

Trismus secondary to valproate treatment in a woman with bipolar disorder: a case report

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Dear Editor,

Muscle contracture is a common symptom of valproate. However, there is no report in the literature of lockjaw (trismus) associated with this drug. We therefore present a case of lockjaw during valproate treatment in a patient with bipolar disorder and hypoparathyroidism.

A 62-year-old Caucasian female was admitted on November, 2015 at a psychiatric unit during a manic episode. Patient was previously diagnosed with bipolar disorder and had manic and depressive episodes in the past. She underwent a total thyroidectomy three months prior to her admission, for suspicion of malignancy (not confirmed by biopsy) and has been since then in treatment for hypothyroidism and iatrogenic hypoparathyroidism with levothyroxine, calcitriol and calcium carbonate. She had no cognitive impairment and no relevant findings in laboratory exams. A cerebral perfusion scintigraphy was performed showing slight hypoperfusion in the frontal lobe and posterior cerebellar areas. It is noteworthy that the patient did not tolerate lithium carbonate due to severe extremity tremors. Therefore, valproate was initiated and gradually increased up to 1000 mg/day. She developed lockjaw three days after. She was unable to open her mouth and also fractured two teeth. She had difficulty in diction and in chewing food. No painful symptom or other muscular manifestation had been reported. Biperiden and clonazepam were prescribed without response. She had no prior symptoms of muscular spasm and she denied previous use of valproate. The diagnosis of valproate-induced trismus was made after other causes of trismus, such as infections, neurological illness and oro-dental abnormalities were excluded. The laboratory tests show no alterations on serum levels of TSH, PTH, phosphate and calcium. Thus, the valproate was replaced by olanzapine, which lead to symptom resolution. Patient has been in follow-up for two years and did not have any trismus symptoms since valproic acid withdrawal.

Trismus is defined as a tonic contraction of the muscles of mastication with mouth opening of ≤ 35 mm¹. It can result in difficulty in activities such as biting, chewing, swallowing and speaking and may further lead to poor oral hygiene, pain and weight loss². Some of the causal factors implicated in this condition are tumors, infections, surgery and radiotherapy complications, and drugs side effect³. There are case reports of trismus induced by succinylcholine⁴ and duloxetine⁵, but none regarding this side effect

with valproate. A recent systematic review of the untoward effects of valproate showed that drug-induced parkinsonism is a relatively common side effect in elderly women⁶. It's known that valproate can safely be used in patients with thyroid and parathyroid dysfunction, once it does not interfere on these hormone levels⁷. The mechanism of how valproate can induce trismus is unclear. A preclinical study found that low concentrations of valproate can induce muscle contractions, which were abolished by indomethacin.⁸ Therefore, prostaglandins may be implicated in the contractile effect of valproate⁸.

In summary, the present study was the first to show a valproate-induced trismus. This case report demonstrates that clinicians need to be vigilant for potential side effects after the beginning of a treatment with a psychoactive drug even when they are not reported in the scientific literature.

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