

Selected Topics: Psychiatric Emergencies



SAFETY OF RISPERIDONE FOR ACUTE AGITATION AND ALCOHOL INTOXICATION IN EMERGENCY DEPARTMENT PATIENTS

Patricia A. Pepa, PHARMD, MS,* Kelly C. Lee, PHARMD, MAS,† Hien E. Huynh, PHARMD CANDIDATE,† and
Michael P. Wilson, MD, PHD, FAAEM, FACEP‡§

*Department of Pharmacy, UC San Diego Health, San Diego, California, †UC San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences, La Jolla, California, ‡Department of Emergency Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, and §Department of Emergency Medicine, Behavioral Emergencies Research Laboratory, Little Rock, Arkansas

Reprint Address: Patricia A. Pepa, PHARMD, MS, Department of Pharmacy, UC San Diego Health, 200 West Arbor Drive, Mail Code 8765, San Diego, CA 92103

Abstract—Background: Acute agitation in the setting of alcohol intoxication is commonly encountered in the Emergency Department (ED). In this setting, expert consensus guidelines recommend haloperidol over second-generation antipsychotics due to their limited safety data in alcohol intoxication. **Objective:** The primary objective was to compare vital sign changes prior to and after risperidone administration between ED patients presenting with alcohol intoxication [ETOH (+)] and without alcohol intoxication [ETOH (–)]. The secondary objective was to assess the effect of benzodiazepine co-administration with risperidone on vital signs. **Methods:** This was a retrospective chart review of patients who received oral risperidone for acute agitation at two university EDs between January 1, 2012 and December 31, 2015. Vital signs (oxygen saturation, systolic and diastolic blood pressure, heart rate, and respiratory rate) were compared in patients who had ingested alcohol with those who had not. **Results:** There were 785 patients without evidence of alcohol intoxication who received risperidone in the ED, and 52 patients with alcohol intoxication who received risperidone. Overall, risperidone with and without alcohol intoxication and benzodiazepine administration had no statistically significant effect on vital signs ($p = ns$ for all comparisons). **Conclusion:** This study suggests that oral risperidone may be a safe option for acute agitation in patients presenting to the ED with alcohol intoxication. © 2017 Elsevier Inc. All rights reserved.

Keywords—acute agitation; risperidone; alcohol intoxication; second-generation antipsychotic

INTRODUCTION

Acute agitation is commonly encountered in the Emergency Department (ED) and may escalate to aggression or violence. When nonpharmacological methods fail, medications are often required. Recent expert guidelines provide recommendations for the management of acute agitation based on available evidence at the time of publication (1). The workgroup of the American Association of Emergency Psychiatry recommends that pharmacological treatment should be based on the most likely cause for the agitation and when an antipsychotic is indicated, second-generation antipsychotics (SGAs) are preferred over first-generation antipsychotics (1). This is due to the lower risks of extrapyramidal symptoms and QTc prolongation with SGAs. However, if the agitation is secondary to a central nervous system (CNS) depressant, such as alcohol, haloperidol is preferred due to few safety data on SGAs in this clinical scenario (1). Risperidone is a SGA commercially available as a tablet, oral solution, and disintegrating tablet, and has been shown to be as effective as intramuscular (IM) haloperidol and lorazepam (2). Second-generation antipsychotics (SGAs), such as

risperidone, have a unique receptor binding profile compared with first-generation antipsychotics like haloperidol. In addition to dopamine receptor blockade, SGAs have antagonistic properties at histamine and alpha-1 adrenergic receptors. Thus, SGAs may have additive CNS depressant effects when given to patients who have ingested other CNS depressants such as alcohol. Additionally, antipsychotics are often given with benzodiazepines for agitation, which could further potentiate the adverse effects of CNS depressants.

Wilson and colleagues reported a statistically significant decrease in oxygen saturation in alcohol-intoxicated patients who received IM olanzapine or IM ziprasidone irrespective of benzodiazepine co-administration (3,4). Interestingly, this was not evident in patients who received oral olanzapine or ziprasidone.

Previous literature has suggested that agitated patients should be offered oral medications whenever possible, to prevent accidental needle sticks, and because oral therapy is preferred by most patients (5–7). Risperidone is available as an oral disintegrating tablet and oral solution, which are convenient for acutely agitated patients who are at risk of medication nonadherence (i.e., “cheeking”).

The safety profile of oral risperidone, with and without a benzodiazepine, on respiratory depression and hemodynamic status for patients admitted with acute agitation and alcohol intoxication, has not been studied. The objective of this study was to investigate the effect of oral risperidone on oxygen saturation in patients with and without alcohol intoxication. Secondary objectives were to determine the effect of risperidone on systolic (SBP) and diastolic blood pressure (DBP), respiratory rate (RR), and heart rate (HR) on patients with and without alcohol intoxication, and to study the influence of risperidone and concomitant benzodiazepine administration on vital signs.

METHODS

Study Design and Setting

This was a retrospective chart review of all patients receiving risperidone in two university EDs between January 1, 2012 and December 31, 2015. Both sites are part of a university hospital system, one being an academic department in an urban setting and the other an ED in a suburban setting. Approval was obtained from the local institutional review board prior to data collection.

Data Collection

Electronic medical records (EMR) of patients who received risperidone in the ED between January 1, 2012

and December 31, 2015 were accessed. Variables were extracted from the study setting's EMR production database using Structured Query Language (SQL) Server Management Studio. Variables extracted from each record included patient identifier, age, sex, triage date/time, discharge date/time, risperidone dose, route and administration times, benzodiazepine dose, route and administration times, opioid administration, antipsychotic administration, International Classification of Diseases, Ninth Revision (ICD-9) and ICD-10 codes, and oxygen saturation, SBP, DBP, RR, HR, and blood alcohol content (BAC).

Additional data were then abstracted from the EMR by two of the study investigators (PP and HH) using a pre-specified abstraction protocol. These investigators were trained in the use of abstracting data from EMR, which tracks laboratory results and clinician charting. Data collected from the EMR included alcohol breath test results, evidence of alcohol intoxication as described by the physician and discharge diagnosis located in the after-visit ED summary. Chart review was conducted in accordance with published methods for this type of study design, with the sole exception that data abstraction was conducted by authors not blinded to the study hypotheses. This was not expected to be problematic given that abstracted variables were not subjective. To improve inter-rater reliability, a chart audit of 65% of the data was performed by a different study investigator.

Inclusion criteria were administration of oral risperidone and documentation of vital signs (oxygen saturation, SBP, DBP, RR, and HR) prior to and within 4 h of risperidone administration. For patients with multiple ED encounters, only the first encounter in which the patient received risperidone was included in the study. Exclusion criteria included patients younger than 18 years old, administration of other antipsychotics or opioids within 4 h of risperidone administration, patients with asthma or chronic obstructive pulmonary disease (ICD-9 codes 496 and 493.3), and respiratory-related discharge diagnoses listed in the after-visit ED summary (i.e., pneumonia, asthma exacerbation).

Study Groups

Patients were separated into two groups: no evidence of alcohol intoxication [ETOH (–)] and evidence of alcohol intoxication [ETOH (+)]. Evidence of alcohol intoxication was defined as having one of the following present in the chart: a BAC or breathalyzer test $\geq 0.08\%$, or if an alcohol level was not obtained but clinician noted in the chart that a patient appeared intoxicated. We expressed BAC as a percentage (weight/volume) and used the following conversion: 100 mg/dL is equivalent to 0.01% (weight/volume).

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