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Selected Topics: Toxicology

DEVELOPMENT OF A PREDICTION MODEL FOR DIAGNOSIS OF ACUTE POISONING IN PATIENTS WITH ALTERED MENTAL STATUS AND ABSENT HISTORY OF ALCOHOL/DRUG INGESTION

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□ **Abstract—Background: Diagnosis of acute poisoning in patients with altered mental status and absent history is a challenging diagnostic problem in clinical practice. Objective: The aims of the study were to develop a simple clinical tool to stratify risk of acute poisoning in patients with altered mental states and no history of alcohol/drug ingestion, and develop a prediction model using initial observations from which a simple risk score could be derived. Methods: The study was carried out on non-trauma patients aged 15 years and older admitted with altered mental states and no history of alcohol or drug ingestion. Univariate analysis and logistic regression were carried out and a score was derived and validated. Results: There were 607 patients included, with mean age of 60.3 years and 54% were male. The regression model performed moderately well on both the training and validation sets with areas under the receiver operating characteristic curve of 0.834 and 0.844, respectively. The risk score correlated with the regression model (R^2 = 0.969). At cutoff thresholds of 20% for the model and 2 for the score, sensitivity and specificity of the regression model (67.6% and 85.6%) and the score (67.6% and 85.4%) were moderate, while positive predictive values were low (43.4%) and negative predictive values were high (94.2%) for both the regression model and the score. Conclusions: A prediction model with a derived risk score was developed with a high negative predictive value and may have potential in assessing risk of poisoning in altered mental status and may have value in a prehospital environment or at triage.** © **2017 Elsevier Inc. All rights reserved.**

□ **Keywords—altered mental status; poisoning; prediction model; risk score; diagnosis**

INTRODUCTION

Altered mental status (AMS) is a common presentation to the emergency department (ED) and is a challenging diagnostic problem in clinical practice. The spectrum of features of AMS include disturbance in activity, arousal, cognition, and perception (1). Other manifestations may include abnormal motor movements (including asterixis, twitching, myoclonus, and seizures) (2).

Drugs and non-pharmaceutical substances are a major cause of AMS, especially in the elderly (3). Acute medical and psychiatric conditions may produce features that resemble drug-induced altered states, including disturbed behavior, delusions, and hallucinations, and are often considered in the differential diagnosis. Ruling out drug-induced psychiatric symptoms is often required in agitated patients referred for psychiatric care.

The accuracy of a clinical diagnosis in AMS by emergency physicians has been found to be moderate (R^2 = 0.807) (4). History of current event, history, and physical examination have been found to be diagnostic in 51%, 43%, and 41%, respectively, of patients with AMS (5). History of a recent new drug or change in

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Table 1. Comparison of Full Dataset, Training Set, and Validation Set

Dataset	Full Dataset	Training Dataset	Validation Dataset
n (%)	607 (100)	485 (80)	122 (20)
Positive cases, n (%)	85 (14)	68 (14)	17 (13.9)
% Male	54.0	54.9	50.8
Mean age, y			
Sample	60.3	60.9	58.0
Males	57.5	57.7	56.8
Females	63.6	64.8	59.3

dose may point to a toxic etiology, particularly in the elderly (6).

When available, an accurate history of recent alcohol, drug, or substance ingestion is crucial to make a diagnosis of acute poisoning. In patients with AMS, however, a history may be unavailable or unclear. Physical examination may reveal specific signs, such as pupillary abnormalities or track marks, and toxidromes may point toward specific drugs. However, individual neurologic signs are not specific to poisoning and may be due to other causes of AMS.

The aim of the study was to develop a simple clinical tool to stratify risk of acute poisoning in patients with AMS and no history of alcohol or drug ingestion. The objective was to develop a prediction model using clinical observations made at first patient contact, including age, smell of alcohol in the breath, and components of AMS, from which a simple score could be derived.

MATERIALS AND METHODS

The study was carried out on a sample of 607 consecutive non-trauma patients aged 15 years and older, admitted during a period of 2 years with AMS and no history of alcohol or drug ingestion. The ED registers more than 100,000 patients a year and is part of an acute general hospital located on an island of 400,000 with a tourism-based economy. Alcohol and drug use is very common.

After obtaining clearance from the data protection office and ethics board, data were collected from electronic clinical notes. Inclusion criteria were age 15 years or older and presenting with AMS, defined as having at least one of the following criteria: depressed consciousness, confusion, psychotic symptoms, agitation, or seizures. Patients with a clear history of alcohol or drug use were excluded. Other exclusion criteria were major trauma or a medical condition immediately detected at triage, including obvious stroke and hypoglycemia.

Age, gender, presence of a smell of alcohol in the breath, unresponsiveness, confusion or aggressiveness, and final diagnosis were recorded for each patient and inserted in a spreadsheet. Final diagnosis was based on the diagnosis made by the caring physician on discharge and was classed as positive if the main diagnosis was alcohol intoxication or medication or drug overdose/toxicity.

Statistical analysis was carried out using the public domain statistical software *R*. Univariate analysis of the predictive variables was carried out to identify significant predictors, using the *Rcmdr* plug-in. The dataset was imported into a data mining GUI plug-in called R.A.T.T.L.E. (R Analytical Tool to Learn Easily). The software was used to partition the dataset randomly using seeding into a training set (80%) for model development and an internal validation set (20%) for testing. Logistic regression was carried out using the training dataset. The regression model was tested on the training and validation datasets and the dataset with predicted probabilities was exported to a spreadsheet for further analysis.

A score was created based on rounded-off regression coefficients for each predictor (the smallest integer greater than the coefficient), and a field was added with the value of the score for each record. Additional fields were created for a range of threshold (cutoff) values for both the regression-based probability (ranging from 0% to 100%, in 5% increments) and for the score (ranging from −1 to 9). Calculations were made to identify the optimal cutoff values for both the regression model and

Table 2. Univariate Analysis of Predictive Variables

Variable	Unadjusted Odds Ratio (95% CI)	χ^2	*p* Value
Age < 50 y	5.84 (3.59–9.49)	58.753	<0.001
Smells of alcohol	26.46 (10.25–68.29)	89.299	<0.001
Aggressive	2.19 (1.03–4.66)	4.300	0.038
Unresponsive	3.10 (1.87–5.15)	20.699	<0.001
Confused	0.16 (0.09–0.28)	47.362	<0.001

Table 3. Logistic Regression Model

Variable	β Coefficient	Standard Error	*z* Value	*p* Value
Intercept	−2.551	0.312	−8.188	<0.001
Age < 50 y	1.442	0.310	4.646	<0.001
Smells of alcohol	3.347	0.646	5.178	<0.001
Aggressive	1.584	0.525	3.018	0.003
Unresponsive	0.809	0.364	2.224	0.026
Confused	−1.149	0.382	−3.012	0.003

χ^2 *p* value: <0.001; Pseudo R^2: 0.517.

Table 4. Risk Score Derived From Regression Coefficients

Variable	β Coefficient	Score
Age < 50 y	1.442	2
Smells of alcohol	3.347	4
Aggressive	1.584	2
Unresponsive	0.809	1
Confused	−1.149	−1