Risk Factors for Delirium Tremens Development

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OBJECTIVE: To identify clinical characteristics associated with inpatient development of delirium tremens so that future treatment efforts can focus on patients most likely to benefit from aggressive therapy.

DESIGN: Retrospective cohort study among patients discharged with diagnoses related to alcohol abuse.

SETTING: University-affiliated inner-city hospital.

PATIENTS/PARTICIPANTS: Two hundred consecutive patients discharged between June 1991 and August 1992 who underwent evaluation and treatment for alcohol withdrawal or detoxification.

MEASUREMENTS AND MAIN RESULTS: Mean age was 41.9 years, 85% were male, 57% were white and 84% were unmarried. Forty-eight (24%) of the patients developed delirium tremens during hospitalization. Bivariate analysis indicated that those who developed delirium tremens were more likely to be African-American, unemployed, and homeless, and were more likely to have gone more days since their last drink, and to have concurrent acute medical illness, high admission blood urea nitrogen level and respiratory rate, and low admission albumin level and systolic blood pressure. In multiple logistic regression analyses, patients who developed delirium tremens were more likely to have gone more days since their last drink (odds ratio [OR] 1.3; 95% confidence interval [CI] 1.09, 1.61) and to have concurrent acute medical illness (OR 5.1; 95% CI 2.07, 12.55). These risk factors were combined for assessment of their ability to predict the occurrence of delirium tremens. If no factors were present, 9% developed delirium tremens; if one factor was present, 25% developed delirium tremens; and if two factors were present, 54% developed delirium tremens.

CONCLUSIONS: Inpatient development of delirium tremens was common among patients treated for alcohol detoxification or withdrawal and correlated with several readily available clinical variables.

KEY WORDS: Delirium tremens; hospitalized patients; detoxification; alcohol-related complications.


Alcohol abuse and dependence are prevalent health problems responsible for substantial morbidity, mortality, and health services utilization with approximately 44 billion dollars spent annually in the United States to treat alcohol-related complications.1 Once alcohol dependence is recognized, formal detoxification and abstinence can be successful in preventing or attenuating further complications. However, detoxification carries some risk, because alcohol cessation can initiate alcohol withdrawal, ranging from mild and asymptomatic to severe and life-threatening. The severest form, delirium tremens, is estimated to occur in approximately 5% to 20% of all patients undergoing detoxification, and of those who experience delirium tremens approximately 5% suffer fatal complications.2-5

Prospectively identifying patients with increased risk of developing severe alcohol withdrawal would be extremely useful to clinicians. Valid multivariable models would allow clinicians to tailor therapeutic decisions based on the risk of delirium tremens development. However, existing literature suggesting associations between patient factors and risk of delirium tremens either lack empirical data or are limited by inadequate sample size or lack of multivariable analyses.6-8 In addition, most studies have focused on detoxification unit settings where patients with concurrent acute medical illnesses are not treated.5-7 Therefore, physicians who assess and treat patients undergoing alcohol withdrawal in acute care settings do not have available sufficient evidence to apply risk stratification criteria to their treatment strategies.

In this study, we estimated the incidence rate of delirium tremens among a cohort of patients admitted to an acute care hospital for evaluation or treatment of alcohol withdrawal or detoxification. We also identified factors associated with delirium tremens development as a first step in helping clinicians develop targeted interventions to decrease the risk of such events.

METHODS

Setting

This retrospective cohort study was conducted among patients admitted to the internal medicine service at Wishard Hospital, a university-affiliated 380-bed inner-city hospital. Inpatient care is managed by approximately 110 housestaff physicians with supervision by general internal medicine and internal medicine subspecialty faculty. Approximately 480 patients are admitted to the internal medicine service per month. The initial evaluation and treatment of alcohol withdrawal and detoxification are determined by housestaff physicians without the use...
of written standardized protocols. However, virtually all such patients receive intravenous fluids with supplemental thiamine, folic acid, and multivitamins as well as scheduled and as needed doses of benzodiazepines. Few patients receive additional or alternative therapies, such as β blockers, magnesium, or clonidine.

Eligibility Criteria

Patients were eligible for the study if they were discharged from the internal medicine service with diagnoses related to alcohol abuse (ICD-9-CM codes 291, 291.3, 291.8, 303.01, 303.9, and 303.93). Patients were excluded if chart review indicated that no alcohol withdrawal treatment or detoxification occurred during hospitalization, or if delirium tremens was present at admission.

Procedures

Consecutive admissions to the internal medicine service between June 1991 and August 1992 with relevant discharge diagnoses were identified for chart review and possible inclusion. Discharge diagnoses, rather than admission diagnoses, were used to increase the sensitivity of cohort identification. Two trained research assistants, blinded to the study objectives, reviewed medical charts to apply eligibility criteria, to determine the severest form of alcohol withdrawal during the admission using predetermined criteria derived from the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition (see Appendix A), and to record vital status at discharge. A 10% random sample of charts was selected to assess interrater and intrarater reliability (κ = 0.7 and 0.8, respectively).

A second pair of trained research assistants, also blinded to the study objectives and outcome assessment, reviewed charts to abstract the following baseline admission variables: age, race, gender, presence of concurrent acute medical illness, history of previous alcohol withdrawal or delirium tremens, concurrent illicit drug use, documented alcohol consumption history, laboratory values, vital signs, and baseline treatment variables (e.g., medications prescribed, intravenous fluid use, and admitting location). We used a second group of abstractors to minimize bias that may have been introduced by a single auditor both applying eligibility criteria and assessing outcomes. A 10% random sample of charts was selected to assess interrater and intrarater reliability (κ = 0.9 and 0.9, respectively).

Statistical Analyses

Differences between patients who developed and who did not develop delirium tremens were examined using Student's t tests for continuous variables and χ² tests for categorical variables. Variables with significance level of p ≤ .10 were then considered in the multivariate analysis. Specifically, we used stepwise logistic regression analysis to determine the net effects of each independent variable while controlling for the others. Only those variables that remained significantly associated with delirium tremens development in the multivariate analysis were retained in the final model. A receiver-operating characteristic (ROC) curve analysis was performed to determine the model's ability to discriminate between patients with and those without development of delirium tremens. All analyses were performed by SAS programs. Bootstrap techniques as described by Efron and Tibshirani were performed to validate our regression model.

RESULTS

From June 1991 to August 1992, 350 consecutive patient admissions with discharge diagnoses related to alcohol abuse were identified: 136 were excluded because these admissions did not include any evaluation of, or treatment for, alcohol withdrawal or detoxification, and 14 were excluded because delirium tremens was present at the time of admission. The remaining patients (n = 200) had a mean age of 41.9 years (range 19–78 years), 85% were male, 57% were white, and 84% were unmarried. Forty-eight (24%) of the patients admitted for alcohol withdrawal or detoxification developed delirium tremens, 4 (8%) of whom died.

Nine factors were considered candidate variables in multivariate analysis because they were associated (p < .10) with delirium tremens development in bivariate analyses: being African-American, being unemployed, presence of concurrent acute illness, being homeless, more days since the last drink, higher admission blood urea nitrogen (BUN) level, decreased admission albumin level, higher admission respiratory rate, and decreased admission systolic blood pressure. History of previous withdrawal events and baseline treatment variables were not associated with delirium tremens development (Table 1).

Two variables were retained in the final model: presence of one or more concurrent acute medical illnesses (odds ratio [OR] 5.1: 95% confidence interval [CI] 2.07, 12.55) and more days since the last drink (OR 1.3; 95% CI 1.09, 1.61) (Table 2). The area under the ROC curve for the predictive model is 0.76. Bootstrap validation techniques revealed that the unbiased estimate of the area under the ROC curve is 0.75. Data documenting the number of days since the last drink were missing in 48 admissions; therefore, the multivariate analyses were performed on the remaining observations (n = 152). Analyses of patient characteristics and outcomes revealed no differences among those who were missing this variable versus those who were not (mean age 44.0 vs 41.3 years, 79% vs 86% males, 54% vs 58% white, presence of delirium tremens 25% vs 24%).

To determine how well the final model predicted delirium tremens events, we developed risk groups based on the presence or absence of the significantly associated risk factors. To simplify the practical use of this instrument, we chose to dichotomize the number of days since