Off-label use of vaptans in children with severe symptomatic hyponatremia due to SIADH

Authors: Tuli Gerdi, Tessaris Daniele, Di Taranto Serena, Matarazzo Patrizia.

Hospital: Department of Pediatric Endocrinology and Diabetology, Regina Margherita Children's Hospital, Turin, Italy

Background:

First chose treatment in euvolemic and hypervolemic hyponatremia is fluid restriction. Compliance is really poor and frequently use of isotonic or hypertonic saline solution is needed to treat euvolemic hyponatremia .
An alternative treatment is represented by non-peptide arginine-vasopressin-receptor antagonists, a new drug class also called vaptans [1,2,3]. The blocking pathway of AVP signaling by vaptans inhibits water resorption and results in excretion of diluted urine or "aquaresis" [4,5]. Vaptans are contraindicated in hypovolemic states but can be a treatment option in euvolemic and hypervolemic chronic hyponatremia. As urine generation is electrolyte free, vaptans make unnecessary repletion of electrolytes.
No data are available in pediatric age, nor trials included any pediatric age patient, so vaptans use is still considered off-label.

Case 1:

A 9-*yo* female with surgically treated suprasellar astrocitoma developed chronic hyponatremia (121 to 128 mmol/l) in SIADH, although no symptoms were present until she had a grand mal seizure episode. As chronic hyponatremia became symptomatic we chose tolvaptan as treatment option in association to orally levetiracetam. Daily dosage was 4 mg, increased to 7.5 mg due to persistent hyponatremia. As expected, she had polydipsia and polyuria lasting for 4 weeks after tolvaptan introduction. Actually, after 15 months of treatment, serum natrium levels are quite normal (131-135 mmol/l), with no adverse effects nor seizure episodes, so levetiracetam treatment was stopped.

Case 2:

A 7-yo boy affected by ROHHAD (rapid-onset obesity, hypothalamic dysfunction, hypoventilation and autonomic dysregulation) syndrome was treated with tolvaptan as he developed SIADH. When he had a severe seizure episode due to hyponatremia (118 mmol/L), he started treatment with orally valproic acid in association to tolvaptan at 5 mg daily dosage, increased progressively to 10 mg daily due to persistent hyponatremia. Actually after 2 years of treatment serum natrium levels range from 137 to 145 mmol/l with no adverse effects nor seizure episodes.

Discussion:

In the last years several trials have assessed efficacy and safety of non-peptide arginine-vasopressin-receptor antagonists, in the treatment of chronic euvolemic or hypervolemic hyponatremia [6,7]. We know that asymptomatic hyponatremia can have neurological adverse effects, especially in young age, so use of vaptans takes an important role and can be considered as an elegant strategy to correct chronic hyponatremia. Vaptans should not be improperly used and are contraindicated in hypervolemic hyponatremia. Also association with other hyponatremia treating strategies is not indicated. In pediatric age use of vaptans is considered off-label as we need more data about effectiveness and safety. The difficulty to treat hyponatremia in children with traditional strategies as fluid restriction, isotonic or hypertonic saline solution or potentially toxic drugs as demeclocycline or urea, forces us to search new treatment options.

Conclusions:

Tolvaptan should be considered as treatment option for symptomatic chronic hyponatremia in pediatric age, due to hypothalamic diseases. More data are needed about effectiveness and safety and serum natrium levels should be carefully monitored. Aquaresis due to vaptans do not cause loss of electrolytes so no repletion is needed.

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Gerdi Tuli

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