DOES TREATMENT OF STATUS EPILEPTICUS SIGNIFICANTLY IMPACT OUTCOME: NO

E. Beghi
Laboratory of Neurological Disorders, Istituto Mario Negri, Milano, Italy
beghi@marionegri.it

Status epilepticus (SE) is a serious clinical condition associated with high morbidity and mortality, although there is controversy about the extent to which these adverse outcomes are associated with SE itself or whether other factors such as cause, age, or treatment affect the outcome. SE frequently occurs in close temporal relationship with an acute metabolic, toxic or structural insult which may vary with age and, if receiving adequate causal treatment, may not recur. In the most comprehensive critical appraisal of the outcome of convulsive SE (the most easily diagnosed and best studied variety of SE) in children [Raspall-Chaure et al. Outcome of paediatric convulsive status epilepticus: a systematic review. *Lancer Neurol* 2006; 5:769-779], the underlying cause was the main determinant of mortality. Age at onset and duration of SE also affected mortality. Aside from mortality, reported adverse outcomes after SE include cognitive impairment, permanent neurological deficits, hippocampal injury, and subsequent epilepsy (ie, repeated unprovoked seizures). The risk of subsequent unprovoked seizures 2 years after a first-ever unprovoked episode of SE ranges from 25 to 40%, which is similar to that reported after a brief first unprovoked seizure. By contrast, more than 50% of children (and adults) with structural brain insults or previous neurological abnormalities will develop epilepsy, which suggests that etiology is the major determinant of subsequent epilepsy.

Overall recurrence of convulsive SE in children is up to 20% at 4 years, 70% of recurrences occurring within 1–2 years of the first episode of SE. Determinants of recurrence are similar to those for subsequent epilepsy. Recurrence of SE will most probably occur in children (and adults) with a history of neurological abnormalities and epileptogenic brain insults even if they are receiving antiepileptic drug treatment. A relapse of a first seizure represented by convulsive SE will probably be prolonged. Moreover, some studies suggest that the major determinant of convulsive SE occurrence is a history of previous convulsive SE. The effect of age at the time of the first episode of convulsive SE on the risk of recurrence is controversial. Neither population-based nor prospective hospital-based studies report a significant association between convulsive SE in childhood and subsequent mesial temporal sclerosis. Lengthy febrile seizures and febrile SE are associated with increased incidence of subsequent partial seizures although the structural basis for these seizures has not been characterized. Intellectual decline caused by seizures or epilepsy is rare and may be confined to certain specific and readily recognizable syndromes.

The effects of treatment on the outcome of SE are still unknown. Studies in children and adults after a first unprovoked seizure suggest there is no difference in recurrence rates and long-term remission between treated and untreated patients. However, there are no studies addressing whether prophylactic treatment after a first convulsive SE episode modifies the risk of subsequent epilepsy. Etiology is the main determinant of morbidity here too. The poorest outcome is reported in acute symptomatic convulsive SE, which is followed by new neurological dysfunction in more than 20% of cases. In the absence of an acute or progressive neurological disorder, morbidity of SE is low, and less than 10% of children with febrile SE and unprovoked convulsive SE develop new neurological deficits attributable to SE itself. Neurological sequelae are reported in more than 50% of patients with refractory SE. However, even in this selected population the poor outcome may still result from the severe underlying brain injury or by the prolonged convulsive SE.

Prehospital diazepam therapy has been associated with convulsive SE of short duration and a reduced recurrence of seizures in the emergency department. However, no data are available on the long-term outcome of these same patients. Regarding refractory SE, no differences between those who received diazepam and midazolam infusions were reported, and an early induction of pentobarbital coma can be followed with less neurological sequelae. The use of propofol before thiopental in children with refractory SE has been recently suggested based on a more favorable side effect profile. However, most of the patients with refractory SE requiring high-dose barbiturates are in the acute symptomatic group and many will have neurological sequelae.

Children with focal abnormalities undergoing resective surgery for refractory SE might be at lower risk of morbidity than children receiving prolonged high-dose suppressive therapy. However, seizure outcome after surgery in children presenting with convulsive SE might not be changed when compared to children undergoing epilepsy surgery from other studies.

Children and adults presenting with a single seizure have a similar outcome of their epilepsy compared to those presenting with multiple seizures, regardless of whether they were treated after the first seizure or not. However, in patients with SE the use of differing therapeutic algorithms and the absence of randomized controlled trials make it difficult to draw conclusions about the effect of therapy on outcome. Even with these limitations, the results of the published reports argue in favor of postponing long-term anti-epileptic drug (AED) treatment in many patients with SE until at least a second seizure has occurred. A poor prognosis and the consequent indication for early and aggressive treatment are dependent mainly upon the presence of variables like symptomatic etiology, certain epilepsy types and syndromes, and the early evolution of the

epilepsy in that particular patient. For these reasons, indiscriminate long-term AED treatment after a single unprovoked SE may not be necessary.