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Vasopressin-2 receptor antagonists (VPAs): potent but potentially dangerous drugs for the treatment of severe hyponatraemia secondary to Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

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Introduction

Hyponatraemia is the commonest electrolyte disorder in clinical practice, affecting around 15-28% of hospitalised patients. A frequent cause is SIADH, and Vasopression-2 receptor antagonists (VPAs) have been licensed for treating SIADH-related hyponatraemia. As usage extends to other causes of hyponatraemia, over-rapid correction and hypernatraemia remains important side-effects. We present a patient with severe SIADH highlighting the need for guidance and vigilance when using these potent drugs.

Case

An 82-year-old female patient was admitted for a total thyroidectomy for papillary carcinoma in December 2014 and commenced on Tri-iodothyronine while awaiting radioiodine ablation. She developed severe hyponatraemia, drowsiness and confusion. On review, she had mild hyponatraemia prior to admission but developed severe hypotonic hyponatraemia post-operatively secondary to SIADH. She was well hydrated, did not have excessive intravenous fluids and was not on any medication that could cause hyponatraemia or SIADH. Despite seven days treatment with fluid restriction and oral Demeclocycline 300mg three times a day her serum sodium remained below 110mmol/l.

We then decided to give a single dose of Tolvaptan 15mg. Tolvaptan is usually initiated in hospital due to the need for a dose titration phase with close monitoring of serum sodium and volume status 4-6 hours after its administration.

Investigations

The initial patient's biochemical test results are shown in the Table 1.

A computerised tomography of her head, chest, abdomen and pelvis did not demonstrate any pathology. Using our in-house protocol for investigating hyponatraemia we ascertained the cause as post-surgery SIADH. Table 2 shows the response to a single 15mg-dose of Tolvaptan.

Table 1

Biochemical test	Results	Reference range
Serum sodium	107	133-146 mmol/l
Serum potassium	3.2	3.5-5.3 mmol/l
Serum urea	3.5	2.5-7.8 mmol/l
Serum creatinine	39	50-120 µmol/l
Thyrotrophin (TSH)	13.3	0.3-4.2 mU/l
Free T_3	2.3	3.1-6.8 pmol/l
Serum osmolality	259	275-295 mosm/kg
Urine osmolality	559	300-1000 mosm/kg
Urine sodium	32	--------
Early morning cortisol	1113	--------

Table 2

Time (hours)	Serum sodium (mmol/l)
0	108
Tolvaptan 15mg given	
6	111
12	117
18	122
24	125
30	126
36	127
42	128
48	128

Response to treatment

Following administration of a single dose of Tolvaptan 15mg we monitored the sodium levels every six hours for 48 hours and maintained fluid intake at 1.5-2L per day. As can be seen from Table 2, the patient's hyponatraemia greatly improved within 48hours. Despite the rapid rise in her serum sodium levels (17mmol/l over 24hours) her neurological symptoms improved and her mental test scores were normal.

Conclusions

- VPAs are potent drugs available for the treatment of hyponatraemia secondary to SIADH. Patients must be well hydrated (not on fluid restriction) and closely monitored to prevent over-rapid correction and hypernatraemia. We recommend 6-8 hourly serum sodium monitoring for the first 24-48 hours after a single dose.
- We believe that after thorough investigation, fluid restriction and a trial of Demeclocycline should still be the first-line treatment for the management of patients with SIADH.

References [Accessed 10th October 2015]
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