Continuous vasopressin replacement in diabetes insipidus

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Abstract
Five children who developed diabetes insipidus as a manifestation of severe brain injury received continuous intravenous treatment with a solution containing both aqueous vasopressin and appropriate crystalloid replacement. Polyuria, hypernatraemia, and decreased urine osmolalities were safely corrected in all patients within eight to 28 hours.

Diabetes insipidus is a well recognised complication of severe brain injury; its presence indicates damage to the hypothalamo-neurohypophyseal axis with associated impairment of vasopressin secretion. The consequent excretion of large volumes of dilute urine can lead to dehydration, hypernatraemia, hypokalaemia, and hypotension if not effectively treated. This report describes an intravenous replacement regimen utilising aqueous vasopressin and appropriate crystalloid replacement in five children who developed diabetes insipidus during the course of their illness and who were admitted to the intensive care unit.

Patients, methods, and results
The injuries sustained by each patient and the corresponding replacement regimens used are summarised in the table. Vasopressin infusion was given as soon as the diagnosis of diabetes insipidus was confirmed: diagnostic criteria included polyuria (>30 ml/kg/day), hypernatraemia, and low urine osmolality (<250 mmol/kg). No patient received osmotic diuretics (mannitol) in the 12 hours before, or during the period of, vasopressin infusion. The regimen constituents were dictated by the fluid and electrolyte balance of each patient and administered in conjunction with our standard restricted volume (10–20 ml/kg/24 hours) treatment for such cases. Two units of aqueous vasopressin were added to each litre of the appropriate crystalloid solution, and the resultant mixture was infused to replace 80–110% of measured urine excretion. The volume of replacement was revised according to the previous hour's urinary output. The serum sodium was recorded every two to four hours and the urine osmolality every 12 to 16 hours. The infusion in each case continued until the clinical and biochemical manifestations of diabetes insipidus

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Summary of clinical presentation, treatment, and patient outcome

Case No	Patient details			Infusion regimen				Results			
	Age (years)	Nature of injuries*	Time of onset of diabetes insipidus (hours)	Urine replaced (%)	Fluid constituents	Duration of infusion (hours)	Total dose of vasopressin (units)	'Time to control' of diabetes insipidus (hours)†	Urine output	Serum sodium	Urine osmolality
1	8	Pedestrian: motor car accident, closed head injury and fractured right femur, severe cerebral oedema	6	80	Half normal saline + 2U vasopressin/l	10	1.6	2	6	9	Died
2	1.5	Pedestrian: motor car accident, closed head injury, cerebral contusions, subarachnoid blood, grade III ventricular haemorrhage	10	100	(1) Sodium lactate (Hartmann's solution) (2) 5% dextrose + 2U vasopressin/l	(1) 12 (2) 36	4.3	8	20	28	Survived: full recovery
3	6	Passenger: motor car, accident, closed head injury, mesenteric lacerations, frontal, parietal, occipital haemorrhage, and cerebral oedema	16	110	4% Dextrose/0.18% saline + 2U vasopressin/l	15	5.4	8	10	16	Died
4	15	Diabetes mellitus—ketoacidosis. Day 3: cerebral oedema	84	100	5% Dextrose + 2U vasopressin/l	12	6.4	8	10	12	Died
5	14	Cyclist: motor car accident, closed head injury and fracture/dislocation C2/C3	6	100	5% Dextrose + 40 mmol potassium chloride + 2U vasopressin/l	8	5.5	7	7	7	Died

*Including computed tomogram.
†Defined as: urine output <2 ml/kg/hour, serum sodium <145 mmol/l, and urinary osmolality >290 mmol/kg.

had resolved—namely, urine volume <2 ml/kg/hr, urine osmolality >300 mmol/kg, and serum sodium concentration <145 mmol/l.

Discussion

The clinical course of post-traumatic diabetes insipidus was first elucidated in 1948.¹ Diagnostic criteria include the excretion of large volumes (>30 ml/kg/day) of dilute urine (osmolality <250 mmol/kg) associated with hypernatraemia (serum sodium concentration >145 mmol/l) in the absence of concomitant diuretic treatment.² The clinical presentation of diabetes insipidus varies,³ but all forms result from inadequate secretion of antidiuretic hormone secondary to disruption of either the supraoptic and paraventricular hypothalamic nuclei, or their neuronal connection to the posterior pituitary gland.

Effective treatment involves the administration of any of a group of synthetic or naturally occurring analogues of antidiuretic hormone by a variety of different methods.⁴ Vasopressin injection (an aqueous solution of the hormone) has a short duration of action (two to eight hours) and is therefore of value in the acute

stages of presentation of diabetes insipidus and its early management. A regimen involving crystalloid replacement of measured hourly urine output, augmented by a small dose (2 U/litre of solution) of aqueous vasopressin has been used successfully in adults. We currently use a similar regimen in children.

In all five cases described, the urine output was reduced to acceptable levels within eight hours of diagnosis and treatment of the diabetes insipidus. In each case, however, the serum sodium took an extra six to 20 hours to decrease to 145 mmol/l.

The advantages of this regimen include the steady decrease in the serum sodium concentration, the convenience of administration, its adaptability to changing fluid and electrolyte demands, and an inherent dose regulation corresponding to changing hourly urine production.

This flexibility is illustrated in case 3 (figure A). Cessation of the infusion at 15 hours coincided with unmasking of persistent diabetes insipidus, while resumption of the replacement regimen brought resolution of symptoms in a further six hours. A possible disadvantage (common to all therapeutic alternatives) is the danger of vasopressin overdosage and associated water toxicity; in case 4 (figure B), the serum sodium concentration fell to 127 mmol/l and was associated with a high urinary osmolality and a urine output of 1 ml/kg/hour. Water overload and cerebral oedema are potential hazards of this treatment; thus the patient's conscious state must be frequently monitored and the intracranial pressure measured if the patient is receiving muscle paralyzing drugs. Frequent biochemical testing (measurement of urine volume every hour, electrolytes every four hours, and urine osmolalities every 12 hours) is also essential. Overall, the average dose of vasopressin administered was 9 mU/kg/hour (range 5–14 mU/kg/hour). This is significantly greater than the intravenous regimen described by Chanson *et al.*,⁵ but compares favourably with other proposed regimens.⁶

This report describes an effective, safe, and convenient method of administration of vasopressin and crystalloid replacement that optimises the physiological state of a head injured patient who has diabetes insipidus. It is likely that this regimen could also be used in children with diabetes insipidus after neurosurgery.

This regimen was introduced to the intensive care unit by Dr Frank Shann.

Variation in serum sodium and urine output, both with and without vasopressin replacement for case 3 (A) and case 4 (B). Hatched lines indicate the period of vasopressin infusion; underlined numbers represent urinary osmolalities.

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