Potassium in the syndrome of inappropriate antidiuretic hormone secretion

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Summary

Serum potassium concentration was normal (≥ 3.6 mmol/l) in 29 of 32 patients with the syndrome of inappropriate antidiuretic hormone excess (SIADH) associated with a bronchogenic carcinoma. In 11 of the patients there was no significant change in serum potassium concentration after correction of the syndrome, by fluid restriction. Hypokalaemia is thus an uncommon finding in SIADH due to bronchogenic carcinomas.

Introduction

Descriptions of the biochemical features of the syndrome of inappropriate antidiuretic hormone (SIADH) excess (Bartter and Schwartz, 1967) emphasize an abnormality of sodium and water homeostasis. Changes in potassium balance are rarely mentioned although a reduced total exchangeable potassium (K_e) was noted in the earliest reported cases (Schwartz *et al.*, 1957) and has since been described together with hypokalaemia in a small number of cases (Jones *et al.*, 1968; Barraclough, 1971). A more recent description of the biochemical features of SIADH (De Troyer and Demanet, 1976) recorded a high incidence of hypokalaemia. In the present authors' experience of over 30 cases of SIADH, hypokalaemia is an uncommon finding and in view of this discrepancy they present their results.

Patient and methods

Thirty-two patients (12 female) with SIADH associated with a bronchogenic carcinoma were studied. Serum sodium and potassium (automated flame photometry), urine and plasma osmolality (freezing point depression) and plasma ADH concentration (Morton, Padfield and Forsling, 1975) were measured after an overnight fast and during recumbency in all patients. In 11 patients repeat measurements were made, under identical conditions, after a period of fluid restriction designed to correct the biochemical abnormalities of SIADH (Bartter and Schwartz, 1967). Results are expressed as mean $\pm$ s.e. mean and the significance of changes

induced by fluid restriction assessed by Student's paired 't' test.

Results

Patients were aged from 49–80 years (58 ± 2). All initially presented with a serum sodium of < 125 mmol/l although at the time of ADH measurement values ranged from 106–135 mmol/l (122 ± 3). Plasma ADH varied widely (6–643 pg/ml) and the values overlapped the normal range (2.5–11 pg/ml) when all states of hydration were considered. Plasma ADH was, however, inappropriately high for the concurrent plasma osmolality (251 ± 3 mosmol/kg, range 218–271) (Fig. 1). Urine osmolality ranged from 276–788 mosmol/kg (583 ± 23). The mean serum potassium concentration for the group was 4.4 ± 0.1 mmol/l (3.1–5.5) and was ≤ 3.6 mmol/l in only 3 patients (3.1, 3.2 and 3.5 mmol/l). Patients with the lowest serum sodium concentrations were not those with the lowest serum potassium. Hyponatraemia was corrected in 11 patients by fluid restriction (118 ± 1.5 to 137 ± 0.9 mmol/l) and although plasma ADH did increase (86 ± 27 to 131 ± 80 pg/ml) there was no significant change in serum potassium concentration (4.42 ± 0.17 to 4.37 ± 0.2 mmol/l). An increase of 0.5 mmol/l was seen in only 3 patients.

Discussion

The acute administration of ADH has been shown to increase renal excretion of potassium in a variety of animal species (Heller and Stephenson, 1950; Kurtzman *et al.*, 1975; Hiatt, Miller and Katayanagi, 1975; Barraclough, 1975). In normal man, ADH given acutely in large doses can produce a moderate increase in the rate of potassium excretion (Barraclough and Jones, 1970) but it does not alter potassium status in more prolonged studies (Stormont and Waterhouse, 1961).

SIADH represents a situation of chronic ADH excess in man, often associated with malignancy. The observations of a reduced K_e (Schwartz *et al.*, 1957; Jones *et al.*, 1968; Barraclough, 1971) have not always been confirmed (Kaye, 1966; Nolph and Schrier, 1970) and in cachectic patients could conceivably reflect a loss of muscle mass.

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While serum potassium does not necessarily reflect overall potassium status, it is important to know whether or not hypokalaemia is likely to be present in SIADH. De Troyer and Demanet (1976) recently described 26 cases of SIADH (without ADH measurement) of varying aetiology and recorded a 62% incidence of hypokalaemia (Serum $K^+ < 3.6$ mmol/l). Among 32 patients, the present authors have seen hypokalaemia in only 3 cases (9%) and have been unable to show consistent changes in serum potassium concentration during correction of the syndrome.

Fig. 1. Relationship of plasma ADH concentration to concurrent plasma osmolality in patients with the syndrome of inappropriate antidiuretic hormone (SIADH) release and in normal subjects. ●, SIADH in carcinoma of the bronchus; ▲, normal subjects (all states of hydration).

This striking difference in 2 series of comparable size may be accounted for by the different modes of presentation. None of the patients described was receiving any agents likely to affect serum potassium concentration. This was not the case in the series of DeTroyer and Demanet (1976). Of their 16 patients with hypokalaemia, 11 had either consumed 'vast quantities' of beer, received 'extensive' intravenous fluids (nature and potassium content not described) or had been given diuretics. It is known that diuretics may produce hypokalaemia and that 'vast quantities' of beer can provide a dilutional hyponatraemia together with profound hypokalaemia (Demanet *et al.*, 1971;

Hilden and Svendsen, 1975). Although the mechanism of the hypokalaemia is ill understood, it is produced by the beer *per se*, without SIADH. It seems possible, therefore, that factors other than SIADH may have contributed to the hypokalaemia in many of the patients. On the basis of these results it is concluded that unprovoked hypokalaemia is an unusual finding in SIADH associated with bronchogenic carcinoma.

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