Seizure 52 (2017) 188–194

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Rescue Medications in Epilepsy Patients: A Family Perspective

Marina Gaínza-Lein[a,b], Robert Benjamin[a,c], Coral Stredny[a], Marlee McGurl[a], Kush Kapur[a], Tobias Loddenkemper[a,*]

[a] Division of Epilepsy and Clinical Neurophysiology, Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA, United States
[b] Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile
[c] Assumption College, Worcester, MA, United States

ARTICLE INFO

Article history:
Received 18 May 2017
Received in revised form 29 August 2017
Accepted 10 October 2017
Available online xxx

Keywords:
Epilepsy
Rescue Medication
Family
Prehospital treatment
Seizure clusters

ABSTRACT

Purpose: The aim of this study was to analyze pre-hospital seizure rescue medication (RM) use in a pediatric epilepsy population, caregiver knowledge and comfort, and prescription patterns.
Method: Cross-sectional observational study based on surveys to families of pediatric patients with epilepsy and based on medical chart review.
Results: One hundred (92.6%) out of 114 families answered the questionnaire. Fifty-five patients were females (55%), with a median (IQR) age of 11 (6-14) years. Eighty-seven (87%) patients had RM prescribed, and 37 (42.5%) used it in the past. In univariate analysis, patients were more likely to have a RM when they had a history of SE ($p < 0.001$), or had seizures $\geq$30 seconds ($p = 0.001$).Patients were not more likely to be prescribed a RM if they were diagnosed at <2 years of age, had $\geq$3 anti-seizure medications (ASM), had a history of seizure clusters or uncontrolled epilepsy, or were currently not on ASMs.In multivariate analysis a history of SE ($p = 0.02$) and seizure duration $\geq$30 seconds ($p = 0.04$) remained significant.
Out of 91 families, 68 (74.7%) prefer a non-rectal RM; this was higher for patients with normal development, and not associated with age or sex. Fifty-three (61%) families reported that they received RM training. Ten (10.1%) parents did not know the RM name, and 31 (35.6%) did not know the administration timing. Forty-five (45%) families had a seizure action plan (SAP), and this was a predictor for knowing the RM name ($p = 0.04$), the administration timing ($p = 0.004$), availability of RM at school ($p = 0.02$), and knowing what to do if the RM fails ($p = 0.008$).
Conclusions: Most patients with epilepsy had a RM, but only 61% reported receiving training. Patients were more likely to have a RM if they had prior SE and longer seizure duration. Families with a SAP were more knowledgeable, and schools were more involved.

1. Introduction

The estimated prevalence of epilepsy in US children is around 1% [1], and 22.5% of these patients are refractory to medications [2]. Status epilepticus (SE), most often defined as a seizure lasting longer than 5 minutes [3], has an incidence of 6.8–41/100.000 per year in adults and children [4], with an higher incidence in infants (135–156/100 000/year) [4–6]. SE has a mortality of 0-3% [5,7,8], and survivors often incur developmental impairments, epilepsy, and recurrent status epilepticus [9,10]. Seizures that last longer than 5 minutes are unlikely to stop spontaneously [11], and prolonged seizures often become progressively more resistant to treatment [12,13]. Therefore protocols recommend the administration of a rescue medication, consistent of a benzodiazepine (BZD), ideally between 5–10 minutes from seizure onset [14,15].

A study showed that the first-line treatment is often delayed in the pre-hospital and in-hospital settings. Only 37.5% of patients received anti-seizure medications (ASM) in the pre-hospital setting [16], and a low number of patients received a rescue medication from their families, even with prior epilepsy or SE diagnosis [16]. Also, a study showed that patients who received a delayed first BZD (> 10 minutes) had a higher risk of dying and a higher risk of receiving third-line medications to treat seizures [17]. Reasons for delayed treatment of prolonged seizures are unclear, especially in the pre-hospital setting. To address this gap in knowledge, we performed a patient family survey to evaluate

* Corresponding author at: Harvard Medical School, Division of Epilepsy and Clinical Neurophysiology, Fegan 9, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States.
E-mail addresses: m.gainzalein@gmail.com (M. Gaínza-Lein), robert.benjamin@assumption.edu (R. Benjamin), coral.stredny@childrens.harvard.edu (C. Stredny), marlee.mcgurl@gmail.com (M. McGurl), kush.kapur@childrens.harvard.edu (K. Kapur), tobias.loddenkemper@childrens.harvard.edu (T. Loddenkemper).

https://doi.org/10.1016/j.seizure.2017.10.007
1059-1311/

the use of rescue medications in pediatric patients with epilepsy, parental knowledge, and prescription patterns.

2. Methods

2.1. Study design

This was a cross sectional observational study. We created a questionnaire detailing the use of rescue medications, which was reviewed by pediatric neurologists, residents and our research team (E-Supplement). We surveyed families in the outpatient setting. All patients arrived with their primary caregiver. If both parents were present both were encouraged to answer the survey jointly. We entered the results into an electronic data capture tool (RedCap), and complemented the data by clinical interviews and chart review. The prescription of rescue medications was done by the primary care providers (21 clinicians: 13 pediatric epileptologists, 5 pediatric epilepsy fellows, 3 nurse practitioners) and it was based on their clinical expertise. We aimed to enroll 100 families. Patients. Boston Children's Hospital institutional review board approved the research protocol, and all participants, parents or guardians gave written informed consent.

Inclusion criteria consisted of: (1) children aged 0-21 years of age, (2) epilepsy diagnosis; (3) a scheduled outpatient epilepsy visit at Boston Children's Hospital, (4) English or Spanish speaker. Exclusion criteria were: (1) psychogenic non-epileptic seizures; (2) infantile spasms; and (3) electrical status epilepticus in sleep.

2.2. Variables

The primary outcome was the prescription of rescue medication in patients with epilepsy. The secondary outcome was the parental level of knowledge about rescue medications. We also looked at other tertiary outcomes: training, availability of an individualized seizure action plan (a plan that guides families, caregivers and schools in case of a seizure, it provides information regarding rescue medication administration, timing, and rescue measures), medication route preferences, medical history, number of ASM, parental report of school involvement, doses, and cost limitation. The training was done during regular clinical practice, and it was evaluated retrospectively.

We compared the recommended weight based dose to the medication doses of the most recent prescription. For rectal diazepam, we used 0.5 mg/kg for age 2–5 years, 0.3 mg/kg for age 6–11 years and 0.2 mg/kg for age 12 years or older, [18] which were rounded to 5, 10, 15 and 20 mg, with a 20 mg maximum, as these are the doses commonly available.[19] For nasal midazolam, we used 0.2 mg/kg with a 10 mg maximum [20,21], and 0.05 mg/kg for oral lorazepam, with 4 mg maximum [22], and we rounded the dose to the closest unit (ie. 2 mg, 4 mg) to calculate if the dose was low, appropriate, or high.

2.3. Statistical analysis

We used descriptive statistics to summarize demographic and clinical characteristics. The evaluation of most variables did not fit a normal distribution; therefore we utilized non-parametric analyses. We expressed continuous variables as median and inter-quartile range (IQR). We analyzed binary outcome variables with Fisher exact test. To determine predictors for receiving a rescue medication we first performed univariate analysis with Fisher's exact test. We created a model with the variables: seizure duration >30 sec (median seizure duration time), history of SE, history of seizure cluster, epilepsy diagnosis < 2 years of age (as rescue medications <2 years are not FDA approved), uncontrolled epilepsy, currently on ASM and 3 or more ASMs. To build the multivariate model we selected the variables with a p-value <0.1. As some bins had zero counts, we performed an exact logistic regression analysis. To evaluate the association of non-rectal route medication application preference to developmental status, age and sex we used logistic regression. We set the two-sided alpha value at 0.05. All statistical analyses were performed with STATA 13 (Stata Corp., College Station, TX).

3. Results

3.1. Patients

We approached 114 families of patients with epilepsy. Five (4.4%) met exclusion criteria, 9 (7.9%) families elected not to fill out the survey due to time constraint, and 100 (92.6%) families participated. Demographics and clinical features are summarized in Table 1.

3.2. Rescue Medications

Out of 100 patients with epilepsy, 87 had seizure rescue medications prescribed (Fig. 1). The prescription range was 90% in children age 0-7 years, 86% in 7-14 years, and 83% in 14-21 years. Thirty-seven (42.5%) patients with a prescribed rescue medication had used it in the past and the median (p25-p75) amount of times they used the rescue medication was 4 (2-8). Twelve (32.4%) parents reported the recue medication was always successful stopping the seizures, 16 (43.2%) said it was successful more than 50% of the time, 4 (10.8%) less than 50% of the time, and 3 (8.1%) said it was never successful. Out of these patients, 24 (64.8%) used it for prolonged seizures (≥ 5 minutes) and 12 (32.4%) for seizure clusters. Families who used the rescue medication for seizure clusters, administered it after a median (p25-p75) of 4 (3-5) seizures.

3.3. Predictors for rescue medications

In univariate analyses, patients were more likely to have a rescue medication prescribed if seizures were on average longer

Table 1
Demographic and clinical characteristics.

Characteristics (N = 100)	N (%)
Females	55 (55%)
Age (years) (mean (SD))	10.7 (5.28)
Race	
White	81 (81%)
Black or African American	2 (2%)
Arabic	1 (1%)
Asian	3 (3%)
Native American/Alaskan Native	0 (0%)
Native Hawaiian/Other Pacific Islander	0 (0%)
Not reported	6 (6%)
Unknown	7 (7%)
Developmental delay	55 (55%)
Ethnicity	
Not Hispanic or Latino	83 (83%)
Hispanic or Latino	11 (11%)
Not reported	5 (5%)
Unknown	1 (1%)
Etiology	
Structural	17 (17%)
Genetic	22 (22%)
Unknown or presumed genetic	60 (60%)
Autoimmune	1 (1%)
Metabolic	0 (0%)

Legend: Race and ethnicity was obtained from the family's demographic information form within the electronic medical record. Some patients prefer to not report their race, and some report it as 'unknown' or not represented with those categories.