharmacoprophylaxis cannot be overemphasized in present treatment scenario, but adequate counselling of the patient, awareness of family members and awareness of physicians involved in emergency care are warranted. It is advised to start naltrexone only after completion of 7-10 days of complete opioid abstinence in routine detoxification⁴ or 48 hours period in case of rapid opioid detoxification⁶.

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