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Implications of atypical antipsychotic prescribing in the intensive care unit☆

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ABSTRACT

Purpose: The purpose of the study was to determine the downstream implications of atypical antipsychotic (AAP) prescribing in the intensive care unit (ICU), including discharge prescribing practices, monitoring, and attributable adverse drug events.

Materials and methods: This retrospective cohort study included patients at least 18 years of age admitted to an ICU that received at least 2 doses of an AAP for documented delirium or avoidance of a deliriogenic medication. Exclusion criteria were documentation of an AAP as a home medication or initiation for a psychiatric indication unrelated to delirium (eg, schizophrenia).

Results: During the 8-month study period, 156 patients were included and 133 (85.2%) patients survived to hospital discharge. Of the survivors, AAP therapy was continued for 112 (84.2%) patients upon ICU transfer and for 38 (28.6%) patients upon hospital discharge. A majority of these patients had evidence of delirium resolution or no indication for continuation documented at discharge. Of the 127 patients with an electrocardiogram ordered during AAP therapy, QTc prolongation occurred in 49 (31.4%) patients. An adverse drug event leading to drug discontinuation was documented in 16 (10.2%) patients.

Conclusions: Because of significant patient-centered implications, AAPs initiated in the ICU require continued evaluation for indication to avoid prolonged and possibly unnecessary use.

1. Introduction

Delirium in the intensive care unit (ICU) is a common disorder affecting approximately 50% (22%-87%) of critically ill patients [1–3]. Unfortunately, delirium is associated with many negative consequences, including prolonged duration of mechanical ventilation, prolonged ICU and hospital length of stay, development of post-ICU cognitive impairment, and increased mortality [1,4–10]. Over the last 15 years, the focus of delirium research has been on the characterization of this comorbidity and its risk factors; the development and validation of diagnostic tools, such as the Confusion Assessment Method-ICU (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC); and the systematic implementation of delirium evaluation on an institutional level [2,11–16]. Data regarding pharmacologic prevention and treatment of delirium are limited. Many risk factors contribute to the development and persistence of delirium, making response to any one pharmacologic or nonpharmacologic intervention challenging to elucidate. Although consensus guidelines for the management of pain, agitation, and delirium in the ICU do not recommend any pharmacologic intervention to prevent delirium, atypical antipsychotics (AAPs) are suggested for treatment to reduce the duration of delirium [17].

Medications initiated in the ICU are often continued at ICU and hospital discharge. A study of 120 elderly ICU survivors found that 14 (12%) patients were discharged with a prescription for an AAP. The AAP was initiated during the ICU admission in 11 of these 14 patients [18]. Risk factors identified for potentially inappropriate discharge prescribing included the number of preadmission inappropriate mediations and discharge service (medical vs surgical). In another single-center, retrospective review of 59 medical ICU patients initiated on an AAP, AAPs were continued in 47% of patients on ICU discharge and in 32% of patients on hospital discharge [19]. These studies highlight a growing concern regarding the prescribing of these agents to inpatients; however, the studies are limited by small sample size in a primarily medical ICU population.

This study aimed to describe the downstream implications of AAP prescribing in multiple ICUs including discharge prescribing, inpatient monitoring, and adverse drug events (ADEs). During the study period, delirium diagnosis in the ICU at our institution was primarily based on clinician assessment because CAM-ICU or ICDSC was not routinely documented. Therefore, we offer a unique position to benchmark AAP prescribing practices and transitions of care across multiple ICUs that do not routinely use an objective diagnostic tool for delirium detection.

Abbreviations: AAP, atypical antipsychotic; ADE, adverse drug event; CAM-ICU, Confusion Assessment Method-ICU; EKG, electrocardiogram; ICDSC, Intensive Care Delirium Screening Checklist; TBI, traumatic brain injury.

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We hypothesized that a notable proportion of patients would receive a discharge prescription for an AAP and sought to identify characteristics of patients more likely to receive a discharge prescription.

2. Methods

Institutional review board approval was granted with a waiver of informed consent. This retrospective, descriptive cohort study included all patients at least 18 years of age who were admitted to an ICU between June 20, 2013, and February 20, 2014, and received at least 2 doses of an AAP while in the ICU for documented delirium or avoidance of deliriogenic medication. Patients were excluded if an AAP was documented as a home medication or if the AAP was initiated for a psychiatric indication unrelated to delirium (eg, schizophrenia).

Five adult, closed ICUs consisting of 120 critical care beds were included in the study: Medical, Surgical, Cardiothoracic Surgery, Neurosciences, and Cardiac. The AAPs evaluated were aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone. During the study period, delirium diagnosis was primarily based on clinician assessment because CAM-ICU or ICDSC was not routinely documented. Medication initiation, monitoring, and discontinuation were conducted at the discretion of the multidisciplinary health care team, which is composed of an attending physician, fellow, resident or physician extender (physician assistant, nurse practitioner), bedside nurse, pharmacist, respiratory therapist, and other allied health staff. All ICUs have a closed staffing model. In general, AAPs, haloperidol, or both were used to manage the delirious patient. No formal delirium management protocol was in place during the study period.

The primary end point was the proportion of ICU survivors discharged from the hospital with a prescription for an AAP. Secondary end points were the proportion of ICU survivors who had an AAP continued on transfer from the ICU, frequency of electrocardiogram (EKG) ordering for QTc monitoring due to AAP use, and a composite of AAP discontinuation due to documentation of an ADE. Adverse drug events evaluated were documentation in the electronic health record of QTc prolongation, extrapyramidal symptoms, seizure, somnolence, or other. QTc prolongation was defined as greater than 470 milliseconds (men) or greater than 480 milliseconds (women) as reported on a 12-lead EKG. QTc data were not collected if the patient had atrial fibrillation/flutter, a ventricular-paced rhythm, or a bundle-branch block. At our institution, providers must document an indication for ordering an EKG; therefore, we were able to retrospectively determine if the EKG was ordered for therapeutic drug monitoring.

Patients were identified by the institutional pharmacy data repository, SAP BusinessObjects Web Intelligence, which generated a report of all patients with an ICU level of care who had an AAP ordered during their stay; patient demographics; order start and stop date/time; medication name, dose, dosage form, frequency, and route of administration; PRN indication; admitting ICU; and hospital service. The remainder of collected data, including preadmission medications, comorbid conditions, hospital and ICU admission and discharge date/time, in-hospital mortality, documented ADEs, and EKG data, were gathered by one investigator (BK) via manual chart review of the institutional electronic health record's admission, discharge, transfer and daily progress notes, medication administration record, and imaging. An a priori–generated data dictionary defined all data collection points and was approved by all study investigators. The institutional electronic health record was implemented at the start of the study period, offering an opportunity to evaluate prescribing practices and documentation of administration, medication monitoring, and ADEs.

Analyses of the transitions of care variables were conducted only in ICU and hospital survivors; however, monitoring and ADEs were evaluated for all-comers meeting inclusion and exclusion criteria. Demographic and clinical variables are summarized as medians and interquartile ranges for continuous variables and proportions for categorical variables. To analyze between-group differences for patients who received a discharge prescription for an AAP and those who did not, 2-tailed Wilcoxon rank sum was used for continuous variables and Fisher exact test was used for categorical data. All analyses were performed using JMP software, version 11.0 (SAS Institute, Cary, NC).

3. Results

Over the 8-month study period, 3232 patients were admitted to or transferred into an adult ICU; and an AAP was ordered for 352 (9.2%) patients. (Fig. 1) Characteristics of the 156 patients included in this study, as well as a comparison between ICU survivors prescribed an AAP at hospital discharge and those who were not, are reported in Table 1. Of the 133 ICU survivors initiated on an AAP while in the ICU, 112 (84.2%) patients had the medication continued on transfer from the ICU; and 38 (28.6%) patients received a prescription at hospital discharge. Discharge prescribing of AAPs was similar regardless of

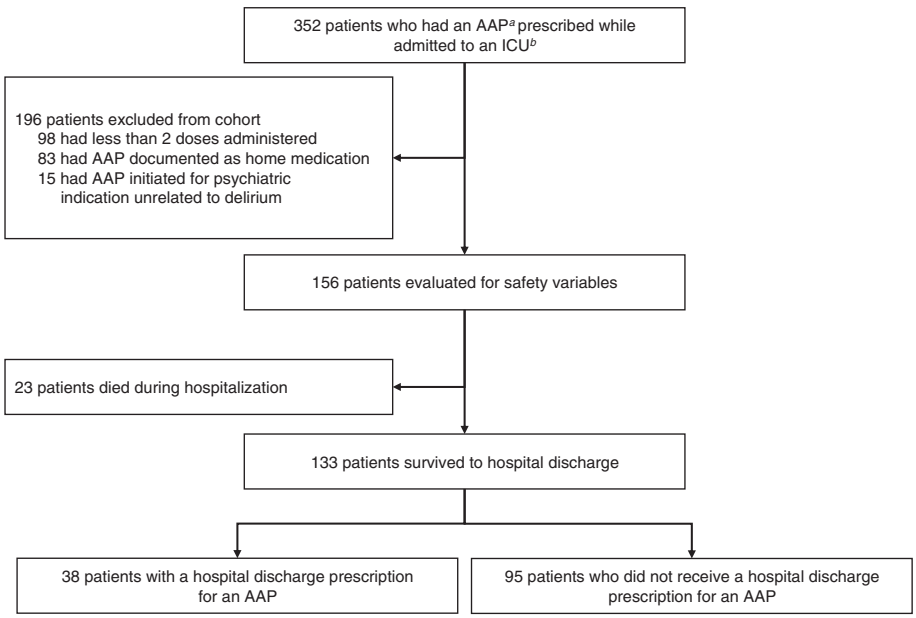

Fig. 1. Enrollment. [a]AAP = atypical antipsychotic; [b]ICU = intensive care unit.