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PREGNANCY AND DIABETES INSIPIDUS


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Diabetes insipidus

Thirst is regulated in man and mammals by osmoreceptors in the supra-optic nuclei of the hypothalamus. An increase in plasma osmolality releases vasopressin from glandular neurones in these nuclei, which is then loosely bound to a carrier protein, neurophysin, and passes down the axons of the supraoptico-hypophysial tract of the posterior lobe of the pituitary gland. Release of vasopressin also occurs, even if plasma osmolality is low, under the stimulus of pain, excitement, alpha-adrenergic agents, opiates, barbiturates and nicotine, and in states of rapid plasma or extra-cellular fluid loss, for example, haemorrhage and burns. Vasopressin release is inhibited by alcohol.

Vasopressin, like its companion hormone oxytocin, is a cyclic polypeptide of 9 amino-acids. Man and most mammals produce arginine-vasopressin, the pig and the hippopotamus lysine-vasopressin. Vasopressin increases the permeability of the distal and collecting tubules of the renal nephron to water, thus potentiating water reabsorption. This action is mediated by cyclic 3:5: adenosine-monophosphate which promotes active sodium ion transport across the cell membrane, and hence osmotic transfer of water. The biological half-life of vasopressin is 20 minutes and the plasma level very low. It is metabolised chiefly in the liver.

Diabetes insipidus, where up to 15 litres of very dilute urine are passed daily, may result from inadequate central release of vasopressin or from a failure of renal tubular response to normal amounts of the hormone.

Central causes include:

a. Basal skull fracture interrupting the supraoptico-hypophysial tract.

b. Suprasellar neoplasms, especially craniopharyngioma.

c. Granulomata (for example, tuberculosis, sarcoidosis, histiocytosis-X) of the hypothalamus or mid-brain.

d. An autosomal dominant gene upon which the acronym DIDMOAD has been bestowed: Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy, and Deafness (sensori-neural).

In the cranial group, up to 25 per cent of cases remain as idiopathic, although in some instances post-viral encephalitis (for example, mumps) has been implicated.

Failure of renal tubular response to vasopressin may result from:


b. Acquired. (i) Chronic hypercalcaemia, for example, parathyroid adenoma, sarcoidosis. (ii) Chronic hypokalaemia, for example, diarrhoea, laxative abuse,

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diuretics, Conn's syndrome, carbenoxolone, liquorice. (iii) Chronic pyelonephritis and analgesic nephropathy. (iv) Heavy metal poisoning and lithium treatment of manic-depressive psychosis.

Investigation of suspected diabetes insipidus should therefore include: (i) Skull radiograph. (ii) Glucose tolerance test. (iii) Assessment of anterior pituitary function. (iv) Renal function tests, including excretion urography as patients with actual diabetes insipidus may secondarily develop hydronephrosis.

Failing any other cause, it remains to distinguish diabetes insipidus from psychogenic polydipsia. This is achieved by measuring urine osmolality before and after 8 hours of water deprivation. In normal subjects and those with psychogenic polydipsia, day-time urine osmolality will rise to at least 800 mOsmol/l, whereas in diabetes insipidus concentration to above 300 mOsmol/l is exceptional and implies severe dehydration which should be avoided by abandoning the test if during it body weight falls by 3 per cent or more. The effect of injected aqueous vasopressin on a repeated test is then observed; nephrogenic diabetes insipidus does not respond.

Treatment of diabetes insipidus, if no other cause is found, may then consist of:

a. Porcine lysine-vasopressin, in oily injection, 5 to 10 units twice or thrice weekly. This is potentially immunogenic.

b. Synthetic lysine-vasopressin in nasal spray.

c. Synthetic arginine-vasopressin analogue (desmopressin DDAVP, 1.des.amino.8.d.arginine vasopressin) as nasal solution 10 to 20 microg. twice daily or as injection 2 to 4 microg daily.

d. Clofibrate, which enhances hypothalmic vasopressin release.

e. Chlorpropamide, carbamazepine, which potentiate renal tubular response to vasopressin.

f. Thiazide diuretics, which paradoxically reduce urine flow in both cranial and nephrogenic diabetes insipidus by up to 50 per cent.

Fluid changes in pregnancy

Normal pregnancy is accompanied by changes in body fluids which have important implications in the management of diabetes insipidus in pregnancy, an unusual clinical combination, Hendricks (1954) describing only 50 cases in a review of the world literature.

In normal pregnancy plasma volume increases by 40 per cent to a peak at 32 to 34 weeks of gestation. Plasma osmolality falls in the first 8 weeks from 290 to 280 mOsmol/l, both total cations and total anions falling by about 5 mmol/l. Glomerular filtration rate increases by 40 per cent so that plasma creatinine and blood urea fall by 40 per cent. The filtered load of sodium ions reaching the renal tubule rises equivalently, thus stimulating renin and aldosterone release, and the extracellular fluid compartment is enlarged and total body water and sodium are raised. The lack of diuresis in response represents the altered fluid
homeostasis of pregnancy, although a water load produces a brisker diuresis than in the non-pregnant state. The hypothalamic osmoreceptors are reset to regard the reduced plasma osmolality as normal, so that vasopressin output does not change markedly.

The effect of diabetes insipidus on pregnancy

Pre-existing diabetes insipidus does not affect fertility, labour, or lactation (Barnes 1976) but problems may arise as follows:

a. Thirst in pregnancy may be a symptom of diabetes insipidus or diabetes mellitus or may occur with nocturia as a temporary disturbance in early normal pregnancy.

b. Even in treated diabetes insipidus severe dehydration can result from hyperemesis gravidarum.

c. Ureteric reflux and hydronephrosis secondary to diabetes insipidus predispose to urinary infection in pregnancy.

d. In hereditary forms of diabetes insipidus, especially the nephrogenic X-linked type, the newborn male baby must be watched carefully for dehydration.

e. General anaesthesia for delivery, or prolonged labour, may lead to dehydration if parenteral vasopressin and intravenous fluids are not given.

Some of these problems are illustrated by Mrs. F., aged 31 years, a recent patient of the British Military Hospital, Munster, who first complained of thirst and polyuria in England in March 1974. At first, diabetes mellitus was suspected, and treated with phenformin to no avail. A diagnosis of diabetes insipidus was then established, and she responded well to porcine vasopressin in oily injection three times weekly. She was admitted to the British Military Hospital, Munster in November 1974 with moderately severe dehydration. She was 12 weeks pregnant and had been vomiting frequently. She had had one entirely normal pregnancy six years before. She improved with increased frequency of vasopressin dosage and through the pregnancy proved to be her own best judge of dosage requirement eventually at full term needing 10 units of vasopressin twice to three times daily by intramuscular injection. The onset of labour was spontaneous and its course uneventful, with the delivery of a healthy child, whom she then fed from the breast happily and successfully. During the puerperium her vasopressin requirements fell progressively until six weeks later she was having her normal 10 units twice or thrice weekly. She has tried intranasal desmopressin but much prefers to have vasopressin injections. Her case is unusual in that in most reported instances the requirement for vasopressin increases only modestly. In a second recent case, Mrs. D., a patient of the British Military Hospital, Rinteln, the dosage of oily vasopressin by injection rose from 10 units twice weekly to 10 units three times weekly during an uneventful pregnancy and labour.

REFERENCES

