

CASE REPORT

SINGLE DOSE OF TOLVAPTAN IN THE MANAGEMENT OF INTRACRANIAL HAEMORRHAGE INDUCED SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE- A CASE REPORT

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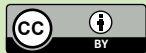
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**ABSTRACT**

Hyponatraemia is a common manifestation of a syndrome of inappropriate antidiuretic hormone secretion in neurological patients admitted to the intensive care unit. We present a case of 62-years old male who presented with loss of consciousness, seizure, and altered mental status and was diagnosed to have right-sided intracranial haemorrhage. The patient underwent evacuation of hematoma and developed persistent hyponatremia secondary to the syndrome of inappropriate antidiuretic hormone. Patient was treated with 3% sodium chloride, loop diuretics, and fluid restriction. There was no improvement in hyponatremia after initial correction and we started on 7.5 milligrams of Tolvaptan. The patient responded within 4 days of starting Tolvaptan. There was no hyponatraemic episode during the follow-up. From this, we want to emphasize that refractory hyponatremia secondary to intracranial haemorrhage should be treated with Tolvaptan.

Keywords: Intracranial Haemorrhage, Hyponatremia, SIADH, Tolvaptan**INTRODUCTION**

Syndrome of inappropriate antidiuretic hormone (SIADH) occurs in 5.34% of neurosurgical patients.¹ Spontaneous intracerebral haemorrhage is a common neurosurgical emergency in the developing country. Hyponatremia is a common manifestation of SIADH that leads to serious complications if not managed properly.² SIADH is common but difficult to treat as many drugs do not work. It occurs due to dysregulation of arginine vasopressin receptor. Fluid restriction is used as a treatment of choice for a long-time but without much good outcome. Therefore, Pharmacological therapy with Tolvaptan can help us to change the management of SIADH with appropriate outcome.

CASE SUMMARY

A 62 years old male, with a past history of Hypertension not under regular medication presented to the Emergency Department with a sudden loss of consciousness and

abnormal body movement for one hour. At a presentation in the Emergency Department, Glasgow Coma Scale (GCS) was 8/15, pulse rate 54 beats per min, Blood Pressure (BP) 210/140 mmHg, respiratory rate 14 breaths/min, and oxygen saturation 96% in room air. Abdominal, Chest, and cardiovascular examinations were normal. Neurological examination showed bilateral pupil sluggish reactive to light, He was immediately resuscitated and intubated, Computed Tomography (CT) scan (Figure 1) of the head was done and it showed a right intracranial haemorrhage involving the thalamus, caudate, and lentiform nucleus.

His blood investigation profiles were Total leucocyte count (TLC) - 14000/mm³ Neutrophil 60%, lymphocyte 35% and eosinophil 3% Platelets-120000/mm³, Haemoglobin (Hb)- 10gm/dl, Urea-58 mg/dl, Creatinine-1.3 mg/dl, Sodium, and Potassium is within normal limit. Total bilirubin 1.6mg/dl in which direct 0.8mg/dl, Total protein 6.9mg/

dl in which albumin 4.1mg/dl, Alanine aminotransferase (ALT) 46 U/L, Aspartate aminotransferase (AST) 35U/L, Alkaline phosphatase (ALP) 102 U/L Prothrombin time (PT) 14 seconds, International normalized (INR) ratio 1.2.

Evacuation of hematoma was done and there was an improvement in GCS from 8/15 to 10/15.

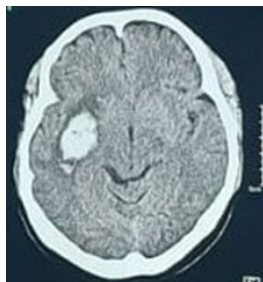


Figure1: Computed Tomography of brain showing right sided intraparenchymal haemorrhage.

The patient was extubated on the third day. He developed a urine output of 50-60 ml/hour. Based on urine specific gravity 1.156, urine osmolality 125 mOsm/kg, serum sodium 128 mEq/L and plasma osmolality 270mOsm/kg, urinary sodium 40mmol/L, the diagnosis of SIADH was made. Fluid restriction was done serial Serum sodium measurement was done daily but there was no improvement in serum sodium. It was persistently below 130 mEq/L (Figure 2). Then, Tablet Tolvaptan 7.5mg was started and there was an improvement in serum sodium, and urine osmolality. The patient was shifted out of ICU on 14. The thyroid function test was normal. He was followed up after 1 week and serum sodium was normal.

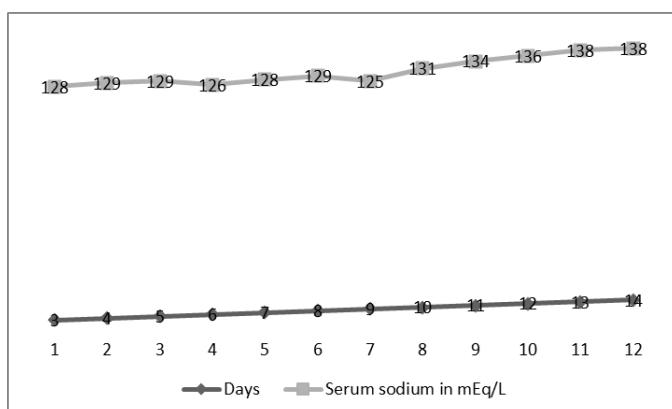


Figure. 2: Serum Sodium during hospital stay

DISCUSSION

The failure to excrete electrolyte-free water from the persistent secretion of anti-diuretic hormone (ADH) despite low serum osmolality usually underlies the development of hyponatremia in SIADH. It has manifestations like loss of consciousness, seizure, decreased urine output, agitation and extubation failure.³ It is associated with increased morbidity and mortality

in patients admitted to hospitals.^{4,5} Fluid restriction, Drugs like demeclocycline, lithium, and loop diuretics in combination with sodium supplementation, and urea tablets but the safest and most effective treatment is still a matter of research.^{6,7}

Vaptans group of drugs has been shown to improve the hyponatremia induced by SIADH.⁸ Tolvaptan is a non-peptide vasopressin antagonist with a $V_2R: V_1R$ selectivity of 29:1 for human arginine vasopressin receptors. Our patient responded to the single dose of Tolvaptan so, we did not use the higher dose as studies have shown that 7.5-90 mg can be used to control hyponatremia.^{7,9} Different studies^{2,5,7} have shown that dry mouth, thirst, elevated liver enzymes and pontine myelinolysis are side effects of Tolvaptan but our patients did not have any of these.

Our patient did not develop hyponatremia in the long-term follow-up. Therefore, Tolvaptan can be used to treat SIADH. Other vaptans groups of drugs like Conivaptan, Lixivaptan, Satavaptan, and Mozavaptan were not used as they were unavailable and our patient responded to Tolvaptan. This patient responded within 4 days of starting treatment with Tolvaptan and studies have shown that the minimum duration of response to treatment is 3.4 days.²

To conclude, Large-scale randomized-controlled trials are required to show the effectiveness of the vaptans group of drugs to treat SIADH.

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