'Sick cell' hyponatraemia and gastrointestinal electrolyte loss

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Summary

A patient with protracted vomiting was noted to have hyponatraemia and hypokalaemia on admission. Isotope dilution studies before treatment revealed profound body depletion of sodium, potassium and water. Treatment with potassium chloride tablets produced a simultaneous rise in serum sodium and potassium concentration without change in urine volume or osmolality, or body weight.

Potassium depletion appears to have contributed to the mechanism of hyponatraemia in this situation, and that replacement of potassium corrected hyponatraemia by effectively re-distributing solute and water across the cell membrane, so that sodium ions which had entered intra-cellular fluid during electrolyte depletion, subsequently returned to extra-cellular fluid after treatment.

Introduction

Complex electrolyte disturbance with prolonged recurrent vomiting may be associated with hyponatraemia. The mechanism is uncertain (Leaf, 1962) but 2 factors are likely. Firstly, sodium deficiency and contraction of extra-cellular fluid (ECF) volume stimulates release of anti-diuretic hormone (ADH). Secondly, impairment of the capacity to excrete a water load promotes water retention and dilution of ECF sodium. This defect in urinary diluting ability is determined by chloride depletion and diminished filtered chloride load, with enhanced proximal tubule chloride and sodium reabsorption, and reduced chloride delivery to the thick ascending limb of the loop of Henle. Active chloride reabsorption at this diluting site, which is impermeable to water, results in the formation of hypotonic urine (Burg, 1976).

When potassium depletion accompanies sodium chloride depletion, renal concentrating ability and water transport across the distal nephron is impaired (Relman and Schwartz (1958). This counteracts the effect of volume-mediated ADH activity. Moreover, thirst is enhanced, and exaggerated water ingestion may be followed by delayed water excretion.

In an ambulant patient with combined sodium and potassium deficiency who was treated initially

with potassium chloride, it was observed that chloride administration did not improve water excretion as judged by urine volume or osmolality, or body weight. Yet serum sodium concentration promptly rose, suggesting that a third factor, potassium deficiency, contributed to the production of hyponatraemia. This conforms with the 'sick cell' hypothesis (Editorial, 1974), in which hyponatraemia is said to result from movement of ECF sodium into intra-cellular fluid (ICF) in exchange for intracellular potassium. Evidence supporting this hypothesis includes studies on a variety of miscellaneous diseases, but not mixed electrolyte deficiencies (Flear and Singh, 1973).

Methods

Serum and urine electrolyte concentrations were measured by flame photometry and chloride-meter, and osmolality by Fiske osmometer. Total exchangeable sodium, and potassium, and total body water were estimated by isotope dilution using ^{24}Na , ^{42}K and titrated H_2O , equilibrating over 24 hr (Belcher and Vetter, 1971).

Case report

A previously healthy 21-year-old female experienced recurrent bouts of painless vomiting with anorexia for 6 weeks. During this period she vomited 6 times/day, with copious volumes for the latter 3 weeks when weakness supervened. Pregnancy was not responsible. Vomiting was not self-induced or accompanied by drug or diuretic abuse or purgation. General condition was satisfactory and the patient remained ambulant. No physical signs were present. BP was 130/80 mmHg.

Investigations

Serum osmolality 241 mosmol/kg; sodium 119 mmol/l; potassium 1.4 mmol/l; chloride 62 mmol/l; urea 4.7 mmol/l; recumbent plasma renin activity 25.4 ng/ml/hr; pH 7.51; PCO_2 33.1 mmHg; base excess +4.4 mmol/l, cortisol 565 ng/ml, glucose 6.2 mmol/l, calcium 2.55 mmol/l.

Urine excretion: volume 1000 ml/24 hr, sodium

2.0 mmol/24 hr, potassium 1.0 mmol/24 hr, chloride 0 mmol/24 hr, osmolality 186 mosmol/kg.

Total exchangeable electrolytes (Skrabal, Arnot and Joplin, 1973); sodium 27.6 mmol/kg (normal 38.1 mmol/kg), potassium 10.4 mmol/kg (normal 39.8 mmol/kg), total body water 28.5 litres (normal 28.2 litres).

Maximum urine osmolality after 12 hr water deprivation: 243 mosmol/kg (when repeated 2 months later this figure was 1153 mosmol/kg).

Chest and plain X-rays of abdomen were normal. Barium meal and cholecystogram normal.

Clinical course

Vomiting stopped following admission to the medical ward. The patient consumed the normal ward diet in which sodium content was approximately 60 mmol/day. Water ingestion remained at the same level throughout the ward stay. The effect of potassium chloride (Slow-K tablets, 104 mmol/day) on serum sodium and potassium concentrations is illustrated in Fig. 1.

The patient quickly regained vigour and her appetite subsequently improved.

Over the following year, bouts of vomiting occurred occasionally for which no physical cause was found. Serum electrolyte concentrations remained within normal limits.

Discussion

The validity of the 'sick cell' concept for producing hyponatraemia has been disputed (Leaf, 1974). In the present case hyponatraemia was probably due to more than one factor and resulted from sustained gastrointestinal losses of sodium, potassium and chloride, uncompensated for by dietary intake or renal conservation. A simultaneous rise in serum sodium and potassium concentrations during potassium chloride therapy revealed the importance of underlying potassium depletion in the causation of this form of hyponatraemia. Two variables which determine serum sodium concentration (Edelman *et al.*, 1958), namely total body sodium and total body potassium, were reduced with the effect that there was relative dilution of residual ECF and ICF solute. The third variable, total body water, was normal presumably because water ingestion had been maintained. Redistribution of solutes across the cell membrane related to external losses of sodium potassium, with water passively equilibrating in concert with solute

movements so that osmolality of ECF and ICF remained the same.

Severe potassium depletion interferes with energy metabolism. The ratio of ECF to ICF potassium concentration, on which cell membrane potential depends, declines with the degree of potassium depletion (Patrick and Hilton, 1979). Performance of the sodium/potassium 'pump' within the cell membrane, which requires metabolic energy for active transport, is reduced. Cellular extrusion of sodium and retention of potassium by the 'pump', which normally controls cell volume, is consequently impaired. Potassium replacement restores cell membrane potential and regenerates the sodium/potassium 'pump', effectively mobilizing sodium from the 'sick cell' as shown by a rise in serum sodium concentration in parallel with serum potassium concentration.

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