Vaptans Are Effective in Treating Hyponatremia in Psychotic Patients: But We Need Treatment Guidelines

To the Editors: Bhardwaj et al[1] recently published a letter to the editor in *The Primary Care Companion for CNS Disorders* focusing on the use of selective vasopressin V_2-receptor antagonists (vaptans) in the treatment of hyponatremia induced by polydipsia. The authors are to be commended for focusing on the problem of hyponatremia in psychotic populations, a condition that is often overlooked and undertreated. They are to be further commended for drawing attention to the vaptans, a new class of therapeutics that effectively treats hyponatremia in a rapid and predictable manner. In the past, treatment options for hyponatremia in this population were suboptimal, but, now, 2 of the vaptans (conivaptan and tolvaptan) are approved by the US Food and Drug Administration and available, which puts clinicians in a much better position to effectively treat this condition. However, one minor correction needs to be made. The authors state that vaptans act by antagonizing both vasopressin 1A and 2 receptors, but this is not entirely correct. For example, both tolvaptan and lixivaptan are selective vasopressin V_2-receptor antagonists. It is a minor point, but it has a bearing on possible side effects. This issue aside, the authors have highlighted an important new treatment option for hyponatremia.

However, we think a cautionary note is necessary. In their letter, Bhardwaj et al[1] correctly state that "fluid restriction is the established method of treating hyponatremia in psychogenic polydipsia." The authors then go on to suggest that "a vaptan should be selected when aquaresis without electrolyte loss is urgently indicated to treat clinically compromising hyponatremia." Despite the attractiveness of using a pure aquaretic agent to correct polydipsia-induced hyponatremia, several issues need careful consideration. First, treatment response to vaptans is brisk and robust in psychotic patients.[2] In our experience, with very few exceptions, abnormal serum Na+ was corrected within 24 hours using the lowest available dose. Next, it has been our experience,[3] and that of others,[4] that polydipsia in psychotic individuals is usually diurnal in nature, resulting in marked variation in serum Na+ over the course of the day. A patient can have a normal serum Na+ in the morning with a markedly abnormal serum Na+ in the afternoon or evening. This is the result of patients drinking excessively throughout the day, which, over time, causes dilutional hyponatremia. But, most of these polydipsic patients self-correct serum Na+ during the night via a water diuresis. Therefore, adding a potent aquaretic agent poses the risk of inducing a rapid overcorrection, possibly leading to the development of osmotic demyelination. Treatment of polydipsia-induced hyponatremia with a vaptan rather than with the established method of fluid restriction requires very careful consideration.[5] There is no question that vaptans are effective for treating hyponatremia, but treatment guidelines regarding "when" and "how" to use them in this population have yet to be developed.

REFERENCES

1. Bhardwaj SB, Motiwala FB, Morais M. Vaptans for hyponatremia induced by psychogenic polydipsia. *Prim Care Companion CNS Disord* 2013; 15(1):
2. Josiassen RC, Goldman M, Jessani M, et al. Double-blind, placebo-controlled, multicenter trial of a vasopressin V2-receptor antagonist in patients with schizophrenia and hyponatremia. *Biol Psychiatry*. 2008;64(12):1097–1100.
3. de Leon J, Verghese C, Tracy JI, et al. Polydipsia and water intoxication in psychiatric patients: a review of the epidemiological literature. *Biol Psychiatry*. 1994;35(6):408–419.
4. Vieweg WV, Robertson GL, Godleski LS, et al. Diurnal variation in water homeostasis among schizophrenic patients subject to water intoxication. *Schizophr Res*. 1988;1(5):351–357.
5. Verbalis JG, Goldsmith SR, Greenberg A, et al. Hyponatremia Treatment Guidelines 2007: expert panel recommendations. *Am J Med*. 2007; 120(11 suppl 1):1–21.

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