DOES TREATMENT OF STATUS EPILEPTICUS SIGNIFICANTLY IMPACT OUTCOME? YES!

T. Tomson
Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden
Torbjorn.tomson@karolinska.se

To question the impact of treatment on the outcome of status epilepticus is to challenge one of the best established dogmas in clinical epileptology.

From animal studies, the evidence is overwhelming that status epilepticus kills neurons. It has also been shown beyond any doubt that status epilepticus induced neuronal death is not simply the result of secondary systemic complications. Even in the absence of convulsive activity, seizures cause neuronal loss as a result of excessive neuronal firing through exitotoxic mechanisms (Meldrum et al., 1973, Sloviter 1987).

The clinical evidence that status epilepticus kills neurons is often limited by lack of information concerning underlying etiology of the condition, duration of status epilepticus, as well as presence or absence of complicating systemic factors. However, also in clinical studies, the evidence of harmful effects of status, in particular generalized convulsive status epilepticus, can not be questioned. Post-mortem examination of patients that die in status epilepticus often reveal brain damage (Corsellis and Bruton, 1983). Findings include decreased neuronal density in hippocampi (DeGiorgio et al., 1995). MRI studies have demonstrated focal cerebral oedema followed by atrophy after prolonged status epilepticus in patients (Nixon et al., 2001).

Case series, retrospective as well as prospective studies of status epilepticus in humans have consistently revealed duration of status epilepticus as a major prognostic determinant. A duration of generalized tonic-clonic status epilepticus exceeding 30-60 minutes is associated with a worse prognosis, which is in line with experimental data. It goes without saying that the best way of preventing cerebral damage, to save brain and life, is to interrupt the seizure activity as soon as possible by active and effective pharmacological treatment.

The best evidence for treatment effects in general comes from randomised controlled trials (RCTs), and it must be acknowledged that there is a shortage of RCTs in status epilepticus. However, for obvious ethical reasons, we cannot expect evidence of the effectiveness of treatment on the outcome of status epilepticus from placebo controlled randomised trials. Nevertheless, one randomised, double-blind study compared the effectiveness of intravenous lorazepam, or diazepam with placebo in patients with continuous convulsive seizures lasting longer than 5 minutes (Alldredge et al., 2001). Seizures terminated more frequently in those given active treatment. Moreover, the rates of respiratory and circulatory complications were higher in the placebo group. Additionally, some other randomised active-control trials have revealed differences in effectiveness between different treatment regimens for early status epilepticus (Shaner et al., 1988; Treiman et al., 1998). Such studies provide sufficient indirect evidence to support the well founded dogma that treatment of status epilepticus significantly impact outcome.

References.

Meldrum B, Vogouroux RA, Brierly JB. Systemic factors and epileptic brain damage. Prolonged seizures in paralyzed artificially ventilated baboons. Arch neurol 1973;29:82-87

Sloviter RS. Decreased hippocampal inhibition and selective loss of interneurons in experimental epilepsy. Science3 1987;235:73-76.

Corsellis JA, Bruton CJ. Neuropathology of status epilepticus in humans. Adv Neurol 1983; 34:129-139.

DeGiorgio CM, Correale JD, Gott PS et al., Serum neuron specific enolase in human status epilepticus. Neurology 1995;45:1134-1137.

Nixon J, Bateman D, Moss T. An MRI and neuropathological study of a case of fatal status epilepticus. Seizure 2001;10:588-591.

Shaner DM, McCurdy SA, Herring MO, Gabor AJ. Treatment of status epilepticus: a prospective comparison of diazepam and phenytoin versus phenobarbital and optional phenytoin. Neurology 1988;38:202-7

Alldredge BK, Gelb AM, Isaacs SM, Corry MD, Allen F, Ulrich S et al. N Engl J Med 2001; 345:631-7

Treiman DM, Meyers PD, Walton NY, Collins JF, Colling C, Rowan AJ, et al. a comparison of four treatments for generelized convulsive status epilepticus. Veteran Affairs Status Epilepticus Cooperative Study Group. N Engl J Med 1998;339: 792-8