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Clinical review

Lesson of the week

Acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution

Do not infuse a hypotonic solution if the plasma sodium concentration is less than 138 mmol/l

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Hyponatraemia (plasma sodium concentration less than 136 mmol/l) is acute if the decrease in natraemia occurs within 48 hours. The major dangers from this are brain cell swelling and herniation. [1 2] Two factors are required for hyponatraemia to develop: a source of electrolyte free water and vasopressin to prevent the excretion of that water.[3] Electrolyte free water is given routinely as maintenance fluids based on formulas developed in studies in healthy children more than 40 years ago. [4 5] There are many reasons to anticipate that vasopressin will be released in sick patients (box).[6] Patients with an acute illness may arrive in hospital with a low plasma sodium concentration because of previous water intake. Hence, to minimise the potential threat of brainstem herniation it is important to measure the plasma sodium concentration if intravenous solutions are to be given.

Causes of vasopressin release

- Hypernatraemia (most important stimulus, but not in these patients)
- Low "effective" circulating volume (greater than 7% decrease in extracellular fluid volume)
- Nausea, pain, anxiety
- Drugs (some act through inducing nausea)
- Afferent stimuli by way of the vagus nerve for example, lung lesions

- Disturbances of the central nervous system (meningitis, encephalitis)
- Metabolic and endocrine disorders for example, hypothyroidism, hypoadrenalism, porphyria

We describe symptomatic hyponatraemia developing over 48 hours in children. In each patient, hypotonic solutions were infused using current guidelines.[7] We related the volume of electrolyte free water given to the decrease in natraemia and assessed whether actions of vasopressin persisted to guide emergency corrective therapy.[8]

We reviewed all patient charts (306 charts) with a recorded diagnosis of hyponatraemia for the past 10 years. Patients were included if their decrease in natraemia was to less than 130 mmol/l and this occurred within 48 hours, if intravenous fluids were given, and if an underlying disease did not compromise renal handling of sodium or water. Thirty patients had acute hyponatraemia. Crucial information was missing for seven, leaving 23 patients in the study group. The median age was five years (range one month to 21 years), with males predominating (18 of 23); 13 developed hyponatraemia in the postoperative period. Fifteen patients were referred to the critical care unit after the development of symptomatic hyponatraemia while receiving intravenous fluids 11 were from the hospital wards and four were transferred from other institutions. Symptoms included seizures (18 patients) and vomiting,17 a warning sign of an increased intracranial pressure. Treatment was withdrawn from five patients after brainstem coning. One patient sustained permanent, severe neurological damage.

Results

All the children received hypotonic fluids while their plasma sodium concentration was less than 140 mmol/l, because of the wide belief in paediatric practice that "maintenance fluids" should be hypotonic.[9] In fact the volume of maintenance fluid given was 50% greater than recommended values in 16 of the 23 patients. This infusion of hypotonic fluids increased the risk of acute hyponatraemia and brain swelling because vasopressin is typically present in this setting.[1 2 10 11] In quantitative terms, some of the electrolyte free water infused was retained in six of the patients because their urine sodium plus potassium concentration was less than 25 mmol/l (fig 1). In six patients more electrolyte free water was infused than needed to cause the observed decline in natraemia (points above line of identity in fig 2). The remainder of the patients had a decrease in natraemia that exceeded the decline if the entire volume of electrolyte free water infused was retained (points below broken line in fig 2). Therefore there was either another non-recorded input of water or the excretion of a large volume of hypertonic urine (a desalination of infused isotonic saline[12]).

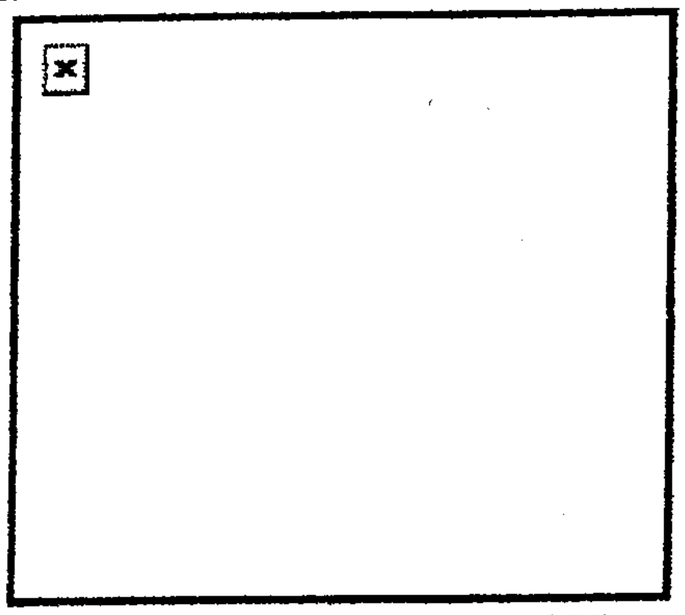

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Fig 1. Concentration of sodium and potassium in urine at nadir observed for plasma sodium concentration in 17 patients (numbers represent rate of urine flow)

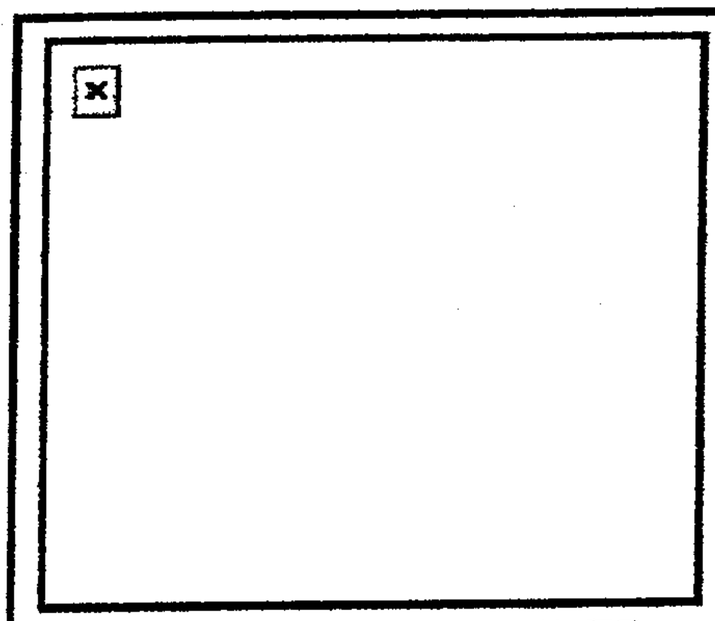

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Fig 2. Comparison of decline in plasma sodium concentration with amount of electrolyte free water given in 17 patients. Difference in sodium concentration was between initial value and that at its nadir

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One objective of our study was to assess the renal actions of vasopressin. Because six patients had very hypotonic urine at their recorded nadirs of natraemia, their plasma sodium concentration might have been much lower before water diuresis began (fig 1). Had their plasma sodium concentration been measured after this large water diuresis, the erroneous conclusion might have been drawn that acute hyponatraemia had never been present. Hence its incidence may be much higher than shown by an analysis of hospital records. Therefore acute hyponatraemia could have been an occult cause of morbidity and mortality.

Another implication of cessation of the release of vasopressin concerns treatment. Treatment for acute, symptomatic hyponatraemia causes a prompt decline in the size of brain cells.[10] Hypertonic saline (3%) is the commonest treatment for shrinking brain cell volume, thereby lowering intracranial pressure. Treatment must be prompt because deterioration may be rapid and irreversible, even when symptoms are mild. Enough hypertonic saline (a total of 5 mmol of

sodium chloride per litre of body water[13]) is needed acutely to lower intracranial pressure sufficiently to minimise this risk (the plasma sodium concentration should be increased by 5 mmol/l over several hours). Because an excessively rapid rate of correction of hyponatraemia might have deleterious effects,[6] hypertonic saline should not be given if there is a brisk water diuresis. For example, the plasma sodium concentration will also increase by 1.2 mmol/l/h if 6 ml of electrolyte free water are excreted per kilogram per hour (total body water is close to 600 ml/kg; 6 ml is a 1% change of 120 mmol/l). Whereas excretion of hypotonic urine indicates that electrolyte free water is being excreted (6 of 17 patients, fig 1), it is also important to consider the rate of urine flow. Little electrolyte free water was excreted in the index oliguric patient (flow 0.16 ml/kg/h). By contrast, the excretion of electrolyte free water was high enough to increase the plasma sodium concentration by close to 3 mmol/l/h in the polyuric index patient who recovered (15 ml/kg/h). Vasopressin continued to act in patients excreting isotonic or hypertonic urine, so hypotonic intake must be avoided in them. With these high urine tonicities a further decrease in natraemia would be anticipated if the urine output was high (index case designated with a urine output of 5.3 ml/kg body weight, fig 1).[12] Finally, vasopressin concentrations may decline abruptly, increasing the excretion of electrolyte free water.

Serious symptoms may become evident when hyponatraemia approaches 120 mmol/l, but there are cases where symptoms become evident with a higher plasma sodium concentration, whereas others tolerate this electrolyte disorder without developing seizures.[14] Apart from underlying conditions that might make a patient more susceptible to seizures, a possible important factor could be the extracellular fluid volume of the brain. If this volume was expanded by a large infusion of isotonic saline, a higher intracranial pressure might be present at a given degree of hyponatraemia. Moreover, because there is a relatively larger proportion of brain cell volume to extracellular fluid volume in young patients, they are more vulnerable to an increase in brain cell volume.

Study limitations

Because of a reporting and referral bias, the incidence of adverse outcomes from hyponaetremia cannot be deduced from these data. Our results highlight the dangers of the routine use of hypotonic solutions when vasopressin acts. The currently used guidelines for maintenance fluids in children admitted to hospital must be changed because they do not take into account the unpredictability of vasopressin secretion. We recommend that the concentration of plasma sodium should be measured when starting an intravenous infusion. If it is less than 140 mmol/l then isotonic and not hypotonic fluids should be given. The use of hypotonic solutions should be reserved for patients who have a plasma sodium concentration greater than 140 mmol/l. If a patient receives intravenous fluid that exceeds 5% of total body water (30 ml/kg) then their plasma sodium concentration should be measured. If an intravenous infusion is started to give drugs, a small volume should be used, and the solution should be isotonic if possible.

Acknowledgments

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Footnotes

Competing interests: None declared.

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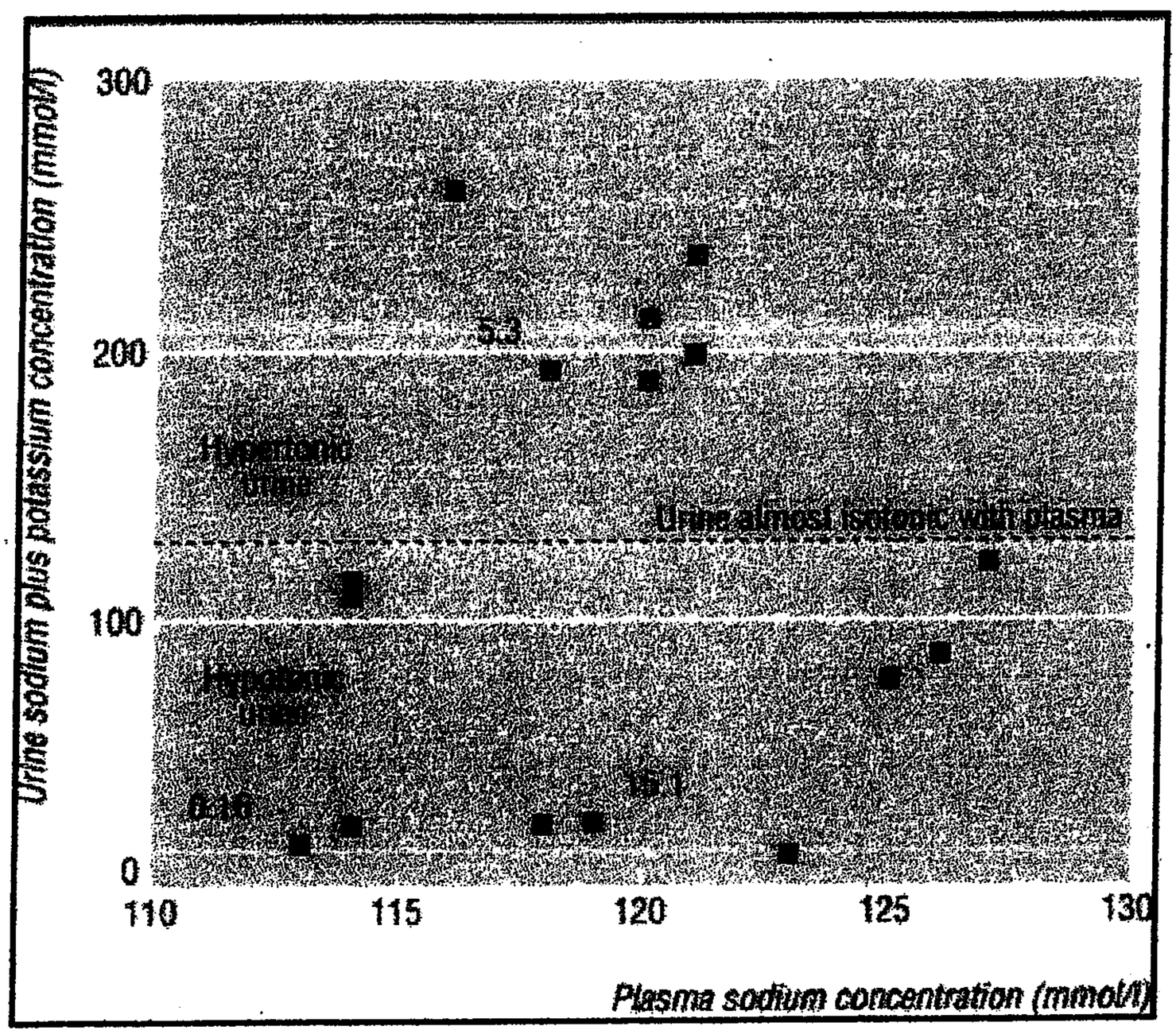

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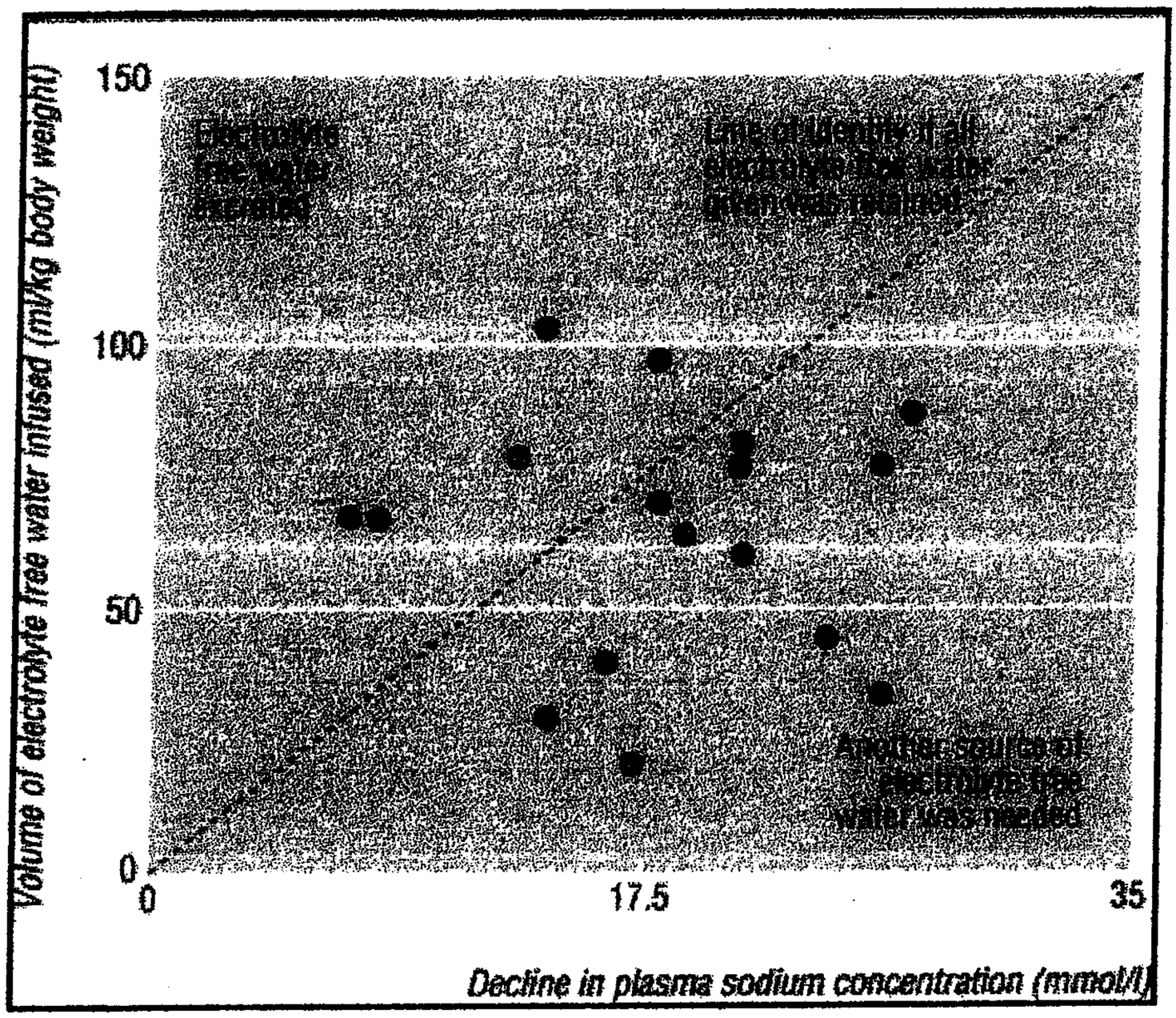

Fig. 2. Comparison of decline in plasma sodium concentration with amount of electrolyte free water given in 17 patients. Difference in sodium concentration was between initial value and that at its nadir

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