Buprenorphine induction using microdosing for the management of opioid use disorder in pregnancy

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Abstract

PURPOSE: Buprenorphine induction in pregnancy requires withdrawal symptoms prior to initiation and has been associated with dissatisfaction and non-compliance.

METHODS: This is a case presentation of a successful buprenorphine induction of a pregnant patient on methadone maintenance, who desired induction onto buprenorphine to minimize the risk of neonatal opioid withdrawal syndrome (NOWS), which severely affected her last child.

CASE PRESENTATION: The patient is a 29 year old G2P1001 at 18 2/7 weeks of gestation, who desired a switch from Methadone to buprenorphine to minimize NOWS in this pregnancy. The patient had a history of IV drug use from 17 to 25 years of age. This pregnancy was complicated by Hepatitis C infection, a history of anxiety and depression, and tobacco use. Her medications included a daily PNV in addition to her methadone. Her prior pregnancy was an NSVD at 37 6/7 weeks of gestation of a female infant weighing 7 pounds 8 ounces, 3 years ago.

She was counseled that buprenorphine maintenance can also be associated with NOWS, and that changes in neonatal treatment across the US using eat, sleep, console allows successful newborn transition and significantly decreases the experience of neonatal withdrawal symptoms and the need for medication. She was also counseled regarding smoking cessation as a means to decrease the risk of NOWS.

Despite these recommendations, the patient was slowly weaning herself down to 30 mg from 68 mg of methadone daily (a decrease of 2 mg qod). This was recommended by the clinic where she was receiving her methadone. The plan had been to abstain from methadone for at least 48 hours, until she experienced moderate withdrawal symptoms before initiating buprenorphine. This is to minimize a precipitated withdrawal in the patient.

Precipitated withdrawal occurs when there is a net decrease in opioid effect. Buprenorphine is a partial opioid agonist which has a high affinity for the $\mu$-receptor, but less intrinsic opioid effect than a pure opioid agonist such as methadone or fentanyl. When buprenorphine is given to a patient with an opioid agonist on board, the partial agonist (buprenorphine) displaces the full agonist from the $\mu$-receptor, and since it activates the receptor to a lesser degree than a full agonist, this results in a net decrease in agonist effect, and the patient experiences severe withdrawal symptoms.

The patient was counseled extensively regarding the possible risks and benefits of buprenorphine microdosing. The main advantage of microdosing is avoiding a precipitated withdrawal. The Prescription Monitoring Program was checked and the
patient had no other prescriptions for opiates. She continued to take her daily dose of methadone 30 mg, while increasing her daily dose of buprenorphine according to the protocol used by Terasaki et al.

The patient did well during the week of buprenorphine micro-dosing, with no complaints of withdrawal or cravings. She continued to be engaged in her prenatal care. She had a normal fetal anatomy scan. Her dose of buprenorphine was increased to 8 mg bid for some withdrawal symptoms in the evening (new onset nausea, vomiting). She had a normal follow-up growth ultrasound at 32 weeks. She was down to 2 cigarettes a day.

The patient underwent an elective induction of labor at 39 weeks and had a spontaneous vaginal delivery of a 3340 gm (7 pound 6 ounce) male infant. Apgar scores were 8 and 9 after 1 and 5 minutes respectively. The FINNEGAN NEONATAL ABSTINENCE SCORE peaked at 5 days of life. Only non-pharmacologic interventions were used. He did not require any opioids for treatment. The patient continued her daily dose of buprenorphine intrapartum and postpartum. Her pain was adequately controlled with NSAIDS and Tylenol. She was prescribed enough buprenorphine until her clinic visit in 2 weeks. She was also referred to GI for treatment of Hepatitis C.

CONCLUSION: A growing body of literature supports micro-dosing of buprenorphine in non-pregnant persons. This approach avoids withdrawal symptoms by slowly displacing the full opioid agonist, and can safely be performed in the outpatient setting. Given the safety profile of buprenorphine and its potential to be a lifesaving intervention, a study of micro-dosing in pregnancy is indicated. This is especially true as overdose deaths exceeded 100,000 last year, with illicit fentanyl now a predominant opioid of abuse.