
Hypernatremia: A known complication of conivaptan

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We report a 30-year-male who was diagnosed case

of craniopharangioma. He was apparently well 2 months back when he had progressive decrease in vision (right > left). He was not able to visualize on lateral vision, and his right side pupil was not reacting to light. He got operated for the same and was shifted for elective ventilation. On 1st postoperative day, his trachea was extubated as computerized tomography (CT) scan was normal. One week after surgery, he suddenly became drowsy. On investigation, there was electrolyte imbalance (Na^+ - 116 mEq/L, K^+ - 2.7 mEq/L). He was started on 3% NaCl infusion along with KCl supplement.

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The electrolyte levels improved gradually over a period of 1 day (Na^+ - 120 mEq/L, K^+ - 3.6 mEq/L) along with improvement in his general condition. Two days later, infusion of the injection conivaptan was started by a nursing staff in the presence of a neurosurgeon and was further monitored by the anaesthesiologist on duty in the Neuro-ICU. He was started on injection conivaptan infusion 20 mg IV over 30 minutes followed by 20 mg IV over 24 h. At the starting point of infusion, the serum sodium level was 123 mEq/L. Subsequent ABG picture showed rapid rise in Na^+ level within 20 minutes (Na^+ - 153 mEq/L, K^+ - 5.5 mEq/L). Within that duration, he became drowsy, irritable and disoriented; therefore, the trachea was intubated to secure the airway. His hourly urine output was 150-200 ml/h, and urine specific gravity remained between 1007-1008. The central venous pressure was also measured, and it was within normal range (9-10 cmH₂O). A repeat CT scan was performed to rule out any intracranial bleed or infarction, and the findings were non-significant.

Electrolyte abnormalities are linked to adverse outcomes and increased mortality in hospitalized patients. While the differential diagnosis for hyponatraemia is diverse, most cases stem from arginine vasopressin (AVP) dysregulation, where hypoosmolality fails to suppress AVP synthesis and release. Despite the long-recognized problem with excess AVP in euvolemic and hypervolemic hyponatraemia, traditional therapeutic options have relied on nonspecific and potentially problematic strategies.^[1]

Conivaptan is a non-peptide inhibitor of antidiuretic hormone (vasopressin receptor antagonist). It was approved in 2004 for the treatment of hyponatraemia (low blood sodium levels) caused by syndrome of inappropriate antidiuretic hormone (SIADH). It inhibits two of the three subtypes of the vasopressin receptor (V1a and V2). Effectively, it causes iatrogenic nephrogenic diabetes insipidus. It is given as loading dose 20 mg IV infusion over 30 minutes and then 20 mg IV as continuous infusion over a 24-h period for 2-4 days. After initial day of treatment, it may be increased to 40 mg/day if necessary. Monitor serum sodium and volume status frequently; a significant increase in serum sodium (>12 mEq/L/24 h) may result in serious neurologic effects. Vaptans can be considered a new effective tool for the treatment of euvolemic and hypervolemic hyponatraemia. Nevertheless, more comparative research of vaptans versus other therapies on clinical grounds is needed to more accurately assess the value of these drugs in the treatment of hyponatraemia.^[2] The single-centre retrospective study from The Methodist Hospital (TMH) compared the effect of hypertonic saline (HS) and conivaptan intervention in the management of 49 patients with

hyponatraemia from January 2009 through November 2010. Regardless of whether the patient was euvolemic or hypervolemic, no significant difference was noted in serum sodium concentration after initiation of treatment or in frequency of over-correction between groups.^[3] However, conivaptan given as a bolus can effectively treat acute hyponatraemia in brain-injured patients.^[4]

Efficacy of vaptans is now well-accepted for management of hyponatraemia over a short period. However, vaptans have not become the mainstay treatment of hyponatraemia yet.^[5] Whereas conivaptan is to be administered intravenously, the other vaptans such as tolvaptan, lixivaptan and satavaptan are effective as oral medication. Tolvaptan is approved for treatment of clinically significant hypervolemic/euvolemic hyponatraemia-serum sodium <125 mEq/L or less marked symptomatic hyponatraemia that has resisted correction with fluid restriction-but not heart failure without hyponatraemia.^[6] Conivaptan is a nonspecific arginine vasopressin receptor antagonist that has been used as therapy in adults who have hypervolemic hyponatraemia due to congestive heart failure.^[7] Intravenous conivaptan is effective for increasing serum sodium levels and may be a potential adjuvant to enhance diuresis in children with cardiac disease.^[8] Further studies are required before conivaptan can be recommended for routine use in children. However, conivaptan has not been approved by the FDA for the treatment of decompensated congestive heart failure. No dose adjustment is necessary in patients with mild or moderate renal impairment and in patients with mild hepatic impairment.^[9] No data are available on the use of vaptans in acute hyponatraemia, and they are not indicated in hypovolemic hyponatraemia.^[10] However, there are case reports where an extremely rapid correction of serum sodium with a typical dosing regimen of conivaptan were seen.^[11] Vasopressin-receptor antagonists, by reversing osmotic shifts, may be novel agents to control ICP and cerebral edema, especially in the setting of falling sodium.^[12]

The one of the possible cause of sudden neurological deterioration in this patient was diabetes insipidus which was ruled out by hourly urine output measurement that was within normal range as was the urine specific gravity. His volume status, adequately measured by central venous pressure, was also in normal limits. The intracranial bleed or infarction was also ruled out by doing a repeat CT scan was normal.

There was no specific indication to start the conivaptan infusion in our patient as he was responding well to the treatment with hypertonic saline. The infusion was started after receiving the instructions from the neurosurgeon as he wanted to see the response of this drug and the infusion of conivaptan was started without consulting the anaesthesiologist on duty. Through this

case report I want to simplify that though conivaptan is not the first line of treatment for the euvoletic or hypervolemic hyponatraemia, but they can be used as a life saving drug for euvoletic or hypervolemic hyponatraemia, when all other common treatment modalities fail. One has to be very cautious while using vaptan group of drugs and also perform the strict serum sodium level monitoring.

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