

Assessment of a Hospital-Wide CIWA-Ar Protocol for Management of Alcohol Withdrawal Syndrome

Arineh Melkonian, MD; Reenal Patel, MD; Albert Magh, MD; Sampson Fern, MD;
and Calvin Hwang, MD, MPH

Abstract

Objective: To determine if a hospital-wide symptom-based alcohol withdrawal protocol may result in significant clinical improvements to patient outcomes, safety, and hospital efficiency.

Methods: Retrospective/prospective cohort study between January 1, 2016 and December 31, 2016 (pre-protocol), and between March 1, 2017 and August 7, July 2017 (post-protocol). Pre-protocol patients were identified retrospectively using International Classification of Diseases, 10th revision codes (F10.1, F10.2, and Z71.4). Post-protocol patients were identified by the use of a unique alcohol withdrawal order set in their electronic medical record. The primary endpoint was average length of stay. Secondary outcomes included death, escalation of care as defined as requiring intensive care unit (ICU) consultation or the rapid response team, average ICU length of stay, respiratory failure, average benzodiazepine usage, and incidence of seizures.

Results: The study included 276 patients in the pre-protocol group and 145 patients in the post-protocol group. There was a significant reduction found in the primary endpoint of average length of stay (7.15 ± 6.5 days vs 5.7 ± 5.6 days; $P=.02$). There was a significant reduction in the average benzodiazepine use, use of adjunctive medications, need for ICU consultation or rapid response team, respiratory failure, average ICU length of stay, use of neurologic imaging, and the need for lumbar puncture.

Conclusion: Implementation of a Clinical Institute Withdrawal Assessment for Alcohol, Revised—based alcohol withdrawal protocol may significantly improve quality of care, patient safety, and treatment effectiveness in a large, mixed medical/surgical, urban community-based academic medical center.

© 2019 THE AUTHORS. Published by Elsevier Inc on behalf of Mayo Foundation for Medical Education and Research. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>) ■ *Mayo Clin Proc Inn Qual Out* 2019;3(3):344-349

From the Department of Cardiology, Newark Beth Israel Medical Center, NJ (R.P.); Department of Medicine, University of California, Los Angeles (A. Melkonian); Department of Pulmonary and Critical Care, Orlando Regional Medical Center, FL (A. Magh); Department of Gastroenterology, New York Presbyterian/Queens, Flushing (S.F.); Department of Medicine, Weill Cornell Medical College, Flushing, NY (C.H.). When the study was conducted, all authors were affiliated with the Department of Medicine, New York Presbyterian/Queens, Flushing.

Alcohol use disorder represents a major substance abuse problem both in the United States and worldwide.^{1,2} In 2010, US health care costs due to alcohol-use disorders was estimated at \$27 billion with more than 1.01 million people hospitalized with alcohol-related diagnoses.^{3,4} The Clinical Institute Withdrawal Assessment-Alcohol, Revised (CIWA-Ar) is a validated, 10-item assessment tool used to quantify the severity of alcohol withdrawal syndrome (AWS) and is meant to guide clinical treatment using benzodiazepines (BZDs).⁵ Oftentimes, nurses perform regular assessments and may administer symptom-triggered BZD therapy based on the CIWA-Ar score. Typically, a CIWA-Ar protocol may be ordered prophylactically in the emergency department but can

be initiated at any point during the hospital stay if alcohol withdrawal is suspected.

A symptom-based protocol for the treatment of AWS aims to accomplish four goals. First, promptly recognize the condition. Second, appropriately select pharmacologic treatment. Third, incrementally administer the treatment medication based on an objective scale. Last, mitigate potential harms from the treatment and/or rapidly escalate care, if required.⁶

Several earlier studies found that use of symptom-triggered AWS protocols resulted in reduced BZD dosage and decreased length of stay (LOS) in dedicated inpatient addiction centers.⁷⁻¹⁰ A similar improvement to LOS and BZD dosage was found in an emergency department clinical decision unit.¹¹ Implementation

of symptom-triggered AWS protocols also showed reductions in duration of AWS treatment, need for mechanical ventilation, and intensive care unit (ICU) mortality in the ICU setting.¹²

However, later studies have not found similar results. One study revealed decreased incidence of delirium tremens but no other improvements.¹³ Implementation of a CIWA-Ar-based protocol in two Veterans Affairs hospitals found mixed results. One study found no reductions in LOS, total BZD use, or safety events.¹⁴ Another study found reductions in the average cumulative BZD use but no improvement to LOS or safety.¹⁵

The authors hypothesized that by using a multidisciplinary approach from initial evaluation in the emergency department through discharge, providing extensive staff training, and optimizing the computerized physician order entry (CPOE) order set, use of a symptom-triggered AWS protocol could result in improvements to safety, quality, and efficiency in a large, urban teaching mixed medical/surgical hospital.

This study was conducted in a large (535-bed), urban, community-based academic hospital. A hospital-wide CIWA-Ar-based alcohol-withdrawal protocol was implemented on February 28, 2017, for all non-pediatric patients. Before implementation, AWS was managed in an individualized, ad hoc fashion. Pharmacologic approaches ranged from scheduled fixed-doses of BZDs, non-symptom-based loading regimens, and nonstandardized symptom-based protocols at the primary teams' discretion. Choices of pharmacologic treatment included a wide array of BZDs (alprazolam, lorazepam, diazepam, clonazepam, and chlorthalidone), barbiturates (phenobarbital), clonidine, and haloperidol. Management in the ICU included use of propofol, midazolam infusion, lorazepam infusion, and dexmedetomidine, in addition to the aforementioned drugs. Medication choice, dosage, and frequency was determined by the prescribing provider and performed by the nursing staff.

METHODS

We performed a retrospective/prospective cohort study using the CPOE (Allscripts SCM, 16.3). This study was approved by the

local institutional review board. All patients older than 18 years of age admitted to the inpatient services between January 1, 2016, and December 31, 2016 (pre-protocol), identified using the International Classification of Diseases, 10th Revision codes for an admission or discharge diagnosis related to alcohol use (codes F10.1, F10.2, and Z71.4) were eligible for inclusion. Pre-protocol patients not prescribed medications for treatment of AWS were excluded.

The AWS CPOE order set was activated on February 28, 2017. Use of the AWS order set was left to each provider's clinical judgment. No initial risk stratification tool was used. Patients treated using the symptom-based protocol between March 1 and August 30, 2017 (post-protocol) were identified within our electronic medical record by searching for the usage of the unique alcohol withdrawal order set. No patients were excluded from the post-protocol population. Patients admitted between January 1 and February 28, 2017, were not included because many health care providers independently began to modify their clinical practice during the 2-month training period.

Because our institution was unable to cohort AWS patients, we opted to pursue a three-pronged strategy. First, we created a CPOE order set that incorporated the CIWA-Ar and forced-decision treatments based on the score. This order set was rigorously assessed for ease-of-understanding and ease-of-use. Second, our institution identified local champions in all relevant departments and hospital units. These local experts, including members of the rapid response team (RRT), were responsible for guiding their colleagues during the first month after activation. These individuals were also responsible for identifying potential safety events during this time. Lastly, we embarked on a global educational effort for all providers between January 1, 2017 to February 28, of 2017. More than 2000 nurses completed a brief (15 minutes) web-based educational lesson about the CIWA-Ar and how to follow the order set. More than 450 physicians and physician-extenders from emergency medicine, internal medicine, general surgery, and obstetrics/gynecology were educated via traditional venues.

The primary endpoint was average length of stay (ALOS). Based on the pre-protocol

TABLE 1. Baseline Characteristics^a

Demographics/Characteristics	Pre-CIWA-Ar (n=276)	Post-CIWA-Ar (n=145)	Student <i>t</i> test <i>P</i> Value
Age, years	48.0±13.5	46.8±12.7	.39
Male, %	84.7	90.3	.13
Prior alcohol withdrawal, %	62.0	57.0	.34
Prior delirium tremens, %	23.5	16.2	.10
Psychosis, %	5.8	6.3	.83
Depression, %	21.4	15.8	.07
Anxiety, %	13.4	15.2	.66
Cirrhosis, %	10.1	8.3	.60
COPD, %	2.5	2.1	>.99
CAD, %	6.5	4.8	.66
CHF, %	1.5	1.4	>.99
Malignancy, %	1.8	2.8	.50
Prior seizure, %	23.9	22.5	.81
INR, s	1.1±0.6	1.1±0.2	.39
ALT, U/L	71.1±78.3	65.4±69.0	.47
AST, U/L	119.5±150.2	122.6±150.6	.84
Total bilirubin, mg/dL	1.3±2.7	1.0±1.0	.19
Creatinine, mg/dL	0.8±0.4	0.8±0.4	.66
Maximum initial CIWA-Ar score	8.5±5.2	8.4±5.2	.88
Mean blood alcohol level on admission	144.4±147.9	142.1±146.8	.89

^aALT = alanine aminotransferase; AST = aspartate aminotransferase; CAD = coronary artery disease; CHF = congestive heart failure; CIWA-Ar = Clinical Institute Withdrawal Assessment of Alcohol scale, Revised; COPD = chronic obstructive pulmonary disease; INR = international normalized ratio.

population of 276, the authors predicted a 0.5-day reduction in the ALOS from the baseline of 7.2 days ($\alpha=.05$). Calculated sample size to detect a change of 7% was 115.

Secondary outcomes included in-hospital death, need for escalation of care as defined as requiring ICU consultation or the RRT, average ICU LOS, respiratory failure (defined as requiring intubation), mean cumulative BZD usage, and incidence of seizures. The authors also tracked 30-day readmission rates, neurologic imaging use, use of medical observers (sitters), use of lumbar puncture, and use of adjunctive medications (defined as use of non-BZDs for symptomatic treatment of AWS).

Baseline characteristics including age, sex, and pre-existing medical diagnoses were collected as well as clinical laboratory data from the first 24 hours including international normalized ratio, alanine aminotransferase, aspartate aminotransferase, total bilirubin,

creatinine, maximum initial CIWA-Ar score, and mean blood alcohol level were collected (Table 1).

Comparisons of continuous variables between pre- and post-implementation were performed using the independent Student *t* test. The Fisher exact test was used for categorical variables. *P* values less than 0.05 were deemed statistically significant; no multiple-test adjustment to the *P* value was done. All analyses were conducted using SAS 9.4 (SAS Institute, Inc., Cary, NC).

RESULTS

There were 276 patients in the pre-protocol group and 145 patients in the post-protocol group included in the study. There were no statistical differences in the baseline characteristics between the pre-protocol and post-protocol groups. The average age of patients in the pre-protocol group was 47.9 years vs 46.8 years in the post-protocol group. Males

constituted 84.7% of the pre-protocol group and 90% of the post-protocol group. Finally, both groups showed similar baseline levels of aspartate aminotransferase, alanine aminotransferase, mean blood alcohol level, and CIWA-Ar scores on admission.

There was a statistically significant reduction found in the primary endpoint of ALOS when comparing hospitalizations pre- and post-protocol implementation (7.2 ± 6.5 days vs 5.7 ± 5.6 days; $P=.018$).

There was a statistically significant reduction in the average BZD use. This was driven mainly by the decrease in lorazepam use (38.8 mg vs 13.2 mg; $P<.001$). There was a statistical reduction in the use of adjunctive medications (24.3% vs. 15.2%; $P=.03$).

Furthermore, we observed a significant reduction in the use of neurologic imaging (53.6% vs 42.8%; $P=.04$) and lumbar punctures (15.2% vs 7.6%; $P=.03$).

We observed significant improvements to patient safety post-protocol. These included avoiding clinical deterioration defined as need for ICU consultation or RRT activation

(34.1% vs 22.1%; $P=.01$) and respiratory failure requiring intubation (13.8% vs 6.9%; $P=.04$). There was no statistically significant difference found in the secondary outcome of in-hospital death, seizure incidence, 30-day readmission rate, or use of medical observers (sitters) (Table 2).

DISCUSSION

Use of a CIWA-Ar-driven protocol in the general medical/surgical hospital setting has not been well validated. Early studies suggested reductions in BZD dosage and LOS whereas later studies only found BZD reduction or no changes at all. Our experience suggests that a comprehensive, CPOE-based protocol with targeted training may result in significant improvements in outcomes, patient safety, and operational efficiency. Results from this study also lend further support the reduction in the need for ICU-level of care as well as adverse ICU-related outcomes.¹⁶⁻¹⁸

Many potential benefits exist for the use of a symptom-based AWS protocol in the general hospital setting. Our study suggests that a

TABLE 2. Outcomes Associated With Implementation of a Facility-wide, Symptom-based Alcohol Withdrawal Protocol

Outcomes	Pre-CIWA-Ar (n=276)	Post-CIWA-Ar (n=145)	Student t test P Value
Length of stay, d	7.2±6.5	5.7±5.6	.02
ICU length of stay, d	1.5±4.4	0.7±2.1	.01
Mean BZD use (in mg of lorazepam equivalents)	49.3±75.2	21.2±30.4	<.001
Mean lorazepam use, mg	38.8±43.8	13.2±19.4	<.001
Mean diazepam use, mg	33.3±44.7	53.4±115.8	.34
Mean chlordiazepoxide use, mg	395.5±483.2	239.0±295.0	.10
Mean alprazolam use, mg	1.0±0.9	3.6±3.4	.26
Adjunctive medication use, %	24.3	15.2	.03
Neurologic imaging use, %	53.6	42.8	.04
Use of 1:1 sitters, mean h/d	1.6±2.7	1.2±2.9	.20
Safety			
In-hospital death, %	1.5	.69	.66
Respiratory failure, %	13.8	6.9	.04
ICU consult or RRT activation, %	34.1	22.1	.01
Seizure during treatment,%	2.9	2.8	>.99
Requiring lumbar puncture, %	15.2	7.6	.03
30-d readmission rate, %	10.5	12.4	.63

BZD = benzodiazepine; CIWA-Ar = Clinical Institute Withdrawal Assessment for Alcohol, Revised; ICU = intensive care unit; RRT = rapid response team.

standardized protocol may be used by most clinical staff, regardless of their department.

The authors believe that the success of this project depended on several key factors. Early buy-in from key clinical personnel throughout the design, planning, implementation, and monitoring phases ensured that the solution set would be practical and easily understood with minimal training. The CPOE order set included specific criteria for care escalation to mitigate safety concerns. ICU consultation was strongly recommended if the CIWA-Ar remained greater than 16 despite medication, or if patients required more than 200 mg of diazepam or 40 mg of lorazepam within 24 hours. By establishing pre-specified safety criteria, non-ICU staff anecdotally reported much less resistance from ICU consultants for care escalation. The authors hypothesize that once general medical unit staff became comfortable with the level of ICU support, they felt more psychologically safe and were willing to administer treatments based on a protocol.

We acknowledge that the CIWA-Ar has not been well studied for patients in severe/very-severe AWS. As a result, the AWS protocol was deliberately crafted to allow intensive care specialists managing these patients in the ICU to use their own clinical judgment to manage their patients. Observed treatment options included continued use of the CIWA-Ar protocol, continuous BZD infusion, dexmedetomidine, and propofol infusion with intubation. However, this study was not designed to specifically study patients in severe/very-severe AWS.

Using estimated 2017 expenses per inpatient day for New York State of \$2729 provided by the Kaiser Family Foundation,¹⁹ we project that the estimated annual cost savings due to decreased LOS alone at our institution will exceed \$1.3 million, irrespective of the reduction in patient harms, need for further diagnostic testing, or decreased need for care escalation.

One common pitfall with quality improvement design and implementation is the lack of sustainability due the reliance on individual clinical decision-making. The authors designed and implemented a solution that would be relatively “turn-key” and require minimal staff retraining by eliminating

multiple clinical decision-making points. We believe that the key to sustainability is the usability of the solution by local staff. Results from this study were shared with all staff at hospital-wide safety meetings. Nursing staff who were present before implementation of this protocol continue to remark positively 2 years post-implementation.

There are a few limitations to our study. First, this was a single-center study. Our experience may not be generalizable to other centers. Our institution strongly values patient safety; thus, safety initiatives typically receive strong consideration from involved staff.

Second, our patient population is extremely diverse and may not mirror that of typical institutions. Although not specifically studied, historically more than 40% of our patients prefer to communicate in a language other than English. By requiring staff to assess the CIWA-Ar as frequently as every 20 minutes, this may have improved provider-patient communication and earlier detection of hypoactive delirium. Thus, cultural factors may have been responsible for lower performance in the pre-protocol phase.

Third, the nonrandomized retrospective/prospective design may have led to unmeasured differences between the two populations. However, the similarity of patient demographics, comorbidities, initial symptomatology, and admission laboratory values decreases this likelihood. Also, the fact that all admissions were included — and not just unique patients — could potentially affect the magnitude of the observed differences. However, we believe that this reflects the nature of the disease and accompanying psychosocial behavior.

Fourth, the method used to identify patients pre- vs post-protocol was decided a priori to assess the performance of the entire CIWA-Ar protocol, not just the medication regimen. Of the 145 post-protocol subjects, only 7 patients did not receive any BZDs during their hospitalization. We believe inclusion of these subjects did not significantly alter the applicability of our findings.

Fifth, the post-protocol study period was relatively limited. It remains unclear how sustainable these results may be over a longer period. But as mentioned earlier, front-line staff members continue to provide very

positive anecdotal reports of the effectiveness of the protocol. The internal institutional patient safety monitoring system has not detected significant deviations from this protocol that have resulted in significant patient harm. Other subsequent institutional initiatives may affect future outcomes.

Last, a limitation inherent to any protocol that involves multiple assessments using multiple providers may be the inability of a caregiver to perform the required steps due to a lack of knowledge, training, or time constraints. The protocol designers attempted to minimize variability through intentional incorporation of forced decisions into the CPOE order set. Further research may be required to assess the extent of protocol variation hospital-wide.

CONCLUSION

Significant debate remains regarding the optimal treatment approach for AWS in the general medical/surgical inpatient population. Earlier studies performed in dedicated alcohol detoxification centers or observation units showed improved outcomes, but results from more recent studies performed in general hospital settings were less conclusive. Our results suggest that implementation of a symptom-based AWS protocol in a general medical/surgical hospital may result in significant improvements to patient safety, operational efficiency, and generate potential cost savings.

Abbreviations and Acronyms: **ALOS** = average length of stay; **AWS** = alcohol withdrawal syndrome; **BZD** = benzodiazepine; **CIWA-Ar** = Clinical Institute Withdrawal Assessment for Alcohol, Revised; **CPOE** = computerized physician order entry; **RRT** = rapid response team

Potential Competing Interests: The authors report no conflicts of interest.

Correspondence: Address to Calvin Hwang, MD, MPH, Department of Medicine, New York Presbyterian/Queens, 56-45 Main Street, Flushing, NY 11355 (cah9096@med.cornell.edu).

REFERENCES

- Lieber CS. Medical disorders of alcoholism. *N Engl J Med*. 1995; 333(16):1058-1065.
- Nutt DJ, King LA, Phillips LD. Independent Scientific Committee on Drugs. Drug harms in the UK: a multicriteria decision analysis. *Lancet*. 2010;376(9752):1558-1565.
- Centers for Disease Control and Prevention. Excessive drinking is draining the U.S. economy. <https://www.cdc.gov/features/costsofdrinking/>. Accessed January 5, 2018.
- National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health. *Alcohol-Related Emergency Department Visits and Hospitalizations and Their Co-Occurring Drug-Related, Mental Health, and Injury Conditions in the United States: Findings From the 2006-2010 Nationwide Emergency Department Sample (NEDS) and Nationwide Inpatient Sample (NIS) (NIH Publication No. 13-8000)*. Bethesda, MD: U.S. Government Printing Office; 2013.
- Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: The revised Clinical Institute Withdrawal Assessment for Alcohol scale (CIWA-Ar). *Br J Addict*. 1989;84(11):1353-1357.
- DeBellis R, Smith BS, Choi S, Malloy M. Management of delirium tremens. *J Intensive Care Med*. 2005;20(3):164-173.
- Saitz R, Mayo-Smith MF, Roberts MS, Redmond HA, Bernard DR, Calkins DR. Individualized treatment for alcohol withdrawal. A randomized double-blind controlled trial. *JAMA*. 1994;272(7):519-523.
- Reoux JP, Miller K. Routine hospital alcohol detoxification practice compared to symptom triggered management with an objective withdrawal scale (CIWA-Ar). *Am J Addict*. 2000 Spring;9(2):135-144.
- Sachdeva A, Chandra M, Deshpande SN. A comparative study of fixed tapering dose regimen versus symptom-triggered regimen of lorazepam for alcohol detoxification. *Alcohol Alcohol*. 2014;49(3):287-291.
- Daeppen JB, Gache P, Landry U, Sekera E, Schweizer V, Gloor S, Yersin B. Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: a randomized treatment trial. *Arch Intern Med*. 2002;162(10):1117-1121.
- Cassidy EM, O'Sullivan I, Bradshaw P, Islam T, Onovo C. Symptom-triggered benzodiazepine therapy alcohol withdrawal syndrome in the emergency department: a comparison with the standard fixed dose benzodiazepine regimen. *Emerg Med J*. 2012;29(10):802-804.
- Sen S, Grgurich P, Tulolo A, Smith-Freedman A, Lei Y, Gray A, Dargin J. A symptom-triggered benzodiazepine protocol utilizing SAS and CIWA-Ar scoring for the treatment of alcohol withdrawal syndrome in the critically ill. *Ann Pharm*. 2017; 51(2):101-110.
- Jaeger TM, Lohr RH, Pankratz VS. Symptom-triggered therapy for alcohol withdrawal syndrome in medical inpatients. *Mayo Clin Proc*. 2001;76(7):695-701.
- Waye C, Wong M, Lee S. Implementation of a CIWA-Ar alcohol withdrawal protocol in a veterans hospital. *South Med J*. 2015;108(1):23-28.
- Eberly ME, Lockwood AG, Lockwood S, Davis KW. Outcomes after implementation of an alcohol withdrawal protocol at a single institution. *Hosp Pharm*. 2016;51(9):752-758.
- Melson J, Kane M, Mooney R, McWilliams J, Horton T. Improving alcohol withdrawal outcomes in acute care. *Perm J*. 2014;18(2):e141-e145.
- Duby JJ, Berry AJ, Ghayyem P, Wilson M. Alcohol withdrawal syndrome in critically ill patients: protocolized versus nonprotocolized management. *J Trauma Acute Care Surg*. 2014;77(6):938-943.
- See S, Nosal S, Brooks Barr W, Schiller R. Implementation of a symptom-triggered benzodiazepine protocol for alcohol withdrawal in family medicine inpatients. *Hosp Pharm*. 2009; 44(10):881-887.
- Hospital Adjusted Expenses per Inpatient Day. Henry J Kaiser Family Foundation. <https://www.kff.org/health-costs/state-indicator/expenses-per-inpatient-day/?currentTimeframe=0&selectedRows=%7B%22states%22:%7B%22new-york%22:%7B%7D%7D%7D&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D>. Accessed May 1, 2019.