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Letter to the Editor

Hyponatremia secondary to SIADH in a schizophrenic patient treated with Quetiapine

1. Introduction

The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is defined as hypotonic hyponatremia, inappropriately elevated urine osmolality relative to plasma osmolality, elevated urine sodium level, expanded extracellular volume, and normal renal, adrenal, and thyroid function (Bartter and Schwartz, 1967). SIADH can be induced by various conditions, including malignant neoplasms, infections (especially pulmonary ones), central nervous system disorders, and numerous drugs (Ramos-Levi et al., 2014). Hyponatremia secondary to SIADH is an uncommon complication of treatment with centrally acting drugs like antipsychotic medications. A recent case control study from the Netherlands described 912 cases of hyponatremia secondary to antipsychotics with reported odds ratio for association between antipsychotic and hyponatremia to be 1.58 (95% CI, 1.46–1.70) (Mannesse et al., 2010).

Quetiapine is an atypical antipsychotic agent, widely used for the treatment of variety of psychiatric conditions and the use of this agent is increasing in the last few years. Frequently reported side effects of this drug include dizziness, dry mouth, nausea, constipation, lethargy, and increased appetite. Prolonged QT interval andhaematological effects are unusual adverse reactions of quetiapine use (Nielsen et al., 2015). Quetiapine-associated hyponatremia is extremely uncommon adverse reactions and only a few reports are available in the literature (Koufakis, 2016). Here, we report a schizophrenic patient who developed hyponatremia after treatment with quetiapine.

2. Case report

A 60-year-old male patient presented to the psychiatrydepartment with exacerbation of schizophrenia after stopping the antipsychotic risperidone for the last 3 months.He had been diagnosed with schizophrenia at the age of 30 years. After admission he was started on quetiapine, the dose of which gradually increased to 800mgper day over a period of two weeks. Third week patient suddenly became lethargic,disoriented to time, place and person, insomniac,severe tiredness, inability to walk and difficulty in breathing. Immediately he was shifted to ICU for further management. He denied consumption of any other drug, dry mouth, and present or past history of excessive water drinking. Other than schizophrenia, his medical history was unremarkable for chronic diseases.

His blood pressure was 130/80 mmHg. Physical examination did not reveal any abnormality. There was no peripheral oedema. Main laboratory findings at the time of shifting to ICU were as follows: serum sodium concentration 106 mmol/L (135–145 mmol/L), serum osmolarity 240 mOsm/L (275–295 mOsm/L), urine sodium concentration 70 mmol/L (< 20 mmol/L), and urine osmolality 260 mOsm/kg. Renal, liver, and thyroid function tests as well as cortisol levels were within the normal limits.In view of these findings, the diagnosis of SIADH was established, according to the criteria described by Bartter and Schwartz (1967). A complete diagnostic workup was performedin the ICU, including thorough laboratory testing, ECG, imaging of brain, chest, and abdomen and gastrointestinal endoscopyto exclude other factors as the potential causes of the syndrome, such as malignancies, infections, and stroke.

His problems werebeing attributed to severe hyponatremia and managed accordingly. Initial management of the patient at the ICU included stopping the offending drug, supportive care, artificial ventilation and intravenous infusion of 150 mL of 3% hypertonic saline solution. After repeating the same procedure three times over a period of three days, serum sodium concentration raised to 120 mmol/L. Subsequently, fluids limitation (500 mL 0.9% saline daily) resulted in the restoration of serum sodium concentration and plasma osmolarity to the normal levels, within the next four days (138 mmol/L and 285 mOsm/L, resp.). Fifth day after admission in ICU,risperidone was restarted due to emergence of psychotic symptoms. Seventh day patient was discharged and in his follow-up visits, his physical and psychiatric status was normal and his blood tests were all within the normal range.

3. Discussion

Quetiapine-induced hyponatremia secondary to SIADH is extremely uncommon adverse eventreported in medical literature (Koufakis, 2016). The exact prevalence of the above association is unknown. Moreover, the possibility of under diagnosis and underreporting of this condition cannot be excluded. In most cases of SIADH associated with drugs, patients have mild, asymptomatic hyponatremia (Ramos-Levi et al., 2014), which is usually go undetected unless blood tests are ordered for some other reason. However, several deaths related to hyponatremia induced by MDMA, cyclophosphamide and carbamazepine have been reported (Fenske and Allolio, 2010). In the reported case, the patient's life was endangered due to dyspnoea triggered by severe hyponatremia.

The exact pathophysiological basis of drug-induced SIADH is still unclear. The stimulation of ADH release and augmentation of ADH action on kidney are believed to be the most probable mechanisms for drug induced hyponatremia.Management of drug-induced hyponatremia secondary to SIADH demandsimmediate discontinuation of the offending agent. In cases of severe hyponatremia, additional actions such as fluid restriction and furosemide administration should be taken (Ramos-Levi et al., 2014). Agents causing nephrogenic diabetes insipidus, such as demeclocycline and lithium carbonate, have been also used for the treatment of the syndrome.

In our case, initial approach was treating the patient with prompt infusion of hypertonic 3% saline solution, due to very low serum sodium levels and severe life endangering situation (delirium and dyspnoea). After a 6 mmol/L increase of serum sodium concentration and stabilization of patient's condition, we continued with a diagnosis-specific, more conservative approach regarding the correction of sodium levels. It is reported that

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symptomatic patients with severe hyponatremia should be treated aggressively to reduce cerebral edema and avoid herniation. However, rapid correction of serum sodium can result in central pontinemyelinolysis and severe, irreversible neurological complications, such as spastic quadriparesis. Patients with chronic hyponatremia are at greater risk from rapid sodium correction, when compared with those with recently (< 48 h) established hyponatremia (Spasovski et al., 2014).

A common cause of hyponatremia in schizophrenic patients is psychogenic polydipsia. Its distinction from SIADH should be based on history of excessive water consumption and opposite results of laboratory tests, such as urine osmolality and urine sodium levels (Dundas et al., 2007). In conclusion, psychiatrists should be aware of this rare, still severe adverse reaction of quetiapine. This case underlines the fact that patients on antipsychotic medication and more specifically on quetiapine should be closely monitored and routinely tested for electrolyte disorders.

References

Bartter, F.C., Schwartz, W.B., 1967. The syndrome of inappropriate secretion of antidiuretic hormone. Am. J. Med. 42 (5), 790–806.
Dundas, B., Harris, M., Narasimhan, M., 2007. Psychogenic polydipsia review: etiology, differential, and treatment. Curr. Psychiatry Rep. 9 (3), 236–241.
Fenske, W., Allolio, B., 2010. The syndrome of inappropriate secretion of antidiuretic hormone: diagnostic and therapeutic advances. Horm. Metab. Res. 42 (10), 691–702.
Koufakis, T., 2016. Quetiapine-induced syndrome of inappropriate secretion of antidiuretic hormone. Case Rep. Psychiatry 2016, 4803132 3 pages.
Mannesse, C.K., van Puijenbroek, E.P., Jansen, P.A., et al., 2010. Hyponatremia as an adverse drug reaction of antipsychotic drugs. Drug Saf. 33 (7), 569–578.
Nielsen, J., Matz, J., Mittoux, A., et al., 2015. Cardiac effects of sertindole and quetiapine: analysis of ECGs from a randomized double-blind study in patients with schizophrenia. Eur. Neuropsychopharmacol. 25 (3), 303–311.
Ramos-Levi, A.M., Duran Rodriguez-Hervada, A., Mendez-Bailon, M., Marco-Martinez, J., 2014. Drug-induced hyponatremia: an updated review. Miner. Endocrinol. 39 (1), 1–12.
Spasovski, G., Vanholder, R., Allolio, B., et al., 2014. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Nephrol. Dialys. Transpl. 29 (2), i1–i39.

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