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【 LETTERS TO THE EDITOR 】

Duloxetine-induced Hyponatremia Can Occur in Not Only Syndrome of Inappropriate Secretion of Antidiuretic Hormone but Also Cerebral Salt Wasting Syndrome

Key words: syndrome of inappropriate secretion of antidiuretic hormone (SIADH), cerebral salt wasting syndrome (CSWS), hyponatremia

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To the Editor I read with great interest the case report of duloxetine-induced hyponatremia by Hamada et al. (1). They diagnosed this case as one of syndrome of inappropriate secretion of antidiuretic hormone (SIADH), but I feel that the possibility of cerebral salt wasting syndrome (CSWS) should also be considered. The test results for SIADH and CSWS are very similar. It is almost impossible to distinguish between the two based on laboratory data alone. The authors found that initial treatment with intravenous fluids improved the symptoms. This is important in differentiating between SIADH and CSWS. In CSWS, hyponatremia is caused by increased sodium excretion due to increased secretion of brain natriuretic peptide and decreased sodium reabsorption from the proximal tubules due to decreased sympathetic stimulation of the glomerular apparatus. Thus, in CSWS, ADH secretion is increased secondary to a decrease in fluid in the body.

One way to distinguish between these two entities is by injecting saline and seeing how the hyponatremia responds. In CSWS, hyponatremia is ameliorated by intravenous infusion of isotonic solutions. In contrast, in SIADH, intravenous infusion may worsen hyponatremia, but hyponatremia is improved by fluid restriction. Thus, the case of Hamada et al. is not a typical one of SIADH, but instead seems to have elements of CSWS.

Of course, hyponatremia in the super-elderly is life-threatening, so the warning in this case report is valuable. Even the super-elderly can develop SIADH, and I reported on a 92-year-old woman who developed SIADH after having the flu (2). My patient improved with hypertonic saline followed by water restriction.

Finally, I would like to speculate on the mechanism by which duloxetine induces hyponatremia in the case of Hamada et al. Duloxetine is a high-risk drug that can cause falls in the elderly. Syncope and orthostatic hypotension can occur at any time during treatment. Duloxetine does not pharmacologically cause CSWS, but even minor falls can cause CSWS in the elderly. For example, I experienced a patient with severe hyponatremia after a simple fall that met the diagnostic criteria for SIADH, but was ultimately diagnosed as CSWS (3). Since there is no mention of a fall in the case of Hamada et al., the above is only speculation. Duloxetine is being prescribed increasingly frequently by many doctors who are not familiar with psychopharmacology, as it is indicated for the management of chronic musculoskeletal pain (4). When used in the elderly, it is recommended that electrolytes be measured at regular intervals.

The author states that he has no Conflict of Interest (COI).

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References

1. Hamada T, Matsuki K, Kondou S, Furukawa S, Onji M. Duloxetine-induced syndrome of inappropriate secretion of antidiuretic hormone in a super-elderly patient. Intern Med **61**: 1099-1103, 2022.
2. Nagamine T. Influenza as a cause of SIADH related hyponatremia. J Clin Diagn Res **13**: OL02, 2019.
3. Nagamine T. Minor head injury might cause cognitive impairment due to severe hyponatremia. Innov Clin Neurosci **18**: 47-48, 2021.
4. Nagamine T. Responsibility of the doctor who prescribes serotonin and noradrenaline reuptake inhibitor (SNRI) for patients with chronic musculoskeletal pain. Psychiatry Clin Neurosci **72**: 45-46, 2018.

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