To the Editors:

Chronic hypernatraemia due to osmoreceptor dysfunction

Plasma osmolality is regulated by the interaction of the kidneys, arginine vasopressin (AVP), and thirst – the last two being stimulated by hypothalamic osmoreceptor signals. Osmoreceptor dysfunction may cause hypernatraemia, hyperviscosity and considerable morbidity, and may be associated with other endocrine dysfunction [1,2]. We report two patients with chronic hypernatraemia and osmoreceptor dysfunction.

Patient 1

A middle-aged, previously healthy, asymptomatic man on no medication, was found to have chronic hypernatraemia. Clinical examination was unremarkable. His serum sodium varied between 146-152 mmol/l. At the conclusion of a standard water deprivation test, urine and serum osmolalities were 512 and 308 mosm/kg, urine output was 45ml/hour, and plasma AVP was 0.15pg/ml (low). Urine osmolality increased to 812 mosm/kg after DDAVP, suggesting partial cranial diabetes insipidus (CDI). He had no thirst during or after the test (adipsic). A short Synacthen test (SST) was sub-optimal. MRI scans revealed a small pituitary, partially empty sella and an absent posterior pituitary “bright signal”.

Patient 2

A middle-aged woman with diabetes mellitus (HbA_{1C} 6.5%), on appropriate medication, had troublesome thirst, polyuria and nocturia. She was obese but otherwise unremarkable. Her serum sodium was 146-149 mmol/l. The water deprivation test, SST and MRI scans of the pituitary were normal.

Screening tests for hyperaldosteronism, hypercortisolism and pituitary dysfunction were normal in both patients. A hypertonic saline infusion test was done [3].

Both patients failed to increase AVP secretion at expected levels of serum sodium and osmolality i.e. their osmoreceptor was reset to a higher threshold. In addition patient 1 was adipsic during and after the test but patient 2 was thirsty and drank 700 ml of water.

These patients had an upward resetting of their hypothalamic osmoreceptor. Patient 1 also had partial CDI and the adipsic syndrome, unlike patient 2 who had normal endocrine function and thirst. The osmoreceptor functions as a "sensor" for both AVP secretion and thirst. Diseases affecting it may cause perturbations of both these elements (patient 1) or affect one independent of the other eg. altered threshold for AVP release with preserved thirst (patient 2). AVP synthesising neurones may also be affected in disease involving the osmoreceptor because of their physical proximity, resulting in complete or partial CDI as in patient 1. Patient 1 is on a fixed fluid intake with close monitoring of his electrolytes and weight. His adipsia places him at high risk of hypernatraemia and hyperviscosity after hypotonic fluid loss and lack of access to water. Patient 2 is on 10 μg of DDAVP at night. Both are well, asymptomatic and normonatraemic.

The contribution of the hypothalamic osmoreceptor and thirst sensation to the regulation of water homeostasis is increasingly recognised [4]. Investigation of chronic hypernatraemia is important in identifying subtle abnormalities in these regulatory mechanisms and avoiding potentially significant morbidity.

Table 1. **Hypertonic saline infusion test**

	Time (min)	*Serum sodium (mmol/l)*	*Serum osmolality (mosm/kg)*	*Plasma AVP (pg/ml)*
Patient 1	0	146	307	0.23
	30	147	312	0.29
	60	150	318	0.53
	90	152	321	0.84
	120	154	327	1.83
Patient 2	0	144	303	0.5
	30	147	315	1.6
	60	147	315	2.1
	90	150	319	-
	120	155	327	4.3

References

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