Antidiuretic function in Sheehan’s syndrome

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Abstract

Twenty patients with postpartum hypopituitarism underwent a dehydration test followed by the administration of synthetic arginine-vasopressin (DDAVP; desmopressin). Panhypopituitarism was confirmed by hormonal assays in the basal state and after stimulation with combined luteinising hormone releasing hormone-thyrotrophin releasing hormone-insulin. All the patients were given replacement therapy with hydrocortisone and thyroid hormones. Results were compared with those in 12 normal women.

Urinary concentrating ability was diminished in the patients as compared with the controls (maximum urine osmolality 688 (SEM 23) mmol (mosmol)/kg in the patients v 967 (SEM 29) mmol/kg in the controls). Also the change in urine osmolality after administration of desmopressin was greater in the patients (v 9.55 (SEM 1.98)% in the patients v 2.49 (SEM 0.96)% in the controls)

Partial diabetes insipidus is apparently common in Sheehan’s syndrome. This association should be borne in mind when managing these patients, especially those in acute failure.

Introduction

Clinical diabetes insipidus is apparently an uncommon complication of postpartum pituitary insufficiency. This is surprising in view of Sheehan and Whitehead’s reports of postpartum anatomical lesions in the posterior pituitary and the hypothalamic secretory neurones in most cases of Sheehan’s syndrome.

Agullo et al reviewed the scanty reports published up to 1969. Most of the 26 cases appeared to be transient polyuria-polydipsia and only a few could be classified as true diabetes insipidus. Single cases were reported subsequently, and in two reports anterior pituitary function was normal.4 5 Little attention has been given to the posterior pituitary in reported large series of Sheehan’s syndrome. Purnell et al reviewed 18 patients and found two cases of polyuria and polydipsia, one of which was transient. Haddock et al found two cases of transient polyuria and polydipsia among 50 patients.

There has never been a systematic study of antidiuretic function in Sheehan’s syndrome and we therefore attempted to investigate a homogeneous series of patients. We report the data obtained using the combined dehydration and arginine-vasopressin test.

Subjects and methods

Twenty patients with the characteristic clinical picture of panhypopituitarism of slow onset after haemorrhagic delivery were included in the study. Total failure of the anterior pituitary was confirmed by a combined luteinising hormone releasing hormone-thyrotrophin releasing hormone-insulin stimulation test. Blood samples were collected every 20 minutes for two hours for determination of follicle stimulating hormone, luteinising hormone, thyrotrophin releasing hormone, prolactin, growth hormone, cortisol, and adrenocorticotropic hormone (ACTH) concentrations. In addition, corticotrophin deficiency was confirmed by a lack of response of the plasma ACTH concentration and urinary 17-hydroxycorticoid excretion to metyrapone administration. Other causes of hypopituitarism were ruled out by the history, results of physical examination, laboratory findings, and radiological evidence. To eliminate the effect of thyroid or adrenal insufficiency all the patients were treated with hydrocortisone and thyroid hormones and return to normal was confirmed by assay of serum cortisol and thyroid hormone values.

The mean age of the patients was 35.3 years (range 21-42) and the average interval since the onset of their disease 7-5 years (range 1-12). Results were compared with those in 12 normal women (mean age 29.5 years, range 22-42).

Protocol

The dehydration tests was conducted using the procedure of Miller et al.10 11 All subjects were deprived of food and water from 7 pm on the evening before the test. Urinary flow and osmolality were measured every hour from 8 am. Maximal urinary concentrating ability was assumed to be achieved when the osmolality did not change by more than 30 mmol (mosmol)/kg in three successive samples. A blood sample was drawn for determination of serum osmolality and 20 mmol desmopressin (DDAVP) given by intranasal spray. The effect of desmopressin on urine osmolality was estimated one hour after administration. If after 24 hours of fasting the urinary concentration plateau was not attained the drug was administered systemically. An Advanced Instruments type 3 D II osmometer was used to determine osmolality.

Results are expressed as means and SEM. Student’s t test was used for statistical analysis.

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Results

Basal data—The mean 24 hour urine volume was 2243 (SEM 145) ml (range 1530-3725), higher than the average output in 52 normal women (811 (SEM 45) ml). Thirteen patients excreted more than 2000 ml and all more than 1500 ml. All the patients had at least one episode of nocturia. The mean 24 hour urine osmolality was 377 (SEM 22) mmol/kg (range 102-536).

After testing the maximal urine osmolality was 688 (SEM 23) mmol/kg (range 515-838) in the patients and 967 (SEM 29) mmol/kg in the controls. This maximal concentration was achieved by 21 hours in the patients and by 16 hours in the controls. At the end of the test serum osmolality was 291 (SEM 0-97) mmol/kg in the patients and 285 (SEM 0-97) mmol/kg in the controls.

After administration of desmopressin the mean change in urine osmolality was +9.55 (SEM 1.98)% in the patients (range +2.59 to +33.70) and -2.49 (SEM 0.96)% in the controls (range -6.93 to +2.44).

In all these results the differences between the two groups were highly significant (p<0.001) (figs 1 and 2).

Discussion

The response to the dehydration test was clearly abnormal in these patients. Compared with the control group they required longer to reach their maximal osmolality, which remained lower.

DDAVP was kindly provided by Ferring Laboratories, Malmo, Sweden.

References


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