SHORT- AND LONG-TERM OUTCOMES AFTER STATUS EPILEPTICUS

Refractory Status Epilepticus Frequency, Risk Factors, and Impact on Outcome

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Arch Neurol 2002;59:205–210

Refractory status epilepticus (RSE) is a life-threatening condition in which seizures do not respond to first- and second-line anticonvulsant drug therapy. How often RSE occurs, risk factors that predispose to this condition, and the effect of failure to control seizures on clinical outcome are poorly defined.

OBJECTIVE: To determine the frequency, risk factors, and impact on outcome of RSE.

DESIGN: Retrospective cohort study.

SETTING: Large academic teaching hospital.

PATIENTS: Consecutive sample of 83 episodes of status epilepticus in 74 patients (mean age, 63 years). Main outcome.

METHODS: Refractory status epilepticus was defined as seizures lasting longer than 60 minutes despite treatment with a benzodiazepine and an adequate loading dose of a standard intravenous anticonvulsant drug. Factors associated with RSE were identified using univariate and backward stepwise logistic regression analyses.

RESULTS: In 57 episodes (69%), seizures occurred after treatment with a benzodiazepine, and in 26 (31%), seizures occurred after treatment with a second-line anticonvulsant drug (usually phenytoin), fulfilling our criteria for RSE. Nonconvulsive SE ($P = .03$) and focal motor seizures at onset ($P = .04$) were identified as independent risk factors for RSE. Eleven (42%) of 26 patients with RSE had seizures after receiving a third-line agent (usually phenobarbital). Although mortality was not increased (17% overall), RSE was associated with prolonged hospital length of stay ($P < .001$) and more frequent functional deterioration at discharge ($P = .02$).

CONCLUSIONS: Refractory status epilepticus occurs in approximately 30% of patients with SE and is associated with increased hospital length of stay and functional dis-

ability. Nonconvulsive SE and focal motor seizures at onset are risk factors for RSE. Randomized controlled trials are needed to define the optimal treatment of RSE.

Long-term Mortality After a First Episode of Status Epilepticus

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Neurology 2002;58:537–541

OBJECTIVE: To evaluate long-term mortality among people with status epilepticus (SE).

METHODS: The authors performed a population-based retrospective cohort study to determine long-term mortality after SE. Between January 1, 1965, and December 31, 1984, all first episodes of SE receiving medical attention were ascertained through the Rochester Epidemiology Project Records-Linkage System. Cases surviving the first 30 days ($n = 145$) were followed until death or study termination (February 1996).

RESULTS: At 10 years, cumulative mortality among 30-day survivors was 43%. The standardized mortality ratio (SMR) at 10 years was 2.8 (95% CI, 2.1–3.5). The mortality rate of those with idiopathic/cryptogenic SE was not increased (SMR = 1.1; 95% CI, 0.5–2.3). The following characteristics of SE increased long-term risk for mortality: SE ≥ 24 hours in duration vs. SE < 2 hours (relative risk [RR] = 2.3; 95% CI, 1.1–5.1); acute symptomatic etiology vs. idiopathic/cryptogenic etiology (RR = 2.2; 95% CI, 1.0–5.1); myoclonic SE vs. generalized convulsive SE (RR = 4.0; 95% CI, 1.3–13).

CONCLUSION: Forty percent of subjects who survived the first 30 days after an incident episode of SE die within the next 10 years. The long-term mortality rate was threefold that of the general population over the same time period. The long-term mortality rate at 10 years was worse for those with myoclonic SE, for those who presented with SE lasting more than 24 hours, and for those with acute symptomatic SE. The long-term mortality rate was not al-

tered in those with idiopathic/cryptogenic SE. We conclude that SE alone does not modify long-term mortality.

COMMENTARY

When studying status epilepticus (SE), it is probably better to be a “splitter” than a “lumper.” The two papers considered here illustrate the complex interplay of variables that contribute to long-term and short-term outcomes following SE. Weighing these variables is important because it allows the physician to prognosticate with a reasonable degree of accuracy, develop an appropriate treatment strategy, and counsel patients and family members.

Although short term outcomes following SE have been well studied, the long-term outcomes of SE survivors have not. Logroscino et al. authored the first study to evaluate 10-year mortality after SE. The study included 184 incident SE cases, excluding incident febrile SE in children. Among the 145 patients who survived SE at 30 days, there was an almost threefold risk of death over ten years, compared with the general population.

The authors used multivariate analysis to identify the factors most closely associated with increased long-term mortality. Significant risk factors for long-term mortality included prolonged SE duration, advanced age, and myoclonic SE, which mirror the risk factors for short-term mortality (1). The authors looked at symptomatic SE (acute, remote, and progressive etiologies), and idiopathic/cryptogenic SE (including SE in the setting of epilepsy of unknown cause). Idiopathic/cryptogenic SE did not have increased long-term mortality when compared with the general population, suggesting that SE alone does not alter long-term prognosis. Etiology is clearly an important variable, however, because the acute symptomatic group (42% of the study population) had twice the long-term mortality of idiopathic/cryptogenic SE.

The means by which SE affects long-term outcomes are not known, but Mayer et al. present evidence that treatment-

resistant SE is associated with prolonged length of hospitalization, serious medical complications, and functional deterioration at discharge. These short-term morbidities in turn are likely to have implications for long-term survival.

Mayer and colleagues document the important point that conventional SE therapy frequently fails. Refractory SE (RSE) in their study was common, occurring in about one third of cases. Independent risk factors for RSE were focal motor seizures at onset, and nonconvulsive SE. Some of the findings in this study stand in apparent contrast to other SE studies, and may be due to the relatively small number of cases analyzed and differences in study populations or treatment protocols. For example, over half of the 26 RSE cases had cessation of SE following the administration of additional phenytoin, or third-line therapy (phenobarbital, in most cases). This response rate far exceeds that seen in the Veterans Affairs SE Cooperative Study, in which only 2.3% of convulsive SE responded to third-line therapy (2).

We now know that some types of SE are associated with significant long- as well as short-term mortality. SE arising as a complication of epilepsy, acute symptomatic SE, and nonconvulsive SE in medically complex patients each have different treatment implications. In order to decrease mortality, we need to understand why our conventional treatment protocols frequently fail. These studies add to our understanding of how etiology and treatment resistance contribute to prognosis. It is hoped that our growing knowledge of these and other factors will lead to targeted therapeutic strategies, and better outcomes.

References

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