SEVERE SYMPTOMATIC ACUTE HYPONATREMIA IN TRAUMATIC BRAIN INJURY RESPONDS VERY RAPIDLY TO A SINGLE 15 MG DOSE OF ORAL TOLVAPTAN: A MAYO CLINIC HEALTH SYSTEM HOSPITAL EXPERIENCE - NEED FOR CAUTION WITH TOLVAPTAN IN YOUNGER PATIENTS WITH PRESERVED RENAL FUNCTION.

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OBJECTIVES

Hyponatremia is common and affects up to 30% of hospitalized patients. It is a powerful predictor of poor outcomes, especially in patients with congestive heart failure or cirrhosis. In traumatic brain injury, hyponatremia results from either the syndrome of inappropriate anti diuretic hormone (SIADH) secretion or from cerebral salt wasting.

Tolvaptan is now well established as a potent pharmaceutical agent to treat symptomatic hyponatremia in patients with SIADH. Nevertheless, over rapid correction is dangerous and potentially lethal. Current literature on the use of Tolvaptan has generally been predicated on clinical experiences with older patients who often have relatively reduced baseline renal function.

We describe the dramatic and rapid normalization and correction of serum Na by 18 mEq/L over 18 hours after a single 15 mg dose in a young man with normal kidney function (eGFR of 126) following symptomatic severe hyponatremia from SIADH following traumatic brain injury.

METHODS/RESULTS

CASE REPORT

A 32-year old Caucasian male was admitted to the Trauma Service of our hospital in November 2013 following a garbage truck motor vehicle accident with a 'semi', with the patient on the passenger side of the truck. He had altered level of consciousness at the scene and was transported to Mayo Clinic Health System Eau Claire Emergency Room as a Level I trauma activation. Significant injuries included acute right posterior 11th and 12th rib fractures, large scalp hematoma, and a small focus of acute intracranial hemorrhage near the vertex of the skull on CT scan, thought to represent subarachnoid hemorrhage. He was intubated earlier on for airway protection. His serum Na on admission was normal at 141 mEq/dL. His serum Na fell during the hospital stay and despite infusions of intermittent timed 250 cc boluses of 3% saline, fluid restriction to 800 cc/day and the use of oral Na tablets, the serum Na continued to fall and was down to 121 mEq/L after several days (Figure 1).

The patient was seen as a nephrology consult for rapidly worsening acute symptomatic hyponatremia. Symptoms of acute hyponatremia included blurred vision, poor memory and cognitive impairment. Since the plan was to start oral Tolvaptan, fluid restriction was discontinued, fluid intake was liberalized and he was educated on the potential effects of Tolvaptan therapy. He received a single dose of 15 mg oral Tolvaptan, given at 1229 pm on the consult day. He was not to receive the next day's dose until after nephrology review. Soon after the Tolvaptan tablet administration, he noticed increased urination, increased thirst and he was soon drinking "tons of water". Serum sodium had rapidly increased overnight to 139 mEq/dL, an increase of 18 mEq over 18 hours, a very rapid rate of correction of 1 mEq/dL/hour (Figure 2).

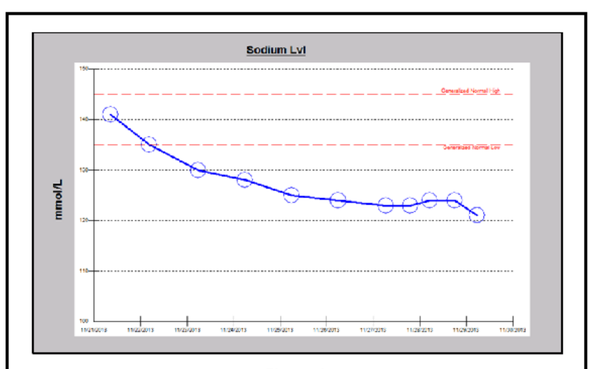

Figure 1

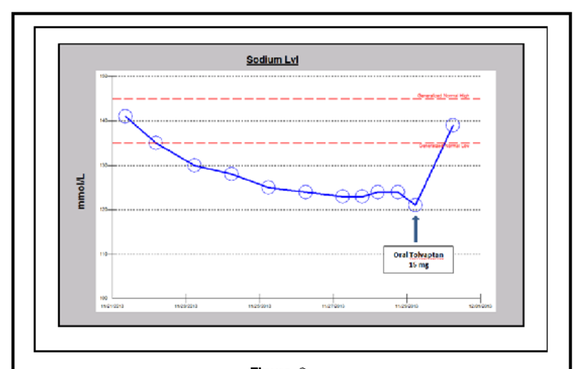

Figure 2

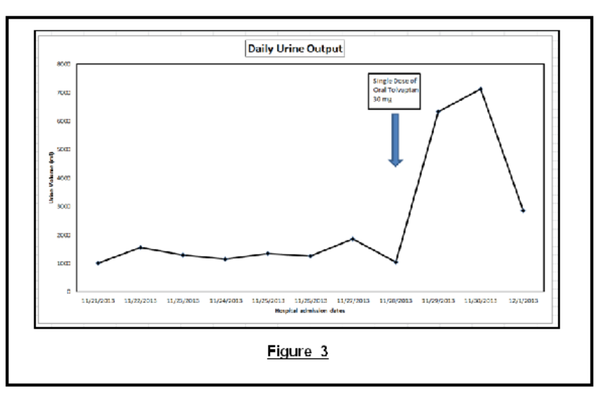

Figure 3

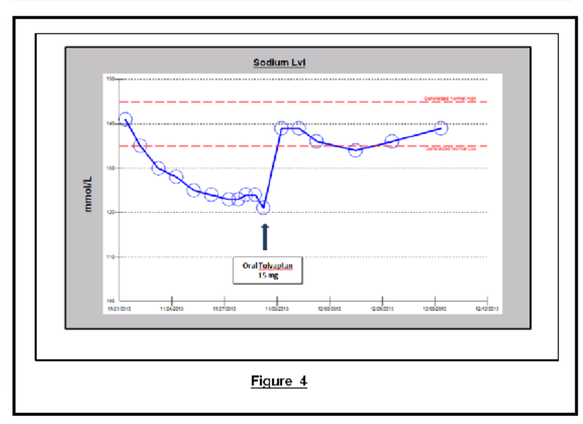

Figure 4

METHODS/RESULTS

Simultaneously, his daily urine output had more than quintupled from 1050 cc to 6325 cc the next day (Figure 3).

Further doses of oral Tolvaptan was promptly discontinued. Concurrent arginine vasopressin level was 1.4 pg/mL, still inappropriately high for a concomitant serum sodium of 121 mEq/dL, consistent with SIADH. Two days after the single oral Tolvaptan dose, the symptoms of blurred vision, poor memory and cognitive impairment had fully resolved and he was discharged home.

A post-hospitalization evaluation in the Nephrology office, a week later, on December 9, 2013 revealed an otherwise normal 32-year old, but with still persistent left gaze diplopia. Serum sodium had remained stable at 139 mEq/dL (Figure 4).

CONCLUSIONS

- Prior studies on oral Tolvaptan for managing symptomatic (chronic) hyponatremia in the SALT-1, SALT-2, EVEREST and SALTWATER trials recruited older patients, age range 64-67 years, with some degree of renal impairment, baseline serum creatinine ~1.3-1.4 mg/dL. The doses of Tolvaptan utilized in these studies were 30 mg/d or higher.
- The very rapid correction of hyponatremia that we observed in our young patient following just a single oral dose of 15 mg of oral Tolvaptan, sustained after eleven days, is extraordinarily remarkable and is the first such report in the literature.
- No such rapid and sustained correction after a single dose of oral Tolvaptan has been previously reported.
- The maximum reported correction of serum sodium within 24 hours were 12 mEq/dl and 13 mEq/dl, respectively, following 15 mg dose of oral Tolvaptan in relatively younger patients, aged 47 years and 51 years, respectively. Indeed, the 51-year old female with one year history of SIADH developed symptomatic hypotension from >6.5 liters of overnight polyuria and ultimately required as little as 3 mg daily dose of Tolvaptan on discharge for maintenance.
- Compared to most other patients previously studied in the literature, our patient was the youngest, and had normal renal function (serum creatinine, 0.76 mg/dL), with an estimated glomerular filtration rate (eGFR) of 126 ml/min/1.73 sq. m BSA.
- We recommend the use of lower doses of Tolvaptan (15 mg or lower) in younger patients with preserved kidney function, more so when treating for chronic hyponatremia, to mitigate against the development of potentially fatal pontine demyelination. Moreover, repeated doses may be unnecessary and potentially contraindicated.

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