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 hypothalamic-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.

Summary of clinical presentation, treatment, and patient outcome

<table>
<thead>
<tr>
<th>Case No</th>
<th>Patient details</th>
<th>Infusion regimen</th>
<th>Results</th>
<th>Patient outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age (years)</td>
<td>Time of onset of diabetes insipidus (hours)</td>
<td>Urine replaced (%)</td>
<td>Fluid constituents</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>6</td>
<td>80</td>
<td>Half normal saline +2U vasopressin/1</td>
</tr>
<tr>
<td>2</td>
<td>1-5</td>
<td>10</td>
<td>100</td>
<td>(1) Sodium lactate (Hartmann’s solution) (2) 5% dextrose+2U vasopressin/1</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>16</td>
<td>110</td>
<td>4% Dextrose/0-18% saline +2U vasopressin/1</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>84</td>
<td>100</td>
<td>5% Dextrose+2U vasopressin/1</td>
</tr>
<tr>
<td>5</td>
<td>14</td>
<td>6</td>
<td>100</td>
<td>5% Dextrose+40 mmol potassium chloride+2U vasopressin/1</td>
</tr>
</tbody>
</table>

*Including computed tomogram.
†Defined as: urine output <2 ml/kg/hour, serum sodium <145 mmol/l, and urinary osmolality >290 mmol/kg.
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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. 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. The clinical presentation of diabetes insipidus varies, 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. 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 paralysing drugs. Frequent biochemical testing (measurement of urine volume every hour, electrolyte every four hours, and urine osmolalities every 12 hours) is also essential. Overall, the average dose of vasopressin administered was 9 μU/kg/hour (range 5-14 μU/kg/hour). This is significantly greater than the intravenous regimen described by Chanson et al., but compares favourably with other proposed regimens.

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.

3 Defoer F, Mahler C, Dua G, Appel B. Post-traumatic diabe-
4 Hartshorne J, Hartshorne E. Vasopressin in treatment of diabe-
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Arch Dis Child 1990 65: 896-897
doi: 10.1136/adc.65.8.896

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