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LETTER TO THE EDITOR

Hyponatremia Associated with Repeated Use of Sodium Valproate

Mehmet Hamdi Orum[1], Aysun Kalenderoglu[1], Oguzhan Bekir Egilmez[1], Murat Eren Ozen[1], Yasar Kapici[2]

[1]Adiyaman University, Faculty of Medicine, Department of Psychiatry, Adiyaman, Turkey
[2]Private Adana Hospital, Department of Psychiatry, Adana, Turkey

To the Editor,

Sodium valproate is one of the medications used in the treatment of schizoaffective disorder, bipolar disorder, and epilepsy. Tremor, drowsiness, Reye-like syndrome, hepatic failure, thrombocytopenia, pancreatitis are the most frequent side effects of this medication (1). Hyponatremia is another serious side effect which has also been previously associated with the use of carbamazepine, oxcarbazepine, clozapine, and selective serotonin reuptake inhibitors (SSRIs) (2). Here, we report the case of a patient with hyponatremia associated with sodium valproate.

The patient was 30 years old. He was being followed-up at a psychiatry outpatient clinic for 10 years, with a diagnosis of schizophrenia. He was using 6 mg/day of risperidone for 3 years. His psychotic symptoms were not taken under control with this treatment, and the parents stated the agitation, threatening behaviour, talking to himself. Previously prescribed drugs used by the patient at the effective dose and time were haloperidol, chlorpromazine, quetiapine, olanzapine, amisulpride, carbamazepine, SSRIs (sertraline and paroxetine), and a few different combinations (e.g., risperidone-olanzapine, risperidone-quetiapine, haloperidol-quetiapine, amisulpride-chlorpromazine). He was started on clozapine 25 mg/day, and it was titrated up to 800 mg/day for control of positive symptoms of psychosis. Sodium valproate was added to the treatment to prevent possible epileptic seizures. The initial dose of sodium valproate was 250 mg/day, and this was titrated up to 1500 mg/day. The patient's initial baseline laboratory data at the time of admission were sodium 137 mmol/L, potassium 5.1 mmol/L, and chloride 101 mmol/L. Upon titration of the sodium valproate to 1500 mg/day, the sodium level was found to be 125 mmol/L, the potassium level 4.1 mmol/L, and the chloride level 96 mmol/L. The serum sodium valproate level at this time was 75.3 mg/L. The patient's thyroid, renal, and liver function tests were within normal limits. The newly developed hyponatremia was attributed to sodium valproate or clozapine as there were no obvious underlying disorders to cause hyponatremia. These two drugs were discontinued. Hyponatremia ceased 10 days after his sodium valproate and clozapine intake was stopped. The patient's laboratory data showed improvement, with the following serum levels: sodium 135 mmol/L, potassium 5 mmol/L, and chloride 95 mmol/L. Hyponatremia was thought to be associated with either sodium valproate, clozapine, both, or an interaction between sodium valproate and clozapine or

Corresponding author: Mehmet Hamdi Orum,
Adiyaman University, Faculty of Medicine,
Department of Psychiatry, Adiyaman, Turkey
E-mail: mhorum@hotmail.com
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another agent. The patient was discharged with his past treatment, risperidone 6 mg/day, at the request of his family.

However, after 2 months of being discharged, he presented to the emergency service with similar complaints. Changes in sodium and potassium levels were observed. He described visual hallucinations in addition to his previous admission. However, it was learned that sodium valproate 1000 mg/day started spontaneously due to the fact that the patient was the first drug to heal itself. It was understood that hyponatremic encephalopathy developed because the brain magnetic resonance imaging examination performed was normal. Haloperidol 10 mg/day was given intravenously until the end of the third day of hallucinations. The sodium level and the condition of the patient returned to normal after 7 days of inpatient treatment. Clozapine was restarted because hyponatremia was thought to be due to sodium valproate. In his follow-up, he did not report hyponatremia after starting 600 mg/day clozapine. Partial remission in psychotic symptoms had also sustained during his follow-up. Written informed consent was taken from the patient in order to publish her data.

There were not much case reports in the literature describe hyponatremia or syndrome of inappropriate antidiuretic hormone (SIADH) as a possible adverse drug reaction associated with use of the antiepileptic drug sodium valproate (3). Ikeda et al. (4), Patel et al. (5), and Bève et al. (6) reported the cases had sodium valproate-induced hyponatremia or SIADH. The mechanism by which sodium valproate could cause hyponatremia or SIADH has not been fully elucidated. SIADH due to drugs can be caused by stimulation of the release of ADH by the hypophysis (7). Sodium valproate could make hypothalamic osmoreceptors less sensitive (2). Hyponatremia due to sodium valproate could be a dose-related side effect (8).

This case report suggests that physicians should be aware that sodium valproate may induce a SIADH-like syndrome with hyponatremia with a high morbidity and mortality (9). Further systemic research should be conducted with respect to anticonvulsant-associated hyponatremia to provide a greater understanding of both its prevalence and etiology.

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