Outpatient Rapid Microinduction of Sublingual Buprenorphine in 3 Days From Methadone for Opioid Use Disorder

Iryna Salapenka, MD[a]; Jaya Sri Konakanchi, MB, BS[b]; and Roopa Sethi, MD[a,*]

The United States is currently facing a public health crisis due to the dramatic increase in opioid use disorder (OUD) and opioid overdose deaths, especially given the coronavirus disease 2019 pandemic.[1–4] Medication-assisted treatment with methadone, buprenorphine, and long-acting naltrexone is considered a safe and effective method to treat OUD.[3,5] Methadone treatment is a preferred treatment for some but has several limitations including risk for respiratory depression and cardiac arrhythmias and QTc prolongation requiring electrocardiogram monitoring, as well as daily clinic visits before the patient can be phased up.[3] On the other hand, due to its properties of less respiratory and central nervous system depression and minimal associations with QTc prolongation, buprenorphine might be preferable to other treatments.[3]

Current buprenorphine induction protocol requires starting an induction procedure when the patient exhibits clear signs of opioid withdrawal using the Clinical Opioid Withdrawal Scale (COWS).[2,3,6–8] For patients who are currently taking methadone, tapering the dose and stopping methadone is preferred. However, this can predispose patients to return to illicit opioid use.[3,9] Furthermore, some patients may decline initiating the procedure due to fear of withdrawal symptoms or avoidance of hospitalization. Rapid microinduction procedure in an outpatient setting can be a desirable alternative approach during initiation without potential withdrawal.

Microdosing or microinduction is a method of using small escalating doses of buprenorphine during initiation of treatment for OUD or for transition from full agonist therapy for OUD treatment. This technique implies a slow buildup of buprenorphine at the opioid receptors with repeated small doses of buprenorphine without precipitated withdrawal.[1,7,10,11] The advantage of this approach is no prerequisite to taper or stop full agonist therapy before initiating buprenorphine. Most studies[5,12–14] on microdosing techniques have been performed in an inpatient setting. Those conducted in an outpatient setting have ranged from 4 to 10 days.[2,9,15–17] Our case report is unique, as we were able to complete the transition from methadone to buprenorphine using the microdosing technique in an outpatient setting in a span of 3 days with minimal withdrawal symptoms in an elderly patient over 65 years of age.

Case Report

A 67-year-old White man, with a history of OUD and on treatment with methadone 72 mg for 3 years, was seen in an outpatient addiction clinic. The patient had been stable on this dose but now needed to transition due to age, excessive sedation, and inability to come to the clinic every 2 weeks for methadone dosing.

His medical history included chronic obstructive pulmonary disease. His psychiatric history included major depressive disorder, benzodiazepine dependence, and OUD.

He started using prescribed oxycodone and fentanyl after a car accident 50 years ago. He used the medications as prescribed for a few years and then switched to intravenous heroin 4 years later due to the belief that "drugs were no more helpful." He had developed tolerance to the medication and would have withdrawal symptoms when he stopped opioid use.

The patient had been diagnosed with OUD and started on methadone, which he had been taking for the past 3 years. He had been on a stable dose but needed to switch treatments due to the reasons mentioned previously. The standard buprenorphine initiation procedure was discussed with the patient and declined by him due to fear of withdrawal symptom development. The alternative method of ultrarapid 3-day microdosing of buprenorphine as an outpatient was discussed and explained to the patient, and he expressed interest in this method.

The 3-day procedure included an initial assessment and 3 half days in the clinic. The time spent in the clinic varied depending on the periods between microdosing and withdrawal symptoms experienced by the patient but did not exceed 4 to 5 hours on average. The patient was seen in the clinic by an addiction psychiatrist, addiction fellow, and nursing staff.

The microinduction procedure was started with 2/0.5 mg of sublingual film of buprenorphine. The film was equally divided into approximately 4 parts of 0.5 mg of

[a]Department of Psychiatry and Behavioral Sciences, University of Kansas Health System, Kansas City, Kansas

[b]School of Medicine, University of Kansas Medical Center, Kansas City, Kansas

*Corresponding author: Roopa Sethi, MD, 3901 Rainbow Blvd, Kansas City, KS 66103 (rsethi@kumc.edu).

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Table 1. Dosing Schedule of Buprenorphine

Day	Buprenorphine Total Daily Dose	Methadone Dose	COWS Score 30 Minutes Before Procedure 1:00 AM	COWS Score in the Middle of Procedure 12 PM	COWS Score at the end of Procedure 2 PM	Withdrawal Symptoms	Withdrawal Medications Used (clonidine 0.1 mg, trazodone 50 mg qhs, ondansetron 4 mg)
1	2 mg/0.5 mg film every 60 min	72 mg	0	0	0	None	None
2	4 mg/0.5 mg film every 30 min	72 mg	0	7	0	Chills, nausea, joint pain, abdominal cramping, diarrhea (1 episode), anxiety	Clonidine 0.1 mg once Trazodone 50 mg qhs taken at night Ondansetron 4 mg during induction
3	8 mg/0.5 mg film every 20 min	72 mg/discontinued the next day	0	2	0	Sweating, anxiety	Clonidine 0.1 mg once

Abbreviations: BID = twice daily, COWS = Clinical Opioid Withdrawal Scale, PRN = as needed, QHS = every hour.

buprenorphine, as that was the lowest dose available at the pharmacy. Each subpart of the film was given in time intervals of a half to 1 hour under close supervision. A methadone dose of 72 mg was administered after every successful induction of buprenorphine for the day. The COWS was administered at the start of the procedure and before each microdosing. Table 1 provides detailed information.

On the second and third days, the dose of sublingual buprenorphine was increased to 4 mg and 8 mg for days 2 and 3, respectively. Mild withdrawal symptoms of sweating, anxiety, nausea, joint pain, abdominal cramps, and loose stool were observed on the second day with a COWS score of 7. At that time, clonidine 0.1 mg and ondansetron 4 mg were administered to mitigate the withdrawal symptoms. Instructions to take trazodone 50 mg at bedtime as needed were provided to the patient.

On the third day, only minor anxiety and sweating with a COWS score of 2 was documented. The patient denied withdrawal symptoms and cravings to opiates. At this point, transition from methadone was complete. Full agonist therapy with methadone was discontinued the next day with no reported consequences. The patient remained opioid abstinent, was withdrawal symptom free, and entered the stabilization phase of buprenorphine treatment.

Discussion

We have described a case in which a patient was transitioned from agonist therapy with methadone to sublingual buprenorphine in an outpatient setting in a short period of 3 days. The patient reached a therapeutic dose of sublingual buprenorphine while taking methadone 72 mg/d without requiring a period of opioid withdrawal prior to initiation and tapering of the daily dose of methadone. During the procedure, supporting symptomatic medications such as clonidine for sympathetic hyperactivity and ondansetron for nausea were effectively used. Following microinduction, the patient was maintained on buprenorphine and did not experience withdrawal symptoms or cravings to illicit opioids.

This case illustrates that barriers to buprenorphine treatment can be overcome by unique techniques such as that presented here.[2] This novel approach can offer advantages for patients and physicians, including short periods of time spent in the clinic, absence of severe withdrawal symptoms, and flexibility of the microdosing regimen.[17]

Observations during this case show that the microdoses during the transition from full agonists to partial agonists should be as small as possible. The available literature in the form of case reports and case series reveals that the starting dose of induction of buprenorphine ranges from 0.2 mg to 0.5 mg.[2] These doses create a positive experience for patients and lead to further compliance with medications for OUD.[2]

The alternative rapid buprenorphine microinduction technique can potentially increase the number of buprenorphine procedures initiated for patients in outpatient settings, especially for those who are transitioning from full agonist therapy without preceding opioid withdrawal and with lower risk to return to opioid use.[2]

Conclusion

Rapid microinduction of buprenorphine in outpatient settings is a new alternative and effective method of initiating treatment with partial agonists for OUD in patients who achieved remission on full agonist opioid replacement treatment including elderly patients. In comparison with traditional guidelines, buprenorphine rapid microinduction technique is beneficial due to the flexible microdosing regimen, short duration of the procedure, no required hospitalization, and use of symptomatic medications targeting withdrawal symptoms. All these advantages lead to better tolerance of transition procedures by patients and lower risk of relapse.

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