



Febrile Status Epilepticus: Time Is of the Essence

Emergency Management of Febrile Status Epilepticus: Results of the FEBSTAT Study.

Seinfeld S, Shinnar S, Sun S, Hesdorffer DC, Deng X, Shinnar RC, O'Hara K, Nordli DR Jr, Frank LM, Gallentine W, Moshé SL, Pellock JM; FEBSTAT study team. *Epilepsia* 2014;55(3):388–395.

OBJECTIVE: Treatment of seizures varies by region, with no standard emergency treatment protocol. Febrile status epilepticus (FSE) is often a child's first seizure; therefore, families are rarely educated about emergency treatment. **METHODS:** From 2002 to 2010, 199 subjects, age 1 month to 6 years, were recruited as part of a prospective, multicenter study of consequences of FSE, which was defined as a febrile seizure or series of seizures lasting >30 min. The patients' charts were reviewed. No standardized treatment protocol was implemented for this observational study. **RESULTS:** One hundred seventy-nine children received at least one antiepileptic drug (AED) to terminate FSE, and more than one AED was required in 140 patients (70%). Median time from the seizure onset to first AED by emergency medical services (EMS) or emergency department (ED) was 30 min. Mean seizure duration was 81 min for subjects given medication prior to ED and 95 min for those who did not ($p = 0.1$). Median time from the first dose of AED to end of seizure was 38 min. Initial dose of lorazepam or diazepam was suboptimal in 32 (19%) of 166 patients. Ninety-five subjects (48%) received respiratory support by EMS or ED. Median seizure duration for the respiratory support group was 83 min; for the nonrespiratory support group the duration was 58 min (p -value < 0.001). Reducing the time from seizure onset to AED initiation was significantly related to shorter seizure duration. **SIGNIFICANCE:** FSE rarely stops spontaneously, is fairly resistant to medications, and even with treatment persists for a significant period of time. The total seizure duration is composed of two separate factors, the time from seizure onset to AED initiation and the time from first AED to seizure termination. Earlier onset of treatment results in shorter total seizure duration. A standard prehospital treatment protocol should be used nationwide and education of EMS responders is necessary.

Commentary

Multiple steps and prerequisites may cause delay and variability in the recognition and treatment of febrile seizures and febrile status epilepticus. Among the challenges are identification of patients at risk of febrile convulsive status and detection of febrile seizures and febrile status epilepticus. If symptoms are noted by nonmedical personnel, including parents or caretakers, seizures and febrile status epilepticus need to ideally be recognized as such. Families either need to bring the patient to medical attention or may need access to acute treatment options and need to know how to apply treatment, and then contact medical providers to determine further work-up and care as indicated. Medical service providers, be it emergency medical services (EMS), emergency department (ED), primary care, or neurologist, may need to have febrile status rescue medications available and need to be able to give initial treatment, recognize treatment failure, and escalate treatment when initial interventions are not effective.

Seizure Detection and Recognition

While the percentage of parents who do not bring their children with febrile status epilepticus to medical attention for prolonged periods of time may be minimal, there are occasional families who elect to wait. Deterrents and distractors from medical care may vary, including limited awareness of acuity and emergency, access to emergency care, long wait times, or relatively more urgent competing family tasks among others. Mutual collaboration to provide children with better access and families in need with better education of this emergency is crucial. Cardiologists and stroke specialists have demonstrated that time to treatment in myocardial infarct patients ("Time is muscle") or stroke patients ("Time is brain") can be improved. This education may also include education regarding varying seizure symptoms and interventions. Despite best intentions and counseling though, seizure onset may occur unwitnessed. To date, there are no clear guidelines regarding the role of novel seizure detection tools, baby monitors, actigraphy sensors, movement sensors, smart clothing, or cameras and other devices detecting seizures, while some of these techniques may benefit patients at risk, allowing easier detection by parents or medical care providers (1).

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Availability and Application of Rescue Medication

Not all parents of children with a history of convulsive febrile seizures and status receive counseling and a prescription for



rescue medications, and the indication, type, and route of administration may continue to spark debates. Even if prescribed, medications may not be readily available at the time of the seizure, or families may remain hesitant to give medications. While our perception of “benign” in febrile seizures and febrile status epilepticus shifts, use of rescue medication regimens likely lags behind this perception.

Decision to Treat and Decision to Escalate Treatment

Parents, caretakers, or EMS may decide not to treat because “it is just another brief febrile seizure.” Many febrile status epilepticus episodes present with recurrent convulsive seizures, and not continuous convulsive movements, thereby making it very difficult for bystanders to determine whether a seizure cluster ended, or whether the patient is in-between two convulsive seizures, or may be in nonconvulsive status, and responsiveness may be impaired in all three situations. Additionally, there may be motor movements that are not seizures. At this point, essentially all patients undergoing cardiac resuscitation also undergo minimal EKG lead placement, frequently even in the ambulance. Acute EEG recordings in the setting, despite greater availability of easily placed caps and electrode systems that could at least in part guide treatment, are currently not routinely performed. Remote EEG reading capability and monitoring may make this more feasible. Additionally, electrophysiological recordings and analysis techniques may now provide further insight into whether seizures self-terminate or continue (2), possibly providing additional information regarding treatment choices.

Identification of Patients at Risk

Improving acute seizure care also includes assessing risk prior to the event. With the advent of new biomarkers, be it electrophysiological, proteomic, or genetic, we may hopefully be able to better identify patients who are more prone to febrile and prolonged seizures. A family history inquiring about familial febrile seizures may open additional genetic testing avenues at this point. Patients at higher risk may require different monitoring, treatment, and prevention strategies than the general population.

Syndi Seinfeld and the FEBSTAT study group set a milestone by providing first benchmarks in febrile status epilepticus, highlighting current acute care practices in pediatric patients with febrile seizures, indicating longer treatment times and greater care variability than some would expect. A common treatment algorithm as suggested by the authors is the first important step to potentially reduce intractability and minimize the percentage of prolonged seizures, in addition to a potential multifactorial intervention at the above-listed febrile status epilepticus prevention, detection, and treatment decision points. The authors show that late-treated seizures lasted longer. While a certain degree of confounding cannot be ruled out, it is conceivable that seizures may be easier to control if treated early. The implications for patients and families, albeit not yet fully known, such as decreased medication application and potentially shortened or no hospital stays, likely fewer complications, improved quality of life, decreased psychological and financial burden on caretakers, and overall

decreased cost, make it worthwhile to rethink our current practice. Allow me to not enter the debate over whether seizures beget seizures and cause long-term structural and functional damage, but this thought deserves further mention in the future, considering other findings from the FEBSTAT study team indicating structural hippocampal changes (3). Similar to radiation exposure, there may ultimately not be a safe minimal duration of exposure to febrile seizures and status in susceptible patients. While “time is of the essence” refers to material damage in contract law, it is also conceivable that time to treatment may also be scrutinized by the medicolegal profession.

Raising More Questions

The article raises more questions than answers and is therefore brilliant and thought-provoking at the same time: How do we recognize seizure onset? How do we identify patients at risk? What is our patient and medical care provider education strategy? What is our work-up and treatment algorithm, considering abundant benzodiazepine treatment choices (lorazepam, diazepam, midazolam, clonazepam, clobazam, and chlorazepate, among others) and administration options (intramuscular, rectal, intranasal, sublingual, and intravenous/intraosseous), in addition to other frequently used medications? Who should be allowed to treat and when should treatment be escalated? Which patients are “over-treated”? When do patients need an EEG, a lumbar puncture, or further neuroimaging? Can spot-check EEGs help in the acute care? Do we track time to treatment consistently, and do we monitor outcomes and follow our patients? In whom does febrile status beget febrile status or epilepsy or psychological deficits? What is the psychosocial burden on patients and families? What are the costs for the healthcare system and for society?

Time Is of the Essence

While the FEBSTAT study team may be able to address some of these questions in the near future, other questions may require further investigation. Insurance providers are moving to bundled care reimbursements, and the reduction of medical care interventions in patient groups may soon provide additional financial incentives for healthcare systems to reduce medical expenses. While some of these measures, such as readmission rates, cannot easily be applied to neurologic conditions and febrile seizures or febrile status epilepticus, time to treatment and adherence to treatment paradigms may be measurable. While some may argue that there is not enough time or funds to do this work beyond FEBSTAT at this point, solutions may include putting some responsibility on caretakers. Electronic tools and improved electronic data capture may at some point fulfill the promise of saving time, research data collection, decision support, and improved care. Hopes are that federal funding organizations, institutions and foundations will renew their commitment to these urgent implementation tasks. Some providers and healthcare systems are also working together and delay almost inevitable reduction of expenses by dedicating funds to care improvement during a specified transition time window. But this time window is closing fast, and in a push to evaluate and implement care changes of febrile status epilepticus, and



to improve and to shorten treatment initiation, there is no time to waste.

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