Implementation and results of a symptom-triggered opioid withdrawal protocol at a Veterans Affairs medical center

Jessa Koch, PharmD, BCPP
Sarah Ward, PharmD, BCPP
Christopher J. Thomas, PharmD, BCPS, BCPP

How to cite: Koch J, Ward S, Thomas CJ. Implementation and results of a symptom-triggered opioid withdrawal protocol at a Veterans Affairs medical center. Ment Health Clin [Internet]. 2017;7(6):282-6. DOI: 10.9740/mhc.2017.11.282.

Abstract

Introduction: The Chillicothe Veterans Affairs Medical Center serves veterans from southern Ohio, Kentucky, and West Virginia, where the rates of non-medical opioid use are some of the highest in the nation. Prior to this project, there was not a standardized practice for the treatment of veterans undergoing opioid withdrawal at the facility. In May 2015, a symptom-triggered protocol was initiated to improve the quality of care and decrease the length of detoxification for veterans treated at the Chillicothe Veterans Affairs Medical Center.

Methods: This paper reflects a 2-phase project that took place from August 2014 through June 2016. Phase 1 focused on the development of a symptom-triggered opioid withdrawal protocol using the Clinical Opiate Withdrawal Scale for assessment and buprenorphine/naloxone or clonidine for treatment. Phase 2 was a retrospective cohort analysis comparing outcomes between group 1, before protocol initiation; group 2, after protocol initiation with clonidine; and group 3, after protocol initiation with buprenorphine/naloxone. The primary outcome assessed was length of detoxification (in days). Secondary outcomes included length of hospitalization (in days) for the index admission, outpatient substance abuse treatment program participation rates, and opioid sobriety rates at 3 months after detoxification.

Results: A statistically significant reduction in the duration of detoxification days was detected after protocol initiation in veterans who received buprenorphine/naloxone or clonidine in accordance with the protocol.

Discussion: This retrospective quality analysis supports the use of a symptom-triggered opioid withdrawal protocol using the Clinical Opiate Withdrawal Scale for assessment and clonidine or buprenorphine/naloxone for detoxification treatment.

Keywords: opioid withdrawal, buprenorphine/naloxone, clonidine

Introduction

Opioid use and abuse in the United States is on the rise. The Centers for Disease Control and Prevention estimates that 46 people in the United States die each day from prescription drug overdose. In 2012, US providers wrote 259,000,000 prescriptions for opioids, which was enough for each person in the United States to receive 1 bottle of opioid pain medication. Data from 2012 illustrated that in Ohio alone, 100 prescriptions for opioid
pain medications were written per every 100 people. West Virginia and Kentucky yielded even more opioid prescriptions than Ohio, at 138 and 128 prescriptions per 100 people, respectively.1 The Chillicothe Veterans Affairs Medical Center (CVAMC) is not immune to the ever-increasing number of patients with opioid use disorder. The CVAMC serves veterans from southern Ohio, Kentucky, and West Virginia, where rates of opioid use are among the highest in the nation.3

The CVAMC is not a licensed outpatient detoxification center, so patients are not admitted to the facility for opioid withdrawal alone. Rather, opioid withdrawal is a secondary condition that needs to be addressed. This may help explain why prior to this project, there was no process in place at the CVAMC to treat veterans undergoing opioid withdrawal. Not only was opioid withdrawal underrecognized, but there was no standardization among providers regarding who received medications and which medications were prescribed for withdrawal. If a medication was provided, it was generally limited to clonidine at varying doses and administration frequencies. The initiation of a symptom-triggered opioid withdrawal protocol was intended to offer evidence-based medical treatment to veterans in the hopes of decreasing length of hospital stay and increasing the number of veterans seeking outpatient rehabilitation treatment.

Opioid withdrawal symptom severity can be measured with a number of assessment tools. Some of these tools include: the Subjective Opiate Withdrawal Scale,2 Objective Opiate Withdrawal Scale,2 and the Clinical Opiate Withdrawal Scale (COWS).3 The COWS assessment was created in 1999 by Wesson and Ling3 to improve upon existing opioid withdrawal measurement tools. The COWS assessment can be completed in 2 minutes using an 11-item rating system. Because of its clinical utility, ease of application, and association with buprenorphine therapy, it has become widely used for assessing opioid withdrawal and was the assessment tool selected to measure opioid withdrawal at the CVAMC.4

Per the American Psychiatric Association substance use disorder guidelines,5 medications for opioid withdrawal include methadone (an opioid agonist), buprenorphine (a partial opioid agonist), and clonidine (an α2-adrenergic agonist). The CVAMC is not currently equipped to prescribe methadone for maintenance treatment of opioid use disorders; therefore, buprenorphine/naloxone was chosen instead of methadone because of the opportunity for continued follow-up with a buprenorphine/naloxone maintenance program at the facility. Clonidine was chosen as an alternative medication option for the treatment of opioid withdrawal in patients who were not candidates for long-term buprenorphine/naloxone treatment. Clonidine was also the preferred treatment option in patients with a history of alcohol use disorder and/or sedative hypnotic use disorder in order to avoid the use of a benzodiazepine with an opioid.

Methods

Phase 1: Implementation of the Symptom-Triggered Opioid Withdrawal Protocol

The protocol was designed by 2 postgraduate year-1 pharmacy residents, the pharmacy residency program director, and an addictionologist. Clinical evidence, clinical experience, and consideration of the prescribing capabilities of the providers at this facility influenced the decision to use the COWS assessment to measure the severity of opioid withdrawal and use clonidine or buprenorphine/naloxone as the opioid withdrawal treatment options. The Substance Abuse and Mental Health Services Administration guidelines were reviewed and guided the creation of the buprenorphine/naloxone dosing protocol.6 The clonidine dosing protocol was based on the clinical experience of the addictionologist. Clinical experience also guided the decision of the COWS scores that determined medication administration doses (Table 1). Because patients may still experience signs and symptoms of opioid withdrawal despite treatment with buprenorphine/naloxone or clonidine, “as needed” symptom medications were included in the protocol. These medications included dicyclomine for diarrhea, ondansetron for nausea and/or vomiting, baclofen for opioid cravings and/or muscle spasms, and ibuprofen for bone/joint pain.

Once the protocol was created, it was presented and approved by the Pharmacy and Therapeutics Committee and the Medical Staff Executive Committee at the facility. The postgraduate year-1 pharmacy residents next worked with the information technology department to create an evaluation and medication order set for opioid withdrawal, as well as a note template for the COWS assessment. Once the creation and approval of the computerized patient record system order sets were in place, the education regarding the protocol could be provided to the appropriate staff. Education was primarily provided to the staff from urgent care, acute psychiatry, and acute medicine. Overall, about 35 educational sessions were held. Some sessions were one-on-one, whereas others were held in a group setting.

Phase 2: Retrospective Cohort Analysis

This was a retrospective cohort quality analysis comparing baseline characteristics and clinical outcomes between 3 treatment arms. The 3 treatment arms were as follows: group 1 included veterans who underwent opioid
detoxification before protocol implementation. Individuals in group 1 were selected based on admission to either the acute psychiatry unit or the acute medical unit at the CVAMC with an admitting diagnosis that included terminology related to opioid dependence or withdrawal between November 1, 2013, and May 26, 2015. Groups 2 and 3 included veterans after the protocol was implemented (after May 31, 2015). Group 2 included veterans who received clonidine in accordance with the symptom-triggered protocol, whereas group 3 included veterans who received buprenorphine/naloxone in accordance with the protocol. Veterans in groups 2 and 3 were identified by the inclusion of the “Clinical Opiate Withdrawal Scale” template note in that veteran’s medical record. All patients included in this quality analysis were identified through the computerized patient record system by either admitting diagnosis or note title. There were no exclusion criteria for this analysis, to allow for a naturalistic design.

Baseline characteristics collected included: sex, race, age, opioid of choice, and comorbid psychiatric conditions. The primary outcome assessed was duration of detoxification as measured by duration (in days) of administration of buprenorphine/naloxone or clonidine compared with duration of detoxification (in days) before protocol implementation. Because buprenorphine/naloxone was not used for acute opioid detoxification prior to the protocol, the duration of clonidine administration was used as the surrogate for length of detoxification in group 1. Secondary outcomes included length of hospitalization (in days) for the index admission, outpatient substance abuse treatment program (SATP) participation after index admission, maintenance of sobriety 3 months after index admission (based on patient self-report in computerized patient record system), and maintenance of sobriety 3 months after index admission in veterans who were maintained on buprenorphine/naloxone. Outcomes were compared between the before protocol initiation group (group 1) and the after protocol initiation groups (groups 2 and 3).

This quality analysis was approved as a quality management project by the Institutional Review Board of the University of Cincinnati and the Veterans Affairs Research and Development Committee.

### Statistical Analysis

Demographic and clinical characteristics were assessed using descriptive statistics: means, standard deviations, and percentages. The primary outcome was assessed using an unpaired t test. The secondary outcome of hospitalization duration was analyzed through an unpaired t test. The secondary outcomes of SATP participation, sobriety at 3 months, and sobriety at 3 months in patients maintained on buprenorphine/naloxone compared with those not maintained on this agent were analyzed through a Fisher exact test.
Results

A total of 111 patients were identified for inclusion in this analysis. The before protocol group, group 1, contained 43 patients; group 2 contained 40 patients; and group 3 contained 28 patients. Demographics among the 3 groups were similar, with most patients being white men with a comorbid psychiatric condition. The most common opioid of choice was heroin, and most patients were considered to be polysubstance users (ie, marijuana, alcohol, cocaine, etc). Of note, there were fewer patients considered to be polysubstance users in group 3 because clonidine was the preferred agent for patients with a history of alcohol use disorder and/or sedative hypnotic use disorder. The demographic characteristics can be seen in Table 2.

The primary outcome analyzed the duration in days of administration of buprenorphine/naloxone or clonidine for detoxification (Table 3). The analysis of the primary outcome detected a statistically significant reduction in detoxification duration in favor of the protocol (clonidine: $P = .0064$, $-1.17$ days; buprenorphine: $P = .0267$, $-1.05$ days). The secondary outcome that measured sobriety 3 months after index admission in patients who were maintained on buprenorphine/naloxone was also found to be statistically significant ($P = .0096$). Of a total of 22 patients who were included in the 3-month analysis, 12 of the 17 who were maintained on buprenorphine/naloxone maintained sobriety.

There was no statistically significant difference detected between the before protocol and after protocol groups in the total duration of hospitalization in days (Table 3). Mean hospitalization duration before protocol initiation was 4.64 days compared with 5.30 days ($P = .4571$) after protocol initiation in individuals who received clonidine, and 5.66 days ($P = .3337$) after protocol initiation in individuals who received buprenorphine/naloxone. Substance abuse treatment program participation before and after protocol adoption did not differ significantly (clonidine group: $P = .6609$; buprenorphine group: $P = .0537$), nor did sobriety at 3 months after index admission (clonidine group: $P = .0978$; buprenorphine group: $P = .1744$). The detoxification durations for groups 2 and 3 were compared, and there was no statistically significant difference ($P = .6382$). For further evaluation of the differences in SATP participation and 3-month opioid sobriety rates before and after protocol implementation, the clonidine and buprenorphine/naloxone groups were combined. There was no statistically significant difference detected for either SATP participation ($P = .1791$) or 3-month opioid sobriety rates ($P = .0627$).

Discussion

Overall, the implementation of a symptom-triggered opioid withdrawal protocol decreased the duration in days that buprenorphine/naloxone or clonidine was administered for

### Table 2: Demographic information

| Demographics            | Group 1 | Group 2 | Group 3 |
|-------------------------|---------|---------|---------|
| Patients, No.           | 43      | 40      | 28      |
| Mean age, y (SD)        | 35.28 (9.8) | 42.25 (13.4) | 38 (11.6) |
| Female, No. (%)         | 2 (4.7) | 2 (5)   | 0 (0)   |
| White, No. (%)          | 41 (95.4) | 36 (90) | 25 (89.3) |
| Comorbid psychiatric conditions, No. (%) | 30 (69.8) | 27 (67.5) | 20 (71.4) |
| Opioid of choice, No. (%) |         |         |         |
| Heroin                  | 36 (83.7) | 20 (50) | 23 (82.1) |
| Short-acting opioids    | 4 (9.3) | 4 (10)  | 4 (14.3) |
| Long-acting opioids     | 0 (0)   | 1 (2.5) | 1 (3.6)  |
| Multiple                | 3 (7.0) | 15 (37.5) | 0 (0)    |
| Polysubstance users, No. (%) | 30 (69.8) | 36 (90) | 15 (53.6) |

### Table 3: Primary and secondary outcomes

| Primary outcome          | Group 1 (n = 43) | Group 2 (n = 40) | P Value | Group 3 (n = 28) | P Value |
|--------------------------|------------------|------------------|---------|------------------|---------|
| Detox duration, d (Mean ± SD) | 3.72 ± 2.28 | 2.55 ± 1.22 | .0064  | 2.67 ± 0.90 | .0267  |
| Hospital duration, d (Mean ± SD) | 4.64 ± 4.60 | 5.30 ± 3.44 | .4571  | 5.66 ± 3.43 | .3137  |
| Substance abuse treatment program participation, No. | 17 | 18 | .6609 | 18 | .0537 |
| Sobriety at 3 mo, No. | 13 | 16 | .0978 | 11 | .1744 |

| Secondary outcomes          | Group 1 (n = 43) | Group 2 (n = 32) | P Value | Group 3 (n = 22) | P Value |
|-----------------------------|------------------|------------------|---------|------------------|---------|
| Buprenorphine/Naloxone NOT Maintained | 0 | 12 | .0096 |
detoxification purposes. This quality analysis did not measure the duration in days that additional “as needed” medications were administered for detoxification. It is possible that concomitant “as needed” medication administration altered the COWS score and administration of the symptom-triggered medication.

Even with the decrease in days that patients underwent acute detoxification (as measured by medication administration), there was not an overall reduction in hospital length of stay. Several factors may account for this. Opioid withdrawal is not deemed to be a life-threatening condition, so patients are unable to be admitted for opioid withdrawal alone. Patients undergoing opioid withdrawal typically have another diagnosis, such as suicidal ideation, infection, etc. Length of overall hospitalization likely accounts for resolution of other conditions rather than opioid withdrawal alone. Another confounding issue that often presents at the VA is SATP bed availability for the 21-day residential program. Many times, veterans may remain on the inpatient unit until a bed is available in the outpatient treatment program.

Substance abuse treatment program participation did not differ between the groups. This is a challenging outcome to assess because programming is typically offered to every patient undergoing withdrawal. However, it should be noted that sometimes patients are denied readmission into residential SATP following several recent admissions, because it can be considered not clinically indicated by the screening team.

Although there were no statistically significant differences in 3-month sobriety rates between the 3 groups, the \( P \) value did trend toward statistical significance when groups 2 and 3 were compared to group 1. With a larger patient population this outcome may have reached significance. Additionally, complete sobriety rates at 3 months could not be collected secondary to some patients not reaching the 3-month postdetoxification point at the time of data collection.

This retrospective quality analysis of a symptom-triggered opioid withdrawal protocol demonstrates that implementing such a protocol can reduce detoxification duration. The steps outlined in establishing this protocol along with the evidence to support its use should provide the foundation for other institutions to adopt a similar protocol.

**Acknowledgments**

This material is the result of work supported with resources and the use of facilities at the Chillicothe Veterans Affairs Medical Center in Chillicothe, Ohio.

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