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Case Report / Olgu Sunumu

Sodium valproate use may result in hyponatremia

Sodyum valproat kullanımı hiponatremi ile sonuçlanabilir

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ABSTRACT

Sodium valproate is a drug used in neurological and psychiatric diseases and has side effects such as tremor, drowsiness, Reye-like syndrome, hepatic failure, thrombocytopenia, pancreatitis. Hyponatremia is another serious side effect of sodium valproate. Here, we report the case of a patient with hyponatremia associated with sodium valproate.

Keywords: Sodium valproate, hyponatremia, side effect

ÖZ

Sodyum valproat, nörolojik ve psikiyatrik hastalıklarda kullanılan ve titreme, halsizlik, Reye benzeri sendrom, karaciğer yetmezliği, trombositopeni, pankreatit gibi yan etkileri olan bir ilaçtır. Hiponatremi, sodyum valproatın bir başka ciddi yan etkisidir. Burada, sodyum valproat ile ilişkili hiponatremi gelişen bir hastayı ele aldık.

Anahtar Kelimeler: Sodyum valproat, hiponatremi, yan etki

INTRODUCTION

Sodium valproate (SV) is an FDA (United States Food and Drug Administration)-approved drug to treat seizures, to prevent migraine headaches, and bipolar disorder (BD). It is also used off-label (for unapproved uses) for other conditions, particularly for other psychiatric disorders. SV has psychiatric, neurological, dermatological, immunological, metabolic, gastroenterological and hematological side effects. Hyponatremia is another serious side effect that has also been previously associated with the use of carbamazepine, clozapine, and selective serotonin reuptake inhibitors (SSRIs) (1). Although cases of hyponatremia associated with SV have also been reported, recurrent use-associated hyponatremia cases are rare (1, 2). We discussed the treatment process and the training process related to compliance with treatment of a male patient who had side effects of hyponatremia due to SV several times in different hospitals and times.

CASE PRESENTATION

The patient is single and unemployed a man born in 1979 who has suffered from BD type 1 since the age of 24. He was admitted to the emergency department with complaints of headache, muscle weakness, irritability, and confusion. He was using quetiapine 300 mg/day per oral (PO), risperidone 3 mg/day PO, and biperiden 2 mg/day PO for nine months for BD in our outpatient clinic, was using desmopressin 40 µgr/day intranasal (IN) with a diagnosis of central diabetes insipidus (CDI) since childhood, and two weeks ago, it was learned that SV was started and the dose was increased to 1500 mg/day PO. The patient's initial baseline laboratory data at the time of admission were sodium 111 mmol/L and potassium 3.9 mmol/L. Drug-induced hyponatremia was considered due to antipsychotic and mood stabilizer use. He was hospitalized with the diagnosis of drug-induced hyponatremia plus BD according to Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) (3). Previously prescribed drugs used by the patient at the effective dose and time were chlorpromazine, olanzapine, risperidone, quetiapine, biperiden, diazepam, lorazepam, alprazolam, lithium, carbamazepine, mirtazapine, fluoxetine, desmopressin, and a few psychotropic combinations, etc. According to the story taken from his parents, after treatment for decreased need for sleep, feeling overly happy, increased sexual desire with various psychotropic drugs had failed, he finally received SV in

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2016 firstly and had a severe hyponatremia with the sodium level of 109 mmol/L and stopped using the SV. The patient had been examined in another city two weeks ago. The family stated that SV could have been rewritten there and that they were not aware of this situation. The serum SV level at this time was 82.9 mg/L. The patient's thyroid and liver function tests were within normal limits. The fasting blood glucose, protein level, and lipid profile were within normal limits. Chest X-ray, electrocardiogram, renal ultrasonography gave normal results. The patient and relatives stated that there was no change in dietary and fluid intake in recent days. The patient had no drug use other than quetiapine, risperidone, biperiden, desmopressin. He had no systemic disease such as hypertension or diabetes mellitus. A history of smoking, alcohol and substance abuse was not available. His family history was unremarkable apart from diabetes mellitus type 2 in his father. The hyponatremia was attributed to SV or unsuitable use of desmopressin as there were no obvious underlying disorders to cause the hyponatremia and firstly SV was stopped. Hyponatremia ceased 6 days after his SV intake was stopped. Quetiapine 300 mg/day PO, risperidone 3 mg/day PO, and biperiden 2 mg/day PO and desmopressin 40 µgr/day IN continued to be used. No additional treatment was applied for adverse effects. Lamotrigine 12.5 mg/day PO was added to treatment and it was titrated up to 100 mg/day PO. The patients and their relatives were informed about the effects and possible side effects of the treatment. No similar side effects were reported during the follow-up of the patient. Psychiatric complaints decreased partially. The patient and his relatives were warned about hyponatremia due to SV use and informed consent was obtained from them for their knowledge. Naranjo Adverse Drug Reaction Probability Scale (NADRPS) score of the patient was 7 (4).

DISCUSSION

This case report was evaluated as a case of hyponatremia due to SV. Because there was a temporal relationship between them, the side effect began with the addition of the drug and completely cured after discontinuation of the drug. Other causes of hyponatremia, such as volume depletion, hypothyroidism, adrenal insufficiency, and diuretic abuse, and vomiting were excluded. On the other hand, the patient has a history of SV-induced hyponatremia. Our patient had a history of CDI and desmopressin use. If desmopressin had not been used, serum sodium would have been elevated (5). However, the serum sodium level was decreased in our patient. It was thought that desmopressin high dose use might cause this condition, but SV was initially discontinued due to the history of SV-induced hyponatremia. The NADRPS score indicates a probable association between drug use and side effect (4). The mechanism by which SV could cause hyponatremia and syndrome of inappropriate secretion of antidiuretic hormone (SIADH) has not been fully elucidated. However, it was speculated that dopaminergic, serotonergic and noradrenergic systems may play a role in SIADH due to SV (6). SIADH due to drugs can be caused by stimulation of the release of ADH by the hypophysis. SV can make hypothalamic osmoreceptors less sensitive, can enhance action of ADH on the kidney, can act directly the kidney, can inhibit the vasopressinase activity, resulting in prolonged vasopressin half-life (1).

Hyponatremia due to SV could be a dose-related side effect. Some authors suggest that this side effect occurs in toxic doses (1). However, the serum SV level of our patient was within normal limits. On the other hand, the reported cases are known to be advanced age patients. Our patient was 39 years old. The number of cases in which the NADPRS score is 7, ie, cases of hyponatremia due to recurrent SV use, is not much. There were no cases of SV-induced hyponatremia accompanied by conditions related to sodium balance such as CDI and desmopressin. Differential diagnosis was difficult because of desmopressin and CDI. We attributed this drug-induced hyponatremia to SV because of the patient's side effect history and the lack of fluid intake change. When hyponatremia occurs, the patient's general medical condition should be reassessed and other organic conditions that may cause hyponatremia should be excluded. Drug dose can be reduced or the drug can be changed (7, 8). In our patient, there was no need for them, and when the drug was stopped supportive treatment was started, the hyponatremia disappeared. World Health Organisation (WHO) defines 'probable' as an event or laboratory test abnormality, with a reasonable time relationship to drug intake (9). WHO also says this relationship cannot be explained by disease or other drugs, response to withdrawal clinically reasonable, rechallenge (not necessary) (9). Factors influencing patients with psychiatric disorder compliance with medication include patient-related influences, physician-related variables, factors related to the patient's environment, treatment-related factors, and side effects. The influence of side effects has been demonstrated in patient's noncompliance with treatment. Sometimes, despite the side effects, some patients continue to be exposed to the drug. The level of functioning of the relatives of the patients, psychiatric or medical diseases which they have should be taken into consideration (10). For these reasons, we have warned the patient and relatives about this side effect.

As a result, this case report suggests that physicians and relatives should be aware that sodium valproate may induce hyponatremia with a low quality of life and low compliance. Further systemic research should be conducted with respect to sodium valproate-associated hyponatremia to provide a greater understanding of both its prevalence and etiology.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

FINANCIAL DISCLOSURE

The authors declared that this study has received no financial support.

ETHICS

The patient's data was used to write this case report within the context of the institutional local ethics approval.

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