Unique Pharmacokinetics of Buprenorphine During Pregnancy

Christopher R. Hollabaugh, BSN, MBA[a]; Brannon Donovan, BA[a]; Salma Velazquez, MD[a]; and Roopa Sethi, MD[b,*]

Buprenorphine is rapidly becoming the preferred treatment in pregnancy for opioid use disorder.[1] However, the literature regarding buprenorphine and its use during pregnancy is still relatively sparse. Research has shown that multiple-day buprenorphine dosing[2] in pregnant women due to the altered pharmacokinetics of gestation[3] is more effective than single-day dosing. As gestation increases, multiple-day dosing causes less withdrawal symptoms and cravings because buprenorphine seems to be metabolized quickly.[1]

Case Report

Ms A is a 35-year-old white woman pregnant for the first time who presented to the addiction clinic at 11 weeks' gestation with a history of opioid use disorder, major depressive disorder, generalized anxiety disorder, and hyperemesis gravidarum. The patient had a 10-year history of taking 40–50 mg of hydrocodone per day, which was prescribed to her for pain management until she developed addiction to the medication. In the addiction clinic at 10 weeks' gestation, she was initiated on buprenorphine 8 mg per day for opioid use disorder while concurrently discontinuing her previous hydrocodone dosing regimen. Medications from other providers included alprazolam, escitalopram, and ondansetron for hyperemesis.

Three days following the initiation of buprenorphine, Ms A reported unrelenting nausea, vomiting, nervousness, anxiety, migraines, lacrimation, abdominal pain, diarrhea, and cravings. She reported complete relief of symptoms with buprenorphine for a few hours after dosing followed by reappearance of the headaches and anxiety thereafter. Ms A stated that her mood had been poor due to the headaches and she generally felt unwell. A urine toxicology screen approximately 20 days after initiation showed a buprenorphine level of 116 ng/mL and a norbuprenorphine level of 624 ng/mL. At follow-up in the clinic, the buprenorphine dose was increased to 8 mg twice a day along with 2-mg midday dosing. After increasing the frequency of the dosing, her headaches and nausea improved. A urine toxicology screen a month after initiation showed buprenorphine levels of 412 ng/mL and a norbuprenorphine level > 1,000 ng/mL. Later, the dose was changed to 8 mg 3 times a day, and the patient's withdrawal symptoms improved significantly with no cravings. This result is consistent with those found in previous literature[2] regarding buprenorphine metabolism during pregnancy.

Buprenorphine is a US Food and Drug Administration–approved medication for opioid use disorder. It is increasingly used in pregnant women because of the availability of providers and ease to obtain the medication compared with methadone.[1] Buprenorphine is a partial agonist at the μ-opioid receptor and has a strong affinity and a slow dissociation rate. This property makes the medication desirable, as it can be used for once-a-day dosing in patients dependent on opiates, thus preventing withdrawal symptoms and reducing cravings.[3]

Currently, dosing of buprenorphine in pregnant women is based on research[4] and dosing recommendations for nonpregnant women. However, studies in the literature have emerged about unique pharmacokinetics of buprenorphine during pregnancy. These studies[1,2] highlight the metabolism of buprenorphine during pregnancy and discuss increased expression of cytochrome (CYP) 3A4 and CYP2D6 at the liver, intestine, and central nervous system in pregnant women. Buprenorphine is metabolized by CYP3A4, hence increased expression will lead to lower plasma levels and less total buprenorphine according to the area under the plasma drug concentration-time curve.[1,2] Thus, in pregnant women, multiple-day dosing may be desirable even if buprenorphine is prescribed at a low dose. As pregnancy progresses, a higher dose of buprenorphine is required to prevent cravings and withdrawal symptoms.[1] Hence, studies[1,3] suggest that women may need higher doses and multiple dosing schedules as pregnancy progresses in an effort to mitigate withdrawal symptoms and cravings throughout pregnancy.

Published online: October 17, 2019.

Potential conflicts of interest: None.

Funding/support: None.

Patient consent: The patient provided consent to publish this case report, and information has been de-identified to protect anonymity.

REFERENCES

1. Bastian JR, Chen H, Zhang H, et al. Dose-adjusted plasma concentrations of sublingual buprenorphine are lower during than after pregnancy. *Am J Obstet Gynecol*. 2017;216(1):64.e1–64.e7.
2. Caritis SN, Bastian JR, Zhang H, et al. An evidence-based recommendation to increase the dosing frequency of buprenorphine during pregnancy. *Am J Obstet Gynecol*. 2017;217(4):459.e1–459.e6.
3. Elkader A, Sproule B. Buprenorphine: clinical pharmacokinetics in the treatment of opioid dependence. *Clin Pharmacokinet*. 2005;44(7):661–680.
4. Bastian JR, Chen H, Tarter R, et al. Pregnancy alters the metabolism of sublingual buprenorphine. *Am J Obstet Gynecol*. 2016;214(1):S163.

[a]University of Kansas School of Medicine, Kansas City, Kansas
[b]Department of Psychiatry and Behavioral Sciences, University of Kansas Medical Center, Kansas City, Kansas
**Corresponding author:* Roopa Sethi, MD, Department of Psychiatry and Behavioral Sciences, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160 (rsethi@kumc.edu).

Prim Care Companion CNS Disord 2019;21(5):18l02390

To cite: Hollabaugh CR, Donovan B, Velazquez S, et al. Unique pharmacokinetics of buprenorphine during pregnancy. *Prim Care Companion CNS Disord*. 2019;21(5):18l02390.

To share: https://doi.org/10.4088/PCC.18l02390