

Water Intoxication during Carbamazepine Treatment

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Carbamazepine has recently been shown to have a vasopressin-like action and, like chlorpropamide, to be effective in controlling polyuria in patients with diabetes insipidus (Hartman, 1972; Uhlich *et al.*, 1972). In the case reported here carbamazepine, which was being given to a patient suffering from depression and psychogenic polydipsia, induced inappropriate secretion of antidiuretic hormone and water intoxication.

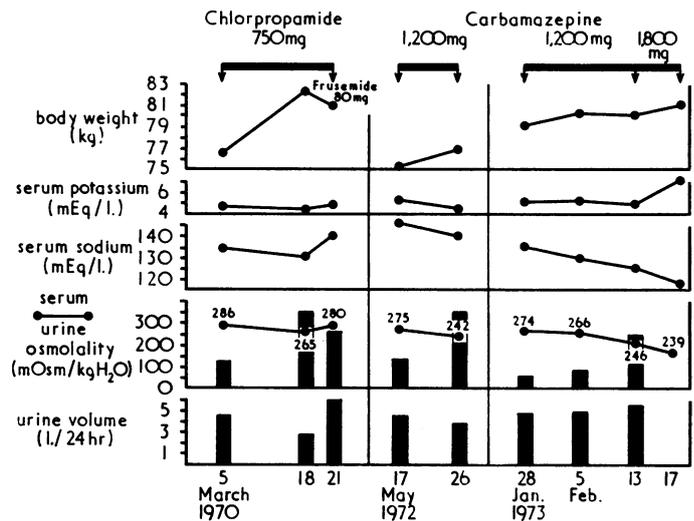
Case Report

A 36-year-old woman was admitted to the metabolic unit of the János Hospital in February 1970 with a tentative diagnosis of diabetes insipidus. She had had polydipsia and polyuria since a head injury at the age of 22. She had also undergone a personality change, and suffered from insomnia, depression, and epileptiform attacks, and had attempted suicide. On admission the patient had a diuresis of 6-7 l./24 hr. She weighed 76 kg. No significant abnormalities or organic neurological disease was found on examination. The serum osmolality was 286 mOsm/kg H₂O, and urine osmolality between 72 and 187 mOsm/kg H₂O. The serum sodium was 134-137 mEq/l., serum chloride 103 mEq/l., and serum potassium 4.7 mEq/l. The serum creatinine was 0.84 mg/100 ml, serum cholesterol 278 mg/100 ml, P.B.I. 5.3 µg/100 ml, and the Hamolsky test was 11.4%. Plasma cortisol levels were 15.5 µg/100 ml at 8 a.m., 10 µg/100 ml at 4 p.m., and 7 µg/100 ml at midnight. The fasting blood glucose was 80 mg/100 ml. One hour after the ingestion of 50 g glucose the blood glucose was 100 mg/100 ml, and after two hours it was 85 mg/100 ml. The results of other examinations were normal. Free water clearance studies carried out during a Carter-Robbins test showed an adequate antidiuretic hormone reserve. A diagnosis of psychogenic polydipsia was established.

The compulsive water drinking was unaffected by intensive tranquillizer treatment. Chlorpropamide 750 mg/day was given to relieve thirst (Hocken and Longson, 1968). The diuresis was reduced by a half and there was a substantial increase in body weight, but the drug had to be stopped because of overhydration, headache, dyspnoea, and hypoglycaemic episodes. The patient was discharged in an improved condition in October 1970.

She was readmitted to hospital in May 1972 and again in January 1973. Because of the epileptic history, character changes, and refractory depression carbamazepine in increasing doses was given. There was some improvement, but an increase in body weight and a decrease in serum osmolality and in serum sodium and chloride concentrations indicated overhydration similar to that observed during chlorpropamide treatment (see fig.).

The antidiuretic effects of carbamazepine were investigated in special studies during the patient's most recent stay in hospital. The abnormal water retention showed a definite relation to the dose of carbamazepine and it was progressive during prolonged treatment (fig.). Because of signs of water intoxication (headache, vomiting, dyspnoea, and confusion) carbamazepine was stopped and frusemide 80 mg was given. Six hours after the start of diuresis the patient's clinical condition improved, as it did when frusemide was given for water retention after chlorpropamide treatment (fig.).



Evidence of water intoxication induced by chlorpropamide and carbamazepine at different times in same patient.

Comment

Previous findings that carbamazepine had an antidiuretic action (Hartman, 1972; Uhlich *et al.*, 1972; Radó, 1973) were confirmed in this case. The clinical condition resembled the syndrome of inappropriate secretion of antidiuretic hormone (Bartter and Schwartz, 1967), as shown by a decreasing urine volume with increasing osmolality and accompanied by a sharp reduction in serum osmolality and sodium concentration, and by an increase in body weight, glomerular filtration rate and urinary sodium excretion. A definite relation was found between the dose of carbamazepine and the antidiuretic effect. A similar relation was found in previous studies with chlorpropamide (Radó *et al.* 1969, 1970 a, 1970 b).

Carbamazepine-induced abnormal water retention does not seem to have been reported before but there have been several reports of chlorpropamide-induced water intoxication, mainly in geriatric patients with diabetes mellitus and in a young patient with neurogenic diabetes insipidus (Cinotti *et al.*, 1972). The similarity of the antidiuretic effects of these two non-hormonal "vasopressin-like" agents has been confirmed in the present case. It has been suggested that they act by potentiating subthreshold amounts of antidiuretic hormone or by enhancing its release, or both (Garcia *et al.*, 1971).

The administration of a drug with an antidiuretic action to a patient with primary polydipsia is potentially dangerous, and the drug-induced syndrome of inappropriate antidiuretic hormone secretion (Hayes and Kaye, 1972) should be borne in mind when a patient on carbamazepine presents with dyspnoea, vomiting, headache, and mental confusion.

References

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