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PREHOSPITAL GLUCOSE TESTING FOR CHILDREN WITH SEIZURES: A PROPOSED CHANGE IN MANAGEMENT

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ABSTRACT

Objective: Many Emergency Medicine Services (EMS) protocols require point-of-care blood glucose testing (BGT) for any pediatric patient who presents with seizure or altered level of consciousness. Few data describe the diagnostic yield of BGT when performed on all pediatric seizures regardless of presenting mental status. We analyzed a large single center dataset of pediatric patients presenting with prehospital seizures to determine the prevalence of hypoglycemic seizures and the utility of repeat BGT in the emergency department (ED). **Methods:** This was a retrospective, IRB-approved chart analysis of all pediatric patients (≤ 14 years) transported by EMS to the Harbor-UCLA pediatric ED over a 2-year period with a chief complaint of seizure. Cases were selected in which witnessed seizures had occurred in the field by family or EMS. Chart review included prehospital, nursing and physician records. Hypoglycemia was defined as blood glucose < 60 mg/dL. Analysis included blood glucose, witnessed field seizure, initial mental status assessed by Glasgow Coma Scale (GCS), and further mental status assessments, along with age, sex, and medical history. Medical records were reviewed for subsequent BGT and patient outcome. **Results:** A total 770 children were transported by EMS due to seizures. Four patients (0.5%) had recorded hypoglycemia in the field, yet only two received treatment to raise blood glucose. Additionally, one child (0.1%) was normoglycemic (81 mg/dL) in the field with hypoglycemia (43 mg/dL) in the ED but required no intervention. Two

were found by EMS to have an ALOC (GCS ≤ 12) and hypoglycemia. Only the patient with hypoglycemia secondary to a suspected glipizide ingestion received ED glucose administration. The most common discharge diagnosis was simple febrile seizure (38.6%). **Conclusion:** Hypoglycemia in the pediatric seizure patient is extremely rare, thus universal field BGT has low utility and potential downstream effects. We propose a novel algorithm for the initial evaluation and management of prehospital pediatric seizures. Although limited to a retrospective analysis of a single medical center, our findings suggest the importance of reassessing prehospital seizure protocols. A larger patient sample should be studied to validate these findings and identify unique cases where glucose testing might be useful. **Key words:** prehospital; glucose; seizure; assessment; pediatric

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INTRODUCTION

In the United States (U.S.), seizure is one of the most common chief complaints resulting in pediatric emergency medical services (EMS) transports.^{1,2} Hypoglycemia is a quickly identifiable and treatable cause of seizure, reflected in the recent GRADE-based Pediatric Seizure Management Guidelines which recommends “systematically screening all seizing children for hypoglycemia” prior to benzodiazepines.³ As such, blood glucose testing (BGT) is almost universally present in prehospital pediatric seizure protocols.^{4,5}

Prior research has questioned the utility of employing ubiquitous and often routine blood glucose testing for all pediatric seizure patients given the rarity of hypoglycemic causes.^{6–8} Vilke et al.⁶ studied 6,018 children who received glucose monitoring by EMS and only 50 patients (0.8%) with seizures required treatment for hypoglycemia. Similarly, Babl et al.⁷ found that only 1.6% of all prehospital pediatric patients required glucose treatment, and many of these treatments were empiric. Routine BGT is also not benign. Children experience pain induced by the healthcare provider and false negative low glucose values often require repeat emergency department (ED) lab testing for confirmation, causing an increased length of stay.^{9,10} To our knowledge, there are few studies that investigate BGT, subsequent ED glucose testing, and patient outcome.

We hypothesized that hypoglycemia is an uncommon cause of seizure in the prehospital setting and that repeated testing of a blood glucose level in the ED is not useful in a patient who has returned to baseline

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mental status. This retrospective study aims to develop a novel, evidenced-based algorithm for seizures that can be used by prehospital providers.

METHODS

A retrospective chart review identified all consecutive pediatric patients (age ≤ 14 years) with the prehospital complaint of seizure who presented to Harbor-UCLA Medical Center in Torrance, California between January 2010 and January 2011. The institutional review board (IRB) at Harbor-UCLA provided approval with waiver of informed consent. Harbor-UCLA Medical Center is a 553-bed general municipal teaching hospital in southwestern Los Angeles (LA) County and is a Pediatric Medical Center (pediatric critical care center).

The single data abstractor (DO), who was trained in assessing prehospital records, was aware of the intent to assess the usefulness of performing a prehospital BGT in all pediatric seizure patients per current Los Angeles County EMS protocol.³ Prehospital management of seizures in children included BGT and administration of midazolam at a dose of 0.1 mg/kg intravenously, intramuscularly, or intranasally. Using a standardized data collection form, the abstractor recorded age, sex, past medical history, Glasgow Coma Scale (GCS)/mental status in the field, glucose in the field, seizing in the field, seizure duration, transport time, GCS/mental status on arrival, glucose on arrival, seizure status on arrival, disposition, and final diagnosis by ED, if discharged, or by inpatient records for admitted patients. All equivocal cases were reviewed by a second investigator (MGH).

Statistical Analysis

Upon completion of patient data entry, the database of seizure patients was converted into native SAS prior to data analysis, using DBMS/Copy, Version 8 (DataFlux Corporation, Carey, NC). Statistical analysis was performed using SAS Version 9.3 (SAS Institute, Carey, NC). Continuous numerical variables were summarized using medians and interquartile ranges (IQRs). Categorical variables, such as gender, whether they were seizing in the field or on arrival, disposition from the ED, past medical history, and final diagnosis are described as proportions. We used the non-parametric Wilcoxon Rank-Sum test to evaluate whether there was any association between field glucose values and seizure upon EMS arrival. Similarly, we used the Wilcoxon test to evaluate whether there was an association between ED glucose values and seizures in the ED. Finally, to assess the relationship between the glucose value in the field and on ED arrival, we compared these values only for those patients ($n =$

232) who had both, using a nonparametric paired test for comparison of medians.

RESULTS

Table 1 outlines the overall results of this study. Of the 770 pediatric seizure patients, 521 (67%) had a glucose recorded on chart review. Four-hundred and sixteen of the patients were male, and upon EMS arrival (of those with documentation), 84 (14%) were actively seizing. When comparing the field glucose among those who were seizing in the field to those who were not, there were no statistically significant nor clinically relevant differences: of those who were seizing, the glucose in the field was a median of 125 (IQR 106–156) vs. 122 (IQR 103–150) for those who were not seizing (Wilcoxon $p = 0.6$). Twelve percent ($n = 86$) of the patients were actively seizing at the time of arrival in the ED. When comparing the ED glucose among those who were seizing in the ED to those who were not, the glucose value was actually higher among those who were seizing in whom the ED glucose was a median of 139 (IQR 104–182) vs. 107 (IQR 96–128) for those who were not seizing (Wilcoxon $p < 0.0001$).

A total of 4 (0.5% overall) patients were found to be hypoglycemic in the field. One of the children reported to be normoglycemic in the field was found upon ED arrival to have a glucose value of 43 mg/dL by venipuncture. However, this patient did not require glucose administration in the ED.

The blood glucose level in the field as compared to the ED was not significantly different. Field blood glucose level demonstrated a median of 123 mg/dL (IQR 103–151), whereas in the ED, the measured blood glucose level on arrival was a median of 111 mg/dL (IQR 97–141). Paired test for difference in blood glucose levels from field to that of the ED showed a median difference of 5mg/dL (IQR 13–28), ($P = 0.1$).

Almost 80% of patients were discharged home and 18% were admitted. The most common diagnosis was seizure related (78%), with simple and complex febrile seizures representing the final diagnosis in 47% of the patients.

Specific Cases

The following are descriptions of the four cases of hypoglycemia in the field.

1. A 2 year-old girl presented with a blood glucose level of 59 mg/dL in the field and a GCS of 14 (Eyes-3, Verbal-5, Motor-6) after a witnessed tonic clonic seizure. Upon arrival to the ED, the patient's GCS improved to 15, she was found to be febrile and had a repeat venous blood glucose level of 149 mg/dL along with a normal

TABLE 1. Descriptive statistics of the 770 pediatric seizure patients transported by EMS.

Documented Seizing on arrival	86 (12.0%)
Seizing in the field	84 (13.9%)
Male gender	415 (54.0%)
Age (years)	Mean = 3.2 Median = 2 (IQR 1–4)
Field glucose tested	Mean = 128.7
N = 521/770 (67.7%)	Median = 123 (IQR 103–151)
Field hypoglycemia (< 60 mg/dL)	N = 4 (0.8%)* GCS was 8, 12, and 15, and one child did not have a GCS in the field that had hypoglycemia.
N = 521	*0.5% of all patients
Arrival glucose (mg/dL)	Mean = 124.3
N = 303	Median = 111 (IQR 97–141)
ED hypoglycemia (mg/dL)	N = 1 (0.3%)
N = 303	There was only one child who had hypoglycemia in the ED (BS = 43), and his/her glucose was 81 in the field. Their transient lethargy and was not treated with glucose in the ED.
Transport time (min)	Mean = 11.3
N = 462	Median = 11 (IQR 7–14)
GCS field	Mean = 12.2
N = 589	Median = 14 (IQR 10–15)
GCS Arrival	Mean = 14.1
N = 606	Median = 15 (IQR 15–15)
Seizure duration (min)	Mean = 5.1
N = 667	Median = 2.5 (IQR 1–5)
Disposition	Discharged = 575 (79.9%)
N = 720*	Admitted = 130 (18.0%)
* 50 dispositions unknown	Transferred = 12 (1.7%) AMA = 3 (0.4%)
Past medical history	None = 282 (42.3%)
N = 667	Febrile seizure history = 153 (22.9%) Seizure disorder = 119 (17.8%) Non seizure diagnoses: Prematurity = 13 (1.9%) Hydrocephalus = 7 (1.0%) Asthma = 6 (0.8%) Autism = 6 (0.8%) Developmental delay = 7 (1.0%) Other = 74 (11.1%) – includes Angelman syndrome, attention deficit hyperactivity disorder, cerebral palsy, fetal alcohol syndrome, gastroschisis, lupus erythematosus, chromosomal abnormalities, hemophilia, histiocytosis, hyperbilirubinemia, meningitis, oligohydramnios, osteosarcoma, Panayiotopoulos syndrome, stroke
Final diagnosis	Simple febrile seizure = 260 (38.6%)
N = 673	Complex febrile seizure = 58 (8.6%) Seizure disorder = 163 (24.2%) Status epilepticus = 41 (6.1%) Other = 151 (22.4%) includes, pneumonia, Apparent Life Threatening Event (ALTE), acute otitis media, autism, syncope, pyelonephritis, pneumonia, diarrhea, subdural or subarachnoid, URI, osteosarcoma, meningitis, head contusion

metabolic panel. The patient was diagnosed with a febrile seizure and admitted for observation due to the episode of hypoglycemia. Subsequently, there were no changes in mental status, and the patient was discharged the following day without need for any glucose administration.

2. A 6 year-old girl presented after a witnessed generalized tonic-clonic seizure lasting for an unknown duration. The prehospital blood glucose level was 38 mg/dL with a documented field GCS of 15. Glucagon 1mg IM was administered. On arrival in the ED, the patient was crying, moving all extremities and pulling on all cardiac leads. No arrival GCS was documented, but per the ED chart, the patient appeared fussy. Her medical history was significant for one previous febrile seizure. In the ED, the patient was febrile and had a normal metabolic panel and venous glucose level 172 mg/dL. She was admitted for observation and had no further hypoglycemic episodes or seizure activity.
3. A 5 year-old girl with a known seizure disorder was transported to the ED after caregivers administered rectal Diazepam for a generalized tonic-clonic seizure lasting approximately 5 min. The prehospital blood glucose level was 50mg/dL with a GCS-8 (Eyes-2, Verbal-2, Motor-4). Enroute to the ED, the patient was given 20 mL of D50W, and a subsequent glucose level in the ED was 259 mg/dL. No GCS was recorded on ED arrival. Her past medical history was significant for severe global developmental delay.

No recurrent seizures or metabolic abnormalities were found and she was discharged from the ED with a diagnosis of recurrent seizure with an underlying seizure disorder. No further glucose was administered.

4. A 6 year-old girl was brought to the ED after a reported tonic-clonic seizure, lasting a few seconds, at home. Paramedics measured a blood glucose level of 20 mg/dL and administered 20 mL of D50W. An initial GCS was not recorded in the field. In the ED, the patient had a GCS of 15 with a venous glucose of 242 mg/dL. Further history elicited concern that the child may have ingested glipizide tablets from the grandfather who was caring for the child at the time of seizure. The patient was initially placed on maintenance fluids with glucose, then advanced to a normal diet, and had no subsequent decline in BGL after a one-day admission.

DISCUSSION

This retrospective analysis of 770 pediatric seizure patients transported by EMS is consistent with prior rates of hypoglycemia associated with seizures in adult patients.¹¹ Prehospital blood glucose levels of <60 mg/dl were recorded in four (0.8%) of the 521 patients who underwent testing or in four of 770 patients (0.5%) overall. While some sources recommend that hypoglycemia be defined as a blood glucose <45 mg/dl, we chose <60 mg/dl to increase our sensitivity for seizures that might have resulted from low values. Even with this increased threshold, we still found hypoglycemia to be extremely rare.

Our data do not support routine BGT of all children with a chief complaint of seizure who demonstrate normal mental status, or baseline mental status, as confirmed by parents and assessed by paramedics in the field. Of the 67.7% of cases where prehospital glucose measurement was performed, only four patients had values less than 60 mg/dL and two received intervention (glucagon or dextrose infusion). Although this was not an interventional trial, one would theoretically need to obtain a blood glucose level on 200 children for every one abnormal glucose value and would have to obtain a blood glucose level on 1000 children for every one abnormal glucose value that requires ongoing treatment.

In this study we also identified one other patient (1 year-old) with a prehospital GCS of 15 and normoglycemia in the field (81 mg/dl) who had a change in mental status to "lethargic" associated with hypoglycemia (43 mg/dl) in the ED. This child ultimately had no documented cause for her isolated episode of hypoglycemia and recovered quickly without any intervention.

Since the natural course of hypoglycemia is persistent altered mental status if not corrected, patients with hypoglycemia-induced seizures are unlikely to return to baseline mental status without an intervention to raise the blood glucose. We found no significant difference between prehospital glucose (mean 128.7 mg/dl) and ED glucose (mean 123.4 mg/dl) in the 232 children that had both of these tests performed. It is therefore reasonable to assume precise measurement of the patient's glucose if checked by EMS. Therefore, a repeat blood glucose measurement is not necessary if the patient has a normal mental status upon presentation in the ED and is euglycemic in the field.

The most common cause of seizures, based on discharge diagnosis, was simple or complex febrile seizure, accounting for nearly half of all seizures (47.2%). This is similar to the data obtained by Vilke et al.⁶ (52%) and Krumholz et al.¹² (48%) in their prehospital pediatric seizure analysis.

The key element to prehospital seizure management is to reduce field seizure times and limit status epileptics, a significant cause of morbidity and mortality that accounts for up to 55,000 U.S. deaths each year.¹³⁻¹⁵ While looking at pediatric and adult EMS seizure calls, Beskind et al.,¹¹ found that prioritizing blood glucose testing *before* giving antiepileptic medications caused a delay to benzodiazepine administration of between 2 to 6 minutes. Eriksson et al.¹⁶, showed that treatment delays of more than 30 minutes in children with seizures lasting longer than 5 minutes were associated with delays in seizure control. Additionally, standard anticonvulsant therapies are more effective at treating seizures of shorter duration.^{17,18} Given the low prevalence of hypoglycemia in our study, delaying anticonvulsant therapy for BGT could have serious consequences including prolonged seizure activity and difficulty achieving seizure control.

Therefore, we created a novel algorithm for the prehospital management of the seizure patient with the approach separated into three categories: those actively seizing, those with GCS measurements <15 or not at baseline per their caregiver, and those at baseline (Figure 1). While incorporating many of the GRADE-based and RAMPART-derived seizure recommendations, our approach focuses on early administration of benzodiazepines, then obtaining a blood glucose level in patients with continued seizure or in those with altered mental status, while avoiding measurements in patients with baseline mental status.^{3,15} Of note that patients who were seizing in the ED tended to have higher blood glucoses, likely as a result of a stress reaction. Thus, it appears that hypoglycemia is a rare cause of seizures in children, and prehospital pediatric patients with status epileptics are statistically more likely to require benzodiazepines rather than glucose to stop seizures.

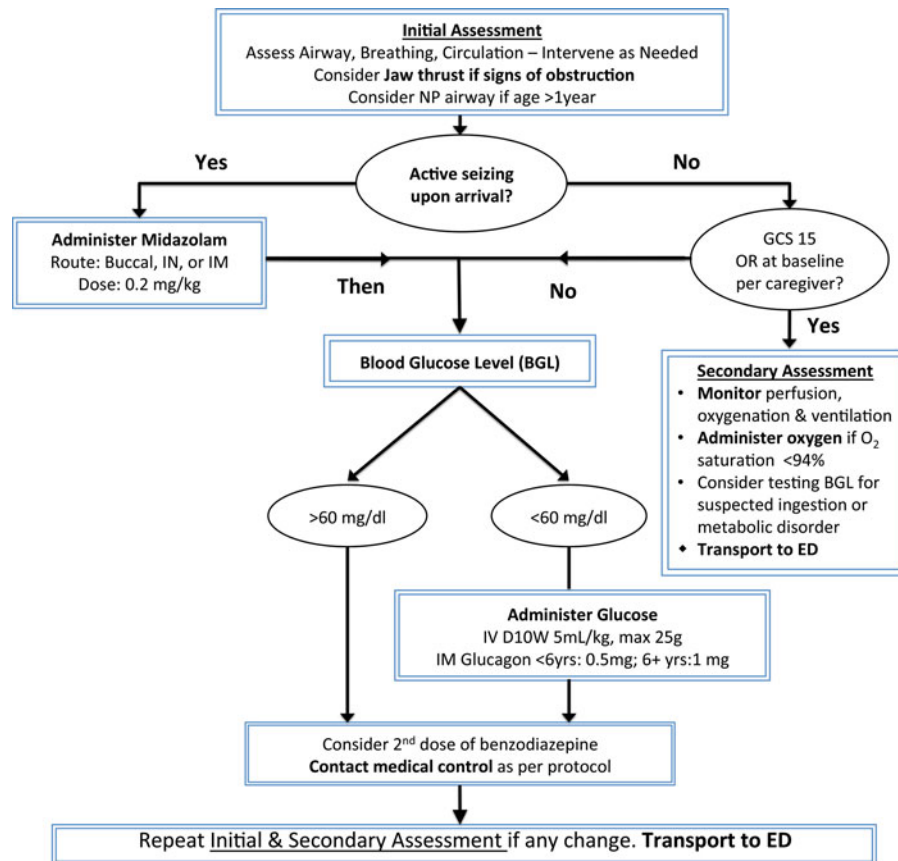


FIGURE 1. Algorithm for prehospital pediatric seizure management. NP: nasopharyngeal. IN: intranasal. IM: intramuscular. IV: intravenous. GCS: Glasgow Coma Scale. PED: Pediatric Emergency Department. BGT: Blood Glucose Testing

While this simplified approach has not been directly studied, it may be possible to decrease time to benzodiazepine administration in the actively seizing patient as well as reduce unnecessary testing.

LIMITATIONS

Field blood glucose was only measured in 521 (67.7%) of our entire cohort. EMS providers may not have checked a glucose level after obtaining a history inconsistent with hypoglycemia-induced seizures or in a patient with normal mental status, and this represents a potential selection bias.

There is also the possibility for misclassification bias, as the study is retrospective and based upon linking a prehospital to an ED database. Only patients categorized as “seizure” by EMS providers were included in this study. It is possible that EMS providers did not classify children with “seizure” who were back-to-baseline or presented with an atypical seizure. Only one investigator abstracted the data which could lead to classification error. However all equivocal cases were reviewed by a second investigator. Also, we only had four patients with hypoglycemia in our patient population, and with such a low frequency event, it is difficult to draw any conclusions about who might ac-

tually benefit from BGT and those who do not. There is a possibility that we could be missing a population (i.e., those with known metabolic disorders or possible ingestions) who should receive glucose testing.

CONCLUSIONS

In this large, single-center retrospective analysis of children presenting with seizures in the field, hypoglycemia was an extremely rare finding in the prehospital or ED setting. Our data suggest that routine prehospital and ED testing of blood glucose levels in this population was of low utility and had minimal clinical significance. We suggest that BGT should instead be performed on the actively seizing patient after the first dose of benzodiazepines, or in the child with persistent altered mental status.

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