

Carbamazepine in the Treatment of Diabetes Insipidus in a Pituitary Dwarf

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SUMMARY

Carbamazepine (Tegretol) has an important role in the treatment of diabetes insipidus. We report a case which showed a most satisfactory response to the agent.

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Diabetes insipidus is classically treated by replacement therapy with various preparations of posterior pituitary hormones. Recently a number of drugs, unrelated to vasopressin, have been shown to possess antidiuretic properties.^{1,2}

These include thiazide diuretics,³ chlorpropamide,⁴ clofibrate⁵ and carbamazepine.⁶ We report a case of diabetes insipidus which responded only to carbamazepine. We are unable to find a similar report in the English literature on the successful treatment with carbamazepine of a patient with combined anterior and posterior pituitary deficiency.

CASE REPORT

A 19-year-old Black female was admitted to hospital for assessment of pituitary function. At the age of 3 years she developed tuberculous meningitis which was successfully treated. Over the next few years it was noted that her growth was stunted. Diabetes insipidus was also suspected, and this diagnosis was confirmed at the age of 6 years. Pituitary snuff was effective in controlling this at first, but thereafter hospital attendance became irregular and infrequent. She was readmitted to hospital when human growth hormone became available; also to determine the effect of oral therapy on her diabetes insipidus. Examination showed an obese, dwarfed female with an infantile facies and no secondary sexual characteristics. Nocturia was marked, 8-10 times each night, accompanied by polydipsia. Urinary output varied from 3 to 4 litres/24 h.

The following tests were performed: 24-hour urinary ketosteroids 1.9 mg (normal 3.5-15.0 mg); 17-hydroxycorticosteroids 5.0 mg (normal 4.0-15.0 mg); luteinising hormone > 25 IU/litre, protein-bound iodine 6.8 mg (normal 2.5-7.5 mg) T₄ 4.8 mg/100 (normal 4.5-5.8 mg/100 ml), T₃-uptake 120% (normal 94-124%).

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TABLE I. INSULIN HYPOGLYCAEMIC TEST

	Blood sugar (mg/100 ml)	Cortisol (μ g/100 ml)	Growth hormones (ng/ml)
Fasting	86	4	1,20
30 min	65	7	0,8
60 min	36	25	0,8
90 min	48	45	0,6
120 min	75	11	0,6

The bone age was 9 years.

Therapy for dwarfism with human growth hormone⁷ was started in November 1972, with 4 IU 3 times a week. Metabolic response over 3 days was confirmed by a decrease in urea, increased calcium excretion and an increase in nitrogen retention. Pretreatment height was 121.8 cm and 6 months later it had increased to 124.2 cm. Treatment for diabetes insipidus was initiated with thiazide diuretics, but this regimen produced no change in urinary output. Chlorpropamide was then given, 250 mg daily, and increased to 500 mg daily, but this also failed to reduce the polyuria. Toxic reactions, notably hypoglycaemia, did not occur. Clofibrate 1 g *b.d.* was substituted, but this was likewise ineffective. Finally carbamazepine was administered, 100 mg *b.d.*, and this dose was increased to 200 mg *t.d.s.*

Urinary output was strikingly reduced to 1 500 ml/day. Carbamazepine was then discontinued, as it was uncertain whether this response was due to the delayed effect of chlorpropamide given 2 weeks previously. This effect may persist as long as 10-15 days after withdrawal of the drug. Urinary volumes again increased. The patient left hospital because of domestic problems, but returned 3 months later, and once again the response to carbamazepine was confirmed. She has been maintained on 100 mg *b.d.* and has had no side-effects from the drug.

DISCUSSION

Hypopituitarism and diabetes insipidus are well-recognised complications of basal tuberculous meningitis.

In patients with ACTH deficiency, the diabetes insipidus is masked due to a lack of cortisol which is necessary for normal diuresis. This can be unmasked by glucocorticoid replacement. In our patient, diabetes insipidus was present because ACTH production was probably normal, as evidenced by the marked rise in plasma cortisol in response to hypoglycaemia. The failure of response to chlorpropamide and clofibrate was probably due to total

TABLE II. RESPONSE TO CARBAMAZEPINE

Date	Treatment	Urine volume/24 h (ml)	Urine osmolarity (mOsm/kg)	Serum osmolarity (mOsm/kg)	Free water clearance (ml/min)
26 June 1972	Nil	4 200	101	306	+2,0
10 August 1972	Tegretol 200 mg t.d.s.	1 200	571	282	-0,85
23 October 1972	Nil	4 800	23	292	+3,06
13 November 1972	Tegretol 100 mg t.d.s.	2 700	132	292	+1,03
16 November 1972	200 mg t.d.s.	2 400	575	284	-1,68
4 May 1973	200 mg t.d.s.	1 200	634	282	-1,04

lack of circulating antidiuretic hormone which might be assumed from the pretreatment urine osmolarity of less than 150 mOsm/kg. A response to chlorpropamide⁸ and clofibrate⁹ requires a small amount of endogenous antidiuretic hormone. Animal experiments support the hypothesis that carbamazepine has a central effect on antidiuretic hormone synthesis or its release.¹⁰

Of all oral drugs used in the treatment of diabetes insipidus, chlorpropamide appears to be the most widely used. However, in patients with both anterior and posterior pituitary deficiency, hypoglycaemia may present a serious problem. Attempts to overcome this have been made by combining it with thiazides¹¹ or diazoxide.¹² We feel that carbamazepine could simplify treatment in such cases,

or in others who fail to respond to other forms of oral therapy.

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