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Diazepam as a component of goal-directed sedation in critically ill trauma patients☆,☆☆,★

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Abstract

Purpose: Limited information addressing the safety and efficacy of diazepam in the intensive care unit, particularly in trauma patients, is available. The purpose of this study is to evaluate the safety and efficacy of diazepam when used in routine clinical practice as a component of a goal-directed sedation regimen in critically ill trauma patients.

Material and methods: This is a prospective observational evaluation of adult trauma patients admitted to an intensive care unit with orders for as-needed midazolam or lorazepam followed by scheduled diazepam. Medication administration and Sedation-Agitation Scale scores were recorded.

Results: Twenty-four patients were evaluated. The most common diazepam dosage was 10 mg every 6 hours, and individual doses ranged from 5 to 30 mg. Sedation-Agitation Scale scores were recorded a median of 20 times per day (interquartile range, 15-24), and the majority (68%) were in the target range. No diazepam-related adverse events were observed.

Conclusions: Based on this limited sample, the use of diazepam as a component of goal-directed therapy appears safe and effective in providing adequate sedation in critically ill trauma patients using an average dosage of 40 mg/d.

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1. Introduction

Agitation is commonly experienced by patients admitted to the intensive care unit (ICU), and sedative agents are administered to prevent excessive anxiety and agitation [1-2]. Undersedation may result in unplanned extubation, whereas excessive sedation may prolong the duration of mechanical ventilation resulting in an increased ICU length of stay [3-4]. A primary goal of administering sedatives in the ICU is to achieve balance between these extremes [4].

Midazolam, lorazepam, and propofol are the most commonly used sedatives in critically ill patients. Surveys indicate that intensivists do not commonly use diazepam for sedation of mechanically ventilated patients [5]. However, it is used for specific indications including muscle rigidity associated with tetanus, alcohol withdrawal syndrome, and delirium tremens [6-9]. One explanation for the lack of diazepam usage in the ICU is its long elimination half-life and concerns about excessive and prolonged sedation [5,10].

Sedation guidelines indicate that diazepam may be appropriate for long-term sedation [4]. Theoretically, diazepam's long half-life and long-acting active metabolites should result in small changes in serum drug concentrations and may decrease fluctuations between severe agitation and oversedation, as well as reduce the need for breakthrough benzodiazepine usage. Although it may represent an alternative to other sedatives by achieving the same target sedation and yet requiring less frequent dosing, there is limited information on the safety and efficacy of diazepam in the ICU, particularly in trauma patients.

The purpose of this study is to evaluate the safety and efficacy of diazepam when used in routine clinical practice as a component of a goal-directed ICU sedation regimen in critically ill trauma patients.

2. Materials and methods

Approval was obtained from the institutional review boards at Orlando Regional Medical Center (ORMC) and the University of Pittsburgh.

2.1. Patients

This was a prospective observational study of consecutive patients managed by the intensivist-led, multidisciplinary surgical critical care service at ORMC between April and December 2006. Inclusion criteria consisted of the following: age greater than 18 years, traumatic injury, admission to an ICU within 24 hours of hospital admission, mechanical ventilation, and initiation of as-needed midazolam or lorazepam followed by scheduled diazepam. Exclusion criteria included the following: neurotrauma with presence of an intracranial hemorrhage or hematoma or Glasgow coma scale score less than 8 without sedation, burn injury more than 25% total body surface area, seizure disorder, pregnancy, administration of neuromuscular blocking agents other than for procedures, and maintenance sedatives other than as-needed benzodiazepines.

2.2. Routine practice

The surgical critical care guideline–based sedation practice at ORMC consists of initial therapy with as-needed intermittent midazolam or lorazepam. When dosing requirements are frequent (ie, every 1-2 hours), scheduled diazepam is added at the discretion of the prescribing physician. Propofol is reserved for refractory agitation. Goal-directed therapy includes hourly monitoring of the Sedation-Agitation Scale (SAS). Efficacy is defined as a target score of 3 to 4 [11]. Pain is managed with opioids. This sedation practice was in place for approximately 5 years at the time of the study.

2.3. Data collection

Data were collected prospectively on all patients. Acute Physiology and Chronic Health Evaluation IV scores were calculated from variables recorded within the first 24 hours of ICU admission [12]. Patients were monitored daily for administration of sedatives, opioids, and concurrent drugs known to interact with diazepam. All dosing information was recorded. Medication administration was also recorded for bedside procedures. Safety was assessed by recording episodes of excessive sedation, defined as SAS scores of 1 to 2. Furthermore, documented adverse drug reactions attributed to diazepam were recorded. For patients receiving intravenous diazepam, hypotension was defined as a mean arterial pressure lower than 60 mm Hg or a decrease in mean arterial pressure greater than 10 mm Hg during the hour following each dose. Intubation status was recorded, and all instances of reintubation were documented.

2.4. Statistical analysis

Data were collected up to 24 hours before starting diazepam. Patients were followed for 7 days following discontinuation of diazepam in the ICU or 7 days following transfer out of the ICU, whichever occurred first. Data are reported as means ± SD or medians with interquartile ranges (IQRs) as appropriate. Student t test was performed using SPSS version 15.0 (SPSS, Inc, Chicago, Ill).

3. Results

3.1. Patient characteristics

Although 25 patients were studied, 1 was excluded because of the initiation of a neuromuscular blocking agent infusion. Demographics of the 24 patients are displayed in Table 1. Twenty-four hours before the initiation of diazepam, patients