Reset osmostat after diuretic treatment

Secretion of anti-diuretic hormone (ADH) is regulated by integrated changes within the circulation which stimulate or inhibit supra-opticohypothalamic osmoreceptors and intravascular volume receptors. Disturbances in endogenous ADH synthesis and release may arise from diuretic treatment, and result in hyponatraemia.[1] This complication may resolve spontaneously after stopping the diuretic; or sodium[2] or potassium,[1] replacement may be needed. Nevertheless, hyponatraemia sometimes persists, suggesting a reset osmostat at a new low level of serum osmolality, which is capable of responding appropriately to further changes in serum osmolality. The elderly may be particularly susceptible to this complication.

Case report

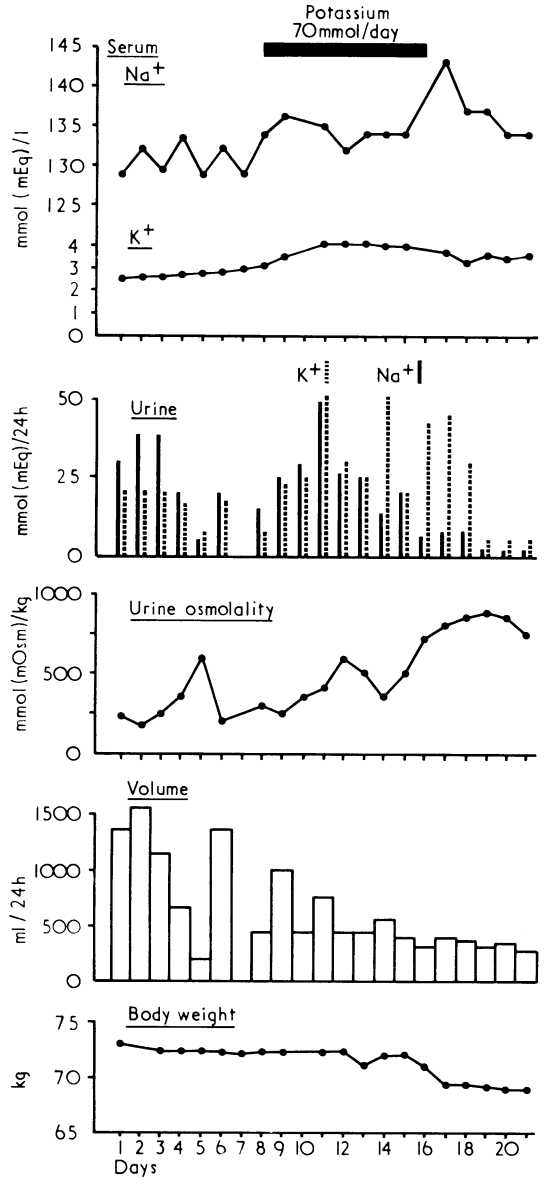
A previously healthy 75-year-old woman was admitted to hospital with drowsiness of three days' duration. She had taken polythiazide 1 mg daily over 10 years for hypertension. There was no cardiovascular, neurological or endocrine disturbance, or oedema. Blood pressure was 130/80 mm Hg, optic fundi were normal. Results of chest and skull *x*-ray examinations, electroencephalography, and brain scan were all normal.

The following values were recorded on admission: serum sodium 127 mmol (mEq)/l; osmolality 275 mmol (mOsm)/kg; potassium 2.3 mmol (mEq)/l; urea 4 mmol (24 mg/100 ml); pH 7·39; Pco_2 4 kPa (30 mm Hg); standard bicarbonate 17 mmol (mEq)/l; plasma renin activity (recumbent) 12·3 ng/ml; plasma aldosterone 195 pmol/l (7 μg/100 ml). Urine excretion on the day after admission: volume 810 ml/24 h, sodium 38 mmol (mEq)/24 h, potassium 30 mmol (m/Eq)/24 h, osmolality 429 mmol (mOsm)/kg; (diuretics stopped on admission).

Intravenous physiological saline (Na concentration ≃ 142 mmol (mEq)/l) was started within hours of admission, and continued for five days (11 litres total). Urine collections recommenced on the last day of infusion; this is shown in the figure as day 1. Serum sodium concentration remained unchanged during saline infusion.

A standard water load was given on day 6, and total exchangeable electrolytes measured on day 7. Sixty per cent of the water load was excreted within four hours: initial urine osmolality of 277 mmol (m0sm)/kg, with urine flow 0·2 ml/minute, changed to urine osmolality of 104 mmol (m0sm)/kg, with urine flow of 4·0 ml/minute. Total exchangeable sodium was 24·1 mmol/kg, and potassium 31·1 mmol/kg.

The figure shows fluid and electrolyte changes during oral potassium gluconate replacement. Fluids were restricted to less than 1 l/day from day 8.



Changes in serum and urine concentrations of potassium and sodium, and osmolality and volume of urine during potassium gluconate replacement in patient with normovolaemic hyponatraemia.

Comment

The development of normovolaemic hyponatraemia after diuretics, which had produced a sustained increase of salt and water excretion, might have resulted from restoration of blood volume by excessive water ingestion without added salt. Failure to correct hyponatraemia by saline infusion provides evidence for a reset osmostat.[3]

A reset osmostat should respond to osmotic stimuli. A normal excretion of a standard water load in the presence of hyponatraemia shows appropriate urinary dilution. With ingestion of water, intravascular volume increases and serum osmolality falls even further, resulting in inhibition of ADH release and water diuresis. Another osmotic response is the excretion of hypertonic urine (hypertonic relative to the patient's serum) during infusion of physiological saline, indicating the presence of circulating ADH.

Hyponatraemia may result from intracellular accumulation and osmotic inactivation of sodium or exchange of intracellular potassium for sodium.[4] Movement of extracellular fluid sodium into the cell would initiate intravascular volume depletion and ADH release. Resultant water retention would then expand intravascular volume to produce dilutional hyponatraemia with suppression of ADH. This hypothesis is supported by the observation that hyponatraemia produced by diuretics may be corrected by oral potassium.[1] Nevertheless, oral potassium replacement in the patient reported here raised the serum potassium concentration and improved renal concentrating ability without correcting hyponatraemia. The serum sodium concentration rose slightly because urine concentration was enhanced after water had been restricted and intravascular volume had contracted.

[1] Fichman, M P, *et al*, *Annals of Internal Medicine*, 1971, **75**, 853.
[2] Roberts, C J C, Mitchell J V, and Donley, A J, *British Medical Journal*, 1977, **1**, 210.
[3] DeFronzo, R A, *et al Annals of Internal Medicine*, 1976, **84**, 538.
[4] Flear, C T G, and Singh, C M, *British Journal of Anaesthesia*, 1977, **45**, 976.

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Hypoglycaemia during treatment of decubitus ulcer with topical insulin

The stimulating effect of insulin on protein metabolism has led to its use as a topical treatment for decubitus ulcers. A case of hypoglycaemia resulting from such treatment is reported.