Hyponatraemia and hypokalaemia during intravenous fluid administration

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ABSTRACT

Background: Hospital-acquired hyponatraemia is associated with excessive volumes of hypotonic intravenous fluids and can cause death or permanent neurological deficit.

Methods: A cross-sectional survey was carried out in 17 hospitals on all children receiving intravenous fluids during 1 day of a specified week in December 2004.

Results: 77 of 99 children receiving intravenous fluids received hypotonic solutions and 38% received >105% of fluid requirements. 21 of 86 children were hyponatraemic, but the electrolytes of only 79% had been checked in the preceding 48 h.

Conclusions: Intravenous fluids should be used with caution as regards the tonicity and volume administered, and with appropriate monitoring of serum electrolytes.

Intravenous fluids are widely used in hospital paediatric practice. Their administration is associated with the development in children of serum electrolyte abnormalities including hyponatraemia (defined here as a plasma sodium concentration of less than 135 mmol/l). Hospital-acquired hyponatraemia can cause death or permanent neurological deficit.[1] It is unclear if this hyponatraemia is due to the use of hypotonic fluids, excessive volumes or both. While sodium chloride 0.45% with glucose 5% solution is hyperosmolar compared to plasma, lack of osmotically effective solutes means that once infused into patients it is hypotonic with reference to the cell membrane (glucose is rapidly metabolised and does not contribute to tonicity).[2]

There are few data on the types and volumes of intravenous fluids given to hospitalised children or on monitoring of serum electrolytes. The aim of this study was to determine the types and volumes of intravenous fluids given to children in hospital in the UK, estimate the prevalence of abnormal serum sodium and potassium levels, and evaluate the use of local clinical guidelines.

METHODS

We conducted a prospective cross-sectional multicentre survey. All members of the Paediatric Research Society were invited to participate in the survey and collect data on all children receiving intravenous fluids in their institution during 1 day of a specified week in December 2004 (including paediatric intensive care unit patients). Patients on neonatal intensive care units were excluded. A standard proforma was used for data collection that included age, weight, diagnosis, indication for intravenous fluids, details of the fluid administered and the timing and results of the last serum electrolyte measurements. The amount of fluid being administered was compared to standard paediatric maintenance fluid recommendations,[3] where 100% maintenance fluid requirements are calculated as 100 ml/kg/day for the first 10 kg, 50 ml/kg/day for the second 10 kg and 20 ml/kg/day for subsequent kilograms body mass. This approach may overestimate fluid requirements[2] but is commonly used in the UK and is recommended in the *BNF for Children*.[4] This audit did not require formal ethical approval.

Fluids administered were classified as hypotonic and isotonic depending upon their osmotically active solutes.

RESULTS

Seventeen hospitals were represented in the data collection, of which 10 were district general hospitals (contributing a median of three patients each) and seven university teaching hospitals (contributing a median of seven patients each). Ninety nine children were receiving intravenous fluids and were a median age of 3.6 years (range 7 days to 16 years), with a quarter being under 12 months of age. The majority of patients (55%) were under the care of general paediatric teams, 25% were under surgical teams and 17% under haematology-oncology teams. The indication for commencing intravenous fluids was decreased oral intake in 48% of cases, nil by mouth perioperatively in 24%, dehydration in 20% and receiving chemotherapy in 5%.

Table 1 shows the type of intravenous fluid given to children; 78% received hypotonic fluids and 43% received fluids without potassium. Figure 1 shows the volumes of fluid given as a percentage of the calculated maintenance fluid requirements, and serum sodium status. At the time of data collection, 16% of children were receiving more than 120% of their calculated maintenance fluid requirements (only four of these 16 were documented as dehydrated). A third of all children were receiving between 95% and 105% of calculated maintenance, and 38% were receiving greater than 105%.

Serum electrolytes had been measured in the preceding 24 h for only 54% of children, and between 24 and 48 h earlier in an additional 25% of children. Six children had never had their serum electrolytes measured, and for one child there were no data. Sodium data were missing for a further six children.

The median serum sodium level was 137 mmol/l with a range of 127–154 mmol/l. Twenty one of 86 children were hyponatraemic (serum sodium

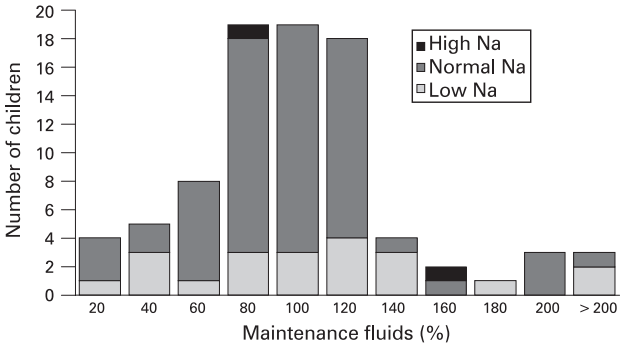

Figure 1 Histogram showing numbers of children on percentage maintenance fluids. 20% indicates up to and including 20% of maintenance, 100% bar is >80% up to and including 100%.

<135 mmol/l), and four of these had serum sodium ⩽130 mmol/l. Fifteen (71%) of these children were receiving hypotonic intravenous fluids and six (28%) received more than 120% of their calculated maintenance fluid requirements. Figure 2 shows the duration of intravenous fluid therapy. The proportion of children found to be hyponatraemic increased with duration from 11/65 (17%) of those having received intravenous fluids for less than 48 h, to 9/17 (53%) of those having received intravenous fluids for 3 days or longer (data missing on four children).

The median serum potassium was 4.0 mmol/l (range 2.3–5.7 mmol/l). Twenty three per cent of children were hyopokalaemic when their serum electrolytes were last measured, of whom 24% were not receiving potassium in their intravenous fluids. In total 46% of children receiving intravenous fluids had a serum sodium or potassium concentration, or both, which were outside the normal range.

Of the 17 hospitals contributing data, 12 did not have a clinical guideline in place for the administration of intravenous fluids to children, although some had clinical guidelines which made reference to intravenous fluid administration (eg, during chemotherapy).

DISCUSSION

Our study found that 24% of children receiving intravenous fluids were hyponatraemic, and that 20% had not had serum electrolytes measured in the previous 48 h. Even when electrolytes were measured, the results did not seem to be acted upon.

There are limitations to a cross-sectional survey. We cannot report on starting sodium/potassium values, renal function or fluid regimes up to the data collection point. Thus we do not comment on causality but can report observed associations. Of the invited clinicians, only those interested took part, and these may hold a particular view. Data were collected, however, on children across institutions in various specialties, with different lead clinicians who are likely to hold varying opinions. A systematic bias is unlikely to be present. We have not attempted to check whether any children were systematically missed.

Over the last decade there have been at least 50 case reports of serious morbidity including at least 27 deaths amongst children who developed hospital-acquired hyponatraemia while receiving intravenous fluids.[5] This is suggested to be due to the use of hypotonic fluids, excessive fluids volumes, the actions of antidiuretic hormone or a combination of these.

Table 1 Type of intravenous fluid being administered

	Fluid type		
	No added KCl	KCl added	Total
Hypotonic			
Sodium chloride 0.18% with glucose 4%	4	6	10
Sodium chloride 0.45% with glucose 2.5%	3	1	4
Sodium chloride 0.45% with glucose 5%	27	31	58
5% glucose		1	1
10% glucose	2	1	3
12.5% glucose		1	1
Total receiving hypotonic fluids			77
Isotonic			
Sodium chloride 0.9%	6	4	10
Sodium chloride 0.9% with glucose 5%		3	3
Hartmann's solution		4	4
Total parenteral nutrition		5	5
Total receiving isotonic fluids			22
Grand total	43	56	99

Hypotonic fluids

In our study 78% of children were given hypotonic fluids, including 71% of those with hyponatraemia; we found that 10% of children were receiving sodium chloride 0.18% with glucose 4%. Hoorn and colleagues have recently published a study showing an association between the development of hospital-acquired hyponatraemia and the administration of hypotonic intravenous fluid.[6] In our study the longer children had been on intravenous fluids, the higher their chance of having hyponatraemia.

The majority of deaths and episodes of neurological injury reported in the medical literature have been associated with the administration of the most hypotonic solutions containing sodium chloride 0.18% or 0.2%. However, administration of sodium chloride 0.45% with glucose 5% solution can also be associated with hyponatraemia leading to the development of permanent neurological sequelae in children,[7] and may also worsen any pre-existing hyponatraemia present at hospital admission. Our study did not differentiate between pre-existing and hospital-acquired hyponatraemia.

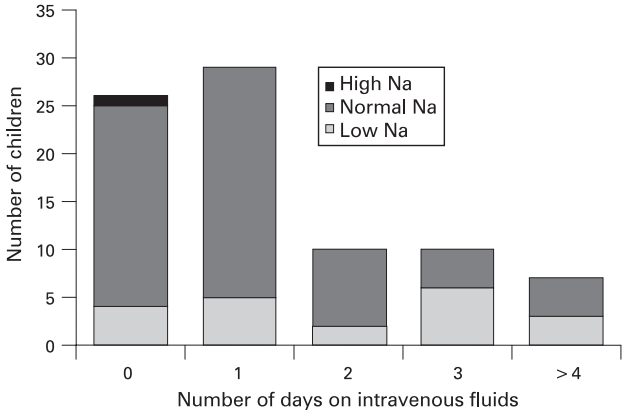

Figure 2 Histogram of number of days on intravenous fluids and the last measured serum sodium level.

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What is already known on this topic

- Hospital acquired hyponatraemia can cause death or permanent neurological deficit.
- Administration of intravenous fluids is associated with hyponatraemia.
- Hypotonic fluids and/or large volumes of fluid are thought to contribute to hyponatraemia.

What this study adds

- Hypotonic fluids are frequently used in children across the UK.
- Volumes of intravenous fluids greater than those required for standard maintenance are frequently administered.
- One in five children on intravenous fluids have not had their electrolytes measured in the preceding 48 h.
- When electrolytes are measured hyponatraemia and/or hypokalaemia are common, but the results do not seem to be acted upon.
- Local guidelines for intravenous fluid administration are infrequently available.

Fluid volumes

In our study one sixth of patients were receiving greater than 120% of the commonly used estimate of maintenance fluid requirement, and only a quarter of these children were deemed to be dehydrated. The fluid volumes commonly given to children may exceed their requirements, especially when unwell.[8] Widely used formulae for fluid calculations date back to the 1950s and are based on the caloric requirements of healthy children by weight. This approach has been challenged, firstly as surface area would more accurately reflect fat free mass and secondly as children in disease states do not have equivalent caloric expenditure to their healthy counterparts.[2] Indeed the *Advanced paediatric life support* (*APLS*) manual and the *BNF for Children* recommend these volumes be adjusted downward for sick and postoperative children. We do not know the calculations that were being used in each institution for fluid requirements, and most had no written guidance on this, but children were receiving large volumes, at least at full maintenance requirements according to APLS formulae. Hyponatraemia was seen at all volumes of fluid administration in our cross-sectional study.

Anti-diuretic hormone

The non-osmotic release of ADH is stimulated by many physiological states commonly encountered during acute illness; these may include pain, pyrexia, nausea, reduced circulating volume (particularly if by more than 8%), drugs, central nervous system infections, and the postoperative state.[9] Elevated anti-diuretic hormone levels can thus exacerbate hyponatraemia, especially when there is administration of high volumes of hypotonic intravenous fluid. Standard formulae for calculating fluid requirements need to be revised in these disease states and isotonic intravenous fluids considered, particularly in those with low sodium (<135 mmol/l).[5]

The majority of contributing hospitals (70%) did not have a guideline for managing children on intravenous fluids. Our study found a lack of recent electrolyte results and poor adjustment of fluid type when electrolytes were available. The *BNF for Children* recommends that "fluids and electrolytes should be monitored carefully and any disturbance corrected by slow infusion of an appropriate solution". It is not explicit as to how frequently monitoring should be done. The lack of evidence, and therefore of evidence based guidelines, may contribute to the prevalence of serum electrolyte abnormalities seen in children receiving intravenous fluids. Prospective randomised trials are needed.

CONCLUSION

Electrolyte abnormalities are common during the administration of intravenous fluids to children, almost half of children having serum sodium or potassium concentrations or both outside the normal range. One fifth of children on intravenous fluids had not had electrolytes measured in the preceding 48 h. Most children were receiving hypotonic fluids at high volumes. It is disturbing that despite increasing awareness of the dangers associated with its use, 10% of children in this study were administered sodium chloride 0.18% with glucose 4%. This Fluid should no longer be available for general use in children following NPSA alert 22.[10] The administration of intravenous fluids should be undertaken with the same degree of caution as that afforded all other drugs. Careful regard should be paid to the tonicity and volume of fluid administered, and to the regular monitoring of serum electrolytes.

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Dr Ben Ramadan was involved in the initial concept and data collection.

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