Journal of Community Hospital Internal Medicine Perspectives

Volume 14 | Issue 6 Article 7

2024

Review of Attributes and Outcomes of Hospitalized Patients with Alcohol Withdrawal

Harsh R Desai
Trident Regional Medical Center, Charleston, SC, USA 29406, rphzdesai@hotmail.com

Joan S Hyland
Florida Orange Park Hospital, Florida, Orange Park, FL, USA 32073

Erica Paulos
HCA Healthcare, Nashville, TN, USA 37203

Eric Shaw
Memorial Health University Medical Center, Savannah, GA, USA 31404

Nayda Pariso-Poldiak,
HCA Healthcare, Nashville, TN, USA 37203

See next page for additional authors

Recommended Citation

Desai, Harsh R; Hyland, Joan S; Paulos, Erica; Shaw, Eric; Pariso-Poldiak,, Nayda; and Patel, Maulikkumar (2024) "Review of Attributes and Outcomes of Hospitalized Patients with Alcohol Withdrawal," *Journal of Community Hospital Internal Medicine Perspectives*: Vol. 14: Iss. 6, Article 7.
DOI: 10.55729/2000-9666.1420
Available at: https://scholarlycommons.gbmc.org/jchimp/vol14/iss6/7

Review of Attributes and Outcomes of Hospitalized Patients with Alcohol Withdrawal

Authors

Harsh R Desai; Joan S Hyland; Erica Paulos; Eric Shaw; Nayda Pariso-Poldiak,; and Maulikkumar Patel

Review of Attributes and Outcomes of Hospitalized Patients with Alcohol Withdrawal

Harsh R. Desai [a], Joan S. Hyland [b], Erica Paulos [c], Eric Shaw [d], Nayda Parisio-Poldiak [c], Maulikkumar Patel [c,d,*]

[a] Trident Regional Medical Center, Charleston, SC 29406, USA
[b] Florida Orange Park Hospital, Florida, Orange Park, FL 32073, USA
[c] HCA Healthcare, Nashville, TN 37203, USA
[d] Memorial Health University Medical Center, Savannah, GA 31404, USA

Abstract

Background: **Alcohol abuse leads to millions of hospital admissions each year in the United States. Alcohol withdrawal syndrome (AWS) is associated with several serious complications, including seizures, delirium tremens, and death. Benzodiazepines have been the mainstay of treatment for hospitalized patients with alcohol withdrawal.**

Objective: **To compare hospital length of stay (LOS) among different protocols for the management of AWS in hospitalized patients.**

Methods: **We conducted a retrospective study of 49,125 adult patients admitted over 4 years (2018−2022) to HCA Healthcare hospitals across the USA with a diagnosis of alcohol use disorder or alcohol withdrawal. Hospital LOS was the primary outcome examined across various treatment groups (chlordiazepoxide, diazepam, gabapentin, lorazepam, phenobarbital). Secondary outcomes included the initial Clinical Institute Withdrawal Assessment (CIWA) score, intensive care unit (ICU) admission rates, readmission rates, and mortality.**

Results: **The average age of patients admitted was 48 years, and the majority (72%) were White males. Lorazepam was the most frequently used protocol and was associated with the lowest LOS (3.96 days). Patients treated with lorazepam had relatively higher initial CIWA scores. Only 11% of patients were admitted to the ICU during their hospitalization, and only 2% were intubated or ventilated. There were no 30-day readmissions, and less than 1% of patients admitted with a diagnosis of AWS died. Other protocols, such as gabapentin, diazepam, phenobarbital, and chlordiazepoxide, were less commonly used and had variable impacts on the outcomes studied.**

Conclusions: **The results of this retrospective study support lorazepam as an effective treatment for AWS management. Future research should focus on comparing the effectiveness of alcohol withdrawal assessment tools in patients with baseline psychiatric disorders.**

Keywords: Alcohol withdrawal, CIWA, Benzodiazepine, Phenobarbital, Lorazepam

1. Introduction

Alcohol is a commonly abused substance in the United States that results in millions of hospital admissions each year requiring clinical management.[1] Alcohol withdrawal syndrome (AWS) increases hospital length of stay (LOS), serious complications such as seizures and delirium tremens, and ultimately mortality.[2] The Clinical Institute Withdrawal Assessment (CIWA-Ar) is an assessment tool to evaluate symptoms of alcohol withdrawal and guide AWS management in the hospital setting.[3] Various treatment protocols have been used for managing AWS and their use has improved clinical outcomes.[4]

The mainstay of treatment of most hospital AWS protocols has been benzodiazepines and phenobarbital. Studies have reported variable outcomes in effectiveness and tolerability when compared against each other. Few studies have suggested that

Received 4 June 2024; revised 1 September 2024; accepted 10 September 2024.
Available online 2 November 2024

* Corresponding author.
E-mail addresses: harsh.desai@hcahealthcare.com (H.R. Desai), shannster12@gmail.com (J.S. Hyland), erica.paulos@hcahealthcare.com (E. Paulos), eric.shaw@hcahealthcare.com (E. Shaw), nayda.parisiopoldiak@hcahealthcare.com (N. Parisio-Poldiak), Maulikkumar.Patel@hcahealthcare.com (M. Patel).

https://doi.org/10.55729/2000-9666.1420

phenobarbital compared to benzodiazepines decreases intensive care unit (ICU) admission, ICU or hospital LOS, all-cause readmission, ED visits, delirium tremens, medication adverse effects, and mechanical ventilation rates.[5-8] Conversely, other researchers did not demonstrate any difference comparing phenobarbital to benzodiazepines on the rate of ICU admission, LOS in ICU or hospital, severity of symptoms, complications/adverse effects, intubation rate, and alcohol-related readmission.[7-11] One study combined phenobarbital with lorazepam and found a reduced LOS.[12] The type of AWS protocol varies among hospitals, whether it involves fixed versus symptom-triggered dosing, or front-loading versus intermittent dosing.[2,13,14] Several researchers have also tried other adjuncts for AWS treatment, including baclofen, dexmedetomidine, chlordiazepoxide, and gabapentin. Again, the results have demonstrated shorter LOS, reduced delirium tremens, or no difference.[15-18] However, a recent meta-analysis comparing benzodiazepine with non-benzodiazepine treatment reported no significant difference in CIWA-Ar scores during the course of AWS.[19]

Interestingly, the symptoms of AWS can overlap with underlying neurological problems such as dementia, delirium, psychiatric conditions, and traumatic brain injury, which can complicate CIWA-Ar and alcohol withdrawal management.[4,20,21] Additionally, a patient's baseline laboratory values, vital signs, or previous history of AWS could serve as important predictors for the severity of AWS.[22,23] The findings from existing prospective and retrospective studies have been limited by sample size, focus on a specific AWS protocol, and consideration of only certain primary and secondary outcomes. Thus, we performed a retrospective study using the robust Enterprise Data Warehouse (EDW) data set across the HCA Healthcare sites to identify risk factors for AWS and compare the effectiveness of different AWS protocols and associated outcomes. We anticipate that findings from our study will help identify optimal AWS treatment strategies. Our retrospective cohort study aims to compare LOS among various drug protocols used for the management of patients admitted with AWS.

2. Methods

2.1. Sample or participants

The patient population included admissions across all HCA Healthcare facilities from July 31, 2018, to July 31, 2022. Study subjects were selected based on the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes. Inclusion criteria included all patients older than 18 years of age with a diagnosis of alcohol use disorder or alcohol withdrawal syndrome. We excluded patients under 18 years of age and those with allergies to phenobarbital, benzodiazepines, or other anti-epileptics studied (Supplementary Figure 1 (https://scholarlycommons.gbmc.org/cgi/editor.cgi?article=1420&window=additional_files&context=jchimp)). The data for this retrospective study were abstracted through the HCA Healthcare Enterprise Data Warehouse (EDW) using the aforementioned ICD-10 codes (Supplementary Table 1 (https://scholarlycommons.gbmc.org/cgi/editor.cgi?article=1420&window=additional_files&context=jchimp)). We initially analyzed eight different protocols (phenobarbital, lorazepam, oxazepam, chlordiazepoxide, midazolam, diazepam, gabapentin, baclofen), but later decided to focus on five of the most commonly used protocols. Therefore, we did not include baclofen, midazolam, and oxazepam in our final analysis due to relatively small sample size (Supplementary Table 2 (https://scholarlycommons.gbmc.org/cgi/editor.cgi?article=1420&window=additional_files&context=jchimp)).

2.2. Data for quantitative outcomes

The primary outcome of focus was LOS among five different protocols studied. The secondary outcomes studied included initial CIWA score, admission triage, discharge disposition, ICU admission, intubation/ventilation rate, alcohol withdrawal-related complications (such as seizures and pneumonia), medication-related adverse effects, and readmission rates/30-day emergency department visits after discharge. The phenobarbital group was the comparison group in our study. The study received an IRB exempt determination and approval (2024-467).

2.3. Statistical analysis

All statistical analyses were performed using the statistical software RStudio. SQL was used to extract the data. Categorical variables were summarized using frequencies and percentages, while descriptive statistics for continuous variables included mean and standard deviation. Patients were categorized and measured as a categorical variable based on which protocol the patients were placed on. Comparative analyses were performed using the *t*-test or Mann–Whitney U test for continuous variables, or cross-tabulations with

Pearson chi-square test or Fisher's exact test for categorical variables, as appropriate, depending upon the type of variable and data normality. All inferential statistical tests were two-tailed and used a tolerance for nominal type 1 error (alpha) of 0.05. The box-and-whisker plot was created using RStudio software.

3. Results

Our study examined 49,125 patients admitted for AWS from July 2018 to 2022 at HCA Healthcare hospitals across the USA. We first analyzed the demographic data of the patients studied. The ratio of males to females was approximately 3:1, and it remained constant across various AWS protocols (Table 1). The mean age of the patient population studied was 48 ± 12.9 years. A significant number of Caucasians (79%) were included in the sample, compared to 9% African Americans and 10% mixed ethnicity. The frequencies of Native Americans, Hispanics, and Asians were less than 1%. Among the admitted patients, the majority had triage scores (based on Emergency Severity Index, Supplementary Table 3 (https://scholarlycommons.gbmc.org/cgi/editor.cgi?article=1420&window=additional_files&context=jchimp)), of either level 2 (emergent, 36%) or level 3 (urgent, 26%). However, only 2% of the sampled population was triaged at level 1 (resuscitation), and less than 1% was triaged as levels 4 and 5. The triage score was not recorded for 36% of the admitted patients.

Among the five protocols we analyzed, lorazepam was the agent of choice for 75.5% of the total number of patients admitted for AWS. Gabapentin (12.10%), diazepam (5.51%), phenobarbital (4.75%), and chlordiazepoxide (2.08%) protocols were less commonly used (Table 1). The average LOS across all protocols was 4.14 days (Table 2; Fig. 1). The LOS for the diazepam group (mean 4.08 days, $p < 0.001$) and the lorazepam group (mean 3.96 days, $p < 0.001$) was significantly shorter compared to that of the phenobarbital group (mean 4.69 days; comparison group). In contrast, gabapentin had a significantly greater LOS (mean 5.03 days, $p = 0.001$) compared

Table 2. The primary outcome, length of stay (LOS) in mean days ± standard deviation for each alcohol withdrawal protocol is presented.

Drugs	LOS (days)
CDP	4.573 ± 5.615
DZP	4.084 ± 4.674 ***
GBP	5.026 ± 5.595 **
LRZ	3.956 ± 4.772 ***
PB	4.686 ± 3.806
TOTAL	4.140 ± 4.866

The phenobarbital group was chosen as a control for comparison with other protocols. T-test is used for statistical analysis, ** p-value ≤0.01, *** p-value ≤0.001. *CDP, Chlordiazepoxide; DZP, diazepam; GBP, gabapentin; LRZ, lorazepam; PB, phenobarbital; LOS, length of stay.*

Table 1. Outlines the basic demographic information obtained from the Enterprise Data Warehouse (EDW) for all drug protocols analyzed.

	CDP	DZP	GBP	LRZ	PB	Total
Age	46.00 ± 12.65	47.58 ± 12.60	50.17 ± 12.55	47.91 ± 12.94	46.01 ± 12.44	48.03 ± 12.88
Sex **						
Female	278 (27.23)	723 (26.72)	1702 (28.62)	9763 (26.30)	511 (21.89)	12,977 (26.42)
Male	743 (72.77)	1975 (72.99)	4196 (70.56)	26,999 (72.74)	1532 (65.64)	35,445 (72.15)
Not Assigned	0	8 (0.30)	49 (0.82)	355 (0.96)	291 (12.47)	703 (1.43)
Race ***						
White	752 (73.65)	2175 (80.38)	4893 (82.28)	29,169 (78.59)	1456 (62.38)	38,445 (78.26)
African American	93 (9.11)	234 (8.65)	527 (8.86)	3210 (8.64)	421 (18.04)	4485 (9.13)
Asian	7 (0.69)	13 (0.48)	29 (0.49)	232 (0.63)	10 (0.43)	291 (0.59)
Hispanic	1 (0.10)	1 (0.04)	3 (0.05)	25 (0.07)	0	30 (0.06)
Native	8 (0.78)	14 (0.52)	11 (0.18)	91 (0.25)	4 (0.17)	128 (0.26)
Multi/Other	160 (16.67)	261 (9.65)	435 (7.31)	4034 (10.87)	152 (6.51)	5042 (10.26)
Not Assigned	0	8 (0.30)	49 (0.82)	356 (0.96)	291 (12.47)	704 (1.43)
Triage Score ***						
1 - Resuscitation	16 (1.57)	60 (2.22)	101 (1.70)	637 (1.72)	17 (0.73)	831 (1.69)
2 - Emergent	452 (44.27)	967 (35.74)	2287 (38.46)	13,222 (35.62)	964 (41.30)	17,892 (36.42)
3 - Urgent	189 (18.51)	697 (25.76)	1371 (23.05)	9970 (26.86)	346 (14.82)	12,573 (25.59)
4 – Semi Urgent	3 (0.29)	16 (0.59)	23 (0.39)	98 (0.26)	14 (0.60)	154 (0.31)
5 – Non-Urgent	0	0	1 (0.02)	3 (0.01)	0	4 (0.01)
Unknown	361 (35.36)	966 (35.70)	2164 (36.39)	13,187 (35.53)	993 (42.55)	17,671 (35.97)
Total	1021	2706	5947	37,117	2334	49,125

The values are presented as age ± standard deviation and the categorial variables as total count in each group with relative percentages in brackets. Some categories did not have the requested variable assigned and they are classified as "Not assigned" line. Chi-square test is used for statistical analysis with phenobarbital as the comparison group, * p-value ≤0.05, ** p-value ≤0.01, *** p-value ≤0.001. *CDP, Chlordiazepoxide; DZP, diazepam; GBP, gabapentin; LRZ, lorazepam; PB, phenobarbital.*

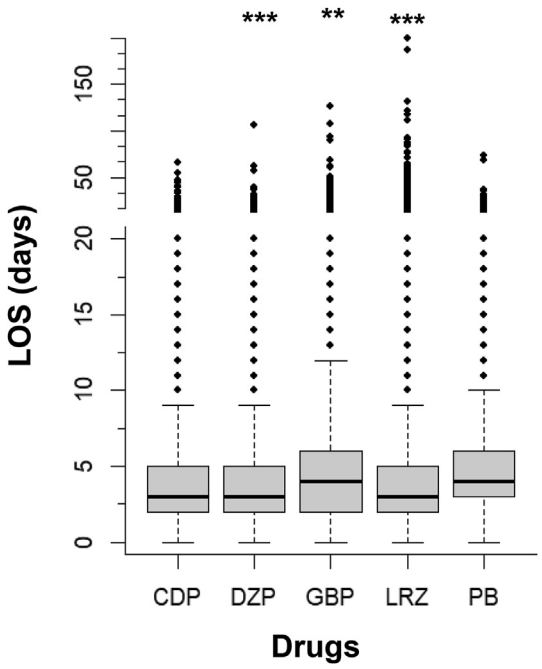

*Fig. 1. The primary outcome, length of stay (LOS), is represented as a box and whisker plot for each alcohol withdrawal protocol. The phenobarbital group was chosen as a control for comparison with other protocols. T-test is used for statistical analysis, p-value ≤0.01, *** p-value ≤0.001. CDP, Chlordiazepoxide; DZP, diazepam; GBP, gabapentin; LRZ, lorazepam; PB, phenobarbital; LOS, length of stay.*

to phenobarbital. However, chlordiazepoxide (mean 4.57 days, p = 0.018) did not show a significant difference in LOS compared to that of phenobarbital.

We used the other secondary endpoints as surrogates to demonstrate that overall patient outcomes were not negatively impacted. The average initial CIWA score was 5.60 (Table 3). The initial CIWA scores for lorazepam (5.94, p < 0.001), diazepam (5.69, p < 0.001), chlordiazepoxide (4.72, p < 0.001), and gabapentin (4.22, p < 0.001) were higher than the CIWA score of 3.54 for the comparison group phenobarbital. Lorazepam was associated with relatively higher CIWA scores and lower LOS. We also looked at initial vitals, such as the Glasgow coma scale (GCS), heart rate, and respirations; however, due to missing data fields for many patients, an in-depth analysis of these values was not performed (Table 3).

We further reviewed the number of ICU admissions and the rate of intubation or ventilation (Table 4). The rate of ICU admissions was 10.60%. The highest rate of ICU admissions was among patients using the lorazepam protocol (4334 patients, or 11.68%), representing 8.82% of the total patient population admitted for AWS. ICU admissions were less prevalent for protocols using diazepam (293 patients, or 10.83%), phenobarbital (201 patients, or 8.61%), gabapentin (377 patients, or 6.34%), and chlordiazepoxide (1 patient). Similarly, the overall intubation or ventilation rate was 1.55%, more frequent for patients on lorazepam protocol (616 patients, 1.65%), and a slightly higher rate for patients on diazepam protocol (59 patients, 2.18%).

We also examined other outcomes such as discharge disposition, readmission rates, and complications (Table 4). The discharge disposition variable considered whether a patient was deceased at the time of discharge. The overall percentage of deceased patients at discharge was 0.47%. Death was somewhat more frequent among patients on lorazepam protocol (197 patients, or 0.53%) and was also notable in other groups, including diazepam (0.41%), gabapentin (0.30%), chlordiazepoxide (0.29%), and phenobarbital (0.13%). Notably, none of the protocol groups had any 30-day readmissions. We also looked at alcohol withdrawal-related complications including medication-related adverse effects, neurological or metabolic complications, etc. We observed a higher prevalence of complications in the following systems: gastrointestinal (13.63%), hematological (7.41%), and neurological (4.64%). The specifics of the complications experienced were not considered as part of the study. Among the patient population we studied, less than 2% had underlying neurological disorders such as Parkinson's, epilepsy, dementia, or traumatic brain injury.

Table 3. Several additional secondary outcomes including heart rate, respirations, body mass index (BMI), Clinical Institute Withdrawal Assessment (CIWA) scores, and Glasgow Coma Scale (GCS) were analyzed for each drug group and mean ± standard deviation.

	CDP	DZP	GBP	LRZ	PB	Total Average	Totals
Pulse†	94.23 ± 17.66	92.58 ± 17.38	90.05 ± 16.22	92.66 ± 17.01	90.82 ± 16.26	92.29 ± 16.94	48,139
Respirations†	17.97 ± 2.81	17.70 ± 2.81	17.38 ± 2.36	17.67 ± 2.68	17.19 ± 2.44	17.62 ± 2.65	48,389
BMI†	25.92 ± 4.70	26.40 ± 4.97	27.14 ± 5.31	26.72 ± 5.08	26.28 ± 4.87	26.71 ± 5.09	47,353
CIWA	4.78 ± 5.15***	5.69 ± 5.72***	4.22 ± 5.04***	5.94 ± 5.91***	3.53 ± 4.74	5.60 ± 5.78	46,732
GCS	14.57 ± 1.15	14.61 ± 1.18	14.68 ± 1.06	14.53 ± 1.29	14.67 ± 1.09	14.56 ± 1.25	24,481

Not all patients had data available for all outcomes. T-test is used for statistical analysis, * p-value ≤0.05, ** p-value ≤0.01, *** p-value ≤0.001. †Top and bottom 1% of sample were dropped to account for data entry errors. *CDP, Chlordiazepoxide; DZP, diazepam; GBP, gabapentin; LRZ, lorazepam; PB, phenobarbital.*

Table 4. The various secondary outcomes including intensive care unit (ICU) admissions, intubation rate, mortality, 30-day readmission, and alcohol induced complications were analyzed for protocol drug group.

	CDP	DZP	GBP	LRZ	PB	Total
ICU Admission* **	1 (0.10)	293 (10.83)	377 (6.34)	4334 (11.68)	201 (8.61)	5206 (10.60)
Intubation* **	0	59 (2.18)	61 (1.03)	616 (1.66)	23 (0.99)	759 (1.55)
Death **	3 (0.29)	11 (0.41)	18 (0.30)	197 (0.53)	3 (0.13)	232 (0.47)
Readmit	0	0	0	0	0	0
Alcohol induced complications						
Blood disorder	164 (16.06)	361 (13.34)	704 (11.84)	5019 (13.52)	449 (19.24)	6697 (13.63)
Drug adverse effect	0	7 (0.26)	46 (0.77)	349 (0.94)	291 (12.47)	693 (1.41)
Gastrointestinal	53 (5.19)	169 (6.25)	359 (6.04)	2705 (7.29)	356 (15.25)	3642 (7.41)
Metabolic	29 (2.84)	55 (2.03)	132 (2.22)	961 (2.59)	309 (13.24)	1486 (1.08)
Myopathy	6 (0.59)	20 (0.74)	72 (1.21)	569 (1.53)	297 (12.72)	964 (1.96)
Nervous System*	42 (4.11)	86 (3.18)	262 (4.41)	1572 (4.24)	316 (13.54)	2278 (4.64)
Neurological condition						
Mental disorder	0	7 (0.26)	46 (0.77)	349 (0.94)	291 (12.47)	693 (1.41)
Parkinson's	4 (0.39)	16 (0.59)	71 (1.19)	452 (1.22)	295 (12.64)	838 (1.71)
Traumatic Brain Injury	0	7 (0.26)	46 (0.77)	349 (0.94)	291 (12.47)	693 (1.41)
Epilepsy	0	7 (0.26)	46 (0.77)	349 (0.94)	291 (12.47)	693 (1.41)
Delirium	12 (1.18)	18 (0.67)	67 (1.13)	599 (1.61)	295 (12.64)	991 (2.02)
Dementia	1 (0.10)	8 (0.30)	54 (0.91)	396 (1.07)	291 (12.47)	750 (1.53)
Total patients in each group	1021	2706	5947	37,117	2334	49,125

The number of patients were noted with relative percentages in brackets. Chi-square test is used for statistical analysis, * p-value ≤0.05, ** p-value ≤0.01, *** p-value ≤0.001. *CDP, Chlordiazepoxide; DZP, diazepam; GBP, gabapentin; LRZ, lorazepam; PB, phenobarbital.*

Notably, a relatively higher proportion of patients in the phenobarbital group experienced alcohol-induced complications or had pre-existing neurological conditions. Since only a small proportion of patients studied experienced complications, a statistical comparison could not be drawn.

4. Discussion

Our study found that management of AWS with lorazepam is associated with a lower LOS and higher initial CIWA scores compared to other commonly used drug protocols we studied. We observed that the number of ICU admissions, intubation rates, and mortality were relatively higher in the lorazepam group, with no difference in readmission rates or alcohol-induced complications. To our knowledge, this is the first study to examine such a large national sample using the HCA Healthcare database.

Patients admitted to the hospital with alcohol use disorder frequently experience AWS, which can be potentially life-threatening and may cause seizures or delirium tremens. Therefore, early recognition and appropriate management are crucial to reducing the risk of complications. Various therapeutic strategies exist for managing AWS; however, there are no standardized nationwide guidelines. Benzodiazepines are commonly used as first-line therapies, but several alternative options have been proposed with varying effectiveness. A lorazepam-based protocol for AWS is most frequently used across HCA Healthcare hospitals in the United States. Studies comparing lorazepam with other benzodiazepines, such as diazepam and chlordiazepoxide,[24-26] have revealed comparable effects. Phenobarbital is emerging as an alternative to benzodiazepines.[6,11] Systematic review, meta-analysis,[27] cohort studies,[28] and retrospective studies[7,10,29,30] have not shown any significant difference between AWS management with phenobarbital and benzodiazepines. Our study favors the use of lorazepam, as it significantly reduces LOS compared to phenobarbital. The differences in the neurochemistry and pharmacokinetics of phenobarbital make it an effective alternative for treating AWS, particularly for patients with contraindications to benzodiazepines or those at risk of severe AWS.[5] Another alternative is the use of gabapentin, which, at high doses, has been associated with a lower hospital LOS, lower mean CIWA-Ar scores, and reduced use of benzodiazepines.[15,31] For patients who may not respond to first-line therapies such as benzodiazepines, other adjunctive strategies have been studied, including dexmedetomidine,[32-35] propofol,[36,37] levetiracetam,[38] and ketamine[13,39] though these have produced mixed results and raised concerns about adverse effects.

There are several assessment tools for withdrawal symptoms, but the CIWA scale has been the most validated. Our study showed that admission CIWA scores were relatively higher for the lorazepam group compared to other protocols. Since the lorazepam group had a shorter LOS, this suggests that lorazepam may be an effective agent for AWS,

regardless of varying initial CIWA scores. Other agents may be helpful when lorazepam or other benzodiazepines are not effective or are contraindicated. Several studies have noted that a symptom-triggered approach resulted in a reduction in overall benzodiazepine usage and duration.[40,41] Clinicians have also employed other strategies, such as fixed dosing or front loading. For example, an early and focused approach with front loading of diazepam in the first 24 h resulted in a reduced hospital LOS.[42] When researchers compared a fixed tapering dose of phenobarbital to a fixed dose of benzodiazepines in trauma and general medical ward, patients had decreased incidence of AWS without significant difference in LOS.[7,10] Additionally, lorazepam-based AWS protocols are relatively standardized compared to phenobarbital, which can have varying dosing among hospitals. Our study cannot distinguish which dosing strategies or regimens were commonly utilized, and this remains a possible avenue for further investigation.

The retrospective design of our study presents several limitations that should be acknowledged. Currently, symptom-triggered management of AWS using the CIWA-Ar is the standard of care. Similarly, our work only considered CIWA-Ar, as it is a standardized and validated scale commonly used across the hospitals in the United States. Many studies have focused on other scales, such as the Sedation agitation scale[43] or the 5-point scale.[44,45] However, the nature of our data allowed us to examine only the initial CIWA-Ar scores, and data were unavailable for some patients. Additionally, we were unable to track how CIWA scores varied during admission. There are limitations to using the CIWA-Ar scale, as patients who lack cognitive or communicative abilities—such as those with delirium or encephalopathy—may not be suitable candidates. Furthermore, if a provider chooses to use a fixed dosing approach for AWS, the CIWA scale may not be administered. This study did not address the effectiveness of other scales, which could be a focus for future research.

Secondly, the choice of AWS protocol can vary based on individual hospital guidelines or a physician's preference, introducing variability and inherent bias. Our study was unable to identify the factors influencing a physician's choice of protocol, such as co-morbidities, physician training, prior patient history, or institution policy. We also could not assess whether other adjuvant agents were used or what dosing regimens were employed, both of which could influence the outcomes. Nevertheless, the results of this study align with previous literature, highlighting the widespread use of lorazepam and its effectiveness in AWS management. It is also worth noting that our study did not include three protocols in the final analysis, as they accounted for less than 2% of combined use. This exclusion could potentially affect the reproducibility and generalizability of our findings. Lastly, the retrospective nature of the study depends on the quality of data available in the database, and there is a possibility of missed cases or inaccurate diagnoses that could potentially confound the results.

In summary, our study shows that lorazepam is a commonly used and effective management approach for AWS in hospitalized patients. Its association with relatively lower LOS can positively influence hospital reimbursement rates and reduce the total healthcare cost per patient.

Ethics information

This research activity was conducted in compliance with the corporate requirements and determined to be exempt from Institutional Review Board (IRB) oversight in accordance with current regulations and institutional policy.

Financial support

The authors did not receive any funding for the present study.

Disclaimer

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

Conflict of interest

The authors declare that they have no competing financial or other conflicts of interests.

Acknowledgements

H.R.D. and J.S.H designed the project, interpreted the data, and wrote and edited the manuscript; E.P. analyzed the data; N.P.P. and E.S. provided input with design and data interpretation; M.P. supervised the project, designed the project, interpreted the data, and critically edited the manuscript. All authors read and approved the final version of the manuscript. M.P. is responsible for the integrity of the work as a whole.

References

1. Pasha AK, Chowdhury A, Sadiq S, Fairbanks J, Sinha S. Substance use disorders: diagnosis and management for hospitalists. *J Community Hosp Intern Med Perspect*. 2020;10(2):117–126. https://doi.org/10.1080/20009666.2020.1742495.
2. Day E, Daly C. Clinical management of the alcohol withdrawal syndrome. *Addict Abingdon Engl*. 2022;117(3):804–814. https://doi.org/10.1111/add.15647.
3. Attilia F, Perciballi R, Rotondo C, et al. Alcohol withdrawal syndrome: diagnostic and therapeutic methods. *Riv Psichiatr*. 2018;53(3):118–122. https://doi.org/10.1708/2925.29413.
4. Farrokh S, Roels C, Owusu KA, Nelson SE, Cook AM. Alcohol withdrawal syndrome in neurocritical care unit: assessment and treatment challenges. *Neurocritical Care*. 2021;34(2):593–607. https://doi.org/10.1007/s12028-020-01061-8.
5. Murphy JA, Curran BM, Gibbons WA, Harnica HM. Adjunctive phenobarbital for alcohol withdrawal syndrome: a focused literature review. *Ann Pharmacother*. 2021;55(12):1515–1524. https://doi.org/10.1177/1060028021999821.
6. Tidwell WP, Thomas TL, Pouliot JD, Canonico AE, Webber AJ. Treatment of alcohol withdrawal syndrome: phenobarbital vs CIWA-Ar protocol. *Am J Crit Care Off Publ Am Assoc Crit-Care Nurses*. 2018;27(6):454–460. https://doi.org/10.4037/ajcc2018745.
7. Nejad S, Nisavic M, Larentzakis A, et al. Phenobarbital for acute alcohol withdrawal management in surgical trauma patients-A retrospective comparison study. *Psychosomatics*. 2020;61(4):327–335. https://doi.org/10.1016/j.psym.2020.01.008.
8. Hawa F, Gilbert L, Gilbert B, et al. Phenobarbital versus lorazepam for management of alcohol withdrawal syndrome: a retrospective cohort study. *Cureus*. 2021;13(2):e13282. https://doi.org/10.7759/cureus.13282.
9. Nguyen TA, Lam SW. Phenobarbital and symptom-triggered lorazepam versus lorazepam alone for severe alcohol withdrawal in the intensive care unit. *Alcohol Fayettev N*. 2020;82:23–27. https://doi.org/10.1016/j.alcohol.2019.07.004.
10. Nisavic M, Nejad SH, Isenberg BM, et al. Use of phenobarbital in alcohol withdrawal management - a retrospective comparison study of phenobarbital and benzodiazepines for acute alcohol withdrawal management in general medical patients. *Psychosomatics*. 2019;60(5):458–467. https://doi.org/10.1016/j.psym.2019.02.002.
11. Sullivan SM, Dewey BN, Jarrell DH, Vadiei N, Patanwala AE. Comparison of phenobarbital-adjunct versus benzodiazepine-only approach for alcohol withdrawal syndrome in the ED. *Am J Emerg Med*. 2019;37(7):1313–1316. https://doi.org/10.1016/j.ajem.2018.10.007.
12. Ibarra F. Single dose phenobarbital in addition to symptom-triggered lorazepam in alcohol withdrawal. *Am J Emerg Med*. 2020;38(2):178–181. https://doi.org/10.1016/j.ajem.2019.01.053.
13. Shah P, McDowell M, Ebisu R, Hanif T, Toerne T. Adjunctive use of ketamine for benzodiazepine-resistant severe alcohol withdrawal: a retrospective evaluation. *J Med Toxicol Off J Am Coll Med Toxicol*. 2018;14(3):229–236. https://doi.org/10.1007/s13181-018-0662-8.
14. Ammar MA, Ammar AA, Rosen J, Kassab HS, Becher RD. Phenobarbital monotherapy for the management of alcohol withdrawal syndrome in surgical-trauma patients. *Ann Pharmacother*. 2021;55(3):294–302. https://doi.org/10.1177/1060028020949137.
15. Levine AR, Carrasquillo L, Mueller J, Nounou MI, Naut ER, Ibrahim D. High-dose gabapentin for the treatment of severe alcohol withdrawal syndrome: a retrospective cohort analysis. *Pharmacotherapy*. 2019;39(9):881–888. https://doi.org/10.1002/phar.2309.
16. Dixit D, Endicott J, Burry L, et al. Management of acute alcohol withdrawal syndrome in critically ill patients. *Pharmacotherapy*. 2016;36(7):797–822. https://doi.org/10.1002/phar.1770.
17. Woods AD, Giometti R, Weeks SM. The use of dexmedetomidine as an adjuvant to benzodiazepine-based therapy to decrease the severity of delirium in alcohol withdrawal in adult intensive care unit patients: a systematic review. *JBI Database Syst Rev Implement Rep*. 2015;13(1):224–252. https://doi.org/10.11124/jbisrir-2015-1602.
18. Liu J, Wang LN. Baclofen for alcohol withdrawal. *Cochrane Database Syst Rev*. 2019;11.6(11). https://doi.org/10.1002/14651858.CD008502.pub6.
19. Pribék IK, Kovács I, Kádár BK, et al. Evaluation of the course and treatment of alcohol withdrawal syndrome with the clinical Institute withdrawal assessment for alcohol - revised: A systematic review-based meta-analysis. *Drug Alcohol Depend*. 2021;220:108536. https://doi.org/10.1016/j.drugalcdep.2021.108536.
20. Wojnar M, Wasilewski D, Zmigrodzka I, Grobel I. Age-related differences in the course of alcohol withdrawal in hospitalized patients. *Alcohol Alcohol*. 2001;36(6):577–583. https://doi.org/10.1093/alcalc/36.6.577.
21. Carter W, Truong P, Sima AP, Hupe J, Newman J, Ebadi A. Impact of traumatic brain injury on clinical Institute withdrawal assessment use in trauma patients: a descriptive study. *Pharm Manag PM R*. 2021;13(2):159–165. https://doi.org/10.1002/pmrj.12385.
22. Goodson CM, Clark BJ, Douglas IS. Predictors of severe alcohol withdrawal syndrome: a systematic review and meta-analysis. *Alcohol Clin Exp Res*. 2014;38(10):2664–2677. https://doi.org/10.1111/acer.12529.
23. Steel TL, Afshar M, Edwards S, et al. Research needs for inpatient management of severe alcohol withdrawal syndrome: an official American thoracic society research statement. *Am J Respir Crit Care Med*. 2021;204(7):e61–e87. https://doi.org/10.1164/rccm.202108-1845ST.
24. Scheuermeyer FX, Miles I, Lane DJ, et al. Lorazepam versus diazepam in the management of emergency department patients with alcohol withdrawal. *Ann Emerg Med*. 2020;76(6):774–781. https://doi.org/10.1016/j.annemergmed.2020.05.029.
25. March KL, Twilla JD, Reaves AB, et al. Lorazepam versus chlordiazepoxide for the treatment of alcohol withdrawal syndrome and prevention of delirium tremens in general medicine ward patients. *Alcohol Fayettev N*. 2019;81:56–60. https://doi.org/10.1016/j.alcohol.2019.05.008.
26. Ramanujam R, L P, G S, Thimmaiah RS. A comparative study of the clinical efficacy and safety of Lorazepam and chlordiazepoxide in alcohol dependence syndrome. *J Clin Diagn Res JCDR*. 2015;9(3):FC10–FC13. https://doi.org/10.7860/JCDR/2015/11887.5678.
27. Pourmand A, AlRemeithi R, Kartiko S, Bronstein D, Tran QK. Evaluation of phenobarbital based approach in treating patient with alcohol withdrawal syndrome: a systematic review and meta-analysis. *Am J Emerg Med*. 2023;69:65–75. https://doi.org/10.1016/j.ajem.2023.04.002.
28. Askgaard G, Hallas J, Fink-Jensen A, Molander AC, Madsen KG, Pottegård A. Phenobarbital compared to benzodiazepines in alcohol withdrawal treatment: a register-based cohort study of subsequent benzodiazepine use, alcohol recidivism and mortality. *Drug Alcohol Depend*. 2016;161:258–264. https://doi.org/10.1016/j.drugalcdep.2016.02.016.
29. Pistore A, Penney S, Bryce R, Meyer C, Bouchard B. A retrospective evaluation of phenobarbital versus benzodiazepines for treatment of alcohol withdrawal in a regional Canadian emergency department. *Alcohol Fayettev N*. 2022;102:59–65. https://doi.org/10.1016/j.alcohol.2022.05.001.
30. Nelson AC, Kehoe J, Sankoff J, Mintzer D, Taub J, Kaucher KA. Benzodiazepines vs barbiturates for alcohol withdrawal: analysis of 3 different treatment protocols. *Am J Emerg Med*. 2019;37(4):733–736. https://doi.org/10.1016/j.ajem.2019.01.002.
31. Morrison M, Udeh E, Burak M. Retrospective analysis of a gabapentin high dose taper compared to lorazepam in acute inpatient alcohol withdrawal. *Am J Drug Alcohol Abuse*. 2019;45(4):385–391. https://doi.org/10.1080/00952990.2019.1602136.
32. Ware LR, Schuler BR, Goodberlet MZ, Marino KK, Lupi KE, DeGrado JR. Evaluation of dexmedetomidine as an adjunct to

phenobarbital for alcohol withdrawal in critically ill patients. *J Intensive Care Med*. 2023;38(6):553−561. https://doi.org/10.1177/08850666231152837.
33. VanderWeide LA, Foster CJ, MacLaren R, Kiser TH, Fish DN, Mueller SW. Evaluation of early dexmedetomidine addition to the standard of care for severe alcohol withdrawal in the ICU: a retrospective controlled cohort study. *J Intensive Care Med*. 2016;31(3):198−204. https://doi.org/10.1177/0885066614554908.
34. Tolonen J, Rossinen J, Alho H, Harjola VP. Dexmedetomidine in addition to benzodiazepine-based sedation in patients with alcohol withdrawal delirium. *Eur J Emerg Med Off J Eur Soc Emerg Med*. 2013;20(6):425−427. https://doi.org/10.1097/MEJ.0b013e32835c53b3.
35. Love K, Zimmermann AE. Use of propofol plus dexmedetomidine in patients experiencing severe alcohol withdrawal in the intensive care unit. *J Clin Pharmacol*. 2020;60(4):439−443. https://doi.org/10.1002/jcph.1539.
36. Sohraby R, Attridge RL, Hughes DW. Use of propofol-containing versus benzodiazepine regimens for alcohol withdrawal requiring mechanical ventilation. *Ann Pharmacother*. 2014;48(4):456−461. https://doi.org/10.1177/1060028013515846.
37. Brotherton AL, Hamilton EP, Kloss HG, Hammond DA. Propofol for treatment of refractory alcohol withdrawal syndrome: a review of the literature. *Pharmacotherapy*. 2016;36(4):433−442. https://doi.org/10.1002/phar.1726.
38. Youland KM, Miller RF, Mahoney LJ, Borgert AJ, Gundrum JD. Levetiracetam as adjunctive therapy for acute alcohol withdrawal syndrome in hospitalized patients. *J Clin Psychopharmacol*. 2014;34(6):704−708. https://doi.org/10.1097/JCP.0000000000000209.
39. Pizon AF, Lynch MJ, Benedict NJ, et al. Adjunct ketamine use in the management of severe ethanol withdrawal. *Crit Care Med*. 2018;46(8):e768−e771. https://doi.org/10.1097/CCM.0000000000003204.
40. Holleck JL, Merchant N, Gunderson CG. Symptom-triggered therapy for alcohol withdrawal syndrome: a systematic review and meta-analysis of randomized controlled trials. *J Gen Intern Med*. 2019;34(6):1018−1024. https://doi.org/10.1007/s11606-019-04899-7.
41. 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 Oxf Oxfs*. 2014;49(3):287−291. https://doi.org/10.1093/alcalc/agt181.
42. Lee JA, Duby JJ, Cocanour CS. Effect of early and focused benzodiazepine therapy on length of stay in severe alcohol withdrawal syndrome. *Clin Toxicol Phila Pa*. 2019;57(7):624−627. https://doi.org/10.1080/15563650.2018.1542701.
43. Sen S, Grgurich P, Tulolo A, et al. A symptom-triggered benzodiazepine protocol utilizing SAS and CIWA-Ar scoring for the treatment of alcohol withdrawal syndrome in the critically ill. *Ann Pharmacother*. 2017;51(2):101−110. https://doi.org/10.1177/1060028016672036.
44. Rastegar DA, Applewhite D, Alvanzo AAH, Welsh C, Niessen T, Chen ES. Development and implementation of an alcohol withdrawal protocol using a 5-item scale, the Brief Alcohol Withdrawal Scale (BAWS). *Subst Abuse*. 2017;38(4):394−400. https://doi.org/10.1080/08897077.2017.1354119.
45. Lindner BK, Gilmore VT, Kruer RM, et al. Evaluation of the brief alcohol withdrawal scale protocol at an academic medical center. *J Addiction Med*. 2019;13(5):379−384. https://doi.org/10.1097/ADM.0000000000000510.