Risk Factors for Apnea in Pediatric Patients Transported by Paramedics for Out-of-Hospital Seizure

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Study objective: Apnea is a known complication of pediatric seizures, but patient factors that predispose children are unclear. We seek to quantify the risk of apnea attributable to midazolam and identify additional risk factors for apnea in children transported by paramedics for out-of-hospital seizure.

Methods: This is a 2-year retrospective study of pediatric patients transported by paramedics to 2 tertiary care centers. Patients were younger than 15 years and transported by paramedics to the pediatric emergency department (ED) for seizure. Patients with trauma and those with another pediatric ED diagnosis were excluded. Investigators abstracted charts for patient characteristics and predefined risk factors: developmental delay, treatment with antiepileptic medications, and seizure on pediatric ED arrival. Primary outcome was apnea defined as bag-mask ventilation or intubation for apnea by paramedics or by pediatric ED staff within 30 minutes of arrival.

Results: There were 1,584 patients who met inclusion criteria, with a median age of 2.3 years (Interquartile range 1.4 to 5.2 years). Paramedics treated 214 patients (13%) with midazolam. Seventy-one patients had apnea (4.5%): 44 patients were treated with midazolam and 27 patients were not treated with midazolam. After simultaneous evaluation of midazolam administration, age, fever, developmental delay, antiepileptic medication use, and seizure on pediatric ED arrival, 2 independent risk factors for apnea were identified: persistent seizure on arrival (odds ratio [OR]=15; 95% confidence interval [CI] 8 to 27) and administration of field midazolam (OR=4; 95% CI 2 to 7).

Conclusion: We identified 2 risk factors for apnea in children transported for seizure: seizure on arrival to the pediatric ED and out-of-hospital administration of midazolam. [Ann Emerg Med. 2014;63:302-308.]

Please see page 303 for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Seizure is the most common chief complaint for pediatric patients in the out-of-hospital setting, accounting for approximately 15% of all emergency medical services (EMS) transports of pediatric patients in the United States.[1] Given the significant morbidity and mortality from prolonged seizures, including risk of permanent neurologic sequelae, treatment is recommended for any seizure lasting more than 10 minutes.[1-3] The sooner the seizure is treated, the more likely it is to be controlled.[1] For this reason, initiating treatment for persistent seizures in the out-of-hospital setting is common practice in EMS systems in the United States. Benzodiazepines are first-line therapy, and their out-of-hospital administration shortens overall seizure duration.[4,5] Traditionally, diazepam was most often used to treat pediatric seizures. However, in the past decade, midazolam has emerged as a favored therapy because of its ease of administration by multiple routes and its rapid onset and clearance, making it less likely to result in adverse effects, including cardiovascular depression and apnea.[2,6-8] Los Angeles County EMS Agency protocol was changed in July 2009, designating midazolam (through the intravenous, intramuscular, or intranasal route) as the treatment for pediatric seizure.

Importance

Respiratory depression is a potential complication of treatment with benzodiazepines, especially in children.[5,6,9-13] The high risk of respiratory depression in several studies has caused some to question the use of benzodiazepines as first-line therapy for seizure.[12] Others have argued that the risk of complications with benzodiazepines may be outweighed by the benefits of reduced seizure duration, which itself could lead to respiratory compromise.[4] There is little knowledge of what other factors may contribute to respiratory depression in children with seizure. It has been suggested that children with developmental delay, those receiving previous seizure medications, and those with high fever may be more susceptible, but this is not well

Editor's Capsule Summary

What is already known on this topic

Seizing children can develop apnea.

What question this study addressed

When is such apnea more likely?

What this study adds to our knowledge

In this multicenter retrospective study of 1,584 children with out-of-hospital seizures, predictors of the 71 who developed apnea were continuing seizure on emergency department arrival and receiving midazolam.

How this is relevant to clinical practice

Although apnea can result from both ongoing seizures and midazolam, these data suggest that the benefit of using midazolam to stop seizures in children outweighs the risk of persistent seizures.

studied.[14] Furthermore, prolonged seizure is likely a risk factor for apnea.[15] Children with persistent seizure activity are more likely to receive medication, so the true contribution of benzodiazepines in the onset of apnea remains unclear. It is important to account for these potential risk factors when evaluating the risk of apnea during paramedic treatment of out-of-hospital seizure. By identifying patients at higher risk of apnea, protocols may be tailored with consideration of these special populations for additional monitoring.

Goals of This Investigation

We sought to quantify the risk of apnea in children presenting with out-of-hospital seizure treated with midazolam by paramedics and to identify other risk factors associated with apnea in this population.

MATERIALS AND METHODS

Study Design and Setting

We conducted a multicenter retrospective chart review of pediatric patients with seizure who were transported by paramedics to the pediatric emergency department (ED) at Harbor-UCLA Medical Center and Los Angeles County/University of Southern California Medical Center during a 2-year period, from January 2010 to December 2011. The study was approved with waiver of informed consent by the institutional review board at both institutions. Harbor-UCLA Medical Center and Los Angeles County/University of Southern California Medical Center are public teaching facilities serving Los Angeles County, with an approximate population of 10 million. Both hospitals are designated pediatric referral centers, as well as pediatric trauma centers, with an annual pediatric ED patient volume of 21,000 and 25,000 at Harbor-UCLA Medical Center and Los Angeles County/University of Southern California Medical Center, respectively. In Los Angeles County, paramedic crews consist of 2 paramedic-level emergency medical technicians (paramedics) stationed at local fire departments. Protocols in Los Angeles County support administration of midazolam by paramedics for seizure termination in any patient actively seizing. The dose may be repeated as needed with online medical control guidance until the seizure terminates. Pediatric patients are defined as aged 14 years or younger, and Los Angeles County pediatric treatment protocols are specific to this age group. Pediatric airway management in the field consists of bag-mask ventilation for children younger than 12 years or less than 40 kg. Intubation is available by protocol for children aged 12 years and older or greater than 40 kg. The average time from dispatch to hospital arrival for pediatric patients transported by paramedics in Los Angeles County is approximately 20 minutes.[16]

Selection of Participants

Inclusion criteria were patients younger than 15 years and transported by paramedics to the pediatric ED with the diagnosis of seizure. Patients with an initial chief complaint of seizure, but who were found to have another diagnosis on pediatric ED evaluation or whose primary complaint was traumatic injury, were excluded. At Harbor-UCLA Medical Center, patients were identified by chief complaint from the base-hospital log of all paramedic transports to the ED. Out-of-hospital care coordinators record all patient transports in a county-sponsored database. At Los Angeles County/University of Southern California Medical Center, an electronic medical record of pediatric ED patients is available. Patients with a chief complaint of seizure or a related discharge diagnosis were identified from an electronic record of all patients treated in the pediatric ED during the study period and screened for those patients transported by paramedics for out-of-hospital seizure. The following diagnoses were included in the search criteria: nonconvulsive epilepsy *International Classification of Diseases, Ninth Revision* (*ICD-9*) 345.00; epilepsy, convulsion, generalized *ICD-9* 345.1; epilepsy, petit mal status *ICD-9* 345.2; epilepsy, grand mal status *ICD-9* 345.3; seizure, grand mal *ICD-9* 345.3; epilepsy, without impairment of consciousness *ICD-9* 345.5; epilepsy (unspecified) *ICD-9* 345.9; epileptic convulsion (unspecified) *ICD-9* 345.9; epileptic seizure (unspecified) *ICD-9* 345.9; febrile convulsion *ICD-9* 780.31; febrile seizure *ICD-9* 780.31; seizure, febrile *ICD-9* 780.31; complex febrile convulsion *ICD-9* 780.32; and other convulsions (seizure not otherwise specified) *ICD-9* 780.39.[17] An initial chief complaint of seizure identified by out-of-hospital personnel and a pediatric ED diagnosis of seizure were required to meet inclusion in the study; therefore, the final patient selection at each institution was similar.

Methods of Measurement

Charts were reviewed by 2 investigators at each institution; at Harbor-UCLA, a nurse practitioner in the division of pediatric emergency medicine and an EMS fellow board-certified in emergency medicine, and at Los Angeles County/University of