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Case Series

Case Series: Lofexidine Treatment of Opioid Withdrawal Symptoms in an Outpatient Setting

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Abstract

In May 2018, lofexidine hydrochloride was approved in the United States for mitigation of opioid withdrawal symptoms to facilitate abrupt discontinuation of opioids in adults. However, the studies supporting its efficacy and safety for treating withdrawal symptoms were all done in the inpatient setting. Here are reported the experiences with 5 diverse patients whose opioid withdrawal symptoms were successfully treated on an outpatient basis. These include patients with opioid use disorder (OUD), patients with chronic pain, and 1 patient with OUD and depression as a co-morbid condition. The cases described here demonstrate how treatment approaches need to be tailored for each patient's situation. The cases illustrate how lofexidine can be used to help mitigate symptoms of opioid withdrawal, across this diverse set of patients and circumstances, in an outpatient setting.

Keywords: *Opioid Withdrawal; Lofexidine; Outpatient Setting; Abrupt Discontinuation; Addiction; Pain Medication*

Abbreviations

DSM: Diagnostic and Statistical Manual of Mental Disorders; OUD: Opioid Use Disorder; SSRI: Selective Serotonin Reuptake Inhibitor

Introduction

Lofexidine hydrochloride, a central alpha-2 adrenergic agonist, was approved in the United States in May 2018 for mitigation of opioid withdrawal symptoms to facilitate abrupt discontinuation of opioids in adults [1]. Lofexidine is not a treatment for opioid use disorder (OUD) but can be part of a complete treatment program for OUD where withdrawal symptom management is needed. Historical comparative studies with clonidine, also an alpha-2 adrenergic agonist, have demonstrated that lofexidine is better tolerated and associated with less systolic hypotension during withdrawal treatment [2].

The lofexidine pivotal clinical trials were conducted in inpatient settings due to the practical demands of the studies [3,4]. Studies in the UK have shown that lofexidine is effective in the outpatient setting as well [2,5-7]. Here are 5 cases of treatment with lofexidine in an outpatient setting in patients with OUD, patients with chronic pain, and 1 patient with OUD and depression as a comorbid condition. All 5 patients met DSM-V criteria for OUD, and all 5 requested to be discontinued from buprenorphine or methadone and were tapered slowly to the lowest dose of these drugs to help manage their fear of withdrawal symptoms. Since many patients experience great difficulty getting off the last lowest dose of these medications, lofexidine was used to help them successfully complete the withdrawal process.

Because written consent for the publication in medical literature was not obtained prospectively from the patients, details are omitted to maintain their anonymity.

Case Presentations

Case 1 (A patient with OUD)

The patient was a 35-year-old man, not using other opioids, who was successfully treated with buprenorphine maintenance therapy for 1 year. He refused to engage in psychosocial therapy and was not willing to attend 12-step recovery meetings. The patient successfully managed his medication and provided negative urine drug testing throughout the maintenance period. His buprenorphine regimen was ultimately reduced over time from 16 mg/d to 1 mg/d. At that point, he was instructed to take buprenorphine 1 mg every other day for 1 week, and then lofexidine was initiated.

He was instructed to take lofexidine 0.18 mg 3 tablets, four times a day for 5 days. After 5 days his dose was reduced to 2 tablets four times a day for 2 days, and then 1 tablet four times a day for 2 days, after which his instructions were to take lofexidine only on an as-needed basis (See table 1).

Days 1 - 5	Days 6 and 7	Days 8 and 9	Days > 7
Three 0.18-mg tablets QID	Two 0.18-mg tablets QID	One 0.18-mg tablet QID	One tablet PRN

Table 1: *Lofexidine regimen as prescribed in the cases.*
PRN, as needed; QID, four times daily.

He successfully discontinued buprenorphine without opioid withdrawal symptoms. However, he was unable to manage the craving and other psychological situations that were cues for him to use opioids. This outcome may have reflected his refusal to accept counseling, which is an important aspect of sustained recovery from substance use disorders [8]. Buprenorphine was restarted, and the patient was instructed to engage in individual psychotherapy. He continues with buprenorphine therapy without any evidence of relapse into active opioid use.

Case 2 (Another patient with OUD)

This patient was a 37-year-old man who had 5 years of ongoing recovery using buprenorphine. This patient was stabilized on 24 mg/d of buprenorphine before he began tapering his dose. His daily maintenance dose was decreased by 4 mg a month until he reached an 8 mg/d dose. Thereafter he was reduced by 2 mg/d for 2 weeks and then to 1 mg/d for 2 weeks. He was then instructed to take buprenorphine 1 mg every other day and then lofexidine was started using the same regimen as described in Case 1.

The patient discontinued without difficulty and has remained abstinent. The patient was seen for another month and was discharged from care thereafter. His urine drug tests were negative for all psychoactive substances prior to his discharge from care.

Case 3 (Patient with chronic non-cancer pain)

This patient was a 50-year-old woman with chronic osteoarthritic pain who had become physically dependent on opioid medications. She was instructed to discontinue the pain medication and was started on buprenorphine 32 mg/d. After she maintained 3 years of documented recovery from opioid use, buprenorphine was slowly tapered by 4 mg each month, ultimately to a dose of 8 mg/d. During maintenance, she was also taking 800 mg of ibuprofen every 6 hours. That medication and dose was continued. After reaching 8 mg buprenorphine daily, her buprenorphine dose was slowly reduced by 1 mg every 2 weeks to a dose of 1 mg every other day. At that time, she was started on lofexidine using the same regimen described in Case 1.

She discontinued lofexidine after a 12-day course. She continues to maintain abstinence from opioid medication while managing her chronic arthritic pain with ibuprofen and physical therapy.

A key point in this particular case is that the patient's use of opioids was for pain and that she did not exhibit the behavioral abnormalities of psychological addiction. Therefore, she did not require counseling or 12-step recovery work.

Case 4 (A patient with chronic post-surgical pain)

This patient was a 57-year-old man with left shoulder chronic pain and a history of multiple shoulder surgeries. He also had alcohol use disorder, for which he had joined a 12-step program. The patient was taking prescription opioids initially but switched to heroin when he could no longer obtain or afford the prescription medications. This patient was initiated on buprenorphine at 24 mg/d. He was maintained on that dose for 2 years without difficulty. During that time, he underwent two surgical procedures on his shoulder. Each time he was instructed to discontinue buprenorphine on the day of surgery and he was instructed to take a prescribed short-acting narcotic medication for 5 days before resuming his maintenance dose of buprenorphine. Before each of his surgeries, he was also treated for pain with ibuprofen 800 mg every 6 hours and he continued that dose.

After completing his physical therapy, he wanted to discontinue use of buprenorphine. As his dose was reduced, he began to complain of increasing pain in his left shoulder. He was started on duloxetine at 60 mg daily in addition to the ibuprofen. Ultimately his buprenorphine was reduced to 1 mg/d and he began lofexidine as prescribed above. He was able to discontinue buprenorphine but continued on duloxetine and ibuprofen.

In this case successful discontinuation of buprenorphine resulted because other treatment modalities were deployed to treat his pain and manage his alcohol use disorder. He complied with prescribed physical therapy and used non-narcotic medications to manage his pain. In addition, he continued 12-step recovery meetings and sponsorship, which helped him manage urges and thoughts about using opioids and alcohol to treat his pain.

Case 5 (A patient with OUD and depression)

Patient was a 45-year-old woman with a history of OUD who began by using prescription oxycodone and acetaminophen for chronic moderate-to-severe musculoskeletal pain due to withdrawal symptoms. She also had developed depression as a result of her chronic pain syndrome. She was successfully stabilized on buprenorphine 16 mg daily and started on a selective serotonin reuptake inhibitor (SSRI). When her pain became better controlled with buprenorphine and 800 mg of ibuprofen every six hours, her depression also improved. She was subsequently weaned off the SSRI, and her buprenorphine was tapered down to 1 mg/d. Her pain and depression remained stable. She was then prescribed lofexidine, again using the schedule described in Case 1 and successfully discontinued use of buprenorphine. Very likely this patient's chronic pain and subsequent depression were exacerbated by opioid-induced hyperalgesia and not ibuprofen-induced hyperalgesia, since she had not been taking ibuprofen initially.

Discussion

This report summarizes our experience with 5 patients, with or without pain, and in one case with depression. All patients were successfully treated in an outpatient setting using lofexidine to treat their withdrawal symptoms while they were being weaned off opioids. When lofexidine was taken as directed, the patients tolerated the medication very well. The report also highlights the need for concomitant psychosocial treatment during medication-assisted treatment, maintenance, and follow-up when necessary after the patients have successfully completed their withdrawal treatment.

The patient in Case 2 underwent psychological counseling and regularly attended 12-step recovery meetings and had a sponsor. When thoughts and urges to use arose, he was able to rely on the tools that he had been taught through counseling and the support of his 12-

step meeting groups and sponsor. On the other hand, the patient in Case 1 did not engage in counseling or 12-step recovery meetings; therefore, when the urge to use returned, he was unable to fend off continued use of opioids.

Case 3 provides an example of physical opioid dependence. This patient did not exhibit any additional psychosocial issues beyond her physiological dependence on the opioids. She was thus able to remain abstinent post-withdrawal treatment without additional interventions. In contrast, Case 4 involved a patient who was addicted to alcohol and thus required post-withdrawal intervention, in this case, participation in a 12-step program.

The patient in Case 5 became dependent on the prescription opioids and was prescribed an opioid-agonist maintenance therapy. Lofexidine was successfully used to discontinue the opioid-agonist. The patient's depression related to her chronic pain may have been in part exacerbated by opioid-induced hyperalgesia.

It is important to note that all comorbid conditions, psychiatric and physical, must be identified and managed to achieve success for opioid withdrawal and subsequent wellness.

Conclusion

The 5 cases presented in this report highlight patient diversity and the necessity to customize treatment approaches based on individual needs. These cases also show the utility of lofexidine to help mitigate symptoms of opioid withdrawal across this disparate set of patients and circumstances in an outpatient setting.

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Conflict of Interest

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