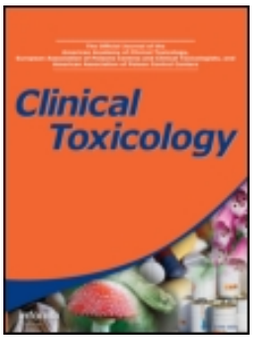

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Letter To The Editor: "Seizures induced by topiramate overdose"

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LETTER TO THE EDITOR

Seizures induced by topiramate overdose

Keywords acute intoxication; topiramate; seizures

To the Editor:

Topiramate (Topamax®) is a relatively new anticonvulsant agent indicated as adjunct therapy for the treatment of partial seizures, Lennox-Gastaut syndrome, and generalized tonic-clonic seizures. It also has been used in the treatment of cluster headache, essential tremor, binge eating disorder, acute mania, Tourette's syndrome, neuropathic pain, bipolar disorder, alcohol dependence, and to facilitate weight loss in obese patients (1–4). The exact mechanism of topiramate action is unknown, although inhibition of voltage-sensitive sodium and calcium channels, potentialization of gamma-aminobutyric acid (GABA) mediated chloride currents, and selective blockade of kainate-activated glutamate receptors are considered (1,3,4,5). Topiramate also weakly inhibits carbonic anhydrase, specifically the activity of CA II and IV isoforms found in the kidney and brain (5). The medical literature on acute topiramate toxicity is limited and contains only six published cases (1–6). According to the best of our knowledge, there is only one article (5) describing status epilepticus in two patients massively intoxicated with topiramate (400 mg/kg and 487 mg/kg). Both patients had a history of epilepsy and were treated with topiramate prior to overdose. We describe the case of a 38-year-old man, with no contributory past medical history, who was admitted to the clinic because of three secondarily generalized tonic-clonic seizures which lasted for about 1–2 minutes each. Each seizure was terminated within one minute after the intravenous administration of diazepam 10 mg. During the third seizure the patient was also given clonazepam 1 mg. According to the history, about two hours earlier, the patient drank alcohol and took 2500 mg of topiramate 2500 mg (31.25 mg/kg) in a suicide attempt (the drug was prescribed to his wife for epilepsy). At the time of admission he was unresponsive (GCS-8), blood pressure was 130/80 mm Hg, heart rate 82 beats/minute, respiratory rate 15 breaths/minute, and body temperature was 36.7°C. Neurological examination showed symmetrical normal-reacting pupils that were deviated to the upper right, normal corneal reflexes, weak and symmetrical deep tendon reflexes, and no Babinski signs. Laboratory results were within the normal ranges, except for a mild metabolic acidosis (arterial pH 7.34, pCO_2 32 mm Hg, pO_2 96 mm Hg, base excess −7.5, and serum bicarbonate 17.3 mEq/L). The serum lactate was 19.8 mg/dL (2.2 mmol/L), blood ethanol level was 60 mg/dL, and urinary pH was 8. Over the next 20 hours, the patient regained consciousness and there were no more seizures during hospitalization. Moderate psychomotor slowing, which was observed the following 24 hours, could be associated with not only intoxication, but also with the intravenous long-acting benzodiazepines. The metabolic acidosis persisted for about 72 hours. Although paradoxical seizures after antiepileptic drugs overdose are unusual, laboratory data suggest that topiramate may have early proconvulsant effects (5,7). McDonald et al. demonstrated that mice treated with topiramate 30 minutes prior to intra-cerebroventricular administration of kainate had longer seizures and higher mortality than did mice given kainate alone. However, anticonvulsant effects were seen in animals treated with topiramate for more than 6 hours prior to pharmacological induction of seizures with kainate (7). The occurrence of secondarily generalized seizures in our patient after the relatively small dose of topiramate (31.25 mg/kg) in comparison to doses described by Fakhoury et al. (5), suggests that acute poisoning may be more severe in those patients who were not previously treated with topiramate.

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