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An Adverse Reaction to Buprenorphine/Naloxone Induction in Prison: A Case Report

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Buprenorphine is a widely used and effective treatment for opiate dependence. Given the alarmingly high rate of post-release opioid overdose,¹ induction of medication-assisted therapy for prisoners may be an important way to decrease the risk of overdose and relapse to opioid use,^{2–4} and a randomized clinical trial at the Rikers Island jail in New York City found that initiating buprenorphine maintenance for heroin-dependent inmates resulted in higher rates of linkage to community treatment upon release compared to those receiving methadone maintenance therapy.⁵ We report a case of probable non-lethal overdose during dose induction of a non-tolerant prisoner.

The patient is a 39 year old woman with a nine-year history of opiate addiction and 10 previous periods of incarceration. Her other medical problems included morbid obesity and bipolar disease, including psychotic depression and anxiety. She reported being abstinent from opioids during her current 9 month long incarceration. She asked to be started on buprenorphine prior to release to prevent relapse to illicit opiate use. While incarcerated, the patient continued her outpatient medications: quetiapine (150 mg bid and 300mg at HS), clonazepam (1mg q am, 2 mg q pm), trazodone (100 mg q HS), citalopram (40 mg q day), haloperidol (5 mg at HS), and benztropine (1 mg at HS).

The patient provided informed consent and was enrolled, upon confirmation of eligibility by the study physician, in a research trial approved by the Office for Human Research Protections and the Miriam Hospital Institutional Review Board whereby inmates at high risk of opiate relapse were begun on buprenorphine/naloxone sublingually within 7 days of release. Four days before her scheduled release, she was initiated on buprenorphine/naloxone therapy at 4 mg sublingually. The next two days the patient received 8 mg daily and was observed without incident for an hour each day after dosing.

About 4 hours after the third day's dose, the patient reported feeling tired and lay down. About 8 hours after her dose, the patient was noted to be very difficult to arouse even with

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the use of “smelling salts.” She remained unarousable throughout the night but had stable vital signs with no cyanosis. She awoke on the fourth day feeling fine and was released from prison. No additional buprenorphine/naloxone was given as she elected to enter residential treatment. She remained drug free for 6 months, but by 12 months relapsed to illicit opiate and benzodiazepine use.

This case represents a fairly typical situation in which a prisoner has a history of opiate dependence and frequent relapse upon release from incarceration. This patient started buprenorphine/naloxone on standard doses for tolerant individuals,⁶ which is the same dose used in the aforementioned clinical trial in New York City with opioid-tolerant inmates.⁵ Given her lack of tolerance and the concomitant use of other psychotropic medications, especially benzodiazepines, it is likely that drug-drug interactions contributed in part to her obtundation. The program Lexi-Interact⁷ recommends that therapy be monitored when buprenorphine is co-administered with other CNS depressants. The moderately severe interactions between these medications increase in incidence and severity when greater than two CNS depressants are used concomitantly: in this case, clonazepam, trazadone, haloperidol, and quetiapine. Because of buprenorphine’s relatively long half-life, administering repeated doses to a non-tolerant patient may lead to an increased risk of overdose due to drug build-up. It would be prudent to start such individuals on no more than 2 mg and to increase the dose more slowly than usual with careful observation, as recommended by the Substance Abuse and Mental Health Services Administration’s “Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction.”⁸

This case suggests that caution should be exercised when inducing buprenorphine for opiate-non-tolerant patients, such as prisoners. Unfortunately, the package insert for buprenorphine/naloxone does not provide a clear dosing schedule for patients who have been abstinent from opiates. Despite the commonly held belief that buprenorphine overdose is rare, similar adverse events can easily occur in patients who are induced too quickly, especially while taking benzodiazepines or other CNS depressants. Future research is needed on how best to initiate buprenorphine/naloxone in non-tolerant patients with a history of institutionalization or incarceration.

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