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Case Report

Successful Rapid Transition from Methadone to Buprenorphine without Bridging Methods: A Case Report

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Abstract

Background: Patients with opioid use disorders often require methadone or buprenorphine during their treatment. For safety and convenience, buprenorphine is preferred over methadone during the treatment course, but transitioning a patient from methadone to buprenorphine can be challenging. Due to the high-affinity and partial agonistic properties of buprenorphine on the μ-opioid receptor, a switch from methadone to buprenorphine can precipitate severe withdrawal if buprenorphine is introduced too soon after methadone discontinuation. To minimize this, numerous methods have been tried to bridge the transition from methadone to buprenorphine. However, this bridging process can be very slow and take many days, and it often requires the use of very low dose transdermal buprenorphine or fentanyl patches that may not be available. These factors can prevent patients from making the switch.

Case presentation: This patient was a 32-year-old male with a history of bipolar disorder and opioid use disorder admitted for psychiatric stabilization and inpatient substance use rehabilitation for daily heroin use. Upon admission, he was started on methadone 80mg daily but desired a switch to buprenorphine, citing its safety profile and accessibility issues with methadone clinics in the past. Transdermal opioids to help with a slow, bridging transition were unavailable, so a direct switch to buprenorphine was attempted under close inpatient monitoring. As expected, he entered moderately severe withdrawal as measured by the Clinical Opiate Withdrawal Scale (COWS). Withdrawal symptoms were managed as needed. Buprenorphine was started at 36 hours post-methadone leading to a significant improvement in withdrawal symptoms, with COWS scores down to the mild range. By 48 hours post-methadone, the patient was fully switched to buprenorphine, and he only experienced ~10 hours of withdrawal symptoms beyond the mild range.

Conclusion: The purpose of this case report is to demonstrate that in inpatient settings it is feasible within 36-48 hours to directly transition from relatively high dose methadone to oral buprenorphine. This contrasts with the commonly held belief that transition must be very slow and gradual. We suggest that clinicians consider more rapid transitions particularly in the inpatient setting where close monitoring and withdrawal-symptom management are available.

Keywords: Bridging; Buprenorphine; Methadone; Opioids; Withdrawal; μ-opioid receptor

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List of Abbreviations

OUD: Opioid Use Disorder

COWS: Clinical Opiate Withdrawal Scale

Background

Between the years 1999 and 2014, the US has witnessed a tripling in the rate of deaths related to opioid use. Consequently, there has been an increased focus in treating opioid use with a primary step being the introduction of an opioid agonist. Both methadone and buprenorphine have been used in managing Opioid Use Disorders (OUD) [1]. A recent meta-analysis, spanning 15 randomized control trials and 36 cohort studies, showed that opioid agonist treatment is associated with lower all-cause mortality rates (RR, 0.47; 95% CI, 0.42-0.53) [2]. Buprenorphine is often preferred over methadone due to its safety and convenience. Buprenorphine, unlike methadone and most other opioids, has a ceiling effect when it comes to respiratory depression, which helps mitigate the risk of fatal overdose. Additionally, as a high-affinity partial agonist of the μ-opioid receptor, the drug can minimize the patient's desire to seek other, more harmful opioids, as these other opioids will not be able to exert their full effects. It is for these reasons that buprenorphine is 6 times less likely than methadone to lead to overdose [3]. Buprenorphine is not only preferable due to its safety, but there is the added convenience with its use that it can be prescribed on an outpatient basis and taken at home. Methadone, on the other hand, must be obtained in-person at designated clinics for each dose when used for OUD. This inconvenience often results in patients not receiving their necessary medication.

Unfortunately, a severe withdrawal reaction is often noted during the switch from methadone to buprenorphine, based on its high-affinity to the μ-opioid receptor and partial agonistic properties leading to replacement of the full agonist methadone. To avoid withdrawal reactions clinicians often wait for methadone levels to get appropriately low which may take up to 96 hours [4] before introducing buprenorphine. The long wait also increases the risks of withdrawal in and of itself. This can result in cessation of treatment with potential

subsequent overdose. To ease this transition, several approaches have been used clinically in this crossover stage of treatment. For example, in the Bernese method, [5,6] buprenorphine (either oral or transdermal) is introduced gradually starting at very low doses. The Stanciu method is another approach where a transdermal fentanyl patch is used as a bridge [7]. However, these methods can be lengthy (often up to ~1 week) and may require access to transdermal buprenorphine or fentanyl patches.

Following is the case of a patient who was able to directly transition from 80mg methadone to oral buprenorphine within 36-48 hours. This direct and rapid transition was done on an inpatient setting with close monitoring and withdrawal symptom management. The case highlights the individualized nature of treatment and can be a reasonable alternative to bridging methods of transitioning from methadone to buprenorphine.

Case Presentation

Mr. A, a 32-year-old male with history of bipolar disorder and OUD, presented for psychiatric stabilization and inpatient substance use rehabilitation. Mr. A used between 5 bags and 1 bundle of heroin daily. He had attended a methadone maintenance program intermittently for a year but had discontinued treatment a few weeks before hospitalization. On admission Mr. A had been without heroin for 2 days and had a Clinical Opiate Withdrawal Scale [8] (COWS) score of 25. The following day, he was started on his previous maintenance dose of 80mg methadone daily, which progressively and predictably decreased his COWS score to 0 (Figure 1A). After 15 days of methadone and further psychiatric stabilization, Mr. A desired a switch from methadone to buprenorphine due to the comparative safety profiles and his difficulty in getting to the methadone clinic. Neither transdermal buprenorphine nor transdermal fentanyl was available. The decision was made to try a direct transition from methadone to buprenorphine; Mr. A's inpatient hospitalization allowed for close monitoring and withdrawal symptom management during this transition.

The last methadone dose of 80mg was given at 8am with COWS beginning to rise over the next 24 hours without methadone (Figure 1B). At 34 hours post methadone, the patient reached a peak COWS of 27, entering the moderately severe withdrawal range. Buprenorphine was introduced at a 2mg dose at 36 hours post methadone. He received an additional 2mg buprenorphine dose 4 hours later (midnight), at which point he fell asleep and slept well through the night. He awoke with COWS back in the mild range of 9 and then 7. After 2 more doses of 2mg buprenorphine, the dose was increased to 8mg twice daily. The patient never again surpassed the mild withdrawal range. This case shows that bridging methods are not always necessary: direct transition is a feasible, reasonable option for an inpatient who can be closely monitored and treated symptomatically for withdrawal.

Discussion and Conclusion

The present case highlights a safe and rapid way to directly transition patients from methadone to buprenorphine. This patient entered moderately severe withdrawal after methadone cessation (COWS of 27), as expected, but his symptoms were managed as needed until buprenorphine was added. Initiating buprenorphine 36 hours after last methadone dose (Figure 1B) brought COWS down from the moderately severe range at nighttime to the mild range (COWS of 9 and then 7) by the following morning-48 hours in total from last methadone dose.

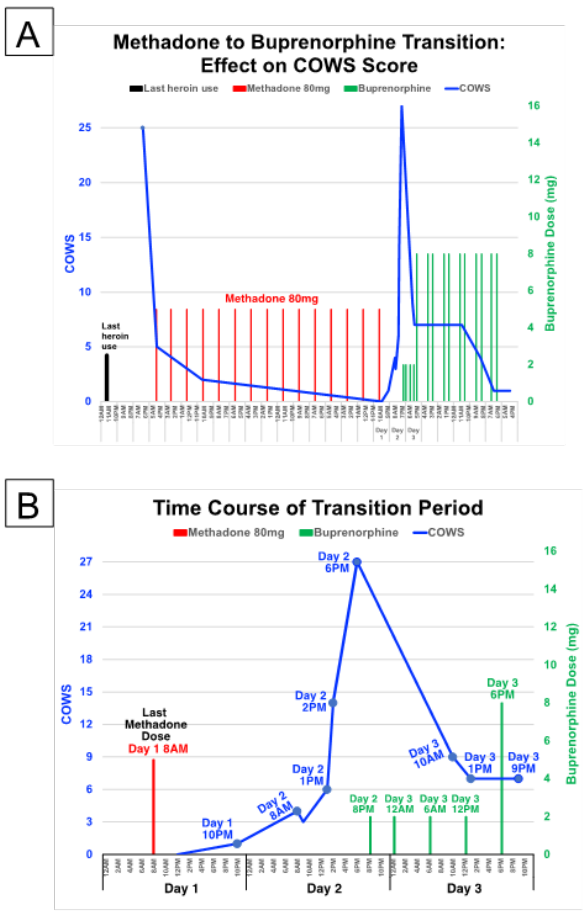

Figure 1: Time course of methadone and buprenorphine administration and the effect on COWS score. A) Methadone (red) to buprenorphine (green) switch with accompanying COWS score (blue) over entire time of case. "Day 1" refers to day of last methadone dose. B) Higher resolution examination of methadone (red) to buprenorphine (green) switch with COWS score (blue) just over days of transition period. "Day 1" refers to day of last methadone dose.

This case provides an alternative to the various bridging methods. The crossover from methadone to buprenorphine within 36 hours, with return to mild withdrawal within 48 hours total, was facilitated by close monitoring and management, it prevented the excess prescribing of opioids, and it meets the current mandate of shorter treatment duration in most settings. It is important to keep in mind that controlling withdrawal symptoms during this transition period is not simply because we want the patient to be comfortable; if patients experience precipitated withdrawal, they are less likely to stay in treatment [6]. Frustration with the process can lead patients to abandon the program or physician they are working with, seek opioids elsewhere, and potentially overdose. The fact that this patient was being treated at an inpatient level of care, in a safe and controlled environment, likely helped the success of this case.

With direct transition, determining the precise time to initiate buprenorphine is difficult-clinicians are encouraged to wait for withdrawal to reach a certain point, but this uses the COWS system which, while validated, [9] is prone to user-to-user variability. Limitations of this case include reliance on a subjective method of withdrawal

assessment. One clinician might rate a patient in moderately severe withdrawal and initiate buprenorphine, while another might rate the same patient as mild and wait. We did wait for the patient to cross into the moderately severe threshold, but our decision was based less on the absolute COWS value and more on the appearance of new symptoms: within a short period, the patient started having a tremor, nasal symptoms, multiple episodes of diarrhea, and muscle aches in addition to his previous symptoms of tachycardia, restlessness, irritability and increased pupil size. The difficulty is that the course of symptoms is different in each patient. One patient may have diarrhea early on, while for another it might not manifest until later, so the guidelines for buprenorphine initiation cannot be symptom-specific.

This case highlights the need for more objective measures of withdrawal. While one would expect that decreasing methadone plasma levels would correlate with increasing COWS scores, the data have not borne this out, [10] so monitoring methadone blood levels to decide when to initiate buprenorphine would not be effective. Further research should focus on identifying biologically-based indications for the appropriate time to initiate buprenorphine. Ultimately, it is up to the physician to determine the most appropriate method given the patient and the setting. However, this case demonstrates that rapid and direct transition is indeed a reasonable option in the inpatient setting where the patient can be monitored and treated symptomatically.

Declarations

Ethics approval and consent to participate: All potential risks, benefits, and alternatives to initiating buprenorphine treatment at 34 hours post-methadone were discussed with patient prior to administration. The patient consented to receiving buprenorphine.

Consent for publication: Consent for publication could not be obtained due to the patient's loss to follow-up. This patient's anonymity was preserved by changing his initials and slightly changing his age. There are no other identifying features in this case report.

Availability of data and materials: Not applicable.

Competing interests: Not applicable.

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Author's contribution: SMP was the medical student working under the attending physician NK in the treatment of this patient. This manuscript was jointly written by SMP and NK. Both authors read and approved the final manuscript.

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Footnotes: Not applicable.

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