removal of reducing substances and uraemic toxins. It would therefore seem justified to conclude that haemodialysis does not improve the glucose tolerance of patients on maintenance haemodialysis, as measured by the intravenous test. Nevertheless, k values are rather uncertain criteria, since plasma glucose disappearance curves are not usually monoexponential. Furthermore, the dynamics of insulin-glucose interactions are imperfectly described by a single parameter.[4] On the other hand, the metabolic performance of patients on chronic haemodialysis is basally depressed, and is intermittently challenged by such stresses as dehydration, blood-pressure and flow changes, and electrolyte depletion. This might explain why we obtained the lowest k values from the tests performed at the shortest time (about 15 minutes) after the dialytic stress. Different test conditions or treatment of data may well give different results.[5] Hence the acute effects of haemodialysis on glucose tolerance are probably weak, transitory, and altogether unpredictable.

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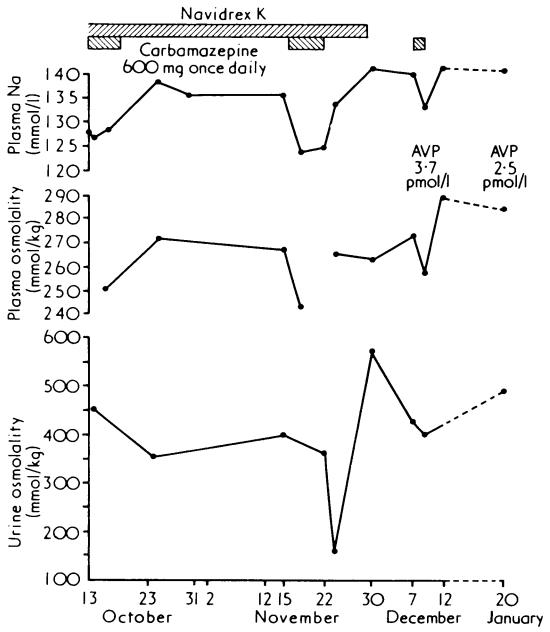
Raised plasma arginine vasopressin concentration in carbamazepine-induced water intoxication

Water intoxication has been reported in patients taking carbamazepine, though in one case there may have been an interaction with other drugs, particularly a thiazide diuretic.[1] Symptomless hyponatraemia has also occurred in patients taking carbamazepine,[2] but the mechanism by which carbamazepine acts is uncertain. We describe a patient who developed water intoxication while taking carbamazepine in whom, using a sensitive and specific radioimmunoassay,[3] we detected an inappropriately high concentration of plasma arginine vasopressin (AVP).

Case report

A 65-year-old woman presented with a two-year history of intermittent pain in the distribution of the right ilioinguinal nerve for which no cause could be found. She also had mild hypertension, which was controlled with methyldopa, propranolol, and cyclopenthiazide (Navidrex K). Carbamazepine 600 mg daily was given for the pain but with no relief, and tiredness and dizziness developed.

After taking carbamazepine for three weeks she was investigated in hospital with the following results: plasma sodium 128 mmol (mEq)/l, plasma urea 3·6 mmol/l (21·7 mg/100 ml), plasma osmolality 251 mmol (mOsm)/kg, urine osmolality 449 mmol/kg, and serum carbamazepine 24·0 μmol/l (6 μg/ml) (optimum range 16-40 μmol/l (4-10 μg/ml)). Carbamazepine was stopped, whereupon the tiredness and dizziness cleared and the plasma sodium and osmolality rose to normal. On two subsequent occasions, before and after stopping Navidrex K, carbamazepine was reintroduced and caused the same symptoms, with a fall in plasma sodium and osmolality (figure). During the last period on carbamazepine, immunoreactive plasma AVP was 3·7 pmol/l (4·0 pg/ml), which was inappropriately high for the plasma osmolality of 257 mmol/kg. Two months after stopping carbamazepine she was no longer hyponatraemic and the plasma AVP concentration (2·5 pmol/l; 2·7 pg/ml) was appropriate for the plasma osmolality (284 mmol/kg). Plasma cortisol at 2.15 pm was 338 nmol/l (12·2 μg/100 ml).



Urine osmolality and plasma sodium, osmolality, and AVP concentrations with and without treatment with carbamazepine and Navidrex K.

Conversion: SI to traditional units—Urine and plasma osmolality: 1 mmol/kg = 1 mOsm/kg. Plasma sodium: 1 mmol/l = 1 mEq/l. Plasma AVP: 1 pmol/l ≈ 1·08 pg/ml.

Discussion

Carbamazepine is one of many drugs that have been associated with inappropriate antidiuresis.[4] Its mode of action is not clearly understood, though it may stimulate vasopressin secretion, impair vasopressin degradation, potentiate vasopressin's renal action, or have an independent, direct effect on the renal tubule. Although there is much indirect evidence that the antidiuretic action of carbamazepine is mediated through an increased plasma vasopressin concentration,[4] some workers have reported low concentrations of immunoreactive plasma AVP in patients taking this drug.[5]

Our patient's hyponatraemia appeared to be related only to carbamazepine treatment. Interaction with a diuretic was excluded, and hyponatraemia recurred on reintroduction of carbamazepine. Furthermore, the hyponatraemia, low plasma osmolality, and high urine osmolality with normal renal and adrenal function could be attributed to the syndrome of inappropriate antidiuretic hormone secretion, and inappropriately high concentrations of plasma AVP were found. This supports the indirect evidence referred to above.[4]

A major problem has been measurement of extremely low plasma concentrations of AVP by either bioassay or immunoassay. With the recent improvement of radioimmunoassay techniques for measuring plasma AVP we expect confirmation that carbamazepine exerts its antidiuretic effect by raising the concentration of endogenous vasopressin.

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