Antidepressant Induced Hyponatremia: Does It Increase The Risk of Neuroleptic Malignant Syndrome in Elderly Patient?

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ABS TRACT:
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INTRODUCTION

Neuroleptic malignant syndrome (NMS) is a rare, life-threatening idiosyncratic reaction secondary to antipsychotic medication. NMS is characterized by muscular rigidity, fever, autonomic instability, and an altered level of consciousness and it is usually accompanied by rhabdomyolysis. This syndrome is supposed to result from an excessively rapid blockade of postsynaptic dopamine receptors (1,2). Although the primary etiological factor is the initiation or elevation in the dose of antidopaminergic agents, there have been reports, albeit rarely, that NMS can be caused by the use of selective serotonin reuptake inhibitors (SSRIs), venlafaxine, and lithium (3).

It is well known that severe hyponatremia can cause neurologic complications such as stupor, seizures, and even coma. Hyponatremia frequently develops in elderly patients and also psychiatric patients. Hyponatremia associated with neuroleptic malignant syndrome has been described as a syndrome of inappropriate secretion of antidiuretic hormone (4).

We have reported an elder patient with recurrent depression taking venlafaxine and olanzapine therapy who developed overt NMS following the hyponatremia.

CASE

A 62-year-old man was admitted to the Emergency Department of a State Hospital due to symptoms including changes in mental status, nausea-vomiting, fever and loss in eating function. Patient’s hyponatremia (serum Na 121 mEq/l) was determined and treated in the hospital. However, the symptoms started again immediately after...
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patient discharge and gradually intensified. Progressively, he had lethargy. He was admitted to our hospital because of unconsciousness, fever, marked muscle rigidity and motor immobility.

His past psychiatric history revealed that he was diagnosed as recurrent depression (according to SCID-I) 6 years ago. He was regularly given oral venlafaxine 150 mg daily and oral olanzapine 2.5 mg daily. He received 10 mg daily olanzapine due to insomnia with his own decision five days before admission.

At admission, his body temperature was 36.7ºC, the blood pressure was 160/95 mm Hg. The pulse was 88 per minute, and respiration rate was 18 per minute. He was extremely rigid and unresponsive. The blood pressure subsequently fell to 80/50 mm Hg. On admission laboratory investigations revealed: hemoglobin 14.6 g/dl, total leukocytes count 10.77 K/µL with 80% polymorphs, serum Na 140 mEq/l, K 3.8 mEq/l, urea 60 mg/dl, creatinine 0.7 mg/dl, random blood glucose 130 mg/dl. Serum muscle enzymes were markedly elevated: creatinine phosphokinase (CPK) 431 u/L (normal up to 200), creatine kinase myocardial muscle (CK-MM) 3.96 ng/ml (normal up to 5), LDH 236 u/L (125–243), aspartate transaminase 59 u/L, alanine transaminase 52 u/L. Urinary analysis showed moderate blood with dipstick, on microscopic examination there were ++ erythrocytes, in urine was +++ protein. We did not detect any food poisoning or any findings consistent with a gastrointestinal infection in this patient or his relatives. There was not psychogenic polydipsia history in our patient.

Antipsychotic drugs were withdrawn after admission and bromocryptine 7.5 mg daily was initiated.

Ten days later, the patients’ muscle rigidity and other symptoms had resolved, and serum CPK level was normalized (37 u/L). The treatment of bromocryptine was gradually stopped. The patient was discharged on the 19th day after admission.

DISCUSSION

We presented a case of neuroleptic malignant syndrome secondary to antipsychotic dose escalation by hyponatremia. The development of hyponatremia has facilitated because of the patient is elderly and use of venlafaxine.

Older age appears to be the major risk factor for SSRIs; incidences were found to be markedly increased in elderly patients, especially with concomitant use of other hyponatremia-eliciting drugs such as (thiazide) diuretics, ACE inhibitors, or laxatives (5). Apparently, this risk of hyponatremia with another medication is not limited to the elderly. In a study, it found the combinations of SSRI or venlafaxine with ACE inhibitors or diuretics to result in about ten fold higher incidences compared with SSRI/SNRI alone (6). However, our patient did not use any antihypertensive medication or other.

It was known that patients with psychiatric disorders such as psychosis and depression have a propensity to develop hyponatremia (7). Psychogenic drugs such as haloperidol, fluphenazine and thioridazine cause hyponatremia by unknown mechanisms. The increasing use of serotonergic agents as adjunctive treatments in schizophrenia highlights the importance of exploring this issue further. It is conceivable that stimulation of 5-hydroxytryptamine (5HT2A) receptors exaggerates the down-regulation of dopaminergic activity already promoted by the antipsychotic agent, thereby potentially enhancing the risk of NMS (8). SSRIs appear to have the potential for antidepressant-associated hyponatremia in elderly patients (9). In a prospective study, the incidence of hyponatremia was 17.2% in patients aged >65 years with venlafaxine therapy (10). This patient has been used venlafaxine and low dose olanzapine last six years. NMS might develop after increase the dose of olanzapine in this patient.

In our case, symptoms of hyponatremia included nausea and disorientation, which seemed to be relatively modest. However, his serum sodium level was 121 mEq/L which could lead to severe symptoms. Appropriate treatments were conducted at an early stage, but patient might have developed NMS after hyponatremia treatment. Perhaps, SNRI and antipsychotic medication may have triggered NMS in this case. Dehydration is another risk factor for NMS. However, this patient had hyponatremia rather than dehydration.

In conclusion, this report shows that NMS may occur following antidepressant-induced hyponatremia; therefore the combination of antipsychotic and antidepressant needed to be used with caution in patients with depression. The changes in metabolism in an elderly patient with depression may lead to life-threatening problems. Clinicians should inform their patients about the use of drugs, drug dose, and side effects.
References:


