Behavioral Health

Case Report

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Successful buprenorphine transition while overlapping with a full opioid agonist to treat chronic pain: a case report

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Abstract: Buprenorphine is a partial mu opioid agonist that has been increasingly utilized to treat patients with chronic pain and opioid use disorder (OUD). The drug has proven to provide significant chronic pain relief at low doses ranging from 75 to 1800 mcg. The conventional buprenorphine transitional process delays its introduction until patients begin withdrawal. However, this process can pose a barrier to both patients and providers due to some patients' inability to tolerate traditional prerequisite withdrawal. To our knowledge, this is a rare reported case to describe a transitional process utilizing buccal buprenorphine in which a patient with chronic pain simultaneously tapered completely off an extended-release (ER) full opioid agonist and uptitrated buprenorphine. The patient was weaned from oxycodone ER 30 mg every 12 h and oxycodone/acetaminophen 10/325 mg 3x/day for breakthrough pain utilizing an unconventional approach. Tapering down to oxycodone ER 20 mg 2x/day for the first 2 weeks was successful. However, reducing to oxycodone ER 10 mg 2x/day for the following 2 weeks presented adherence difficulty and increased breakthrough pain. At this time, buccal buprenorphine was added at 300 mcg daily for 3 days. From days 4 to 6, buprenorphine was increased to 300 mcg 2x/day and oxycodone ER decreased to 10 mg daily. Six days later, oxycodone ER was discontinued and oxycodone/acetaminophen continued as needed. The patient exhibited no signs of withdrawal and adequate relief of symptoms through this tapering process. At the 1-month follow-up, the patient was doing well and was being treated solely with buprenorphine and oxycodone/acetaminophen to control her breakthrough pain. After 5 months, buprenorphine was increased to 600 mcg 2x/day and her oxycodone/acetaminophen decreased to 5/325 mg 3x/day as needed. From the start of the patient's taper to her current transition, the patient reduced her morphine milligram equivalent (MME) dosage from 135 MME to 22.5 MME. The Clinical Opioid Withdrawal Scale (COWS), which measures the severity of a patient's opioid withdrawal symptoms, was consistently less than 5. This buprenorphine schedule demonstrated a successful tapering approach for this patient because she had reported improved quality of life and function. A patient-centered osteopathic treatment approach was utilized when the patient presented with mid-taper adherence difficulty. Transitioning patients from full to partial opioid agonists could become an important practice standard for patient safety not only for formal pain management practices but also in primary care, family practice, and even geriatric offices.

Keywords: buprenorphine; chronic pain; opioids; withdrawal.

Buprenorphine is a partial mu opioid agonist that has been increasingly utilized to treat patients with chronic pain and opioid use disorder (OUD) [1]. The drug has proven to provide significant chronic pain relief at low doses ranging from 75 to 1800 mcg; higher doses ranging from 2 to 24 mg are utilized to treat patients with OUD [2]. Additionally, buprenorphine at this higher dosage has been shown to augment the analgesic effect when the dose is divided 3 times a day (TID) to 4 times daily (QID) [3]. The medication can be administered orally, sublingually, by injection, or as an implant [1].

Buprenorphine has a high receptor binding affinity compared to a full opioid agonist. When this medication overlaps at higher buprenorphine doses, the full agonist is displaced from the mu receptor, resulting in precipitated withdrawal [4]. The conventional buprenorphine transitional process delays its introduction until patients begin withdrawal, demonstrating a Clinical Opioid Withdrawal

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Scale (COWS) [5] score of ≥5 [6]. However, this process can pose a barrier to both patients and providers due to some patients' inability to tolerate traditional prerequisite withdrawal, leading to relapse to opioid use [6]. The smaller receptor saturation associated with lower buprenorphine doses, notably those utilized for chronic pain (75 to 1800 mcg), brings a reduced risk for precipitated withdrawal when utilized with full mu agonists [7]. The risk can be further reduced by decreasing the amount of daily opioid use to 30 morphine milligram equivalent (MME) or less prior to initiating therapy [7].

Alternative strategies have emerged in practice, most notably a micro-dosing induction schedule for buprenorphine introduced in 2010 that has been dubbed "the Bernese Method." [8] It was theorized that the pharmacokinetics of buprenorphine, its slow dissociation from the receptor, and its relatively long half-life made it improbable that the repetitive administration of very small doses with sufficient dosing intervals would precipitate opioid withdrawal [8]. Over time, buprenorphine would accumulate at the receptor and gradually replace the full mu agonist (e.g., fentanyl, heroin) [9]. Buprenorphine demonstrates a ceiling effect for respiratory depression with dosage increases, mitigating the risk of both withdrawal and respiratory depression when overlapped with a full mu agonist [9].

Multiple case studies have demonstrated successful transition to buprenorphine maintenance by overlapping with high doses of full mu agonists [4, 8, 10]. Studies with 8 patients [4], 2 patients [8], and 1 patient [10] have shown that patients with OUD have tolerated the process well while experiencing, at most, mild opioid withdrawal and craving. A systematic review with 24 patients showed a transition to buprenorphine with cessation of opioid agonists in 21 (87.5%) patients [6]. Titration methods have varied, but they all follow the same concept. Buprenorphine dosage usually starts at approximately 0.25 mg daily and is titrated up to 12 mcg to 16 mg daily over 7–10 days [10]. The full mu agonist is either tapered slowly or stopped once the desired dose of buprenorphine is reached.

This case report describes a transitional process with buccal buprenorphine in which a patient with chronic pain tapered completely off her extended-release (ER) full mu opioid agonist while simultaneously up titrating the buprenorphine. It was not an induction but rather a variation of previously tried methods and concepts that have utilized buprenorphine for the treatment of OUD and chronic pain. Specifically, buprenorphine was utilized in this case to assist the taper.

Case description

A 70-year-old white female with a history of fibromyalgia, Lyme disease, knee osteoarthritis, lumbar radiculopathy, and peripheral neuropathy presented to our clinic in September 2021 for management of chronic thigh, forearm, and radicular back pain. Her associated symptoms included numbness, paresthesias, and muscle spasms. Her pain level was 6/10. She was on opioids since 2013. She was consented for this case report (both in-person on hardcopy and verbally) a few months after the transition period, and she provided informed consent for publication. Due to adverse effects, it was decided that it would be best to wean her opioid medications, which included oxycodone ER 30 mg every 12 h with oxycodone/acetaminophen 10/325 mg TID as needed for breakthrough pain. The plan was to wean her off the oxycodone ER over the course of 6 weeks by reducing the dosage in 2-week steps, starting with 20 mg twice daily (BID), then 10 mg BID, and finally 10 mg daily before stopping it completely. The intention was to convert her treatment to buprenorphine at that time. Tapering down to oxycodone ER 20 mg BID for the first 2 weeks was successful. However, reducing to oxycodone ER 10 mg BID for the following 2 weeks presented adherence difficulty and increased breakthrough pain to QID. Her pain level increased slightly to 7/10. At this time, buccal buprenorphine was added at 300 mcg daily for 3 days, followed by 3 days with buprenorphine increased to 300 mcg BID and oxycodone ER decreased to 10 mg daily. Six days later, oxycodone ER was discontinued and oxycodone/acetaminophen continued as needed (Table 1). The patient exhibited no signs of withdrawal and reported adequate relief of symptoms through this tapering process.

Medications included pregabalin 300 mg nightly, eszopiclone 3 mg nightly, clopidogrel 75 mg daily, atorvastatin 80 mg nightly, and levetiracetam 750 mg BID.

Osteopathic structural examination and considerations

No deformities, swelling, or erythema were noted in the thoracic and lumbar spine. Bilateral hypertonicity of the paraspinal muscles was felt. Gait was equal and symmetric. Osteopathic manipulative treatment (OMT) was not utilized due to the patient's noncompliance with in-person visits and time constraints.

Table 1: Daily buprenorphine dosage overlapping with oxycodone ER.

Days	Oxycodone ER[a], mg	Buprenorphine[b], mcg
0	20	0
1	20	300
2	20	300
3	20	300
4	10	600
5	10	600
6	10	600
7	0	600

[a]Extended-release total daily dosage; [b]Buccal buprenorphine (Belbuca) daily doses.

A patient-centered osteopathic treatment approach was employed when the patient presented with mid-taper adherence difficulty. Rather than continuing the conventional method of a strict taper and allowing the patient to experience withdrawal symptoms, we adopted a more humanistic method. During the osteopathic palpatory examination, we explained the examination findings, the osteopathic philosophy on pain, and the evidence-based science behind our pain management plan [11]. This allowed us to educate the patient and to develop trust, which ultimately reinforced the patient-physician relationship. When treating patients with chronic pain, it is also important to address the biopsychosocial elements such as anxiety, substance use, and other stressors. Osteopathic considerations of these mind-body connections as a means of decreasing biomechanical and biochemical stressors can be beneficial for patient buy-in and treatment adherence [12].

Results and follow-up

At the 1-month follow-up, the patient was doing well and was being treated solely with buprenorphine and oxycodone/acetaminophen to control her breakthrough pain. Her pain level was 4/10. Her oxycodone/acetaminophen 10/325 mg dosage was initially continued QID as needed and eventually weaned down to TID after 1 month of maintenance therapy. The buprenorphine dosage was increased to 450 mcg BID at 2 months after transition in response to the increased pain associated with her heightened activity level. After 5 months, buprenorphine was increased to 600 mcg 2x/day and her oxycodone/acetaminophen decreased to 5/325 mg 3x/day as needed. Her pain level was 2/10. From the start of the patient's taper to her current transition, the patient reduced her MME dosage from 135 MME to 22.5 MME. During the initiation of buprenorphine therapy, she had a daily opioid usage of 90 MME. Her retrospectively calculated COWS score was consistently less than 5 at every visit [5].

Discussion

This buprenorphine schedule demonstrated a successful tapering approach for this patient because she had reported improved quality of life and function. She was motivated to continue utilizing buprenorphine while decreasing the frequency of her oxycodone/acetaminophen. If necessary for pain management, her dosage could be increased to a maximum of 900 mcg BID [2]. The remaining goal is to determine the optimal dose for her for the maintenance phase in order to limit the use of a breakthrough medication.

Tapering of opioid medication is indicated in circumstances including the occurrence of adverse events or known side effects such as opioid-induced hyperalgesia, hypogonadism, or immune dysfunction [13]. However, patient anxiety regarding how tapering may affect their function can make it difficult for them [14]. In this case, the patient remained comfortable during the transition by starting with a higher initial dose (300 mcg) of buprenorphine to provide adequate pain relief.

Although the duration needed to achieve buprenorphine maintenance may take longer with this method compared with the conventional tapering strategy, it may be helpful for patients fearing withdrawal [8]. It is also convenient, because it avoids the need for patients with anxiety, impulsivity, or work and family responsibilities to undergo the transition process through active withdrawal in a supervised clinic setting [10]. This method should be highlighted as a convenient alternative to buprenorphine use that is favorable and safe, because the pharmacokinetics of buprenorphine exhibit a ceiling effect on the respiratory depression and the ability for rapid titration [10]. Additional research involves utilizing other buprenorphine products such as transdermal patches and higher-dose buprenorphine-naloxone–like medications to treat pain and to facilitate transitions.

Transitioning patients from full to partial opioid agonists could become an important practice standard not only for formal pain management practices but

also in primary care and even geriatric offices. Geriatric patients on opioid analgesia are at risk of falling or developing respiratory depression, constipation, and cognitive deficiencies that adversely affect patient safety [15]. Adjustments should be done while still allowing the patients to function and maintain their independence [15].

Limitations

The study lacks biopsychosocial objective measures such as the Beck/Hamilton depression scales to observe the patient's fear of withdrawal and stressors before, during, and after the taper. The COWS score was calculated retrospectively through chart documentation and confirmed at follow-up visits. A standardized pain instrument was not utilized, as the primary concern was function and/or withdrawal symptoms as opposed to quantitative numbers. The initial tapering decision was made on a subjective assessment by the physician and patient as it was clinically appropriate. Subjective improvements in quality of life and function can be better observed with pain disability questionnaires. This single case limits the generalizability of the findings and external validity due to the subjective measures listed above.

Conclusions

This is a rare reported case to describe a transitional process utilizing buccal buprenorphine in which a patient with chronic pain simultaneously tapered completely off an ER full opioid agonist and uptitrated buprenorphine. Prospective randomized trials comparing these tested strategies to traditional buprenorphine transition that utilize validated tools measuring long-term indicators of success such as retention and mortality are warranted.

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