Transient hyperammonemia associated with postictal state in generalized convulsion

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Abstract Previous studies revealed that transient hyperammonemia was noted after generalized convulsion. This study was undertaken to analyze the association between postictal state and serum ammonia levels. Adult patients presenting to the emergency department with seizures were included. Serum ammonia and other blood tests were compared between patients with full recovery of consciousness after generalized convulsion and those who had not completely regained consciousness. Patients who had not completely regained consciousness (7 of 7, 100%) had higher rate ($p = 0.035$) of hyperammonemia compared with patients who had fully regained consciousness (4 of 10, 40%) and higher level of serum ammonia (246 ± 96 mg/dL vs. 102 ± 99 mg/dL, $p = 0.006$). All patients who showed postictal consciousness level impairment on arrival at the emergency department had elevated serum ammonia at that time. Transient hyperammonemia is associated with postictal confusion.

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Introduction
Many physical and biochemical abnormalities may be found after an episode of generalized convulsion. Previous studies showed changes in prolactin [1] and creatine kinase [2]. Other previous studies also found that changes in the neuronal receptors and cerebral blood flow after seizure may contribute to the postictal state [3,4]. Recently, studies have revealed transient hyperammonemia after seizure [5,6]. The hyperammonemia seemed to last only for a short time. The present study was designed to analyze the time relation between hyperammonemia and postictal consciousness state.

Methods
We performed this study in the emergency department (ED) of a medical center after receiving the approval from...
The center’s ethics committee (KMUH-IRB-980142). This prospective convenience sampling study occurred from April 2009 to October 2009 and was assisted by part of the ED staff. We included the adult patients (older than 18 years) who had been brought to our ED because of generalized convulsion but had stopped convulsive movement by arrival at ED. The presentation for the diagnosis of generalized epilepsy was defined as generalized convulsive limbs, face, and eye movement lasting more than 1 minute, including a change in consciousness. Postictal confusion also had to be present. The patients had to have a history of epilepsy or a witness who could describe that they had the typical convulsive movements of an epileptic seizure. Patients presenting to the ED with unstable respiratory and hemodynamic status requiring emergency intervention were excluded. The exclusion criteria included airway obstruction or respiratory distress necessitating immediate intubation, systolic blood pressure less than 90 mmHg, and hemodynamic unstable arrhythmia. A neurologist was consulted for any uncertain diagnosis, etiology, or treatment of seizures.

The patients were separated into two groups according to the initial consciousness level when they presented to the ED. The consciousness level was evaluated by emergency physician according to Glasgow Coma Scale and orientation to place, time, and person. The patients who had abnormal consciousness as determined by Glasgow Coma Scale (<15) or who showed disorientation were defined as incomplete consciousness recovery. Patients with clear consciousness were allocated to one group and patients who had not completely regained consciousness were allocated to the other group. Patients with underlying diseases or comorbidities that may have impaired their level of consciousness were excluded from further analysis.

Patients received blood tests and other diagnostic studies according to their clinical needs. We also reviewed the current medication regimen of each patient, especially valproate. The blood test included complete blood cell counts, urea nitrogen, creatinine, sodium, potassium, calcium, ammonia, aspartate aminotransferase, alanine aminotransferase, and glucose. If the ammonia level was high (greater than 80 µg/dL), it would be rechecked after an interval of between 1 hour and 3 hours.

For statistical analysis of continuous variables, a Mann-Whitney U test was performed. The Chi-square test or Fisher’s exact test was used for categorical variables.

Results

Thirty-one patients with seizure were referred to our ED. Fourteen were excluded because of the following reasons: 9 patients with underlying impaired consciousness because of a history of cerebrovascular disease, brain tumor, or head injury and 5 patients with comorbidities of active diseases, including hyperosmolar hyperglycemia status, lymphoma, sepsis, uremia and hemolysis, elevated liver enzymes, and low platelet count syndrome. Among the 17 enrolled patients, 10 showed a full recovery of consciousness and 7 demonstrated a various degrees of impaired consciousness on arrival at the ED. Although the patients were usually referred to our ED shortly after their seizures, the interval between seizure onset and ED arrival in both groups was difficult to assess because most patients and the witnesses were unable to report the exact time of their seizure onset.

The blood test results are shown in Table 1. The group with impaired consciousness had a higher percentage of elevated serum ammonia (7 of 7, 100% vs. 4 of 10, 40%, p = 0.035) and a higher average serum ammonia level (246 ± 96 µg/dL vs. 102 ± 99 µg/dL, p = 0.006) than the group with a full recovery of consciousness. Patients with impaired consciousness all had elevated ammonia levels with a minimum level of 136 µg/dL. Four patients in the group with full recovery of consciousness had higher serum ammonia levels: 98 µg/dL, 101 µg/dL, 173 µg/dL, and 355 µg/dL. All patients in both the groups had clear consciousness by 1–2 hours later when the follow-up blood tests were performed. All but one patient had their elevated ammonia levels decreased to the normal range on this follow-up examination, and that single patient’s ammonia decreased from 162 µg/dL to 101 µg/dL. Other blood tests did not reveal any significant difference except that the group with impaired consciousness had a higher proportion of leukocytosis (85.7% vs. 20%, p = 0.015). One patient in the group with full recovery of consciousness and two patients in the impaired consciousness group had received valproate with the drug levels 18.1 µg/mL, 31.3 µg/mL, and 29.8 µg/mL.

Discussion

Among the patients in our ED because of seizures, those patients who were still in the impaired consciousness state all showed hyperammonemia. Subsequently, they recovered from consciousness and their follow-up ammonia levels were also markedly decreased. Those patients who had already regained full consciousness also showed lower ammonia levels.

In previous studies, transient hyperammonemia has been observed in generalized convulsive seizure because of a variety of causes [5,6]. It is still unknown if all generalized convulsion results in transient hyperammonemia. Under normal conditions, serum ammonia would be produced from muscle metabolism [7]. During a generalized convolution, muscles may be heavily contracted and produce lots of ammonia which overwhelms liver metabolism. Once the seizure stops, typically the liver rapidly extracts the ammonia. It has been shown that serum ammonia is also elevated after heavy exercise [8].

The postictal state has been defined as "manifestations of seizure-induced reversible alterations in neuronal function but not structure"[9]. The consciousness could not recover in a short period after generalized convolution. After consciousness has been regained, patients may also complain of being unable to think clearly, poor attention and concentration, poor short-term memory, decreased verbal and interactive skills, and a variety of cognitive defects specific to individuals. Impaired consciousness level and a confused state were usually observed and have been attributed to neurotransmitter abnormalities; however, there is currently no direct evidence for neurotransmitter...
depletion following seizures [10]. Seizures result in changes of neuronal receptors and cerebral blood flow [3,4]. Hyperammonemia causes disturbances of consciousness as observed in hepatic encephalopathy and other metabolic diseases [11]. Some symptoms of postictal confusion are similar to hepatic encephalopathy.

There are several limitations in this study. First, we did not record the consciousness and serial serum ammonia level changes during the postictal state. At ED, we only documented the initial consciousness level and the follow-up consciousness level 1–2 hours later. Although all patients’ consciousness recovered uneventfully at follow-up, the ammonia level and consciousness level may show better correlation with serial follow-up. Second, the postictal state was defined by clinical evaluation without electroencephalography. Some patients may still be in nonconvulsive state as convulsive movement stops. In our study, all patients’ consciousness recovered uneventfully. In a review of the time course, all patients had only a single seizure episode. Third, the number of patients was small. However, this study has demonstrated a significant difference in the hyperammonemia between patients with incomplete consciousness recovery and patients with clear consciousness.

The results of this study showed that transient hyperammonemia is associated with postictal consciousness impairment with regard to time course. Further study is needed, however, to determine whether the hyperammonemia causes any other symptoms of postictal state.

References


