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Hyponatremia induced by stable high dose risperidone in bipolar disorder: A case report

Bipolar bozuklukta stabil yüksek doz risperidon sonrası oluşan hiponatremi: Bir olgu sunumu

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Abstract

Risperidone is a commonly prescribed atypical antipsychotic. Hyponatremia has been reported rarely as an adverse effect of risperidone. We report a case of a patient with bipolar affective disorder, who developed the syndrome of inappropriate antidiuretic hormone secretion, probably induced by high dose risperidone. A 60-year-old male with bipolar affective disorder, who was on risperidone 6 mg per day and sodium valproate 1200 mg per day, developed lethargy, unsteady gait, disorientation for the past 4 days followed by fever and productive cough with yellow sputum. Laboratory screening revealed that the serum sodium level was 117 mol/L, the urine sodium concentration was 106 mmol/L and plasma osmolarity was 260.57 mmol/Kg. A diagnosis of the syndrome of inappropriate antidiuretic hormone secretion was made. Risperidone was thought of as a precipitating agent and changed over to olanzapine resulting in improvement in hyponatremia. In this patient, high-dose risperidone treatment was the most probable cause, and the mechanisms may be related to risperidone's high affinity for the 5-hydroxytryptamine 2A and dopamine 2 receptors.

Keywords: risperidone, high-dose, syndrome of inappropriate antidiuretic hormone secretion, bipolar affective disorder

Öz

Risperidon genellikle kullanılan bir atipik antipsikotiktir. Hiponatremi nadiren risperidonun bir yan etkisi olarak bildirilmiştir. Bipolar affektif bozukluğu olan, uygunsuz antidiüretik hormon salınımı sendromu gelişen, muhtemelen yüksek doz risperidonun neden olduğu bir hastayı sunuyoruz. Bipolar duygulanım bozukluğu olan ve günde 6 mg risperidon ve günde 1200 mg sodyum valproat kullanan 60 yaşındaki bir erkek hastada letarji, dengesiz yürüme, son 4 gün boyunca yönelim bozukluğu, ardından ateş ve sarı balgamla karakterize öksürük gelişti. Laboratuvar taraması sonucunda serum sodyum seviyesi 117 mmol/L, idrar sodyum konsantrasyonu 106 mmol/L idi ve plazma ozmolaritesi 260.57 mmol/Kg olarak hesaplandı. Uygunsuz antidiüretik hormon salınımı sendromu olarak değerlendirildi. Risperidonun çökeltici bir madde olduğu düşünülmüş ve tedavisi olanzapine değiştirilerek hiponatremisi düzeltilmiştir. Bu hastada yüksek doz risperidon tedavisi en muhtemel neden olup, oluşum mekanizması risperidonun 5-hidroksitriptamin 2A ve dopamin 2 reseptörlerine yüksek afinitesi ile ilişkili olabilir.

Anahtar kelimeler: risperidon, yüksek doz, uygunsuz antidiüretik hormon salınımı sendromu, bipolar affektif bozukluk

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Introduction

Risperidone is a commonly prescribed atypical antipsychotic, with high affinity for the 5-hydroxytryptamine 2A (5-HT2A) and dopamine 2 (D2) receptors [1]. Common adverse effects of the drug are dizziness, akathisia, extrapyramidal symptoms, weight gain, and other autonomic adverse effects [2]. Hyponatraemia has been reported more with typical than with atypical antipsychotic agents, more often in schizophrenia than in other psychosis [3]. A literature search revealed two reports of risperidone-induced hyponatremia, and nine such cases have been reported at a Dutch pharmacovigilance centre [4-6]. Here, we report a case of hyponatremia induced by high stable dose of risperidone in a male with bipolar affective disorder.

Case report

A 60-year-old male with a diagnosis of bipolar affective disorder was brought by his family to medical emergency room. According to his family, the patient developed lethargy, unsteady gait, disorientation for the past 4 days followed by fever and productive cough with yellow sputum, and the patient was admitted. The patient's medication at the time of admission included risperidone 6 mg per day and sodium valproate 1200 mg per day. He had been in remission for the last two years on the current medications.

His physical examination revealed fever (101° F), tachycardia (108 beats/min), high blood pressure (150/100 mmHg), moderate dehydration as shown by dry skin and disorientation of time, place and person. Respiratory system examination showed crepitations in the right lower zone.

His blood investigations revealed serum sodium was 117 mmol/L (normal range 136-145 mmol/L), serum potassium was 4.68 mmol/L (normal range 3.6-5.2 mmol/L), urine sodium was 106 mmol/L, plasma osmolarity was 260.57 mmol/Kg, uric acid was 3.6 mg/dl (normal range 3-7 mg/dL) and total leucocyte count was 7800/mm3 (4500-11000/ mm3) with the dominance of the neutrophils as 71%. Hemoglobin, blood sugar, albumin, and liver and renal function tests were normal. Creatine kinase was 513 U/L on the third day. Chest X ray revealed features consistent with aspiration pneumonia. There was no evidence of excessive fluid intake or psychogenic polydipsia. The patient was diagnosed with the syndrome of inappropriate antidiuretic hormone secretion (SIADH) based on his clinical presentation and his blood work. He was treated with parenteral antibiotics (Lactagard 1000 mg/500mg Injection: Cefoperazone and Sulbactam, Ipca Laboratories Ltd, India) and oral fluid restriction. Considering physical condition of the patient, the antipsychotics drugs were reduced to a dose of 1000 mg/day for sodium valproate and 3 mg/day for risperidone. But hyponatremia and delirious symptoms persisted between the day 2 and day 4. Considering worsening of the physical symptoms, the antipsychotics were withheld for a day; they were restarted due to the precipitating manic symptoms. Though physical conditions were improved, manic symptoms and hyponatremia persisted. Risperidone was thought of as a precipitating agent and changed over to olanzapine resulting in improvement in manic symptoms and hyponatremia over the next 2 days. The patient was discharged on sodium valproate 1200 mg/day and olanzapine 7.5 mg/day. On subsequent two follow ups, he was maintaining well and his serum electrolyte estimation was within the normal range.

Written consent was taken from the patient.

Discussion

The patient's SIADH developed when receiving risperidone at high dose and resolved after the drug was discontinued. The causal relationship is also supported by the Naranjo Adverse Drug Reaction Probability Scale with a score of 4 on a 0- to 13-point scale, and it has been reported that high-dose risperidone is the possible cause of the SIADH [7].

The mechanism linking risperidone to SIADH remains unclear. It was postulated that by its antagonistic action at 5-HT2A and 5-HT7 receptors in the medial preoptic area/anterior hypothalamus, it can disinhibit antidiuretic hormone (ADH) secretion resulting in water reabsorption by aquaporins [8]. Long-term blockade of D2 receptors also can result in the hypersensitivity hypothalamic dopaminergic pathways involved in the regulation of water consumption and ADH release [9]. Furthermore, dopamine 2 blockers have been proposed as facilitators of ADH response and high dose treatment with risperidone can enhance this response [10]. As a result, high-dose risperidone might have triggered SIADH in our patient. Contrary to our report, risperidone have also been used in the treatment of psychogenic polydipsia with associated hyponatremia; however, their role is not clear as there are reports of both improving and causing polydipsia [11]. Though we found improvement in hyponatremia and manic symptoms in our case after shifting to olanzapine, there are reports of hyponatremia with olanzapine also. The only antipsychotic consistently found to have a beneficial effect on polydipsic behavior and development of hyponatremia is clozapine, may be due to its lower binding affinity to D2 receptors [12].

In conclusion, we suggest that, in patients with bipolar affective disorder, high doses of risperidone may cause SIADH. Therefore, we recommend that clinicians should regularly evaluate serum electrolyte levels to detect SIADH in suspected patients with bipolar affective disorder, just like they are advised to do in schizophrenia using high-dose risperidone treatment.

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