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LETTER TO THE EDITOR

Seizures in nonketotic hyperglycaemia

Dear Sir,

The association between focal seizures and hyperglycaemia was first reported in 1965[1]. The disorder is characterized by hyperglycaemia, no ketoacidosis, full consciousness (or minimal depression of sensorium) and focal seizures. We report 21 patients, who presented with seizures and nonketotic hyperglycaemia (NKH). This is a large case series. The aim of this report is to study clinical and laboratory characteristics of seizures in NKH.

A retrospective study was done in a teaching hospital. Inclusion criteria were (1) hyperglycaemia (plasma glucose more than 11.11 mmol/l), (2) seizures, and (3) seizure stopping after control of the hyperglycaemia. Patients with seizures explained by causes other than hyperglycaemia were excluded from the study. Of the 21 patients, 9 were men (43%) and 12 were women (57%) who developed seizures and NKH (23 events). One patient had three events. Six patients had a previous history of diabetes mellitus (DM). Fifteen patients had no previous history of DM. They presented with seizures and NKH, and were diagnosed with DM in the index admission. Of the 21 patients, 3 were DM type 1 (14.3%) and 18 were DM type 2 (85.7%). The average duration of seizures before admission was 5 days (range 1–14 days). The average duration of seizures in each episode was 3 minutes (range 1–5 minutes). Total of 22 events (95.65%) were partial seizures, and 1 event was an unclassified tonic-clonic seizure. Among the 22 partial onset seizures, 14 were epilepsia partialis continua, 6 became secondarily generalized tonic-clonic seizures, and 2 were complex partial seizures (CPS). In all 20 events of partial seizures without CPS, seizures started in one extremity or the face: 14 started in an upper extremity, 5 in the face, and 1 in a lower extremity. Partial seizures started slightly more often on the left side (12 cases) than the right side (8 cases). At the time of the seizure, the average plasma glucose value was 32.61 mmol/l (range 16.11–61.33 mmol/l). The average calculated serum osmolarity was 302 mOsm/l (range 288–323 mOsm/l). When the seizures stopped, the average plasma glucose value was 11.3 mmol/l (range 4.11–21.67 mmol/l).

Neurologic manifestations, particularly seizures, may provide the first clinical clue to the presence of NKH. Focal motor seizures are the most common type[2]. However, seizures in NKH are still not fully appreciated by physician and patient. Our patients took an average of 5 days before they got the correct diagnosis and treatment. Knowledge of this condition may shorten the time to diagnosis and decrease the discomfort of patients. Every patient who presents with seizures especially focal seizures should have an immediate determination of plasma glucose levels. Seizures in NKH happen equally in both sexes. In 15 of the 21 patients (71.4%), seizures were the earliest manifestation of DM and led to discovery of DM in these patients. Most of patients had type 2 DM. Although 3 of the 21 patients had type 1 DM, none of them had ketoacidosis during the seizure. This finding may be explained by the fact that ketosis has an anticonvulsant action, due to intracellular acidosis increasing glutamic acid and decarboxylase activity leading to increased levels of GABA[3]. Epilepsia partialis continua was the most common type (60.87%) of seizure in our series, as previously reported[2]. Interestingly, we found 2 (8.7%) of our patients presented with CPS. Our finding confirmed previous reports of CPS induced by hyperglycaemia[4]. The mechanism of seizures in NKH is still debated. The possible mechanisms are hyperglycaemia or hyperosmolarity, a low level of gamma aminobutyric acid (GABA), and focal ischaemia. Each mechanism, considered alone, is unsatisfactory. Mean plasma glucose value in our report was 32.61 (16.11–61.33 mmol/l), and osmolarity ranged from normal to a moderate value (288–323 mOsm/l). Almost all of our seizures in NKH patients have plasma osmolarity less than the classical diagnostic level (320 mOsm/l) of NKH. In addition, mean plasma glucose ranged from normal to hyperglycaemia (4.11–21.67 mmol/l) when seizures stopped. So, the explanation of hyperglycaemia or hyperosmolarity alone is unsatisfactory. In addition, the Krebs cycle in NKH is inhibited, GABA metabolism is increased and the levels may be decreased, thus lowering the threshold for seizure activtiy[3,5].

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The clinical and laboratory characteristics features of hyperglycaemic-induced seizures are: (1) moderately severe hyperglycaemia (plasma glucose > 16.11 mmol/l); (2) moderate hyperosmolarity (plasma osmolarity > 288 mOsm/l); (3) seizures, especially focal seizures; (4) seizures stopping immediately after normalizing plasma glucose and plasma osmolarity. All of the patients had a normal CT-scan brain finding and did not require antiepileptic drugs (AEDs). Focal seizures in NKH are refractory to AEDs and respond best to insulin and rehydration. In all the patients seizures ceased on correction of the hyperglycaemia. This is important, because such seizures are refractory to the usual AEDs.

Yours sincerely,

Professor Somsak Tiamkao
Tongchai Pratipanawatr
Department of Medicine

Siriporn Tiamkao
Department of Pharmacology

Benjaporn Nitinavakarn
Department of Radiology

Verajit Chotmongkol
Suthipun Jitpimolmard
Department of Medicine
Faculty of Medicine
Khon Kaen University
Khon Kaen 40002, Thailand

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