Childhood Status Epilepticus Associated Short-Term Mortality in Kano Nigeria

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Abstract

Objective: Determine the childhood status epilepticus (SE) – associated short-term mortality in Kano, Nigeria

Methods:1408 Children with SE, ages 30 days to < 15 years, managed using a standardized protocol with point-of-care EEG-video, were enrolled into a cohort upon arrival to emergency units in Kano, Nigeria with prospective recording of SE and clinical data into a REDCap database. Age-specific mortality rates, and odds ratios for clinical predictors of short-term SE associated mortality were determined. Hypoglycemia was defined as RBS of < 2.2 mmol/l or < 3.0 mmol/l in severely malnourished children. Benzodiazepine resistant (BR) SE was defined as persistence of SE after 2 weight-appropriate doses of a benzodiazepine.

Results: Death within one month of hospital discharge, or short-term mortality was 21% (300 of 1408); 267 of 1408 (19%) died prior to hospital discharge. Short-term mortality was higher among females (24%) than males (19%). Mortality was higher among the infants (1-11 months; 43%), and children ≤ 5 years (20%), and was lowest among children ages 6-9 years (11%). Age less than 1 year, hypoglycemia (OR = 7.15; 95% CI = 4.18, 12,22), SE duration > 30 minutes (OR = 1.35; 95% CI = 1.05, 1.75) and BR SE (OR – 2.75; 95% CI = 1.48, 5.12) were significantly associated with higher risk of death.

Conclusion: SE-associated mortality is high in northern Nigeria, even with a standardized diagnostic and treatment protocol, point-of-care EEG-video, and trained SE treatment teams. Infancy, hypoglycemia, BR and prolonged SE are all associated with higher SE-associated mortality.

Materials and Methods

Childhood Status Epilepticus & Epilepsy Determinants of Outcome (SEED)

- Deep phenotype of 1551 children with SE
  - point-of-care EEG-video
  - Detailed clinical assessments
    - MRI, EEG-video
- Clinical predictors of outcome
  - Mortality & morbidity
  - Epilepsy among those who survive SE as 1st seizure
    - Potential model of epileptogenesis for future studies
  - Benzodiazepine-resistant ("Established") SE
- Genomic predictors of outcome (GWAS)
  - H3Africa Controls

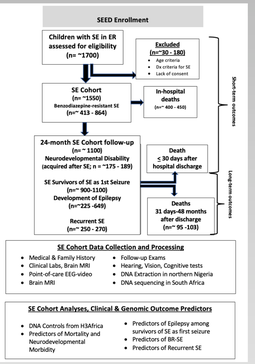

Fig. 1. SEED Overview

SEED Enrollment and Data Flow in Emergency Paediatric Units (EPU)

- **Waiver of Consent** if Child with SE dies within four (4) hours of Registration
- **SEED Staff in EPU 24/7**
  - SEED EEG tech, 2 EEG-video systems
  - SEED Nurse
- **EPU Staff with SEED training**
  - Nurses/Nurse Matron
  - Physicians
- **EEG-video performed upon EPU arrival**
- **REDCap®-based Data Systems**
  - Android tablets – direct upload
  - Data Management, AKTH, Kano
  - Data Coordinating Ctr, Vanderbilt
- **Blood specimens for DNA**
  - Obtained soon after enrollment
  - Blood specimens digitally tracked
  - Storage @-80°C and DNA extraction at Bayero U Kano
  - DNA analysis & GWAS, Wits + Vanderbilt

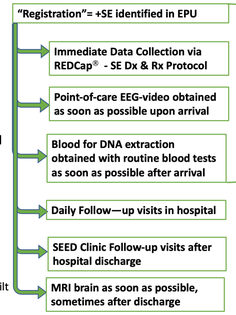

Fig. 2. SEED EPU Data Flow

Paediatric Status Epilepticus (SE) Protocol#
(*Point-of-Care EEG-Video as part of SE Protocol)

Time Line	Intervention
0-5 min Stabilization*	❖ Stabilize patient (airway, breathing, circulation, exam) ❖ Oxygen, Finger stick glucose – Rx hypoglycemia ❖ Prepare Benzodiazepine for administration
	*Continued seizures → No seizures
1-20 min Phase One Rx	❖ Midazolam IM or IV (repeat dose once if continued seizures) ❖ IF Midazolam IM and IV not available, Diazepam or Lorazepam
	*Continued seizures → No seizures
20-40 min Phase Two Rx	**Choose one of the following second treatment choices** ❖ IV phenobarbitone, phenytoin, valproic acid, or levetiracetam
	*Continued seizures → No seizures
40-60 min Phase Three Rx^	**Choose a third treatment choice – consult neurology or ICU team** ❖ If phenobarbitone given in Second Phase, may give an additional 10-15 mg/kg of phenobarbitone IV, and/or ❖ Administer a second phase treatment from above not previously used in this patient, and/or ❖ Paraldehyde IM 0.2-0.35 mL per kg, or 1 ml per year of life, max dose 10 mL

#Modified from Glauser, et.al. *Epilepsy Currents* 2016;16(1):48-61

Fig. 3. SEED Status Epilepticus Protocol

SEED enrolled 1551 children with status epilepticus (SE) who presented to one of four participating pediatric emergency units (EPUs) in Kano northern Nigeria. An overview of the SEED Study is shown in figure 1. SEED SE teams composed of EEG technologists and nurses were available 24 hours per day, 7 days per week in the four EPUs, and identified children upon arrival to the EPU , and coordinated emergency care and implementation of the SEED SE protocol with the EPU nurses and physicians, all of whom received training in the SEED protocol. Clinical assessments and EEG-video studies were performed upon arrival, or as soon as possible after arrival to the EPU. All clinical data, study data, laboratory data, and outcomes were directly recorded into standardized case report forms (CRFs) at the bedside by full-time SEED trained study nurses, with data directly uploaded to the SEED data coordinating center. During the enrollment period EEG-video was performed on all children with SE or suspected SE, with EEG used in clinical care decisions. All children with SE in the participating EPUs also received the standardized treatment protocol. Consent was obtained in over 98% of eligible study subjects for enrollment into the SEED cohort study. Consent was waived, with approval from the Ethics Committee, for children who died within 4 hours of arrival to the EPU and parents were not available for consent.

The SEED cohort is followed daily in hospital prior to discharge, and then is followed in a specialized SEED clinic following discharge to obtain long-term outcome data.

Results

At the time of abstract submission 1408 children were enrolled in the BRIDGE study; 267 of 1408 children with SE died prior to hospital discharge (19%), and 300 of 1408 children with SE (21%) died within 30 days of discharge.

- **SE-associated short-term mortality by age**
  - 1-11 months = 43%
  - 12 months - ≤ 5 years = 20%
  - 6-9 years = 11%
- **Identifiable Risk Factors for SE-associated Short-Term Mortality (with 95% CI)**
  - Hypoglycemia, OR = 7.15 (4.18, 12.22)
  - SE > 30 minutes OR= 1.35 (1.05, 1.75)
  - BR SE OR = 2.75 (1.48, 5.12)

Conclusions

- Short-term SE associated mortality is very high in northern Nigeria
- The most significant risk factors are young age, especially age < 12 months of age, and hypoglycemia.
- Malnutrition is common among children with SE in northern Nigeria. The contribution of malnutrition to SE-associated short-term mortality is currently under study in the SEED project.
- Failure to respond to benzodiazepines (or "Established SE") is also a risk factor for mortality.
- Genomic and other clinical risk factors for short-term and long-term mortality are underway.

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