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Clinical commentary

Clinical course and long-term outcome in children with alteration of consciousness underwent continuous EEG monitoring: A prospective observational study in Thailand

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ABSTRACT

The study aims to explore the clinical course and long-term outcome in children with altered consciousness who underwent cEEG monitoring. A prospective observational study was conducted in neonatal and pediatric intensive care units from 1 September 2014 through 31 March 2017. Standard 10–20 cEEG monitoring was applied. Twenty children were included in this study. Their ages ranged from 1 day to 142.7 months (median age 40.6 months). Continuous EEG was commenced from 5 h to 5 days after the onset of alteration of consciousness (median 40.2 h). The range of EEG monitoring duration was 6.7–256.3 h (mean 50.4 h). Four patients (20%) had preexisting neurological diseases, which were 2 epilepsy, adrenoleukodystrophy and unknown cause of brain atrophy. Eleven patients (55%) had principle neurological diagnosis and the others 9 (45%) had systemic illnesses. Sixteen patients (80%) had clinical seizures prior to the commencement of cEEG monitoring. Fifteen patients (75%) received antiepileptic drugs before cEEG monitoring. NCSE was diagnosed in 25%. Comparison of patients' characteristics and long-term outcome between the NCSE and non NCSE groups, there was statistical significance between the two groups only with respect to epileptiform discharges. The patients are being follow up for a period of 24 months after the end of cEEG monitoring. The outcome of patients divided into those with a favorable outcome and those with poor outcome according to modified Rankin scale. The patients with isoelectric EEG background had relatively poorer outcomes than those with normal or slow background activities. The overall mortality rate for the entire population was 15%.

1. Introduction

Acute repetitive seizures and status epilepticus are common neurologic pediatric problems causing admission to intensive care units [1,2]. Most status epilepticus is convulsive; however about 25%–50% can be a non-convulsive status epilepticus (NCSE) [3]. NCSE and related non-convulsive seizure (NCS) are defined as ongoing seizure activity without clinical correlation [4]. Common presentations of NCSE include wandering confused epileptic patients and impaired conscious critically ill patients [4]. About 7–47% of pediatric patients with alteration of consciousness had NCSE detected by continuous electroencephalography (cEEG) [5–17]. Experimental models and pathologic studies demonstrate neuronal damage from status epilepticus to be due primarily from generalized convulsive status, whereas most morbidity from NCSE appears to be caused by underlying illness rather than to the NCSE itself [18]. Recent studies show the more persistent the NCSE, the more difficult to treat and the higher the morbidity and mortality rates [19] (Alexis et al., 2013 [23]). Further, there is increasing evidence that high seizure burdens, often classified as electrographic status epilepticus, are associated with worse short-term outcome [19–22]. In contrast, electrographic seizures were not associated with worse long-term outcomes [23]. In addition, electrographic status epilepticus had greater odd ratio of in-hospital death [24]. However, data on clinical course and eventual long-term outcome in children with alteration of consciousness underwent cEEG monitoring is limited. Therefore, we conducted a prospective observational study on children with alteration of consciousness in the intensive care units of a major referral hospital to explore the results of cEEG monitoring and its clinical course and the long-term outcome.

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2. Methods

A prospective observational study was conducted in infants and children who had altered consciousness and were admitted to the neonatal and pediatric intensive care units of Bhumiboladulyadej Hospital, which is a tertiary medical care level and a referral hospital, from 1 September 2014 to 31 March 2017.

Continuous EEG (cEEG) was underwent in all ICU patients with alteration of consciousness regardless prior convulsion or not. Digital video EEG machine (Nihon Koden-1200) with 21 electrodes according to the International 10–20 system was utilized. The minimum monitoring duration was 6 h. If a cEEG was suggestive for either NCS or NCSE, the patient would be monitored until these cEEG characteristics disappeared for at least 24 h. Treatment of NCS and NCSE followed the national guideline for convulsive status epilepticus.

Characteristics of NCS and NCSE were defined using standard terminology [22]. The NCS was defined as an abnormal paroxysmal electrical activities event that is different from the background activities with duration longer than 10 s, a temporal-spatial evolution in morphology, frequency and amplitude, and a plausible electrographic field without clinical association. The NCSE was defined as either a 30-min electrographic seizure or a series of recurrent independent electrographic seizures totaling more than 30 min in any 1-h period (50% seizure burden). Background activity was categorized into 3 groups: normal, slow, and attenuated with featureless or isoelectric.

Patient's information, intubation status, time from alteration of consciousness to commencement of cEEG monitoring, cEEG monitoring duration, underlying diseases, etiology of alteration of consciousness, types of seizures, blood electrolytes, brain imaging, antiepileptic drug therapy prior to cEEG monitoring, ventilator support, length of stay in the ICU and in the hospital were collected as baseline data.

To determine the clinical outcomes, Modified Rankin Scale was used upon clinical evaluation at one month after the cEEG monitoring and at subsequent follow-up visits in the outpatient clinic. Modified Rankin Scale of 1 and 2 were classified as having favorable outcome; whereas, modified Rankin Scale from 3 to 6 were classified as having poor outcome.

Descriptive analysis was applied. Comparison between the NCSE and non NCSE groups and the association of each variable with neurological outcome were determined by chi-square for categorical variables and Mann-Whitney U test for continuous variables. The significant level of inclusion for subject variables was primarily set at $p < .05$. All statistics were performed on SPSS Statistics 19.

Informed consent was obtained from patient's parents or legal guardians. This study was reviewed and approved by the Bhumiboladulyadej Hospital Ethics Committee.

3. Results

There were 20 children admitted ICU with alteration of consciousness and undergone cEEG monitoring. Table 1 summarized demographic and baseline clinical data.

There were 5 patients (25%) who had cEEG indicating NCSE. Among these patients, 3 of NCSE were diagnosed when cEEG recording was commenced. Sixteen patients had abnormal EEG background activities consisted of slow background in 12 and low amplitude in 4. The EEG in 4 patients with initial slow background became normalized 24 h later. The detailed of cEEG findings are shown in Table 2.

One patient who had NCSE died during cEEG monitoring due to cardiac arrest. Therefore, nineteen patients left for evaluation to determine the outcome. The patients are being follow up for a period of 24 months after the end of cEEG monitoring. One patient was lost to follow-up visit after being seen one month after discharge. He had normal neurological function and seizure freedom without medication. Four patients (20%) had normal cEEG and

Table 1
Demographic and clinical data of 20 patients.

Characteristic	Number	Description
Gender	20	Boy 11 Girl 9
Median age (mo.)	40.6	Range 1 day-142.7 mo.
Hospital admission	20	PICU 19 NICU 1
Average time to cEEG monitoring (hrs.)	40.2	Range 5–120
Average monitoring time (hrs.)	50.4	Range 6.7–256.3
Preexisting neurological disease	4	Adrenoleukodystrophy 1Epilepsy 2 Brain atrophy (undermined syndrome)1
Average blood sodium (mEq/L)	138.1	Range 130–148
Etiology of alteration of consciousness		
• Neurological condition	11	Infratentorial ependymoma 1 Hypoxic ischemic encephalopathy 1 Seizure 4 Urea cycle defect 1 Subdural hemorrhage 2 Varicella encephalitis 1 FIRES 1
• Other conditions	9	Pneumonia 4, Myocarditis 1, Intussusception s/p reduction 1, Sepsis 1, SLE1 Toxic shock syndrome 1
Patients receiving brain imaging	16	CT 9 MRI 3, CT and MRI 4
Clinical seizure	16	
• Generalized tonic clonic	4	
• Tonic	4	
• Focal clonic	7	
• Complex partial	1	
Patients with seizures receiving antiepileptic drug (AED) before cEEG	15	Phenobarbital 9, Phenytoin 8, Valproate 3, Topiramate 2, Levetiracetam 2 Vigabatrin 1
• 1 AED	9	
• 2 AEDs	2	
• 3 AEDs	3	

Table 2
cEEG findings in 20 patients.

cEEG Findings	Number	Description
Electroencephalographic seizures (NCSE)	5	Multifocal seizures 5
• Immediately after cEEG commencement	3	Intractable epilepsy 1, Urea cycle defect 1, Subdural hemorrhage1
• Later	2	Myocarditis with cardiac arrest, FIRES
Focal epileptiform discharges	8	
cEEG background	16	
• Slow background	12	
• Amplitude less than 10 μV/isoelectric	4	Myocarditis with cardiac arrest 1, Hypoxic ischemic encephalopathy 1, Urea cycle defect with brain herniation1, Varicella encephalitis 1
Normal over time	4	Pneumonia with respiratory failure 2, 1st unprovoked complex partial seizure 1, Intussusceptions s/p reduction 1

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