

Original Research

A Retrospective Comparison of the Effectiveness of Buprenorphine Versus Baclofen for Acute Opioid Withdrawal

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Abstract

Background

A significant impediment to opioid cessation or dose reduction is mitigating withdrawal severity that has been shown to affect the course of opioid dependence. Current guidelines recommend the use of buprenorphine and methadone over alpha-2 adrenergic agonists. Baclofen, a GABA-B agonist, has promising results as an adjunct agent for opioid withdrawal but has not been compared to buprenorphine. This study compared the ability of buprenorphine and baclofen to mitigate acute opioid withdrawal.

Methods

This was a single-center, retrospective chart review of 63 patients with diagnosed opioid use disorder that received scheduled buprenorphine or baclofen for 3 days, in addition to as-needed medications during 2 distinct time periods (pre-2017 and 2017-2020). Patients were admitted to the inpatient detoxification unit at Gateway Community Services in Jacksonville, FL.

Results

The results showed that patients achieving detoxification success were 11.2 times more likely to be exposed to baclofen than buprenorphine (95% CI 3.32 - 37.83, $P < .001$). Completion of detoxification protocol (baclofen 63.2% vs buprenorphine 72%, $P = .649$) and incidence of orthostatic hypotension (15.8% versus 0%, $P = .073$) were not significantly different between the 2 groups.

Conclusion

Patients treated with baclofen had a lower frequency of secondary medication use for acute opioid withdrawal than patients treated with buprenorphine. This raises an interesting question of whether baclofen is comparable to buprenorphine for treating opioid withdrawal. A prospective, randomized, controlled trial in a larger patient population is warranted to determine this difference.

Keywords

opioid-related disorders; opioid-related disorders/therapy; opioid withdrawal; substance withdrawal syndrome; buprenorphine; baclofen; inpatient detoxification; substance abuse treatment centers

Introduction

The opioid epidemic has plagued the United States (US) over the past 20 years, accounting for approximately 450 000 deaths.¹ From 2010 to 2018, the rate of inpatient hospital stays

related to opioid use has increased about 50% nationwide and nearly 100% in Florida.² More recent opioid dependence data have shown an association with early adulthood (18-25 years) opioid misuse, nonmedical use of prescription

opioids, and increasing illicit fentanyl use.³⁻⁵ In addition to the significant death toll, the overall economic impact of abuse of and dependence on prescription opioids, as well as fatal overdoses, was estimated to account for \$78 billion in national spending in 2013.⁶ A significant barrier to opioid cessation or dose reduction is withdrawal severity. Providers who are able to mitigate acute opioid withdrawal severity can reduce treatment dropout rates.⁷ However, an actual link between withdrawal severity reduction and a change in chronic opioid dependence has yet to be established.

The 2020 American Society of Addiction Medicine (ASAM) guidelines support opioid agonists (methadone and buprenorphine) over alpha-2 adrenergic agonists such as clonidine, lofexidine, and guanfacine, as they have shown to be more effective in reducing symptom severity and improving retention in opioid withdrawal treatment.⁸ While partial mu-receptor agonist buprenorphine, and full agonist methadone, have comparable efficacy in terms of retention and opioid abstinence, buprenorphine has greater dosing flexibility and can be prescribed in either outpatient or inpatient settings.⁹ In 2018, lofexidine became the first medication to gain US Food and Drug Administration (FDA) approval for opioid withdrawal.¹⁰ Interestingly, the current ASAM guidelines fail to mention the use of the antispasmodic baclofen, which is thought to alleviate withdrawal anxiety through gamma-aminobutyric acid (GABA-B) modulation.⁸ Despite nationwide implementation of non-opioids in hospital protocols, there is a paucity of scientific literature comparing these agents to buprenorphine.

Baclofen is FDA-approved to manage reversible spasticity and is used off-label for alcohol use disorder and opioid withdrawal.¹¹ Several studies have shown that GABA-B agonism in rats suppresses self-administration of cocaine, ethanol, nicotine, methamphetamine, and heroin.¹²⁻¹⁶ Akhondzadeh and colleagues demonstrated that patients treated with baclofen and clonidine had comparable mean short opiate withdrawal (SOW) scores on days 0-3, with those treated with baclofen having lower mean scores on days 7 and 14.¹⁷ A different post-hoc analysis by Ahmadi-Abhari and colleagues, also revealed that baclofen significantly alleviated withdrawal symptoms 10 days sooner than clonidine.¹⁸

None of the buprenorphine products have been FDA approved for opioid withdrawal management, but are often used off-label for this indication.^{19,20} Existing data comparing buprenorphine to non-opioid agonists greatly favors buprenorphine over clonidine. According to a 2010 meta-analysis by Meader, 7 studies demonstrated that buprenorphine was more effective than clonidine in managing acute opioid withdrawal and retention rates.²¹ A 2005 study by Raistrick et al also demonstrated a strong trend towards buprenorphine being more effective than lofexidine but the confidence interval crossed the value of 1, which could not prove superiority.²² In a randomized trial by Ziaddini et al, buprenorphine was as effective as clonidine in controlling withdrawal symptoms.²³

Currently, ASAM guidelines for opioid withdrawal management do not include recommendations regarding opioid agonists and baclofen. Though the literature is limited, baclofen has been shown to display similar effects for withdrawal severity with a lower incidence of orthostatic hypotension compared to clonidine. The purpose of the current study was to evaluate the differences in clinical efficacy between buprenorphine and baclofen in mitigating acute opioid withdrawal within 48 hours.

Methods

Setting

This was a single-center, retrospective chart review of patients seen between January 1, 2017, and September 1, 2020, at Gateway Community Services (GCS) detoxification facility in Jacksonville, Florida; the University of Florida Institutional Review Board approved the study guidelines to protect and maintain patient confidentiality. GCS is a private, non-profit drug and alcohol rehabilitation center for adults and adolescents. Services include residential, outpatient, and inpatient detoxification. Upon admission to inpatient detoxification, a patient's past medical history (ie, psychiatric and substance abuse) and prescribed medications in the outpatient setting are reconciled. The patient is then physically examined for signs or symptoms of intoxication, and a blood alcohol content and urine drug screen are performed. All female patients are given a pregnancy test. Patients with opioid use disorder are then seen by a licensed psychiatrist and of-

ferred medication-assisted therapy with either buprenorphine, methadone, or extended-release naltrexone. If patients decline to receive buprenorphine, they are offered non-opioid options. The non-opioid options consist of a scheduled baclofen dose for 3 days in addition to other as-needed (PRN) medications for severe withdrawal (eg, clonidine, non-opioids for body aches, anti-diarrheal, anti-nausea medication, etc). Benzodiazepines and phenobarbital are administered PRN only if concomitant alcohol or benzodiazepine detoxification is necessary to prevent seizures. For the purposes of our study, we collected data from patients using buprenorphine tapered over a 3-day course in addition to non-opioid agents.

The buprenorphine taper is completed across 3 days in accordance with the drug enforcement agency “3-day” rule under Title 21, Code of Federal Regulations, Part 1306.07(b), allowing providers who are not registered narcotic

treatment programs or DATA waived to administer buprenorphine for the purpose of relieving withdrawal symptoms while arranging a patient treatment program.²⁴ The change in protocol was due to buprenorphine’s superiority for retention in withdrawal treatment, reduction in withdrawal severity, and reduction in mortality compared to non-opioid alternatives.^{21,23,25} The protocol includes performing a baseline Clinical Opiate Withdrawal Scale (COWS) score and vital sign assessment.²⁶ The buprenorphine taper is started once the patient is in mild withdrawal according to the COWS score, in order to reduce the risk for precipitated withdrawal per Substance Abuse and Mental Health Services Administration (SAMSHA) provider clinical support system (PCSS) guidelines.²⁷ Thus, the 2 groups included in our study were patients receiving scheduled baclofen or buprenorphine in addition to PRN agents. **Figure 1** depicts the protocol design.

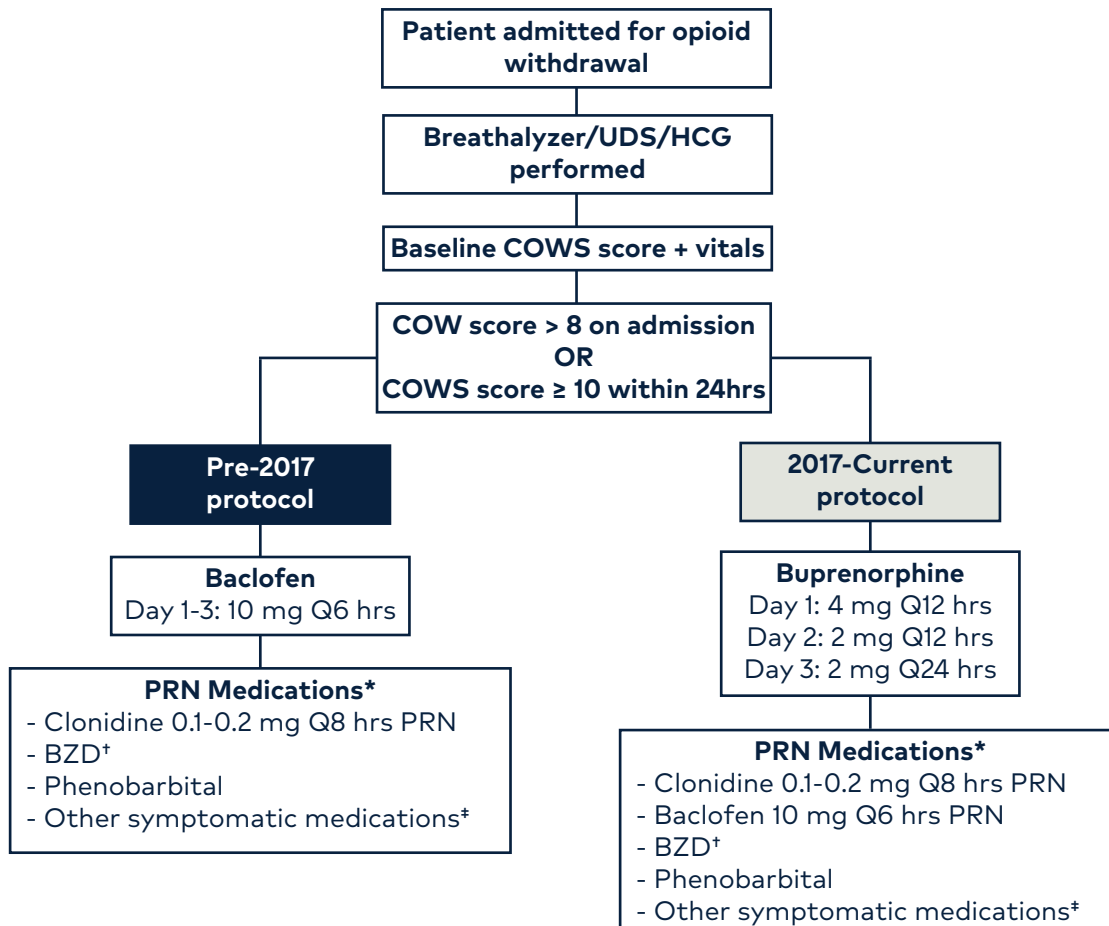


Figure 1. A flowchart shows Gateway Community Services protocol for acute opioid withdrawal intake. *If patient experiences severe withdrawal; +Clonazepam, lorazepam, chlordiazepoxide; *Antidiarrheal, anti-nausea, constipation, muscle aches/pain

Sampling

Study inclusion criteria were patients over 18 years old and receiving scheduled buprenorphine or baclofen, a diagnosis of opioid use disorder defined by ICD-9/10 code (304.00, 304.01, 304.02, 304.03, 304.70, 304.71, 304.72, 304.73, 305.50, 305.51, 305.52, 305.53, F11.24), and a COWS score greater than or equal to 8 on admission or greater than or equal to 10 within 24 hours of admission. Exclusion criteria were patients receiving PRN medication first prior to starting the drug protocol (ie, buprenorphine or baclofen) at the time of admission, those concomitantly prescribed baclofen, buprenorphine, or an alpha-2 adrenergic agonist prior to admission, those with a history of allergy to buprenorphine and baclofen, patients lacking a daily COWS score, blood pressure rate, heart rate, or respiratory rate documentation during admission, or those with a urine drug screen positive for methadone. Patients with a methadone positive urine drug screen were also excluded given its prolonged half-life (24-150 hours), which could potentially affect the COWS scores during the hospital stay. The authors decided on the COWS score of greater than or equal to 8 on admission or greater than or equal to 10 within 24 hours of admission for both study groups in an attempt to include patients with mild to moderate baseline withdrawal severity, which most accurately represents the real-life patient population experiencing acute opioid withdrawal. Scores less than 8 on admission could potentially indicate

that the patient still has opioids in their system, increasing the risk for precipitated withdrawal upon buprenorphine administration. Precipitated withdrawal would not be a factor in patients receiving baclofen, as it does not possess opioid receptor binding. The patient selection process is shown in **Figure 2**. We report how we determined our sample size, all data exclusions (if any), all data manipulations, and all measures in the study.

Interventions

Per the study protocol, patients in the baclofen group received 10 mg baclofen by mouth with food every 6 hours for 3 days, in addition to other PRN medications for severe opioid withdrawal symptoms that were not responding to the baclofen protocol. A hold on baclofen was initiated if patients had an observable change in neurological status or deterioration in mental status for which the provider was contacted. As a result of holding medications for the aforementioned reasons, patients may have received a total daily dose of 10 to 40 mg. PRN medications for severe withdrawal symptoms included 0.1 to 0.2 mg clonidine every 8 hours for systolic blood pressure (SBP) greater than 160 mmHg or diastolic blood pressure (DBP) greater than 90 mmHg, antidiarrheal medication (ie, loperamide), anti-nausea medication (ie, ondansetron), constipation medication (ie docusate, milk of magnesia), body ache medication (ie, acetaminophen or ibuprofen), chlordiazepoxide (25-50 mg), clonazepam (0.5-

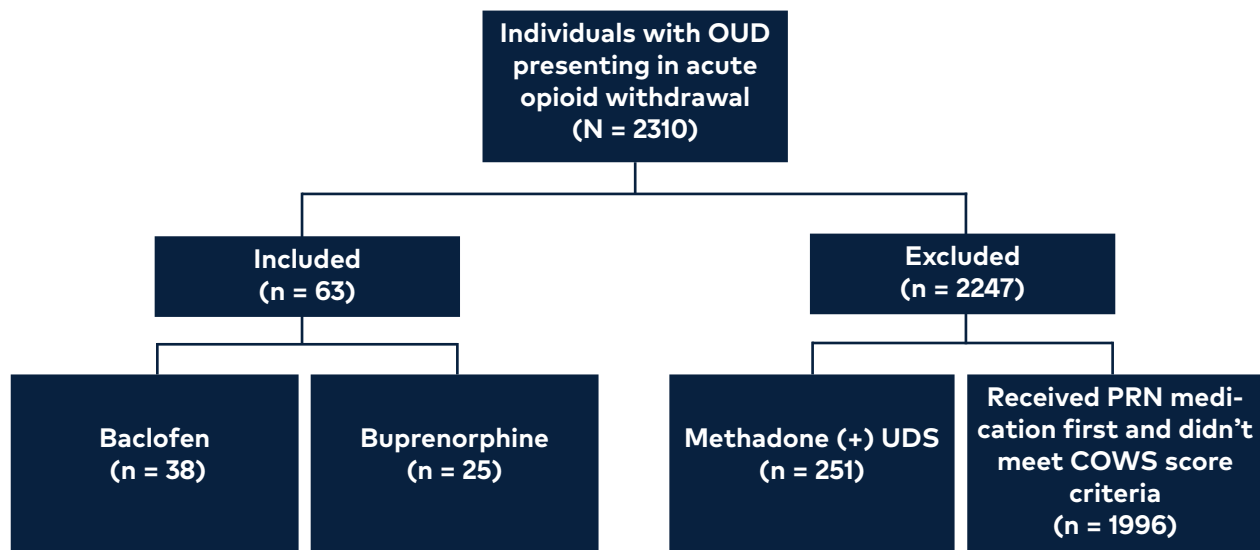


Figure 2. A flowchart shows patient inclusion and exclusion criteria during the study period.

2 mg), lorazepam (0.5-1 mg), and phenobarbital (30-60 mg) for alcohol or benzodiazepine detoxification. Hold parameters for clonidine were a SBP less than 90 mmHg or a DBP less than 60 mmHg and a heart rate below 60 beats per minute. If phenobarbital was initiated, then clonidine was discontinued due to the risk of central nervous system and respiratory depression effects, psychomotor impairment, hypotension, and orthostasis.

Patients were clinically monitored and began the buprenorphine protocol once mild withdrawal symptoms were observed. Patients then received a twice-daily dose of 2 to 12 mg buprenorphine tapered for 1 to 3 days, in addition to the previously mentioned PRN medications, including baclofen for severe withdrawal that was not responding to buprenorphine alone.

Outcomes

The primary objective of the study was to determine detoxification success or failure. Detoxification success was defined as patients who solely received scheduled medications in detoxification (baclofen or buprenorphine) and conversely, detoxification failure was defined by patients who required additional withdrawal agents (ie, baclofen group receiving clonidine and buprenorphine group receiving baclofen or clonidine) in addition to the scheduled medications.

The secondary objectives of the study were to determine detoxification protocol completion and incidence of orthostatic hypotension. Detoxification protocol completion was defined as patients receiving all scheduled medication doses for days 1-3. The incidence of orthostatic hypotension was defined as a SBP less than 90 mmHg.

Sample Size

The observed proportion of success for baclofen and buprenorphine was 73.9% and 20%, respectively. Therefore, the observed proportional difference between success in the baclofen and buprenorphine groups was 53.9%. Our study included 38 patients in the baclofen group and 25 patients in the buprenorphine group.

Statistical Methods

Continuous nonparametric data were represented as a median (interquartile range 25 to 75%) and analyzed using a Mann-Whitney U-test. The primary outcome was assessed using a stepwise logistic regression model, controlling for predictors using a *P* value of less than .1 for inclusion. Secondary outcomes with categorical data were presented as frequencies and percentages and analyzed using chi-squared/Fisher's exact test. A *P* value of less than .05 was considered statistically significant. A post-hoc analysis of power was performed using our observed proportional difference in the above sample size. All data were analyzed using SAS® for Windows (version 9.4 or later).

Results

Participant Flow and Baseline Characteristics

Of the 2310 charts identified, 63 study participants met the inclusion criteria for final analysis. 2247 participants were excluded from the study primarily due to having a urine drug screen positive for methadone (*n* = 251), or for receiving a PRN medication first, or failing to meet the COWS score criteria (*n* = 1996). The median age was similar between groups (baclofen = 40.1 years vs buprenorphine = 38.9 years); most patients were male (baclofen = 57.9% vs buprenorphine = 60%), White (baclofen = 84.2% vs buprenorphine = 92%), and unemployed (baclofen = 73.7% vs buprenorphine = 84%). Patients reported using fentanyl (48%) and other opioids (ie, morphine, hydrocodone, oxycodone, and hydromorphone [48.6%]) as the primary substance of abuse. Regarding pertinent past medical history, more baclofen patients had hypertension (baclofen = 26.3% vs buprenorphine = 8%) and were actively prescribed more antihypertensive medications inpatient (baclofen = 10.5% vs buprenorphine = 4%). More buprenorphine patients had a mental health diagnosis (baclofen = 26.3% vs buprenorphine = 56%) but were not prescribed more psychiatric medications inpatient (baclofen = 10.5% vs buprenorphine = 8%). Drug screens were comparable at baseline between both groups except having the combination of oxycodone, opiates, and fentanyl which was greater in the buprenorphine group (baclofen = 27.8% vs buprenorphine = 58.3%). Baseline COWS scores were higher in the buprenor-

phine vs baclofen group (13.6 vs 11.9), but each indicated the upper limit of mild withdrawal to the lower limit of moderate withdrawal. None of the compared baseline characteristics were found to be statistically significant. Complete baseline criteria can be seen in **Table 1**.

Outcomes

Primary. A chi-squared/Fisher's exact test was performed on all the baseline criteria regarding the primary outcome of detoxification success or failure using the stepwise logistic regression model. It was determined that the medication

Table 1. Baseline Characteristics

	Baclofen (n = 38)	Buprenorphine (n = 25)	P value
Age, median (IQR)			.432
	40.1 (35.0 – 42.0)	38.9 (32.0 – 45.0)	
Gender, n (%)			.278
Male	22 (57.9)	15 (60.0)	
Race, n (%)			.462
Caucasian	32 (84.2)	23 (92.0)	
Non-Caucasian	6 (15.8)	2 (8.0)	
Employment status, n (%)			.919
Unemployed	28 (73.7)	21 (84.0)	
Living status, n (%)			.099
Homeless	12 (31.6)	4 (16.0)	
Independent	16 (42.1)	17 (68.0)	
Dependent	10 (26.3)	4 (16.0)	
Primary substance problem, n (%)			.305
Other opioids/synthetics	18 (48.6)	12 (48.0)	
Past medical history, n (%)			
Cardiovascular condition	10 (26.3)	2 (8.0)	.435
Respiratory condition	3 (7.9)	2 (8.0)	.999
Hepatitis C	3 (7.9)	2 (9.1)	.649
Mental health diagnosis	18 (26.3)	14 (56.0)	.895
Seizure history	11 (28.9)	12 (48.0)	.417
Home medications, n (%)			
Antihypertensive	4 (10.5)	1 (4.0)	
Psychiatric	4 (10.5)	2 (8.0)	
Drug screening, n (%)			.212
Fentanyl only	7 (19.4)	4 (16.7)	
Oxycodone, opiates only	7 (19.4)	3 (12.5)	
Oxycodone, opiates, and fentanyl	10 (27.8)	14 (58.3)	
None	12 (33.3)	3 (12.5)	
Baseline COWS score, median (IQR)			
	11.9 [10.0-14.0]	13.56 [10.5-15]	
Length of stay (days), median (IQR)			
	5.42 [3.45-7.77]	5.13 [2.84-7.39]	

Table 2. Outcomes

Outcome(s)	Baclofen (n = 38)	Buprenorphine (n = 25)	Odds ratio	Between-group difference (95% CI)	P value
Detoxification success, n (%) [*]	28 (73.86)	5 (20)	11.20	3.32-37.83	< .001
Completion of detoxification, n (%) [†]	24 (63.2)	18 (72.0)	-	-	.649
Incidence of orthostatic hypotension, n (%) [*]	6 (15.8)	0 (0)	-	-	.073

^{*}Primary outcome

[†]Secondary outcomes

^{*}Exploratory outcome

group (baclofen vs buprenorphine) ($P < .001$) and living status ($P < .099$) met the significance level for addition into the initial model controlling for predictors with a P value of less than .1. Upon further stepwise selection, living status did not have a significant relationship with our primary outcome and was removed. The final model included only the drug group (baclofen vs buprenorphine) as the independent variable. Patients who experienced success had 11.2 times higher odds of being exposed to baclofen versus buprenorphine (95% CI: 3.32 – 37.83, $P < .001$).

Secondary. Completion of the detoxification protocol was not significantly different between groups (baclofen: 63.2% vs buprenorphine: 72%; $P = .649$). Orthostatic hypotension was also not shown to be significantly different between groups (baclofen: 15.8% vs buprenorphine: 0%; $P = .073$). Complete primary and secondary outcome data can be seen in **Table 2**.

Discussion

This was the first known retrospective study to compare and assess the clinical effectiveness of buprenorphine and baclofen in an inpatient detoxification facility. Patients achieving detoxification success, requiring no PRN medications for opioid withdrawal, were more likely to be prescribed baclofen than buprenorphine. There were no significant differences in the completion of the detoxification protocol and the incidence of orthostatic hypotension.

Our primary finding was unexpected since buprenorphine is the preferred agent for opioid withdrawal and is widely used as a first-line

agent across healthcare systems. Baclofen is not mentioned in the 2020 ASAM guidelines and is likely used to a lesser extent as an off-label agent.⁸ This recommendation by ASAM is primarily due to buprenorphine’s mechanism of action and established literature showing reduced opioid-related mortality.²⁷ Buprenorphine is a partial agonist at the mu-opioid receptor producing supraspinal analgesia and euphoria, thereby reducing withdrawal symptoms.²⁸ Interestingly, this partial receptor agonism may have a protective effect on respiratory depression risk when co-administered with other full opioid agonists. This effect was demonstrated in a retrospective study showing that increased frequency of non-prescribed buprenorphine use was associated with a lower risk of opioid overdose.²⁹ Additionally, in 2018 Larochelle et al demonstrated that prescribed buprenorphine after a non-fatal opioid overdose was associated with significantly reduced opioid-related mortality within a 12-month follow-up period.³⁰ Baclofen, on the other hand, modulates the GABA-B receptor inhibiting the ventral tegmental area cell bodies from depolarizing and releasing dopamine to the nucleus accumbens. This reduces dopamine-related drug-reinforcing effects.³¹ Baclofen has not demonstrated opioid-related mortality benefits to the authors’ knowledge and has been shown to increase overdose risk with concomitant use of opioids.³²

However, our primary outcome raises an interesting question of whether baclofen is comparable to buprenorphine for mitigating opioid withdrawal. If proven in future studies, it could significantly impact current guidelines and protocols. Institutions may also prefer baclofen in

a controlled setting since its mechanism does not pose a risk for precipitated withdrawal, unlike buprenorphine. This is a major benefit in an era where chronic fentanyl use has made initiation of buprenorphine complex due to the risk for precipitated withdrawal. As mentioned earlier, buprenorphine may still depress the central nervous system, a risk that increases with concomitant opioid use. Buprenorphine historically is initiated when COWS scores are mild to moderate to ensure it does not displace any existing full opioid agonists (eg, heroin, fentanyl).³³ From a cost-savings perspective, a 3-day scheduled course of baclofen is approximately 4 times less expensive than a scheduled buprenorphine taper. Given that the patients treated with baclofen in our study required fewer PRN medications, this could potentially result in overall drug cost savings. Regarding both drugs' schedule statuses, baclofen is not a controlled substance unlike buprenorphine, which is a Schedule III drug.^{11,20} Furthermore, baclofen requires less frequent monitoring from an outpatient perspective. It also may be continued after detoxification, unlike buprenorphine, which adheres to the "3-day" rule set forth by the DEA for administration. Many facilities are not registered as a buprenorphine treatment center, exceeding this "3-day" rule, as this adds another level of complexity regarding regulatory restrictions by the DEA. Our study duration of 3 days is shorter than previously documented inpatient detoxification withdrawals ranging from 3 to 12 days. This is largely due to unavailable COWS score documentations past 2 days and the GCS "3-day" rule for acute detoxification with buprenorphine. Therefore, the comparable literature, based on study duration, would be another inpatient detoxification study conducted by Umbricht et al in which patients received a 3-day course of intramuscular buprenorphine, oral clonidine, or oral methadone, followed by a clonidine transdermal patch on the fourth day.³⁴

We were unable to detect a significant difference in the completion of the detoxification protocol or the incidence of orthostatic hypotension between groups in our study. Orthostatic hypotension has been analyzed in prior literature as it is a potential drug-related adverse event that can negatively impact blood pressure and increase fall risk.³⁵ Our data showed that patients treated with baclofen

had a greater clinical incidence of orthostatic hypotension, but this difference was not statistically significant. This could be due to its mechanism of action or because more patients in this group were prescribed antihypertensive agents at baseline. The number of baclofen doses held due to symptomatic hypotension was not documented.

Baseline COWS scores were similar to those in previous literature, indicating mild to moderate withdrawal.^{17,23,36,37} Our data were from an inpatient detoxification facility comparable to other studies, except for Lintzeris et al, which was conducted in an ambulatory setting.³⁶ In our study, we reported baseline urine drug screen results, which showed fentanyl-positive rates ranging from 17 to 20% between groups, and negative drug screen results from 12.5 to 33.3% between groups. Given the substantial increase in fentanyl use across the US, our data could be considered more generalizable for this patient population. Historically, authors have solely reported study populations as using heroin or opioids and have not provided specific urine drug screen results. Negative urine drug screens may be a result of the short half-life of fentanyl, shorter duration and frequency of use prior to admission to detoxification, or the use of illicit fentanyl analogues, which are unable to be identified. Future studies are needed to analyze illicit fentanyl use and duration of occurrence within a urine drug screen. Our data showed a greater clinical incidence of orthostatic hypotension with baclofen use than Ahmad-Ahbari and colleagues, who reported an overall incidence of approximately 3%.¹⁸ It is unclear in that study how many patients received concomitant antihypertensive medications. Lastly, our study analyzed the completion of a detoxification protocol, which is not the same as treatment retention; therefore, a comparison to previous literature is not appropriate for this metric.

Our study design has several limitations. COWS scores were not obtained in a consistent frequency among patients during detoxification. As a result, this restricted us from performing a direct comparison between both medication groups and identifying differences in withdrawal severity between agents over the course of admission. However, COWS scores were obtained at baseline and after initiation of buprenorphine, and did not subsequently wors-

en. This indicates that buprenorphine-treated patients did not have falsely-elevated COWS scores due to precipitated withdrawal requiring more withdrawal agents as compared to baclofen. Future studies should implement a standardized schedule for obtaining COWS scores for every patient to address this limitation.

Other limitations include the use of a proxy as a primary outcome, variability with the interpretation of detoxification completion, the impact of the COVID-19 pandemic occurring during the buprenorphine group period, and lastly the use of a post-hoc analysis for power in a retrospective study. Our primary outcome, defined as patients who received more than 1 medication for opioid withdrawal, served as a proxy for detoxification failure. This criterion was pre-established by several addiction-trained psychiatrists and has not been evaluated in prior literature. This outcome revealed patients in the baclofen group required fewer PRN medications to manage withdrawal. However, clinical evaluation comparing buprenorphine and baclofen is still limited and warrants further research to prove non-inferiority or superiority. The secondary outcome, assessing the completion of the detoxification protocol, is subject to bias and confounding variables. It may falsely represent patients who recovered sooner than the 3-day course hence not “completing” the protocol. As a result, this outcome should be interpreted with caution. GCS has a standardized protocol for the taper and maintenance of each medication, but patients may require deviation from the set procedure in certain clinical scenarios. Thus, not all patients received the same total daily dose of buprenorphine and baclofen during the study.

The COVID-19 pandemic has had a major impact on mental health and those diagnosed with opioid use disorder. People with opioid use disorder have disproportionately higher rates of psychological trauma and mental health problems at baseline, which can be further exacerbated by social isolation during quarantine.³⁸ While policymakers and practitioners have created new strategies to break down barriers to treating opioid use disorder and expand resources, many individuals were still negatively impacted.³⁹ Our study included patients treated with buprenorphine who

received this drug therapy during the beginning of the COVID-19 pandemic from 2019-2020. While not statistically significant, patients receiving buprenorphine also had nearly twice the incidence of a mental health diagnosis (56% vs 26.3%) versus the baclofen group, highlighting the potential clinical impact on our primary and secondary outcomes as well as the potential for a reduced number of patients seeking detoxification at hospitals in fear of being infected with COVID-19.

Lastly, we performed a post-hoc analysis of power, which is a controversial method of data calculation. It is controversial to conduct a power analysis in this way, as the power calculation cannot be acted on as the study has been completed.⁴⁰ However, power analyses calculated retrospectively can detect whether a statistically insignificant result was due to an inappropriately small sample size, since observed power is directly related to the *P* value.⁴⁰ A reasonable alternative to using observed power is a 95% confidence interval. Given that our confidence interval for our primary outcome contains a large range (3.32- 37.83), we can assume a less precise estimate of the observed proportional difference and our data should be interpreted with caution as a result.

Conclusion

Our study results offer the first known retrospective comparison of baclofen to buprenorphine, the current gold standard, for acute opioid withdrawal. Patients achieving detoxification success were more likely to be exposed to the baclofen protocol versus the buprenorphine taper. Completion of the detoxification protocol and incidence of orthostatic hypotension were not significantly different between groups. These results warrant a prospective, randomized, controlled trial to determine the true difference in effect between agents.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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