
Tolvaptan for treatment of iatrogenic hyponatremia

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A 9-year-old girl, underwent surgery for hypothalamic astrocytoma. She had a normal hormonal profile before surgery. Her weight was 49 kg. She underwent hourly urine output monitoring, daily serum sodium and serum and urine osmolality monitoring [Table 1]. She did not have any neurological deficits after surgery. From the third postoperative period, she developed diabetes insipidus. She received vasopressin 5 units subcutaneously for every episode of urine output more than 200 ml/h. As she required frequent injections of vasopressin, she was started on the oral tablet desmopressin 100 µg daily. On the third day of desmopressin treatment, she developed the hyponatraemia. The desmopressin was stopped and 3% hypertonic saline was started to target increase in serum sodium concentration by 0.5 mEq/h. Her hyponatraemia worsened in spite on hypertonic saline infusion. The central venous

pressure monitoring was not done to determine the volume of the patient. There was no significant change in heart rate and blood pressure indicating that the volume was probably normal or more. The urine output reduced as the serum sodium concentrations dropped. The serum osmolality reduced and urine osmolality increased during hyponatraemia. From the available data, the hyponatraemia seemed to be due to hypervolaemia (desmopressin intake). A trial of fluid restriction was not given as the cause of hyponatraemia was definitely desmopressin. Hence she was started on oral tablet tolvaptan 15 mg daily. On the second day of receiving tolvaptan, her serum sodium concentration started increasing [Figure 1]. She received tolvaptan for 3 days. Her serum sodium gradually normalised, and on day 18 after surgery, her serum sodium concentration was 137 mEq/L. Her diabetes insipidus settled and she did not require any hormone supplement. At 6 months of follow-up, she has a normal hormonal profile.

Hyponatraemia is defined as a serum sodium levels <135 mmol/L. Hyponatraemia is common and can be challenging to manage. It is often encountered in neurosurgical practice. This disorder is most of the time due to the syndrome of inappropriate antidiuretic hormone (SIADH) secretion, which causes euvolemic or hypervolaemic hyponatraemia. The causes of SIADH are malignant disease, intracranial pathology and some medications.^[1]

The only pharmacological therapy approved for the treatment of hyponatraemia due to SIADH is the class of vasopressin receptor antagonists (vaptans).^[1,2]

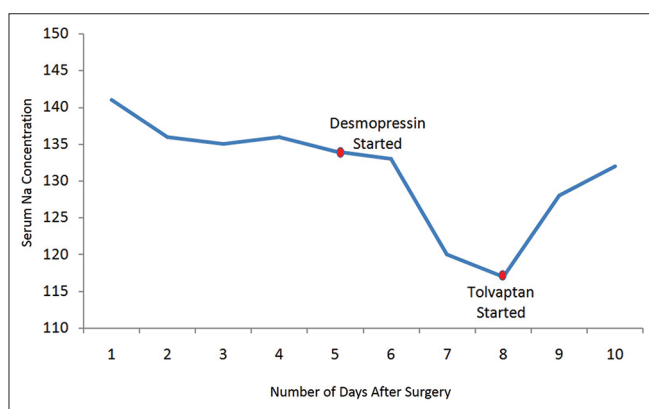
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Table 1: Daily serum sodium, urine output, serum and urine osmolality chart

Day	Serum sodium (mEq/L)	Urine output (mL)	Serum osmolality (mOsm/L)	Urine osmolality (mOsm/L)
1	141	1600	282	360
2	136	3380	280	468
3	135	5600	Not available	Not available
4	136	7200	Not available	Not available
5	134	4650	281	389
6	133	2350	278	366
7	120	2100	274	570
8	117	2000	261	550
9	128	4000	268	541
10	132	4300	268	299

**Figure 1:** Trend of daily serum sodium and effect of drugs

Tolvaptan is one of the potent, highly selective, and orally effective nonpeptide antagonists of arginine vasopressin. It is a selective oral antagonist of the V₂ receptor causing a dose-dependent increase of dilute urine. Tolvaptan has been used for euvolemic and hypervolaemic hyponatraemia. The daily doses of tolvaptan ranges from 15 to 60 mg.^[3] Two randomized, placebo-controlled, double-blind phase three clinical trials (SALT-1 and SALT-2) showed the effectiveness of the oral tolvaptan compared with placebo in increasing serum sodium concentrations.^[2] Tolvaptan is well-tolerated, the common side effects with prolonged use are nausea, dry mouth, pollakiuria and polydipsia.^[3]

In the present case, the child had developed hyponatraemia due to desmopressin. The desmopressin is a long-acting vasopressin agonist. There is a wide inter-individual variation in dose requirement and dosing intervals.^[4] Dilutional hyponatraemia is a serious adverse effect of

desmopressin. This complication mostly develops in the patients within 14 days or less after starting the medication.^[5] The oral tablet form has unpredictable absorption. The usual recommended dose is 100 µg daily. In the present case, the effect of desmopressin was prolonged resulting in the failure of the treatment of hyponatraemia even after stopping desmopressin and starting hypertonic saline infusion. Though vaptans are recommended for the chronic hyponatraemia due to the pathological conditions, tolvaptan was given in this case to combat the effect of desmopressin resulting in the successful management of hyponatraemia.

Desmopressin should be avoided in the acute and sub-acute stage of hyponatraemia after the neurosurgical intervention. If patients develop the refractory hyponatraemia due to desmopressin use, tolvaptan is effective in restoring the normal serum sodium concentration.

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Conflicts of interest

There are no conflicts of interest.

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