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Original Article

Etiology, clinical course and response to the treatment of status epilepticus in children: A 16-year single-center experience based on 602 episodes of status epilepticus

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ABSTRACT

Objective: evaluation of etiology, clinical course and response to the treatment of status epilepticus (SE) in children, with particular investigation of superrefractory SE.
Materials and methods: The retrospective study included children with convulsive SE aged 0.2–18 years, treated from 1995 to 2011. Status epilepticus is defined as a continuous seizure or intermittent seizures without full recovery of consciousness between seizures for at least 30 min. Refractory SE is diagnosed if SE lasts for more than 60 min, while superrefractory SE if SE continues or recurs 24 h or more after the onset of an anesthesia therapy, including those cases that recur after reduction or withdrawal of an anesthesia. The etiology was summarized in five categories: idiopathic/cryptogenic, remote symptomatic, febrile SE, acute symptomatic and progressive encephalopathy. The patients were treated according to the same hospital protocol. Midazolam iv and diazepam rectally were given as the first line drugs, phenobarbital/phenytoin iv as the second line drugs. If they failed, third line drugs, midazolam and thiopental were given in continuous intravenous infusion. The medication was defined as effective if seizure clinically stopped within 20 min, without recurrence within the next 6 h. Midazolam was assessed as effective even if it failed as the first line, but was effective in intravenous infusion as the third line drug.
Results: The study consisted of 602 SE in 395 children. There were 305 (50.7%) refractory SE episodes, and 43 (7.1%) of superrefractory SE. Idiopathic/cryptogenic and febrile SE was the most common etiology in the first SE, while progressive encephalopathy and remote symptomatic was in recurrent and superrefractory SE. The most effective drugs were: midazolam (306/339) given in mean dose of 0.4 mg/kg (range 0.1–1.2 mg/kg), thiopental (47/57) in mean dose of 4 mg/kg (range 3–5 mg/kg), phenobarbital (91/135) in dose of 20 mg/kg. Midazolam successfully stopped 306/339 SE episodes (90.3%), 67 SE (21.9%) by equal or lower dose than 0.2 mg/kg as the first line drug, while all other 239 episodes (78.9%) were

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stopped by intravenous infusion in range 0.2–1.2 mg/kg/h (mean 0.4 mg/kg/h) as the third line drug. Adverse effects were frequent in superrefractory SE (60.5%). In 15 patients, corticosteroids contributed to the reduction of seizure recurrence after anesthetic withdrawal and cessation of epilepsia partialis continua. Case fatality rate was 5.1% in all patients, while 21.3% in patients with superrefractory SE.

Conclusion: Status epilepticus in children was characterized by heterogeneous etiology, prolonged duration and commonly good response to midazolam only given in high doses. Superrefractory SE was not so rare in children, especially among the patients with progressive encephalopathy.

1. Introduction

Status epilepticus (SE) is one of the most urgent conditions in paediatrics and requires fast and appropriate treatment. It is defined as an acute epileptic condition characterized by continuous seizures (partial or generalized, convulsive or non-convulsive) for at least 30 min, or by 30 min of intermittent seizures without full recovery of consciousness between seizures.[1] Refractory SE (RefSE) is diagnosed if SE lasts for more than 60 min. Superrefractory status epilepticus (SuperRefSE) is defined as status epilepticus that continues or recurs 24 h or more after the onset of anesthesia therapy, including those cases that recur after reduction or withdrawal of anesthesia.[2] Convulsive SE in childhood is more common, it includes a different range of causes and a lower risk of death compared with adults.[3] Mortality rate in children with SE has decreased from 6% to 3%, probably due to earlier treatment and better intensive care facilities.[4] Shorvon highlighted that the main aim in SE treatment is prevention of brain damage caused by direct effect of epileptic activity, so it is important to interrupt both clinical and electrical manifestation of the seizures.[5] Treiman et al. compared four ways of SE treatment in a large multicentric double-blind randomized study with 518 patients included.[6] In initial SE treatment, lorazepam was effective in 52,2%, phenobarbital in 49,2%, combination of phenytoin and diazepam in 43.1% and phenytoin in 36.8%. The management of SE might be challengeable because SE is not a single entity and comprises different electro-clinical syndromes with various etiologies. Thus, the treatment of all SE by the same algorithm could have certain disadvantages. Particularly, the management of refractory SE could be associated with many difficulties. Costello and Cole recommended aggressive management of SE and highlighted that giving an appropriate dose of the first- and second-line anticonvulsive medication is very important.[7] The excessive dose of initial medications is far less associated with SE morbidity compared to prolonged seizure activity and treatment in ICU. It is suggested that neurologists with EEG knowledge should be consulted during the early stage of SE treatment.[7]

This manuscript presents a single center experience concerning etiology, clinical course and response to the treatment of a large number of convulsive SE episodes, with particular emphasis on the most complicated group of patients with superrefractory SE.

2. Materials and methods

The retrospective study included first and recurrent convulsive SE episodes in children aged 0.2–18 years treated in Institute for Mother and Child Healthcare of Serbia in the period from January 1995 to January 2011. Recurrent SE was defined as repeated SE at least 48 h after cessation of the previous SE, either during the same or new hospitalization. The patients were treated in intensive care unit (ICU) and neurological department. The criteria for ICU admission were: seizing on admission with no response to initial treatment in emergency room by diazepam rectally (0.5 mg/kg) or midazolam intravenously (0.1–0.2 mg/kg), prolonged duration of seizures, severity of underlying disorder, disturbances of consciousness and vital functions. The patients with only electrographic features of SE, without any clinical manifestations such as electrical status during slow-wave sleep and other SE with no motor manifestation as absence seizures were excluded. Patients with the loss of consciousness due to underling disorder, and with including motor manifestation of seizures such as epilepsia partialis continua, were included in the study. Etiology of SE was summarized in five categories[8]: idiopathic/cryptogenic, remote symptomatic, febrile SE, acute symptomatic and progressive encephalopathy. Cryptogenic/idiopathic SE included SE in patients with generalized or focal idiopathic epilepsies and/or epilepsies of unknown etiology. Remote symptomatic SE was defined as SE caused by previous hypoxic ischemic encephalopathy, intracranial hemorrhage, cerebral palsy, CNS abnormalities, including malformations and vascular abnormalities and previous head injury or surgery. Febrile seizure which lasted for more than 30 min was defined as febrile SE. Acute symptomatic SE was caused by acute brain disease or injuries including CNS infections, cerebrovascular insults, acute systemic disease, hypertension, drugs and acute metabolic disorders. Progressive encephalopathy included different disorders with progressive course: neurodegenerative, metabolic, neurogenetic, malignant and neurocutaneous disease. Etiology distribution was analyzed in the group of first, recurrent and superrefractory SE episodes. SE duration was divided in six groups: 30–60 min, 60–90 min, 90–180 min, 180–360 min, 360 min-24 h and more than 24 h. All patients with seizures were treated in the Institute according to the same protocol and neurologist was consulted in early or