Current Practice Patterns in the Management Of Alcohol Withdrawal Syndrome

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ABSTRACT

Objective: The aim of this study was to examine current practice patterns surrounding the management of alcohol withdrawal syndrome (AWS) in the Northeast region of the United States.

Methods: A survey questionnaire with several treatment options related to current practice in the management of AWS was developed. All hospitals with 100 beds or more located in the Northeast region were selected, and 512 surveys were mailed to pharmacy directors of those hospitals.

Results: Responses from 90 hospitals in nine states were included in the analyses. For the treatment of mild, moderate, and severe AWS, most institutions utilized protocols or guidelines (66%, 73%, and 67%, respectively). However, two-thirds of the hospitals indicated that guidelines or protocols were not in place to treat benzodiazepine (BZD)-refractory AWS. A BZD-only treatment strategy was selected as the first choice for mild and moderate AWS (74% and 54%, respectively), whereas a BZD regimen in combination with a variety of other agents, including haloperidol, dexmedetomidine, phenobarbital, or propofol, was frequently used in the treatment of severe and BZD-refractory AWS.

Conclusion: The findings suggest that considerable heterogeneity exists, particularly in the treatment of severe and BZD-refractory AWS, among hospitals in the Northeast. Given that current guidelines focus mainly on BZD therapy, the results of this survey highlight the need for updated practice guidelines utilizing other treatment strategies.

Keywords: alcohol withdrawal syndrome, survey, pharmacists, benzodiazepine therapy, guidelines

INTRODUCTION

The most recent mortality data available from the Centers for Disease Control and Prevention estimate there were 33,171 alcohol-related deaths in the United States in 2015, which is an 8% increase from the 2014 national data that showed 30,772 alcohol-related deaths. In addition, the total estimated cost of excessive alcohol consumption increased from $223.5 billion in 2006 to $249 billion in 2010. Alcohol withdrawal is commonly encountered in the inpatient setting. The incidences of alcohol withdrawal syndrome (AWS) are approximately 8%, 16%, and 31% in all hospitalized, postsurgical, and trauma patients, respectively.

Because alcohol dependence has become a major public health problem in the United States, many hospitals face challenges in treating patients with AWS, which is characterized by a wide array of symptoms including autonomic hyperactivity, tremor, agitation, hallucination, and seizures. Delirium tremens (DTs), an acute episode of delirium caused by alcohol withdrawal, is the most severe form of AWS, potentially leading to intensive care unit (ICU) admission or death. Some studies estimate that 3% to 5% of hospitalized patients with AWS progress to DTs.

The only benzodiazepines (BZDs) that are approved by the Food and Drug Administration for the treatment of AWS are chlordiazepoxide and diazepam; however, other BZDs are often used because no single agent has proven superior to the others. The choice of BZD in the management of AWS may be influenced by rapid onset of action for quick agitation control, longer duration of action to lessen potential wearing off and breakthrough symptoms, or shorter duration of action to lessen prolonged sedation in elderly patients or those with compromised hepatic function. When given for AWS, BZDs may be prescribed as either a fixed or symptom-triggered dosing regimen. Studies have shown that symptom-triggered treatment results in a decreased cumulative dose of BZDs and decreased duration of treatment compared with fixed-dose regimens. Alternative medications that have been studied for the treatment of acute alcohol withdrawal include valproic acid, carbamazepine, phenobarbital, gabapentin, clonidine, propofol, antipsychotics, dexmedetomidine, and ketamine. In particular, phenobarbital, propofol, dexmedetomidine, and ketamine have been investigated extensively as adjuncts to BZD therapy for BZD-refractory AWS in the ICU setting.

While BZDs are considered a mainstay for AWS treatment, there are significant variations among hospitals with regard to a choice of adjunctive pharmacological agents. Furthermore, there are no universally accepted guidelines for the management of AWS, although evidence suggests that formalization of an alcohol withdrawal protocol can potentially reduce the total daily dose of BZDs, duration of treatment, and the occurrence of DTs. Therefore, the purpose of this study was to survey current practice patterns in the management of AWS.

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Methods

This paper-based survey was sent to pharmacists practicing at hospitals in the Northeast region of the United States. The study was approved by the institutional review board at the Western New England University. The survey questionnaire was developed by the investigators: three pharmacists board-certified in either pharmacotherapy or psychiatry, and one PhD in pharmacy (health outcomes and pharmacy practice) with expertise in survey research. The questionnaire included two sections. Most of the survey consisted of multiple-choice questions with checkboxes, but respondents were allowed to write in their answers if they were not listed. The first section included questions about each institution’s current practice in the management of AWS using four clinical scenarios. Each scenario included several treatment options. The scenarios represented four main categories of AWS severity (mild, moderate, severe, and BZD-refractory). In scenarios of mild, moderate, and severe AWS, all patients were treated for AWS in non-ICU settings, while in the BZD-refractory AWS scenario, a patient was admitted to the ICU. The second section included demographic questions regarding the role of respondents, hospital type, and hospital location. (The full text of the survey is available online at: www.ptcommunity.com/journal/article/full/2018/3/aws-survey.)

All hospitals with 100 beds or more located in nine Northeastern states—Connecticut, Massachusetts, Maine, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont—were identified from the 2016 American Hospital Association Guide to the Health Care Field. A pilot survey was sent to 10 randomly selected hospitals from the list of included hospitals. The content of the questionnaire was revised to reflect comments received from the pilot group. In May 2016, 512 surveys were mailed to pharmacy directors with a statement that the questionnaire could be delegated to an appropriate staff member if necessary. Each survey included a postage-paid return envelope and a postage-paid postcard with a respondent identifier. Respondents were instructed to mail the postcard separately from the survey to maintain anonymity. The postcards were used to determine nonrespondents. The postcard included a checkbox to indicate whether a participant would like to enter a random drawing to win one of twenty-five $20 gift cards for a major online retailer. A reminder postcard was mailed to all nonrespondents three weeks after the initial survey. To optimize the response rate, between June and July 2016 an additional 140 survey packets were mailed to clinical pharmacists practicing at the nonrespondent hospitals, who were identified using various data sources, such as hospital websites and pharmacy residency directories.

Statistical analyses included descriptive statistics (means, standard deviations, frequencies, and percentages) and Fisher’s exact test. All analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute, Inc., Cary, North Carolina). A P value less than 0.05 was considered statistically significant.

Results

Of 504 hospitals eligible for the study (eight questionnaires were excluded due to the incorrect mailing address or lack of an inpatient alcohol withdrawal treatment program), a total of 90 surveys (18%) were completed and included in the analyses.

Table 1 Comparison of Hospital Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Eligible Sample (N = 504)</th>
<th>Respondents (n = 90)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teaching hospital, n (%)</td>
<td>280 (56)</td>
<td>54 (60)</td>
</tr>
<tr>
<td>Number of hospital beds, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100–299 beds</td>
<td>312 (62)</td>
<td>52 (58)</td>
</tr>
<tr>
<td>300–499 beds</td>
<td>114 (22)</td>
<td>18 (20)</td>
</tr>
<tr>
<td>≥ 500 beds</td>
<td>78 (15)</td>
<td>16 (18)</td>
</tr>
<tr>
<td>Not reported</td>
<td>0</td>
<td>4 (4)</td>
</tr>
<tr>
<td>State, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connecticut</td>
<td>24 (5)</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Massachusetts</td>
<td>61 (12)</td>
<td>17 (19)</td>
</tr>
<tr>
<td>Maine</td>
<td>10 (2)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>New Hampshire</td>
<td>12 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>New Jersey</td>
<td>76 (15)</td>
<td>12 (13)</td>
</tr>
<tr>
<td>New York</td>
<td>170 (34)</td>
<td>22 (24)</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>135 (27)</td>
<td>24 (27)</td>
</tr>
<tr>
<td>Rhode Island</td>
<td>11 (2)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Vermont</td>
<td>5 (1)</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Total percent may not add up to 100 due to rounding.

To assess nonresponse bias, key hospital characteristics of the respondents (n = 90) were compared with the overall sample (N = 504) using Fisher’s exact test (Table 1). There were no significant differences between the two groups in regard to teaching status, state, and hospital bed size ($P > 0.05$).

The questionnaires were completed by pharmacists working in the clinical setting (50%) and pharmacy directors or managers (45%). Half of respondents reported that their institutions offered substance treatment services in inpatient and/or outpatient settings. Most hospitals (78%) had fewer than 500 beds, but a majority of the hospitals (60%) were affiliated with a medical residency program. The most common tool for routinely assessing the severity of AWS was the Clinical Institute Withdrawal Assessment of Alcohol Scale, Revised (61%), followed by the Richmond Agitation Sedation Scale (22%), the Riker Sedation–Agitation Scale (7%), and the Modified Minnesota Detoxification Scale (6%). In addition, most respondents (72%) reported that their institutions had protocols or guidelines for the management of AWS. At about half of the hospitals, AWS protocols or guidelines had been updated within the prior two years. The survey asked about the use of alcohol for AWS management; alcohol use was allowed at 19% of hospitals.

Although most hospitals utilized protocols or guidelines when treating mild, moderate, and severe AWS (66%, 73%, and 67%, respectively), only 30% of respondents indicated that guidelines or protocols were implemented to treat BZD-refractory AWS (Figure 1). A BZD-only treatment strategy was selected as the first choice for mild (74%) and moderate (54%) AWS, whereas a BZD regimen in combination with other non-BZD agents was most frequently used in the treatment of...
whereas dexmedetomidine (55.3%) was used most frequently in treating BZD-refractory AWS (Figure 3). As shown in Figure 4, respondents reported using phenobarbital most often for the treatment of both severe and BZD-refractory AWS when they chose a non-BZD regimen.

DISCUSSION

While BZD has been a mainstay of therapy for the treatment of AWS, limited recommendations are available, particularly with regard to the use of non-BZD agents as an adjunct to BZDs. In addition, non-BZD recommendations are inconsistent among guidelines. In the 2004 American Society of Addiction Medicine Practice Guidelines Committee’s Management of Alcohol Withdrawal Delirium guidelines, sedative-hypnotic agents, including BZDs and barbiturates, are recommended as the primary agents for the management of AWS.11 These guidelines recommend consideration of pentobarbital or propofol in patients whose agitation is not adequately controlled with large doses of BZDs.11 The 2010 National Institute for Clinical Excellence guidelines for alcohol use disorders published in the United Kingdom recommend BZDs or carbamazepine as the first line for withdrawal symptoms.24 In terms of DT treatment, lorazepam, olanzapine, and haloperidol are recommended as treatment options.24 More recently, the 2015 Veterans’ Affairs/Department of Defense clinical practice guideline for the management of substance use disorders recommends BZDs for moderate-to-severe AWS.25 In the case of mild-to-moderate withdrawal, however, if the risk of BZDs is determined to outweigh the benefits for reasons such as inability to adequately monitor the patient or adverse reactions, consideration of other medications such as carbamazepine, gabapentin, or valproic acid is recommended, with the strength of this recommendation rated as weak.25 There have been no publications surveying practice patterns in the management of AWS in the United States since the last national survey conducted by Saitz and colleagues in 1995.26 Given that substantial variability exists in recommendations for managing AWS, including assessment tools and treatment regimens, the present survey aimed to evaluate current practice patterns surrounding the inpatient management of AWS in the Northeast region of the United States. A multicenter survey of inpatient pharmacologi-
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Figure 3 Use of Non-Benzodiazepine (BZD) Agents When BZD-Based Regimen With Other Agents PRN Was Chosen

![Bar chart showing the use of non-benzodiazepine agents when BZD-based regimen with other agents PRN was chosen.]

- BZD = benzodiazepine; PRN = as needed.

Figure 4 Use of Non-Benzodiazepine (BZD) Agents When Non-BZD-Based Regimen Was Chosen

![Bar chart showing the use of non-benzodiazepine agents when non-BZD-based regimen was chosen.]

- BZD = benzodiazepine.

Cal management strategies for alcohol withdrawal conducted in 104 acute-care hospitals in the United Kingdom observed that only 60% of these hospitals had a formalized protocol in place. Furthermore, the existing protocols had wide variability in recommendations for vitamin dosing, duration of treatment, fixed versus symptom-triggered dosing, and sedative medication of choice. The results of the survey prompted its authors to conclude that there is an urgent need to standardize care in the United Kingdom. Similarly, the findings from our survey will be valuable in demonstrating a potential need for establishing a standard of care for AWS treatment.

For the treatment of mild or moderate AWS, most respondent hospitals utilized guidelines or protocols (Figure 1). In addition, BZD-only regimens were the most commonly used in both mild and moderate AWS scenarios, and lorazepam was the first agent of choice (Figure 2). In contrast, this report suggested a
lack of consensus on treatment strategies for severe and BZD-refractory AWS. When a patient with severe AWS was treated in the intermediate care unit, which was shown on the survey as a severe case scenario, 74 of the respondents reported using a BZD-based regimen with other agents as needed, but there was considerable variation in selecting other non-BZD agents, including haloperidol (51%), clonidine (23%), phenobarbital (19.3%), and valproic acid (9%) (Figure 3). When treating a patient with BZD-refractory AWS in ICU settings, much more variety existed regarding the treatment regimens utilized. This was partly because only 33% of hospitals used standardized protocols or guidelines for the treatment of BZD-refractory AWS.

In this survey, a patient consistently showing a high severity of AWS despite a treatment with at least 35 mg of lorazepam over the first three hours was presented as an example of a BZD-refractory AWS case. Of 60 institutions where such patients were treated, 53 respondents reported that they would use other non-BZD agents with or without BZDs. Phenobarbital was the first agent of choice when a non-BZD-based regimen was chosen (Figure 4), whereas dexmedetomidine or propofol was most frequently used in combination with BZDs (Figure 3).

There are several limitations to our survey. The primary limitation is a relatively low response rate (18%), but the investigators examined whether survey respondents (n = 90) were representative of eligible institutions (n = 504) by comparing key hospital characteristics of the two groups. Although the number of respondents from four states—Rhode Island, New Hampshire, Maine, and Vermont—was three or fewer, the investigators believe that, overall, the findings from this study are representative of all the hospitals surveyed. In addition, in the present survey, hospitals located only in the Northeast region were surveyed due to limited research resources. This survey, however, provides preliminary data for future nationwide surveys. Another limitation is that all respondents were pharmacists, not prescribers. Nonetheless, the investigators believe that it is valid to use pharmacists as a representative sample for this survey because hospital pharmacists are not only well informed of treatment protocol but also actively involved in its development and implementation.

CONCLUSION

The findings suggest that there was no widely accepted consensus among hospitals on how to treat severe and BZD-refractory AWS. The results of the survey point to the urgent need for updated uniform practice guidelines utilizing other non-BZD treatment strategies, particularly for more severe AWS. Furthermore, a national survey is needed to determine whether AWS treatment regimens in the Northeast region are representative of practice patterns in the United States.

REFERENCES