

Topiramate and metabolic acidosis: a case series

Kelly Groeper MD, Mary Ellen McCann MD, Mark A. Rockoff MD

Department of Anesthesiology, Boston Children's Hospital, Boston, MA

Introduction: Topiramate is a relatively new anti-epileptic drug that has been approved for use as adjunctive therapy for partial and primary generalized seizures in adults and children greater than two years of age.¹ It appears to have a favorable safety profile², however there have been reports of metabolic acidosis occurring in both adults and children. We present four pediatric surgical patients who were taking topiramate for seizure control and were found to have a significant metabolic acidosis when a baseline arterial blood gas was obtained in the operating room.

Methods: After Institutional Review Board approval, medical records of patients receiving topiramate who were found to have a metabolic acidosis on initial blood gas analysis after induction of anesthesia, but prior to beginning a major surgical procedure were reviewed. Data collected included patient age, surgical procedure performed, a brief medical history and arterial blood gas results.

Results: Four patients were identified in a four-month period. They ranged in age from 2 to 14 years. All of the patients had been on topiramate for greater than six months. None were previously known to have a metabolic acidosis. The surgical procedures performed included posterior spinal fusion in two patients and placement of electrocortography grids and strips for seizure monitoring in the other two patients. Arterial blood gas values are indicated in the table.

	pH	pCO ₂ (mmHg)	HCO ₃	Base Deficit
Patient 1	7.33	32.6	17.4	6.8
Patient 2	7.38	38	22.9	1.3
Patient 3	7.33	31.5	16.4	8
Patient 4	7.35	34	19.2	5
Mean ± SD	7.35±0.02	34±2.8	19±2.9	5.3±2.9
Normal value	7.35-7.45	35-48	22-27	-2 to 3

Discussion: Topiramate is a widely used anti-epileptic drug with multiple mechanisms of action including blocking of sodium channels, enhancing gamma aminobutyrate (GABA) activity, and blocking glutamate receptor subtype activity.³ Topiramate has also been found to weakly inhibit carbonic anhydrase.⁴ This inhibition of carbonic anhydrase may cause a metabolic acidosis, most likely from a renal tubular acidosis rather than from a more central mechanism.⁵ Metabolic acidosis may be a more frequent side effect of topiramate than generally appreciated. It is important to recognize the possibility that a metabolic acidosis might exist in a patient undergoing a surgical procedure and anesthesia, since a metabolic acidosis may be mistaken as a sign of inadequate intravascular volume, poor circulatory function, hypoxemia, or even malignant hyperthermia. Therefore, patients receiving topiramate as a part of the anti-epileptic regimen should have preoperative laboratory testing that includes determination of venous bicarbonate levels. When abnormally low levels are found, alkaline urine can confirm the renal nature of the acidosis. It may be appropriate to administer bicarbonate replacement therapy if significant acidosis is detected. In any case, anesthesiologists should be aware of the potential renal tubular acidosis in patients receiving topiramate therapy.

References:

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