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Oral ADH Antagonists for Hyponatremia in Subarachnoid Hemorrhage

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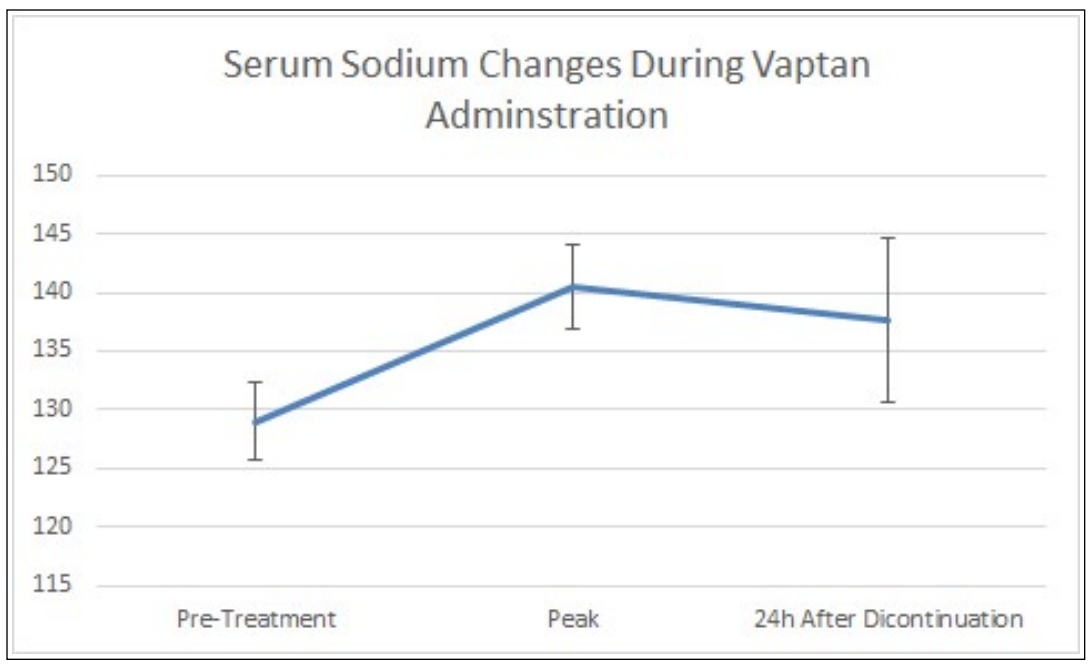
Introduction

Hyponatremia ia a commonly encountered problem in patients with subarachnoid hemorrhage and has been demonstrated to lead to worsened long term outcomes in this patient population(1). Treatment modalities are varied (intravenous hypertonic saline, corticosteroids, urea, among others) and none is accepted as the standard of care(2,3).

Vaptans are a family of vasopressin receptor antagonists used to treat hyponatremia associated with heart failure, cirrhosis and SIADH. They have been demonstrated to be safe in patients weith neurological injury(4). Here we investigate the utility of tolvaptan, an orally administered agent, in patients with subarachnoid hemorrhage and hyponatremia.

Methods

Patients who developed hyponatremia (serum sodium </= 130mMol/L) within 14 days of a ruptured intracranial aneurysm and who were managed in an ICU were included in the study. Tolvaptan was initially dosed at 15mg per day for a total of 3 doses. The dose was increased by 15mg daily (to a maximum dose of 45mg) if serum sodium did not normalize (135mMol/L or greater). IV fluids (0.9% saline) were administered at a rate of 100ml/hr during drug treatment.



Results

Seven patients met inclusion criteria. The average serum sodium level of patients prior to administration of tolvaptan was 129 mMol/L. The drug was administered for an average of 4.1 days. Two of the eight patients required at least one dosage increase due to lack of response. All patients had an increase in sodium levels with an average daily correction of 5.9mMol/L. The average peak sodium concentration was 140.5 mMol/L and was reached in an average of 2.1 days. Compared to pre-drug administration, patients demonstrated a 172% increase in urine output in comparison to a 168% increase in fluid intake. The average sodium concentration 24 hours after discontinuing medication was 137.5mMol/L. Of the 6 patients whose hospital stay was greater than 24 hours after final dose, four were noted to have recurrent hyponatremia.

Conclusions

Tolvaptan appears to adequately correct hyponatremia associated with subarachnoid hemorrhage, however the effect may not be durable. As expected, urinary outputs were increased by drug administration but euvolemia was maintained via intravenous and oral fluids. Further investigation is required to assess the safety and utility of vaptans in the setting of subarachnoid hemorrhage.

References

1: Mapa B, Taylor BE, Appelboom G, Bruce EM, Claassen J, Connolly ES Jr. Impact of Hyponatremia on Morbidity, Mortality, and Complications After Aneurysmal Subarachnoid Hemorrhage: A Systematic Review. World Neurosurg. 2016 Jan;85:305-14

2: Mistry AM, Mistry EA, Ganesh Kumar N, Froehler MT, Fusco MR, Chitale RV. Corticosteroids in the Management of Hyponatremia, Hypovolemia, and Vasospasm in Subarachnoid Hemorrhage: A Meta-Analysis. Cerebrovasc Dis. 2016;42(3-4):263-71.

3: Human T, Cook AM, Anger B, Bledsoe K, Castle A, Deen D, Gibbs H, Lesch C, Liang N, McAllen K, Morrison C, Parker D Jr, Rowe AS, Rhoney D, Sangha K, Santayana E, Taylor S, Tesoro E, Brophy G. Treatment of Hyponatremia in Patients with Acute Neurological Injury. Neurocrit Care. 2017 Jan 4.

4: Buckley MS, Patel SA, Hattrup AE, Kazem NH, Jacobs SC, Culver MA. Conivaptan for treatment of hyponatremia in neurologic and neurosurgical adults. Ann Pharmacother. 2013 Sep;47(9):1194-200.