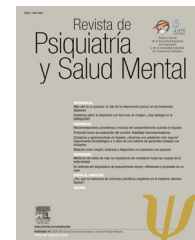


# Revista de Psiquiatría y Salud Mental

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## SCIENTIFIC LETTER

### Metabolic acidosis and topiramate. Use of Winters' formula<sup>☆</sup>

### Acidosis metabólica y topiramato. Utilidad de la fórmula de Winters

Topiramate is a drug introduced in Europe in 1995 for the treatment of hard-to-control epilepsy. The drug is also effective in the treatment of bipolar disorder, migraines, neuropathic pain, alcohol dependence, essential tremor, obesity and eating disorders. One of its side effects is hyperchloremic metabolic acidosis without anion gap,<sup>1,2</sup> which can appear in up to 40% of the patients who receive topiramate at therapeutic doses; it is more frequent and severe in the case of acute poisoning.<sup>1</sup> However, in the cases of acute intoxication, it is usually associated with other drugs, which can also influence acid-base balance. We report the case of a patient who presented with metabolic acidosis after an overdose of 2 drugs, one of them being topiramate.

This was a 38-year-old woman with a history of gastric reduction due to obesity and cluster B personality disorder. She was on treatment with venlafaxine, mirtazapine, topiramate and lorazepam. She came to emergency treatment for autolytic-intention medicine overdose with topiramate and lorazepam of uncertain dosage and time. Upon arrival the patient was found to be Glasgow 14, tending to somnolence, with the rest of the examination being normal. She was given activated charcoal. The analytical analyses showed hyperchloremic metabolic acidosis with normal anion gap: pH 7.29, pCO<sub>2</sub> 41 mmHg, bicarbonate 19.7 mmol/l, excess of bases  $\square$ 6.9, chlorine 113.4 mmol/l, and anion gap 14.6. After 18 h her level of consciousness improved, being in Glasgow 15, and the pH was normal, although low levels of bicarbonate (18.2 mmol/l) and hyperchloremia (117 mmol/l) persisted. Nevertheless, given her clinical stability, the patient was discharged after psychiatric assessment.

Topiramate, besides potentially causing metabolic acidosis, can also produce central neurogenic hyperventilation. This is probably due to its inhibitory effect on the carbonic anhydrase in the brain and to the subsequent LCR acidosis.<sup>2</sup> In such a situation, the clinical picture develops with hyperventilation, arterial hypotension and different degrees of altered consciousness and cognitive functions.<sup>1</sup>

In these cases, gastric lavage and administering activated charcoal are of little use because topiramate is very rapidly absorbed.<sup>1</sup> The perfusion of sodium bicarbonate as treatment for acute intoxication with acidosis is controversial.<sup>1,2</sup> However, some authors recommend administering alkaline solutions in cases of acidosis secondary to chronic treatment.<sup>3</sup>

In the case that we present here, topiramate might be responsible for the metabolic acidosis with normal anion gap that the patient had. However, when we apply Winter's formula (expected pCO<sub>2</sub> = 1.54 × HCO<sub>3</sub> + 8.36 ± 1.11), we see that the expected pCO<sub>2</sub> is 38.7 ± 1.11 mmHg, a value less than that presented by our patient. This formula is extremely useful for calculating the value of pCO<sub>2</sub> starting from a specific value of serum bicarbonate. Consequently, when the pCO<sub>2</sub> values are different from that expected when applying Winter's formula, it can be concluded that there is another process that is influencing the genesis of acidosis. In this case, the discrepancy between the expected and real pCO<sub>2</sub> values led us to suspect the presence of a component of respiratory depression attributable to the benzodiazepines. It can be interpreted that the presence of other toxic substances (such as the benzodiazepines in this case) can eliminate the compensatory respiratory effect secondary to acidosis produced by topiramate. The conclusion is that the finding of abnormally elevated pCO<sub>2</sub> with respect to the degree of existing acidosis can alert one to the possible presence of a component of respiratory depression that can be produced by other toxic substances.

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Paula Rubio, August Supervía\*, Alfons Aguirre, José Luís Echarte

*Servicio de Urgencias, Hospital del Mar, Barcelona, Spain*

\* Corresponding author.

*E-mail address:* [asupervia@parcdesalutmar.cat](mailto:asupervia@parcdesalutmar.cat) (A. Supervía).

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