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Original article

Early predictors of status epilepticus-associated mortality and morbidity in children

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Abstract

Background: Early predictors of status epilepticus (SE)-associated mortality and morbidity have not been systematically studied in children, considerably impeding the identification of patients at risk. *Objectives:* To determine reliable early predictors of SE-associated mortality and morbidity and identify the etiology of SE-associated sequelae in Japanese children. *Methods:* We conducted a prospective multicenter study of clinical findings and initial laboratory data acquired at SE onset, and assessed

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[1] Appendix 1

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outcomes at the last follow-up examination. In-hospital death during the acute period and neurological sequelae were classified as poor outcomes. *Results:* Of the 201 children who experienced their first SE episode, 16 exhibited poor outcome that was most commonly associated with acute encephalopathy. Univariate analysis revealed that the following were associated with poor outcomes: young age (⩽24 months); seizure duration >90 min; seizure intractability (failure of the second anticonvulsive drug); biphasic seizures; abnormal blood glucose levels (<61 or >250 mg/dL); serum aspartate aminotransferase (AST) ⩾56 U/L; and C-reactive protein (CRP) levels >2.00 mg/dL. Multivariate analysis revealed that young age, seizure intractability, abnormal blood glucose levels, and elevated AST and CRP levels were statistically significant. *Conclusions:* Young age and seizure intractability were highly predictive of poor outcomes in pediatric SE. Moreover, abnormal blood glucose levels and elevated AST and CRP levels were predictors that might be closely associated with the etiology, especially acute encephalopathy and severe bacterial infection (sepsis and meningitis) in Japanese children.

Keywords: Status epilepticus; Prognosis; Predictors; Acute encephalopathy

1. Introduction

The incidence, causes, and prognosis of pediatric status epilepticus (SE) vary worldwide because of distinct environments, socioeconomic conditions, and genetic susceptibility to acute neurological disorders; i.e., the incidence of febrile seizures is much higher and that of bacterial meningitis is lower in Japanese children than in other children. SE predictors have been extensively studied in adults; however, these studies might not provide reliable information for the prediction of pediatric SE because the etiology in children is distinct from that in adults. Early SE predictors have not been systematically studied in children, considerably impeding the identification of patients at risk.

Influenza-associated encephalopathy cases, in which the initial presentation usually includes SE, have increased markedly in Japan since the 1994–1995 influenza epidemic; this prompted the Japanese Ministry of Health, Labour and Welfare to initiate a national survey of influenza-associated encephalopathy in 1998. During the 1998–1999 epidemic, 148 cases with a mortality of 31.8% and a morbidity of 27.7% were reported [1]. Such acute encephalopathies are caused by pathogens other than influenza, and although they are a common cause of acquired brain damage in Japanese children, the pathophysiology remains unknown. These encephalopathies have been collectively termed as acute encephalopathy with inflammation-mediated status epilepticus (AEIMSE) [2]. Early diagnosis of AEIMSE is often difficult because laboratory results, including data from cerebrospinal fluid (CSF) analysis and neuroimaging, are often unremarkable for several days after SE onset [3–5]. Therefore, we initiated a prospective multicenter status epilepticus study to determine the reliable early predictors of SE-associated mortality and morbidity and elucidate the etiology of SE-associated brain injury in Japanese children.

2. Methods

2.1. Study design

The Status Epilepticus Study group includes researchers belonging to 25 hospitals who have been studying the etiology and prognosis of pediatric SE since 2005. The 25 hospitals included 7 intensive care units and 18 local hospitals. Most pediatric SE patients in Tottori prefecture, eastern Shimane prefecture, and northern Okayama prefecture were referred to one of these participating hospitals. Tottori Prefecture Central Hospital serves severely ill pediatric patients living in the north-western part of Hyogo prefecture and Tottori prefecture. Kagoshima University Hospital, which serves severely ill pediatric patients in Kagoshima City, participated in this study. This group has been enrolling pediatric patients who suffered seizures ⩾20 min. Between August 1, 2005 and March 31, 2010, over 250 patients aged 1 month–16 years were consecutively enrolled in this study.

SE was defined as any seizure >30 min or a series of recurrent seizures >30 min without complete recovery of consciousness in this study. Patients with SE of any etiology were the participants of this study. The episodes of first SE during the study period were used for statistical analysis.

We used the modified version of the classification of SE etiology proposed by Maytal et al. (Appendix 2) [6]. Clinical findings from each patient were used to identify outcome predictors: these included demographic data, previous neurological conditions, factors commonly associated with SE, SE characteristics, health status at SE onset, and laboratory data. Prior neurological conditions included past seizures, comparative mental and motor development, and past neurological insults. Factors associated with SE included pyrexia and exposure to proconvulsant drugs (theophylline