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Buprenorphine Induced Respiratory Depression: A Case Report

Katie Cole, MS[1], **Thu Nguyen**[1], **Tanvir Singh**[2]

[1] College of Medicine and Life Sciences, The University of Toledo, Toledo, OH 43614

[2] Faculty, Department of Psychiatry, The University of Toledo, Toledo, OH 43614

Email: kaitlin.cole@rockets.utoledo.edu

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Abstract

Due to buprenorphine's low maximum effect on respiratory depression because it is a partial agonist at the mu opioid receptor, it is generally considered a safe medication for treating opioid drug dependence. However, in combination with benzodiazepines or other comorbidities, it has been shown that buprenorphine can result in serious respiratory depression. We present the case of a 64-year-old female with a history of type 2 diabetes mellitus, asthma, obstructive sleep apnea, hepatitis C, hyperlipidemia, and hepatic steatosis who presented to the detox unit for alcohol and cocaine dependence and withdrawal. Although her initial presentation was for alcohol and cocaine withdrawal, her medical history was significant for opioid use disorder with multiple prior admissions to the detox unit. In consideration of this, buprenorphine therapy was initiated as part of her opioid dependence treatment. However, when given the standard dosage of buprenorphine, she was found to be sleeping upright in her chair three hours later with reduced O2 saturation. The patient received 1.2 mg of Narcan and had to be intubated because of buprenorphine induced respiratory depression. This case illustrates the potential effects of buprenorphine on respiration status.

Keywords: Buprenorphine, Respiratory Depression, Suboxone, Opioids

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1. Introduction

Over the past two decades, negative incidents related to prescription opioids have dramatically increased across the United States (1). When left untreated, opioid use disorder can escalate to overdose, potentially leading to mortality. Medication treatments FDA approved to treat opioid withdrawal include methadone (an opioid receptor full agonist), naltrexone (an opioid receptor antagonist), and buprenorphine (an opioid receptor partial agonist) (2). At adequate doses, methadone can prevent the euphoric effects of opioids, prevent withdrawal symptoms, and reduce cravings (3, 4). Some significant adverse effects of excessive methadone accumulation include sedation, respiratory depression, and respiratory arrest. Therefore, methadone prescribed in clinics for opioid withdrawal is heavily controlled, and patients undergoing treatment are required to attend frequent appointments for monitoring and dose adjustments. (5). Naltrexone, a non-selective opioid antagonist, is another treatment commonly used for maintenance therapy in opioid dependency. It binds to the mu-opioid receptor, blocking the effects of opioids and has led to increased retention rates in treatment (6). Unlike the others, buprenorphine is an effective long-term maintenance treatment for opioid dependency due to its neurophysiological properties of being a partial mu-opioid receptor agonist with high receptor affinity (7). Buprenorphine blocks opioid effects at adequate doses and prevents overdose; however, it has been shown to cause less respiratory depression due to its profile as a partial agonist (8). It has been shown that as a partial agonist, buprenorphine exhibits an earlier plateau effect in respiratory depression commonly referred to as a “ceiling effect” (9). Over a maximum daily dose of 32 mg, buprenorphine demonstrates a ceiling effect for respiratory depression but does not exhibit a ceiling effect for its analgesic properties (10,11). Therefore, increasing the dosage of buprenorphine in treatment has little to no effect on increasing its therapeutic action. This property makes buprenorphine stand out as a more manageable treatment compared to its counterparts, however respiratory depression may still occur in patients with comorbidities or using combined drugs. Patients undergoing treatment with buprenorphine for opioid dependency exhibit reduced responses to hypoxia and hypercapnia (12). In patients with sleep disordered breathing such as obstructive sleep apnea, this could contribute to an increased respiratory depressive effect. Cases of respiratory depression from buprenorphine have also been linked to intravenous polysubstance abuse, most often involving benzodiazepines (13). We report a case of respiratory depression in a patient receiving sublingual buprenorphine for treatment of opioid use disorder.

2. Case Presentation

Our patient is a 64-year-old female with a history of type 2 diabetes mellitus, asthma, obstructive sleep apnea, hepatitis C, hyperlipidemia, and hepatic steatosis who presented to the detox unit for alcohol and cocaine dependence and withdrawal. Her past psychiatric history included bipolar disorder, schizoaffective disorder, and major depressive disorder with psychotic features with multiple past visits to the detox inpatient unit for alcohol withdrawal and chronic opioid use disorder which had previously been treated with buprenorphine. Reportedly, she was drinking about half a fifth of whiskey daily as well as one gram of cocaine a day for several years. Her urine toxicology report was positive for benzodiazepines, cocaine, and tricyclic antidepressants which alluded to the patient taking benzodiazepines prior to her arrival at the hospital. During admission, the patient was responding adequately to the Clinical Institute Withdrawal Assessment (CIWA) protocol with symptomatic treatment. Although she presented for alcohol and cocaine withdrawal, the patient has had a known history of opioid use disorder and, given this history, was initiated on buprenorphine as part of her treatment. She received 2 mg of buprenorphine sublingually at 3 p.m. and 4 mg at 4 p.m. Around 7 p.m., the patient was found to be sleeping upright in her chair. A nurse woke her up to check her vitals; however, the patient began to vomit a large amount of yellow emesis. The nurse noted the patient to be excessively drowsy but arousable. Upon vital assessment, her oxygen saturation was 68%. A rapid response was called while the patient continued to doze off in her chair. When rapid response arrived, the patient’s oxygen saturation read 95% but quickly dropped into the high 60s. Oxygen was administered, and the patient was also given a total of 1.2 mg of Narcan intramuscularly without improvement in mental status or oxygenation. On initial arterial

blood gas in the detox unit, she was severely acidotic with a pH of 7.12 and her pCO2 was elevated at 85. The patient was subsequently taken to the emergency room from the detox unit. In the ER, she was found to have pinpoint pupils, tachycardia, but was arousable and in no respiratory distress. Repeat blood gas on BiPAP showed continuing acidosis of 7.07 and pCO2 of 100. Because of her worsening respiratory acidosis, the patient was transferred to the ICU and intubated. Physicians determined the patient had acute hypercapnic respiratory failure, possibly secondary to buprenorphine use. She was extubated after respiratory stabilization a day later and was transferred to the floor for further evaluation and respiratory failure.

3. Discussion

Previous reports of buprenorphine induced respiratory depression have often occurred among individuals who use benzodiazepines concurrently or have other underlying comorbidities. Buprenorphine is known to have a ceiling effect; however, it can cause respiratory depression in certain cases with concurrent medical issues and benzodiazepine use (14). Our patient's urine toxicology was positive for benzodiazepines, indicating exposure prior to admission. As benzodiazepines may potentiate opioid-induced respiratory depression, there is a question as to whether concomitant exposure may have contributed to the effects observed with buprenorphine. In our patient's case, 6 mg of buprenorphine in total was administered, which this dosage has generally been considered to carry a low risk of significant respiratory depression. Studies have shown that buprenorphine induced respiratory depression and decreased oxygen saturation between doses of 8 mg and 32 mg (13). Others have shown that respiration can be maximally suppressed after administration of 16 mg of buprenorphine sublingually (15). In patients with concurrent respiratory issues such as obstructive sleep apnea, we recommend careful monitoring of respiratory status after administration of buprenorphine. Also, our patient experienced her episode a few hours after she had been administered buprenorphine. Compared to other opioids, like fentanyl, which is known to cause respiratory depression almost immediately, buprenorphine toxicity might not be observed right away. Clinicians should continue to monitor for respiratory depression throughout the patient's hospitalization and remain aware of this risk in future patient encounters. Furthermore, our patient has an extensive history of inpatient detoxification where she has received uncomplicated symptomatic treatment with buprenorphine. As stated earlier, the patient required multiple rounds of Narcan, which is typical of acute buprenorphine overdose (16). This suggests a primary role for buprenorphine induced respiratory depression in our patient. We recommend careful monitoring of respiratory rates and oxygen saturations in patients who are even on standard doses of buprenorphine, especially when they are sleeping as respiratory depression can cause serious complications in patients and a prolonged hospital stay.

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