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Course and Treatment of Buprenorphine/naloxone Withdrawal: An Analysis of Case Reports

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Abstract

Currently published information on buprenorphine-naloxone withdrawal recommends a gradually decreasing dosage over weeks to months. In this case report, abrupt cessation of buprenorphine/naloxone at various doses, and after variable durations of treatment, resulted in mild opiate withdrawal lasting over approximately 1–2 days that did not require additional opioid medication or only specific symptom-relieving, non-opioid, medications. Lengthy withdrawal regimens might prolong withdrawal symptoms unnecessarily, perhaps increasing the risk of re-addiction. Controlled studies of buprenorphine/naloxone withdrawal regimens over varying time frames would help to illuminate the most effective means of opioid discontinuation and inform clinical care.

Introduction

Early recommendations regarding withdrawal from buprenorphine/naloxone indicated that a taper should be gradual over several weeks or longer. This recommendation was not based on clinical research, but rather on general experience with maintenance therapy with methadone. Early on, clinicians preferred gradual tapers in cases of elective withdrawal from buprenorphine/naloxone. With time, however, cases of abrupt withdrawal from buprenorphine began to appear. Described experiences did not jibe with clinical fears regarding the potential extent and severity of withdrawal symptoms. This general observation found voice at the morning panel discussion during the annual meeting of the American Academy of Addiction Psychiatry (AAAP) in December 2011.

Since publications on buprenorphine/naloxone recommend a taper period, at times lasting weeks or months[1, 2], some clinicians unfamiliar with buprenorphine/naloxone withdrawal utilize lengthy withdrawal regimens. Currently no clinical trial has focused on the specifics of opiate withdrawal symptom severity over the course of varying lengths of buprenorphine/naloxone withdrawal. We now report several cases of buprenorphine/naloxone withdrawal following abrupt cessation of this medication. These cases reflect common themes discussed at the AAAP meeting.

Case Reports

Three men and one woman comprised these four case reports. They ranged in age from 25 to 63 years (mean 45 years). One was employed, one retired, one disabled, and one unemployed. Two were single, one married, and one divorced. Ethnicity included two Caucasian Americans, one African American, and one American Indian. Two patients had become dependent on opioid medications through use of illicit heroin and other opioid drugs, and two developed iatrogenic opioid dependence, one following surgery and the other

as a result of opioid prescribing related to chronic pain. Prior to buprenorphine/naloxone maintenance therapy, each had received a variety of other treatment modalities for opioid dependence (i.e., drug-free programs and counseling, clonidine, and methadone). All had experience with methadone maintenance with the exception of the 25 year old individual.

Case 1 had been receiving buprenorphine-naloxone 12/3 mg for 15 months. Prior to beginning buprenorphine/naloxone treatment, the patient had a driving-while-intoxicated offense and had an outstanding warrant. When appearing for the court hearing, the patient was unexpectedly incarcerated for two weeks. Buprenorphine/naloxone or other withdrawal medication was not administered in jail. On the day following his last buprenorphine/naloxone dose, the patient experienced mild withdrawal "like a cold" that lasted for one day. Non-steroidal anti-inflammatory drugs (NSAIDS) relieved these symptoms. Following release from incarceration, the patient resumed buprenorphine/naloxone and has continued in recovery for 32 months.

Case 2 was unexpectedly incarcerated while taking buprenorphine/naloxone 16/4 mg, which had been prescribed for several weeks. Previously incarcerated suddenly while dependent on heroin and later while dependent on methadone, the patient was experienced with sudden withdrawal associated with other opioid substances. Buprenorphine/naloxone withdrawal involved mild symptoms that included myalgia/arthralgia, increased lacrimation and minimal rhinorrhea described as being present for two days. Upon release the patient resumed buprenorphine/naloxone maintenance treatment.

Case 3 had received buprenorphine/naloxone 16/4 mg for two months when a life-threatening illness in the family resulted in a sudden departure over a weekend. When the prescribed buprenorphine/naloxone medication ran out during the week, mild symptoms "like a regular cold" for occurred for one day after the last Buprenorphine/naloxone dose was ingested. Although the patient possessed clonidine pills left over from an earlier methadone withdrawal (prescribed during a transfer to buprenorphine/naloxone), the symptoms were not severe enough in the patient's judgment to warrant taking medication. Upon returning, buprenorphine/naloxone maintenance was resumed. Five months later, similar circumstances resulted in the patient again running out of buprenorphine/naloxone. Similarly, withdrawal symptoms were reported to be mild lasting for one day. Although aware that buprenorphine/naloxone maintenance could be arranged in the distant city, the patient opted to go though buprenorphine/naloxone withdrawal and brief buprenorphine/naloxone abstinence rather than arranging for guest-dosing.

Case 4 had been escalating the prescribed buprenorphine/naloxone 20/5 mg dose taking 150% more than prescribed (or buprenorphine/naloxone 30/7.5 mg daily). Since this was the third instance of buprenorphine/naloxone non-compliance, the patient was informed that buprenorphine/naloxone maintenance would be discontinued. Subsequently the patient presented to the clinic two days after the last dose of buprenorphine/naloxone, complaining of "severe" withdrawal symptoms and requesting further buprenorphine/naloxone. Pertinent findings included pulse of 62, respirations of 16, blood pressure within normal limits, and the patient was afebrile with no other abnormal findings. Two hours later, vital signs remained essentially unchanged. Buprenorphine/naloxone was denied, but patient was offered 24 hours of inpatient observation and/or clonidine. This was declined and the patient returned home.

Author Comments

These individuals manifested minimal signs of opiate withdrawal over 1–2 days and either reported minimal discomfort or showed no objective signs of opiate withdrawal following

abrupt discontinuation of chronic buprenorphine/naloxone treatment in doses ranging from 12/3 mg to 30/7.5 mg daily. Opiate withdrawal symptoms reported included arthralgia, myalgia, rhinorrhea, and lacrimation. One accepted symptom-relieving NSAIDs; two others opted not to utilize clonidine, although it was available. Three were not averse to resuming buprenorphine/naloxone maintenance therapy; and in the fourth case buprenorphine/naloxone withdrawal was reported to be severe, but no evidence of opiate withdrawal was observed on physical examination.

Buprenorphine/naloxone has been used to withdraw patients from methadone because of its mild opiate withdrawal properties upon discontinuation. In a described method administered to five opioid-dependent individuals, pre-treatment with clonidine was undertaken, followed by oral naltrexone 25 mg (which precipitated opioid withdrawal symptoms), with administration of buprenorphine/naloxone upon manifestation of opiate withdrawal, which was then tapered over several days [3]. The mild withdrawal observed with buprenorphine/naloxone may result from its mu opioid partial agonist activity as well as the high affinity of buprenorphine for the mu opioid receptor and slow dissociation from that receptor when stopped abruptly [4].

Sudden or rapid withdrawal from buprenorphine/naloxone results in a short period of mild opiate withdrawal. Buprenorphine/naloxone withdrawal over weeks to months might unnecessarily prolong opiate withdrawal. However, one issue that studies of opiate withdrawal using buprenorphine/naloxone have failed to address to date is that of the rapid rate of relapse that has been observed following withdrawal of any duration and which is similar to that observed[1, 2] with other opioid withdrawal regimens[5]. Whether taper using buprenorphine/naloxone is short or lengthy, it is clear that ongoing treatment after opioid cessation is needed. This might include naltrexone, psychosocial intervention, or some combination.

Determination of the most effective means of opioid taper using buprenorphine/naloxone warrants further study. Questions regarding how to most effectively taper this medication over a period of a few days would be helpful. For example, does rapid taper to a 4/1 mg/d dose have some clinical advantage or is it a disadvantage? Is discontinuation from a higher buprenorphine/naloxone dose better tolerated? Severity and duration of withdrawal symptoms associated with rapid (several days) versus longer (28 days) taper should be undertaken to inform current clinical care.

To conclude, sudden cessation of buprenorphine/naloxone maintenance produced minimal morbidity in this series of 4 cases, despite chronic exposure to relatively large doses ranging from buprenorphine/naloxone 12/3 mg to 30/7.5 mg. No evidence that abrupt cessation of buprenorphine/naloxone is medically dangerous was found. However, further research is needed to inform rapid withdrawal protocols and to determine the most effective post-buprenorphine/naloxone treatment of opioid addiction.

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