 Syndrome of Inappropriate Antidiuretic Hormone Secretion Associated with Pramipexole in a Patient with Parkinson’s Disease

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The syndrome of inappropriate antidiuretic hormone secretion (SIADH) can be caused by a variety of drugs. Dopaminergic drugs might enhance the secretion of the antidiuretic hormone arginine vasopressin by reducing γ-amino butyric acid release through the dopaminergic receptor in supraoptic nucleus. A 75-year-old woman with Parkinson’s disease developed asthenia, delirium, aggravated parkinsonian symptoms, and hyponatremia along with the diagnostic criteria for SIADH during dose escalation of pramipexole. After pramipexole withdrawal, these symptoms disappeared, and sodium levels returned to normal values. The serum sodium levels of patients receiving pramipexole should be monitored, especially during dose escalation.

Key Words: Pramipexole, SIADH, Hyponatremia.

A 75-year-old woman visited our neurology outpatient clinic because of feeling of leg weakness. She had chronic obstructive pulmonary disease and diabetes mellitus that was well controlled with 2 mg glimepiride. Upon neurological examination, she had a masked face, bradykinesia, a stooped posture, and limb rigidity that was more severe on the right side; she was diagnosed with Parkinson’s disease. The medication taken by this patient was summarized in Figure 1. Her treatment started with 100 mg amantadine and 0.375 mg pramipexole per day, and her clinical symptoms slightly improved. After two weeks, the dosage of pramipexole was increased to 0.75 mg per day, and 0.375 mg alprazolam and 100 mg aspirin per day were added because of anxiety and mild white matter changes on T2-weighted magnetic resonance images of the brain. After ten weeks, the dosage of pramipexole was increased to 1.125 mg per day.
per day, and levodopa/carbidopa/entacapone at 150/37.5/600 mg (Stalevo 50 tid) per day was added to treat postural instability and increased rigidity. After three additional weeks, she was admitted to our hospital because of asthenia, frequent falling, more aggravated rigidity, and dysarthria. Biochemical studies showed a serum sodium level of 128 mEq/L, a serum potassium level of 4.7 mEq/L, a serum chloride level of 94 mEq/L, a serum urea level of 23.1 mg/dL, and a serum creatinine level of 0.84 mg/dL. On the third day in the hospital, 50 mg sertraline was added. On the fourth day in the hospital, Stalevo was switched to carbidopa/levodopa at 37.5 mg/375 mg per day, and domperidone 30 mg per day was added. On the fifth day in the hospital, 25 mg quetiapine was added because of delirium. On the sixth day in the hospital, sertraline was switched to 10 mg escitalopram, and biochemical studies showed a serum sodium level of 115 mEq/L, a serum potassium level of 4.6 mEq/L, a serum chloride level of 83 mEq/L, a serum osmolarity of 247 mOsm/kg, a urine osmolarity of 311 mOsm/kg, a urine sodium level of 56 mEq/L, a urine potassium level of 21.7 mEq/L, and a urine chloride level of 51 mEq/L. A thyroid function test was normal. She did not have any clinical evidence of adrenal insufficiency. She also did not have any hypervolemic features, such as subcutaneous edema, or any hypovolemic features, such as orthostatic hypotension, increased pulse rate, or dry mucous membranes. She did not have weight loss or any clinical symptoms that were related to malignancy. The serum levels of alpha-fetoprotein, cancer antigen-125, carbohydrate antigen 19-9, and beta-human chorionic gonadotropin were in normal range. She was diagnosed with SIADH possibly induced by a drug. The clinical symptoms and the serum sodium levels improved after stopping pramipexole. On the 19th day in the hospital, which was also the day of discharge, her medication consisted of 100 mg amantadine, carbidopa/levodopa at 225 mg/1,125 mg, 30 mg domperidone, 80 mg propranolol, 25 mg quetiapine, 5 mg donepezil, 10 mg escitalopram, 2 mg glimepiride, 0.125 mg clonazepam, 0.375 mg alprazolam, 100 mg aspirin, 10 mg amloidipine, 100 mg losartan, and 2 mg warfarin per day because of deep vein thrombosis, and biochemical studies showed a serum sodium level of 135 mEq/L, a serum potassium level of 4.6 mEq/L, and a serum chloride level of 101 mEq/L. Two weeks after discharge, amloidipine and losartan were stopped because of low blood pressure. On the 27th days after discharge, biochemical studies showed a serum sodium level of 135 mEq/L, a serum potassium level of 3.3 mEq/L, and a serum chloride level of 102 mEq/L.

**Discussion**

Our patient developed SIADH 21 days after increasing the dosage of pramipexole, and SIADH disappeared after pramipexole withdrawal. The temporal relationship between the development/disappearance of SIADH and the pramipexole dosage suggests a possible cause-effect relationship between pramipexole and SIADH.

The development of SIADH associated with amantadine has been rarely reported.4,5 Although our patient continued to take amantadine, SIADH disappeared after pramipexole withdrawal. Therefore, SIADH was associated with pramipexole in our patient. SSRIs can also induce SIADH.6 Our patient took sertraline after the development of hyponatremia, and ser-

| Drug            | Admission | Discharge |
|-----------------|-----------|-----------|
| Pramipexole     | 0.375 mg  | 1.125 mg  |
| Amantadine 100 mg | 0.75 mg   |           |
| Glimepiride 2 mg |           |           |
| Aspirin 100 mg  |           |           |
| Alprazolam 0.375 mg |        |           |
| Stalevo 150 (50 tid) |       |           |
| Sertraline 50 mg |           |           |
| Escitalopram 10 mg |          |           |
| Carbidopa/levodopa |          |           |
| Domperidone 30 mg |          |           |
| Quetiapine 25 mg |           |           |
| Propranolol 80 mg |           |           |
| Donepezil 5 mg  |           |           |
| Clonazepam 0.125 mg |        |           |
| Warfarin 2 mg   |           |           |
| Amlodipine 10 mg |           |           |
| Losartan 100 mg |           |           |
| Serum Electrolyte (mEq/L) | Na 128 K 4.7 CI 94 | Na 115 K 4.6 CI 83 | Na 135 K 3.3 CI 101 | Na 135 K 3.3 CI 102 |

**Figure 1.** Overview of medication taken by this patient. The dosages are the amount taken daily. The gray-colored columns mean the durations of taking drugs.
In one case, SIADH developed during first two weeks of pramipexole therapy,\textsuperscript{10} and in the other case, SIADH developed during dose escalation of pramipexole,\textsuperscript{7} as with our patient. Pramipexole might facilitate AVP secretion in some patients, which is a prerequisite for developing SIADH. The serum sodium levels of patients receiving pramipexole should be monitored, especially in the first few weeks after starting therapy and during dose escalation.

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