



# Syndrome of Inappropriate Secretion of Antidiuretic Hormone Due to Olanzapine Use

## Olanzapin Kullanımına Bağlı Gelişen Uygunsuz Antidiüretik Hormon Sendromu

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### ABSTRACT

Hyponatremia secondary to syndrome of inappropriate secretion of antidiuretic hormone (SIADH), which is characterized by the sustained release of antidiuretic hormone (ADH) from the posterior pituitary gland, is a less-known but life-threatening complication of treatment with antipsychotic medications. We report a patient who was using olanzapine due to the diagnosis of schizophrenia and presented with status epilepticus. The patient's medical history and biochemical blood and urine test results were suggestive of SIADH and revealed that hyponatremia was secondary to SIADH, induced by olanzapine use. The patient was treated successfully with olanzapine discontinuation, fluid restriction, and hypertonic/normal saline infusion. The possible adverse effects of olanzapine on sodium–water balance should always be kept in mind while prescribing it, and we suggest that clinicians should closely monitor electrolytes, particularly sodium, in patients on atypical antipsychotic medications such as olanzapine.

**Keywords:** Olanzapine, hyponatremia, syndrome of inappropriate secretion of antidiuretic hormone, antipsychotic medications, schizophrenia

### ÖZ

Posterior hipofizden antidiüretik hormonun (ADH) sürekli salınımı ile karakterize uygunsuz ADH sendromu sonucu gelişen hiponatremi, antipsikotik ilaç tedavisinin az bilinen ama yaşamı tehdit eden bir komplikasyonudur. Bu makalede status epilepticus tablosunda başvuran, şizofreni tanısı ile olanzapin kullanan hastayı sunduk. Hastanın uygunsuz ADH sendromunu işaret eden medikal öyküsü, biyokimyasal kan ve idrar sonuçları, hiponatreminin olanzapin kullanımına bağlı gelişen uygunsuz ADH sendromundan kaynaklandığını ortaya koymuştur. Hasta, olanzapininin kesilmesi, sıvı kısıtlaması ve hipertonic/normal salin replasmanı ile başarıyla tedavi edilmiştir. Olanzapin tedavisi planlandığında, su-sodyum dengesi üzerine olası etkilerinin akılda tutulmasının, olanzapin gibi atipik antipsikotik ilaç kullanan hastaların başta sodyum olmak üzere elektrolitlerinin yakından takip edilmesinin önemini tekrar vurgulamak isteriz.

**Anahtar Kelimeler:** Olanzapin, hiponatremi, uygunsuz antidiüretik hormon sendromu, antipsikotik ajanlar, şizofreni

### INTRODUCTION

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is characterized by the sustained release of antidiuretic hormone (ADH) in the absence of either osmotic or non-osmotic stimuli or by enhanced renal action of ADH. It is characterized by dilutional hyponatremia (<135 mmol/l), increased urine sodium levels (>20 mmol/l), inappropriately elevated urine osmolality (>100 mOsm/kg) relative to plasma osmolality (<280 mOsm/kg), and expanded extracellular volume in euvoletic patients taking no diuretics, with normal cardiac, hepatic, renal, adrenal, and thyroid functions. SIADH can be induced by various conditions, including malignancies (carcinomas: bronchogenic, pancreatic, prostatic, thymoma, lymphoma, mesothelioma), pulmonary diseases (asthma, pneumonia, tuberculosis, empyema), central nervous system disorders (meningitidis, encephalitis, cerebrovascular accidents, subarachnoidal hemorrhage, head trauma), and numerous drugs (vasopressin, desmopressin, oxytocin, antidepressants, antipsychotics, carbamazepine) (1).

Olanzapine is an atypical antipsychotic agent indicated for the first-line treatment of schizophrenia and moderate-to-severe

manic episodes in bipolar disorder. In psychiatric patients on antipsychotic medications in whom psychogenic polydipsia is excluded, hyponatremia, a life-threatening complication, occurs secondary to SIADH. Similar to other antipsychotics such as chlorpromazine, amisulpride, fluphenazine, haloperidol, trifluoperazine, risperidone, and clozapine, olanzapine causes hyponatremia by stimulating inappropriate release of ADH. In a systemic review by Meulendijks et al. (2) it was concluded that antipsychotic drug-induced hyponatremia does not seem to be dose dependent or associated with age or gender (3-5). We report a patient presenting with life-threatening severe hyponatremia caused by SIADH, induced by olanzapine treatment; this has been rarely observed in the literature, with only a few relevant reports.

### CASE PRESENTATION

A 49-year-old female using 40 mg olanzapine daily for the past 6 years due to the diagnosis of chronic schizophrenia was brought to the emergency room in a postictal confusional state following a witnessed episode of generalized tonic-clonic seizure and vomiting. There were no other chronic diseases, malignancies,

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concomitant medications, or compulsive drinking in her medical history. Shortly after admission, she had respiratory arrest, and she was therefore intubated and transferred to the intensive care unit (ICU).

Her hemodynamic parameters and oxygenation was found to be normal. No peripheral edema or hypovolemia findings such as tachycardia, postural blood pressure changes, dry mucous membranes, or poor skin turgor were observed. Her physical examination was unremarkable, with normal electrocardiography and echocardiography findings. Her cranial and abdominal CT scans did not reveal any abnormal findings; however, infiltration was observed in the right lung, suggesting the need for aspiration on chest CT scan. Her temperature was 36.4°C, and total blood count, renal functions, liver enzymes, and thyroid hormone levels were within the normal limits. Laboratory testings revealed the following: hyponatremia (Na: 114 mmol/l) with K: 3,48 mmol/l, Cl: 82 mmol/l, Ca: 82 mmol/l, serum osmolality: 238 mOsm/kg, urinary Na: 51 mmol/l, urinary osmolality: 274 mOsm/kg, and urine density: 1010. Seizures were attributed to severe hyponatremia, and the patient's medical history and all the clinical and laboratory findings mentioned above revealed that hyponatremia was secondary to SIADH, induced by olanzapine use.

Discontinuation of olanzapine, restriction of fluid intake, and treatment with hypertonic/normal saline resulted in the resolution of hyponatremia (6 h: 122 mmol/l, 12 h: 125 mmol/l, 24 h: 129 mmol/l, 36 h: 138 mmol/l). In addition, antibiotherapy for suspicious aspiration pneumonia was initiated shortly after the admission to the ICU. She was extubated on day 2, with completely normal neurological examination. She did not experience any further convulsions. Along with oral antibiotherapy and psychiatric suggestions, including follow-up visits, she was discharged at the end of day 4 with approval for the use of her results in this case report.

## DISCUSSION

Hyponatremia is a more frequent dangerous adverse reaction of olanzapine treatment than thought previously. In the World Health Organization (WHO) global individual case safety report database system, olanzapine was the second most common antipsychotic associated with hyponatremia after risperidone (6).

Animal studies have suggested that the inhibitory effect of dopamine (D<sub>2</sub>) on the release of ADH is blocked by D<sub>2</sub> receptor antagonists such as haloperidol and domperidone, and it has also been shown that ADH response to a hypertonic stimulus is potentiated by D<sub>2</sub> antagonists. Because olanzapine is a selective monoaminergic antagonist with high binding affinity to D<sub>2</sub>, serotonin, muscarine, histamine, and adrenergic receptors, it causes SIADH by its antagonism to D<sub>2</sub> receptors (7, 8).

While consulting a psychiatric patient with hyponatremia symptoms, it is important to rule out psychogenic polydipsia, a clinical disorder that occurs in 6% to 20% of psychiatric patients and is characterized by hyponatremia, polydipsia, and polyuria, in differential diagnosis. The key differences are low urinary osmolality (<100 mOsm/kg) and low urinary sodium levels (10 mEq/L) in patients with psychogenic polydipsia who also have a history of excessive water consumption. Cerebral salt wasting (CSW), which

has similar laboratory and clinical findings as SIADH, is also an important diagnosis to consider in hyponatremic patients. It presents as low serum osmolality, high urine osmolality, and a high urine sodium level, similar to SIADH, but with a fundamental difference: hypovolemic hyponatremia. High levels of natriuretic peptides and fractional excretion of uric acid may also help differentiate between CSW and SIAH, although the key difference is the volume status of the patient. In this case, euvoletic hyponatremia with high urinary osmolality and urinary sodium levels but low serum osmolality revealed that hyponatremia was secondary to SIADH, induced by olanzapine use.

## CONCLUSION

The possible adverse effects of olanzapine on sodium–water balance should always be kept in mind while prescribing it, and we suggest that clinicians should closely monitor electrolytes, particularly sodium, in patients on atypical antipsychotic medications such as olanzapine. Patients and their family members should be informed about hyponatremia symptoms, and emphasis should also be laid on the importance of the early identification of hyponatremia.

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