Case Report

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Quetiapine-Induced Syndrome of Inappropriate Antidiuretic Hormone Secretion: A Challenging Case

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ABSTRACT

Hyponatremia due to syndrome of inappropriate antidiuretic hormone secretion (SIADH) occurs as a rare but clinically important phenomena in various conditions including malignant neoplasms, infections, and central nervous system disorders, and as an adverse effect of numerous drugs. To the authors' knowledge, there are a few reports on SIADH associated with quetiapine in the literature. This case presents a 58-year-old woman receiving quetiapine for the treatment of bipolar disorder. The patient was hospitalized due to generalized tonic-colonic seizure. After checking her laboratory tests, she was found to be hyponatremic, and the treatment began accordingly. The situation was resolved after discontinuation of quetiapine therapy. Quetiapine was thought to be the cause for the patient's symptoms, and she was diagnosed with SIADH induced by this medication. Close monitoring of the sodium level is recommended in patients taking quetiapine.

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Introduction

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) accounts for approximately one-third of all cases of hyponatremia that is known as the most frequent electrolyte disorder. In order to diagnose SIADH, it is important to ascertain about the euvolemic

state of extracellular fluid volume, via both clinically and laboratory measurements (1). Electrolyte changes of SIADH includes hyponatremia, urinary osmolality of more than 100 mOsm/kg, urinary sodium concentration of more than 40 mmol/l, and plasma uric acid of less than 200 µmol/l (1).

IADH can be induced by various conditions, including malignant neoplasms, infections (especially pulmonary ones), central nervous system disorders, and a large number of medications (2).

Quetiapine, a second-generation antipsychotic (SGA), is widely used for various psychotic and mood disorders. SGAs share a high affinity for serotonin (5-HT2A), but a relatively low affinity for dopamine (D2) receptors. Compared with other SGAs, quetiapine has a further unique profile that is a high affinity for histamine (H1) (3, 4).

Prolonged QT interval and hematological effects have been also described as unusual adverse reactions of quetiapine use. Still, quetiapine-associated hyponatremia is generally uncommon, and only a few relevant reports are found in the literature (5-8).

Case Report

A 58-year-old woman patient presented to the emergency department with generalized tonic-colonic seizures. She was diagnosed with bipolar disorder about 20 years prior to this last admission. Up to 3 weeks prior to the initiation of quetiapine, she was taking trifluprazine (6 mg daily, orally) and sodium valproate (500 mg daily, orally) for 2 years. Due to bothersome extrapyramidal symptoms on trifluperazine, quetiapine (100 mg daily, orally) substituted trifluprazine, while sodium valproate remained at the same dose. Quetiapine dose was increased to 150 mg at night after a week. Three weeks after the initiation of quetiapine, patient had a seizure. Her medical history was unremarkable for any other chronic diseases or drug abuse.

The patient was normotensive (blood pressure: 130/85 mmHg). Physical examination did not reveal any abnormal findings. Peripheral edema was absent. Her main laboratory findings on admission were as follow. Serum sodium concentration was 109 mmol/l (normal range: 135-145 mmol/l), urine sodium concentration was measured as 72 mmol/l (normal range: < 20 mmol/l), and urine osmolality was 264 mOsm/kg. Renal, liver, and thyroid function tests as well as cortisol levels proved to be within the normal limits. Brain magnetic resonance imaging (MRI) was done, and showed no abnormality. According to these findings, the diagnosis of SIADH was established.

Because her hyponatremia resolved after the discontinuation of quetiapine, this medication was thought to be the culprit drug in this case. Then, the patient was decided to receive olanzapine instead quetiapine. Finally, her symptoms were controlled on olanzapine (5 mg daily, orally), and sodium valproate (500 mg daily, orally) without any complaints.

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent may be requested for review from the corresponding author.

Discussion

The exact pathophysiological background of drug-induced SIADH is still unclear. However, stimulation of ADH release and increase of ADH renal action are believed to be the most probable mechanisms. In most cases of drug-associated SIADH, patients have mild, asymptomatic hyponatremia (2). Even though several deaths related to hyponatremia induced by ecstasy (methylene dioxy methamphetamine or MDMA) have been reported in the literature (2).

The proposed mechanism by which a substance interferes with the normal secretion and action of ADH depends on that substance. Drugs that stimulate the release of ADH from the posterior pituitary gland include nicotine, phenothiazine, and tricyclic antidepressants (TCAs). Some drugs increase or potentiate the renal action of ADH. They include

desmopressin, oxytocin, and prostaglandin synthesis inhibitors. Drugs that cause SIADH by means of mixed or uncertain mechanism of action include chlorpropamide, carbamazepine, cyclophosphamide, and vincristine (9).

It is estimated that psychotropic drugs are administered to approximately 50% of institutionalized older patients (10).

A systematic review of reported cases was conducted to evaluate the relationship between hyponatremia and SIADH with the use of selective serotonin reuptake inhibitors (SSRIs), including fluoxetine, fluvoxamine, paroxetine, and sertraline. According to the study, fluoxetine is the SSRI most commonly reported to cause hyponatremia and therefore, SIADH. However, the mechanism of action responsible for SSRI-induced SIADH is not exactly known (11).

In this case, quetiapine was suspected to induce hyponatremia due to the recent prescription (3 weeks before) of this medication; but in Koufakis study, the situation happened after 3 months of prescription (7). Both cases were old woman patients. As sodium valproate may also induce hyponatremia (12, 13), this patient was taking this medication for more than 20 years without any particular complaint associated with it, and SIADH developed shortly after the initiation of quetiapine; so underlying causes and previous drugs should be considered before adding quetiapine in such patients.

Quetiapine-induced SIADH is extremely uncommon, as concluded from the few relevant reports found in the medical literature. Still, the exact prevalence of the above association is practically unknown. Moreover, the possibility of under diagnosis and underreporting of this condition cannot be excluded (5-8). In conclusion, clinicians should be aware of this rare, still important, adverse reaction of quetiapine. Close monitoring of the sodium level is recommended in patients taking quetiapine.

Conflict of Interests

Authors have no conflict of interests.

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