

UNINTENTIONAL RAPID OPIOID DETOXIFICATION: CASE REPORT

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SUMMARY

Background: Naltrexone is a competitive opioid antagonist and is often used to maintain abstinence in detoxified opioid dependent patients. However, it can precipitate an accelerated withdrawal when ingested by an individual with concurrent opioid use.

Methods: We report the case of a 28 year old male with opioid dependence syndrome presenting with chaotic symptoms following ingestion of naltrexone. Symptomatology, management is described and literature in this area is reviewed.

Results: Accidental or surreptitious ingestion of naltrexone in a patient with concurrent opioid use can precipitate symptoms typical of opioid withdrawal in addition to other varying symptomatology. Most cases would require sedation and management of concurrent vomiting and diarrhoea.

Conclusions: Clinicians, especially those providing substance abuse and emergency care, need to be aware of the possibility of an accelerated and possibly life threatening withdrawal associated with naltrexone ingestion in an incompletely detoxified patient with opioid dependence.

Key words: addiction – detoxification – emergency – opioid - naltrexone

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INTRODUCTION

Naltrexone is a pure opioid antagonist and acts a competitive antagonist at opioid receptor sites (Fuller & Sajatovic 2005). It is commonly used to prevent relapse in detoxified opioid dependent patients or to complete the process of detoxification under anaesthesia as a part of a procedure called ultra rapid opioid detoxification (UROD) (Rabinowitz et al. 2002). If ingested by an individual who is simultaneously using opioids, it can precipitate an immediate withdrawal - which may have potentially dangerous consequences (Fuller & Sajatovic 2005, Quigley 2001). We report the case of a 28 year old opioid dependent male who presented with symptoms of opioid withdrawal following ingestion of naltrexone and review the literature in this area.

CASE REPORT

A 28 year old male was brought by his relatives to the casualty after having been given 25

mg of Naltrexone by a private practitioner. The patient had been on treatment for opioid dependence with this practitioner. He had claimed abstinence from opioids for the preceding two weeks. As his claim was corroborated by his wife, a urine analysis before naltrexone institution was omitted. Within five minutes of the ingestion of drug, he started to have symptoms which were typical of opioid withdrawal. These included sweating, yawning, lacrimation, cold sweats, pain in the abdomen, piloerection and severe body aches. As his symptoms started to worsen, he was referred to the hospital where additional symptoms recorded were tachycardia (110 beats/minute) and dilated but reactive pupils. His vitals were stable and he was responding normally to verbal commands. The systemic and neurological examinations were essentially normal. The family revealed that he had been dependent on opioids and nicotine for ten years and had undergone numerous unsuccessful treatment efforts. Also revealed was a history of complex partial seizures

with occasional secondary generalization since childhood; he had been treated with antiepileptic drugs, but not in the last 10 years. There was a history of untreated intermittent epileptic episodes in this period. He was initially prescribed 0.2mg of clonidine and 2mg of Lorazepam orally. Within a few minutes his symptoms increased in intensity. He was observed to be restless and thrashing around the bed, and not responding to verbal commands. He also had a generalized tonic posturing of the body, which was controlled by an intravenous bolus of 10mg of diazepam. Thereafter, an intravenous access was established. Routine blood biochemistry was within normal limits. An electrocardiogram revealed a sinus tachycardia. He was shifted to the critical care unit where his vitals remained stable and oxygen saturation normal. He continued to remain agitated and confused, had clouded consciousness, was not responding to verbal commands, and was muttering incoherently. About 1-2 hours after the ingestion of drug he also had two episodes of passage of loose stools over which he had no apparent control or awareness of. Symptoms of opioid withdrawal continued as before. For control of agitation he was prescribed 5 mg of intravenous diazepam 4 hourly. All the above symptoms continued for the next 12-14 hours where after he started to improve gradually. The initial symptoms to resolve were lacrimation, yawning and mydriasis, which disappeared by about 20-24 hours. By about this time, his sensorium also started to clear up and by about 30 hours post naltrexone ingestion the only remaining symptoms were pain in the legs and insomnia. At this stage he revealed that he had been taking opioids while on detoxification treatment and that he had not expected the 'reaction' to naltrexone to be so severe. The exact profile of the opioids used by him was not clear but apparently included raw opium, dextropropoxyphene, diphenoxylate, codeine containing cough syrups and heroin at different times and in varying dosages and combinations depending on their availability. A urine analysis for opioids done 7 days post naltrexone ingestion was negative for opioids.

DISCUSSION

In usual circumstances naltrexone should not be given until a patient is opioid-free for 7-10 days as determined by urine analysis; in case of doubt, a naloxone challenge is recommended (Fuller & Sajatovic 2005). When instituted the initial naltrexone dosage should be 25mg, and if there are no withdrawal symptoms another 25mg can be given after one hour (Fuller & Sajatovic 2005). Maintenance regimens can vary as per individual requirements (Fuller & Sajatovic 2005). However, some researchers have used low doses of naltrexone to hasten the completion of opioid detoxification (Mannelli et al. 1999). In addition, naltrexone has also been used under deep sedation or general anaesthesia to hasten the process of detoxification called UROD (Rabinowitz et al. 2002).

Oral absorption of naltrexone is rapid, with peak plasma concentrations occurring after about 3 hours and metabolic activity continuing for as long as 72 hours; but this is subject to varying degrees of absorption from the gut and variable first pass metabolism (Ferrari et al. 1998). Therefore, in opioid users who have inadvertently taken naltrexone, it can continue to displace opioids from receptors for as long as 2-3 days post-ingestion.

A review of case reports on accidental naltrexone ingestion precipitated/accelerated withdrawal reveals the following features. There are typical opioid withdrawal symptoms in all cases; however, while their intensity is greater than usual, they have been reported to begin as soon as five minutes after ingestion of naltrexone and to last from 24 hours (Boyce et al. 2003, Quigley & Boyce 2001, Yeo et al. 2003) to as long as 48-72 hours (Mannelli et al. 1999). Incontinence and vomiting has been observed in almost all cases (Boyce et al. 2003, Bristow et al. 2001, Mannelli et al. 1999, Quigley & Boyce 2001, Yeo et al. 2003). In addition, confusion and clouded consciousness has been described (Boyce et al. 2003, Mannelli et al. 1999, Yeo 2003). In extreme cases, general anaesthesia and intubation with ventilation has been required (Boyce et al. 2003, Mannelli et al. 1999). The need for anaesthesia does not seem to be related to the dose of naltrexone; reportedly

having been required following the ingestion of doses as low as 50mg (Mannelli et al. 1999) and 150mg (Boyce et al. 2003).

The management in all the reported cases has been symptomatic: sedation with benzodiazepines or anaesthetic agents, antiemetics, intravenous fluids, non-opioid analgesia and anti-spasmodic agents being the mainstays (Boyce et al. 2003).

The nature and intensity of symptoms following accidental naltrexone ingestion in opioid users can vary greatly. However, it is important to recognize the possibility of such a reaction in patients with a history of substance abuse presenting with chaotic symptoms. Clinicians involved in emergency care should be ready to anticipate the need of measures such as general anaesthesia and intubation in such patients, if such a need arises. Our case also demonstrates the importance of a psychiatrist being sure of a patient's abstinence status in all patients being started on naltrexone.

There are obvious similarities between the procedure of UROD and an accidental naltrexone induced withdrawal subsequently managed with deep sedation. However, the major difference is that while the duration of anaesthesia in UROD has been typically described as being 4-6 hours post opioid-antagonist ingestion (Collins et al. 2005), in each of the 'accidental' cases reviewed above, at the corresponding time period of 4-6 hours, the withdrawal symptoms were at their peak and would have necessitated a reinstatement of sedation had it been stopped. Possible reasons for this disparity may include patient preparedness, lack of adjunctive treatment such as clonidine, or that patients may not be as 'withdrawal-free' after UROD as claimed (Mannelli et al. 1999). For instance, the withdrawal profile of patients who have undergone UROD with naltrexone is similar to the withdrawal profile of those detoxified with

clonidine or buprenorphine at 16 hours post naltrexone ingestion and about 10-12 hours after the end of anaesthesia in the former and at the corresponding time period in the latter (Collins et al. 2005). Therefore, it is important that for future studies to assess the actual status of residual withdrawal symptoms in patients who have undergone UROD as compared to patients who are detoxified sans opioid antagonists. This would have an important bearing on the future use of a potentially dangerous procedure such as UROD.

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