Hypernatraemic gastroenteritis in critically ill children

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Introduction

Hypernatraemic dehydration is a recognised complication of diarrhoeal disease in children, and yet the management of dysnatraemia and rehydration remains controversial. Both hypernatraemic dehydration itself [1], and complications of its management, have been associated with seizures, neurological insult, and death .[2 3 4] The symptoms of hypernatraemia are predominantly neurological and include tremor, irritability, hyperreflexia and lethargy.[2 5] It has been reported that neurological symptoms occur in most children with serum sodium greater than 158 mmol/l.[2]

Traditional teaching has held that hypernatraemic dehydration should be treated with hypotonic solutions (0.45% saline), in order to drop the sodium no faster than 10 - 15 mmol/l/day (0.4 – 0.6 mmol/l/hour). [2 3 6 7 8] It has been demonstrated that the blood-brain barrier limits the passage of electrolytes (but not water), allowing far slower equilibration of electrolytes in the brain than elsewhere in the body.[8] Therefore, as serum sodium falls with rehydration, the decrease in extracellular fluid osmolality may result in cerebral oedema. Slow correction of dehydration and the dysnatraemia may be partially protective against this process.[8]

The awareness of the high incidence of hyponatraemia in children treated with traditionally large volumes of hypotonic solutions has focused attention on both the volume and the tonicity of maintenance fluids. [9 10 11] In hypernatraemic gastroenteritis, rehydration fluid with higher sodium content (near isotonic) may protect against an abrupt fall in serum sodium. [2 3 7] However, the relationships between type of rehydration fluid, volume of fluid administered, rate of correction of dysnatraemia, and clinical outcome have not been conclusively delineated.

Presented here is a retrospective study of children with moderate to severe hypernatraemia, associated with dehydrating gastroenteritis, who were admitted to the paediatric intensive care unit (PICU) of a paediatric teaching hospital in a developing country. Comparison is made

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between the volume and sodium content of intravenous rehydration solutions, the rate of correction of serum sodium, morbidity, and mortality.

Methods

PICU discharge summaries were screened for children with hypernatraemia and gastroenteritis who were admitted to the PICU at Red Cross Children's Hospital in Cape Town, South Africa, over a 6 year period from 1 January 1997 – 1 January 2003. From 1997 to 2000 the PICU consisted of an 11 bed medical unit, which was combined in 2000 to form a 22 bed multi-disciplinary unit with 24 hour intensivist cover. Eighty-six hospital records were identified from the screening process and 59 found to fit the inclusion criteria. Two had inadequate documentation and were also excluded.

Gastroenteritis was defined as the passage of frequent loose or watery stools. Moderate to severe hypernatraemia was defined as serum sodium ≥ 150 mmol/L within 2 hours of PICU admission. Children with mild hypernatraemia in the range of 145 – 150 mmol/L were excluded from further analysis unless their next sodium within 2 hours of PICU admission was > 150 mmol/l.

Data collection

The following data were gathered from the medical record: gender, age, date of admission and discharge from PICU, admission and discharge weights, clinical assessment of hydration, history of excess salt administration, admission arterial blood gas parameters, serum electrolytes at admission, 24 hours, and peak sodium, type and amount of intravenous fluids administered, presence of seizures, evidence of pre-existing or co-morbid neurological disease, need for mechanical ventilation, evidence of acquisition of a new neurological deficit, and mortality. Data were not collected after the first 24 hours in PICU.

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A co-morbid neurological condition was defined as an infective, ischaemic or hypoxic neurological insult occurring during the PICU stay. A newly acquired neurological deficit was defined as a proven or suspected defect of vision, hearing, fine motor, or gross motor function, documented in the medical record at the time of hospital discharge, but which was not present at the time of the admission. Adverse outcome included seizures which occurred after commencement of fluid treatment in PICU, the acquisition of a new neurological deficit at the time of hospital discharge, or death.

Ethics approval for the study was obtained from the Research Ethics Committee of the University of Cape Town.

Fluid management during the study period

During the early part of the study period (1997 – 2000), fluid rehydration guidelines for hypernatraemic gastroenteritis had not been established and fluids of varying tonicity were used. During the latter part of the study period (2000-2003), the recommended intravenous solution for rehydration, maintenance, and replacement of ongoing abnormal losses (where applicable), was Half Darrow's Dextrose (per 1000 ml: Na 61 mmol, K 17 mmol, Cl 51 mmol, Lactate 26 mmol). Maintenance intravenous fluid requirements were based on traditional recommendations[11] although ventilated children were routinely fluid restricted to two-thirds of maintenance requirements. Percentage dehydration was assessed clinically and rehydration fluid requirements were calculated as an additional 50 ml/kg/day for 5% dehydration, and an additional 100 ml/kg/day for 10% dehydration, and this was replaced over 24 hours. If ongoing abnormal losses due to watery stool were estimated at > 25 ml/kg/day, this volume would be added to the prescribed intravenous fluid volume. In severely ill children, enteral feeds would usually be delayed, and the sum of the maintenance, rehydration, and replacement fluid volume would be delivered as a single intravenous fluid prescription, hereafter referred to as the total intravenous infusion (as distinct from bolus resuscitation fluid for hypovolaemia).

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Six hourly weighing and measurement of serum sodium were recommended. The guideline recommended that if both sodium and weight remained static, the rate of fluid administration should be increased, whereas if the sodium fell too quickly and the weight remained static, fluid with higher sodium content should be administered. Due to the limitations of retrospective data collection, data were collected on the rate, volume, and type of the initial total intravenous infusion only.

Due to the retrospective nature of the study, it was often difficult to ascertain from the records which children were considered to be shocked, and what criteria were used to define shock. Therefore for the purposes of this study, children who were administered >10 ml/kg boluses of isotonic fluid for resuscitation (usually, but not always, Ringer's lactate) were deemed to be shocked. Sodium bicarbonate was used frequently during the first part of the study period in an attempt to correct the acid-base disturbance, but was no longer recommended during the latter part of the study period.

Data are presented as median (range), and n (%). Data were analysed by the Fisher's Exact test for categorical data, and the Mann-Whitney test for continuous data. Fifty seven children were studied, with a median age of 151 days (14 - 953) and median weight of 5.9kg (1.8 – 8.7).

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Results

Clinical and biochemical data of the study population are presented in Table 1. Forty six (81%) children were shocked. The median volume of isotonic resuscitation fluid was 39 ml/kg (0 – 180 ml/kg). Thirty seven (65%) of the children were clinically assessed as being at least 10% dehydrated. Median percentage increase in weight on discharge was 6% (-20 to 27). Median admission sodium was 165 mmol/l (145 – 199) (two children had initial serum sodiums of 145 and 147 mmol/l, with the repeat sodiums 165 and 153 respectively within the first two hours of PICU admission). The median volume of total intravenous infusions administered was 6 ml/kg/hr (144 ml/kg/day) (2 – 24 ml/kg/hr). One child had a pre-existing neurological condition, while 9 others

had co-morbid neurological conditions. See Table 2. In 12 patients (21%) a history of salt administration due to incorrect preparation of formula feeds or oral rehydration solution was obtained.

Rate of fall of serum sodium

The median rate of fall of sodium was 0.6 mmol/l/hr (14.4 mmol/l/day) over the first 24 hours, falling to 151 mmol/l (134 – 171) at 24 hours. Children were divided into 2 groups, those with a rate of fall of sodium >0.6 mmol/l/hr (n=23) and those with a rate of fall <0.6 mmol/l/hr (n=33). See Table 3. Children with a rate of fall of sodium greater than 0.6 mmol/l/hour were more likely to have a co-morbid neurological condition (30%) than those with a rate less than 0.6 mmol/l/hour (6%) (p=0.04). There was no significant difference in the incidence of seizures occurring post initiation of fluid treatment in PICU (p=0.43) or adverse outcome (p=0.31) between these two groups.

Sodium content of total intravenous infusions

Median sodium concentration in intravenous infusions was 61 mmol/l (0 – 154 mmol/l). Children in the early years of the study period (1997 – 1999) received intravenous fluid infusions with a lower sodium content, median 61 mmol/l (0 - 61) compared to the later years (2000 – 2003), median 61 mmol/l (40 – 154) (p=0.005).

To assess the effect of the type of total intravenous infusion administered, patients were divided into those who received infusions containing at least 61 mmol/l sodium, and those who received infusions containing less than 61 mmol/l sodium (see Table 4). Forty five children (79%) received infusions containing at least 61mmol/l of sodium, with median admission sodium 164 mmol/l, falling to median 151 mmol/l at 24 hours. Twelve (21%) children received intravenous infusions containing less than 61mmol/l of sodium, with median admission sodium 166 mmol/l, falling to 151 mmol/l at 24 hours. Median rate of fall of sodium was 0.5 mmol/l/hour compared to 0.9

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mmol/l/hour (p=0.06) respectively, but there was no statistical difference in incidence of seizures (p=1) or adverse outcome (p=1).

Seizures

Seizures were documented in 29 children (51%), with 15 (52%) occurring before admission to PICU and 14 (48%) occurring after commencement of fluid therapy in PICU. Only those in the latter group were analyzed with respect to fluid management, as the seizures in the first group were independent of PICU management.

The 14 children (25%) who had seizures post PICU admission did not have significantly higher serum sodiums on admission (168 vs.164 mmol/l) (p=0.19). See Table 5. There was also no significant difference in the sodium concentration of total intravenous infusions (median sodium 61 mmol/l in both groups) (p=1) nor in the rate of fall of sodium over the first 24 hours (0.63 vs. 0.5 mmol/l/hour) (p=0.11), compared to the group of children without seizures or with seizures occurring prior to PICU admission. The incidence of shock was no different in children with or without seizures in PICU (p=0.27). Five children (36%) with seizures occurring in PICU had co-morbid neurological conditions, compared to 5 children (12%) in the group with no seizures or seizures occurring before PICU admission (p=0.11).

Outcome

Four children (7%) died, 5 children (9%) developed a newly acquired neurological deficit, and 14 children developed seizures after PICU admission i.e. there was an adverse outcome in 23 children (40%). See Table 6. One child with a pre-existing neurological condition was excluded from the outcome analysis. Children with adverse outcome were more likely to have a co-morbid neurological condition (39%) than those with good outcome (5%) (p=0.006).

There was no significant difference in the volume of total intravenous infusions administered between those children with adverse outcome and those with good outcome (5 vs. 6 ml/kg/hour)

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(p=0.52), nor in the volume of isotonic resuscitation fluid administered to these two groups (38 vs. 43 ml/kg) (p= 0.75). A higher admission potassium was significantly associated with adverse outcome (p= 0.017) and the admission sodium also trended towards this (p= 0.068).There was no association between shock, pH, or requirement for ventilation, and adverse outcome (p=0.35, p=0.62, and p=0.36 respectively).

The median sodium content of the total intravenous infusions was 61 mmol/l in children with both adverse and good outcome. Comparing children in these 2 groups, median admission sodium was 172 mmol/l vs. 163 mmol/l (p=0.068), both falling to median 151 mmol/l at 24 hours (p=0.49), with rate of fall of 0.63 and 0.48 mmol/l/hour respectively (p=0.083).

Multivariate analysis, using stepwise logistic regression, was done to compare the rate of fall of sodium (p= 0.31), the sodium concentration in maintenance infusions (p= 0.59), the admission potassium (p= 0.014), the administration of sodium bicarbonate (p= 0.52) and the study time period (1997 – 1999 vs. 2000-2003) (p= 0.18) with adverse outcome. The only factor that was associated with adverse outcome was the admission potassium, with an Odd's Ratio of 1.92 (95% Confidence Interval 1.14 – 3.22).

Further multivariate analysis, using stepwise logistic regression, found that seizures occurring post PICU admission were associated with a higher risk of either developing a new neurological deficit on discharge from hospital or with death (Odd's Ratio 6.87; 95% Confidence Interval 0.72 – 65).

When comparing PICU admission in the early vs. late phase of the study period with adverse outcome, using logistic regression, there was a trend towards less risk of adverse outcome for those children admitted in the late phase (after 2000), but this was not significant (Odd's Ratio 0.38, 95% Confidence Interval 0.11 – 1.29).

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Discussion

Hypernatraemia associated with gastroenteritis has been reported to be declining in developed countries, due to the use of low-solute infant formula feeds and the availability of oral rehydration solutions. [13 14] In developed countries hypernatraemia is now more commonly a hospital-acquired disease in children with other illnesses.[6] In the developing world, hypernatraemic dehydration is reported as becoming more common, a finding that has been attributed to the increased use of formula feeds.[15] This study shows that it remains an important problem in the Southern African context.

The study demonstrates that the majority of children with moderate to severe hypernatraemia associated with gastroenteritis survive to hospital discharge without significant neurological sequelae. The mortality rate of 7% is similar to the mortality rates of 3 – 13% reported for hypernatraemic gastroenteritis in general paediatric populations.[13 16] It should be noted that this study population included critically ill children with severe dehydration and metabolic acidaemia, who required large volume rehydration and fluid resuscitation. Many were shocked and septicaemic on admission and would be expected to have a higher mortality rate when compared to the studies in the literature, which report on children in general paediatric wards. Of the 4 deaths, 3 were related to the severity of the primary illness. The fourth child was encephalopathic on presentation, but also had a too rapid decrease in serum sodium which may well have contributed to his subsequent death. See Table 7.

Neurological sequelae were present in 9% of the patients. Dunn et al have previously reported a neurological complication rate of 11 – 15% in children with hypernatraemia, although the majority of children had serious underlying conditions other than gastroenteritis.[6] It was found that significantly more children with adverse outcome had a co-morbid neurological condition, although it is difficult to disentangle the effects of underlying sepsis, haemodynamic compromise, and cerebral oedema due to iatrogenic fluid shifts. While 29 (51%) of the children had seizures documented at some point during this illness, only 14 of these seizures occurred after

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commencing intravenous fluid therapy in PICU and could be considered to potentially be as a result of treatment. It is notable that the occurrence of seizures post PICU admission was not related to admission or peak serum sodium or the rate of fall of sodium. These seizures were, however, associated with a higher risk of either developing a new neurological deficit on discharge from hospital or with death.

Another admission factor associated with outcome was serum potassium, which was higher in the adverse outcome group and shown to be significant with multivariate analysis. It is difficult to account for this association, and it is debatable whether this finding is clinically significant. However, it has been suggested that potassium is an important factor in aiding the entry of water into cells and that potassium should be included in rehydration solutions once adequate urine output is confirmed. [2 18]

The rate of correction of hypernatraemia has been reported as being the most important aspect of the management of hypernatraemic dehydration, and it has been recommended that the rate of correction of serum sodium should not to exceed 15 mmol/l/day or 0.6 mmol/l/hour. [2 8 16 18] In this study group, serum sodium fell at an appropriate median rate of 0.6 mmol/l/hour, although higher admission sodium was associated with faster fall, as were co-morbid neurological insults. Admission sodium and a faster rate of fall of sodium showed a trend towards a higher risk of adverse outcome, but multivariate analysis showed that these associations were not significant.

The rate of fall of sodium will depend on net water balance and net sodium balance. The optimum sodium concentration that should be administered to maintain a safe fall in serum sodium has been a matter for debate. The historical consensus has been to administer a hypotonic solution, and sodium concentrations of 30 – 77 mmol/l have been recommended. [2 3 4 15 16 17] More recently there has been a tendency to use solutions with higher solute load (77 - 154 mmol/l) in order to prevent a rapid fall in sodium which might cause cerebral oedema.[7] These changes in practice

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may have been influenced by the controversy surrounding hospital-acquired hyponatraemia and intravenous maintenance solutions.[9 10 11]

No difference was found in the volume of total intravenous infusions, or resuscitation fluid, which was administered to children with good outcome compared to adverse outcome. The majority of children in this study received a hypotonic intravenous infusion containing 61 mmol/l sodium. Although there was a trend towards more rapid fall in serum sodium in children who received infusions containing < 61 mmol/l of sodium, there was no difference in outcome between these children, and those who received infusions containing more sodium. See Tables 4 and 6. Multivariate analysis also showed that there was no association between the sodium content in total intravenous infusions and adverse outcome.

This study has several limitations, primarily related to the retrospective nature of the data collection. Note-keeping in the early part of the study period was less comprehensive and for this reason only the initial rehydration fluid data were recorded and the precise calculations of a tonicity balance is not possible. Subsequent changes to the fluid regimen in the PICU stay may have affected either serum sodium or clinical outcome. Enteral feeds may have been started in some children, although data on the volume and composition of feeds were not collected. It is also possible that improvements in PICU care and organization could have resulted in differences in outcome between the early and later parts of the study period.

Although all children had hypernatraemia in association with diarrhoeal disease, some had also received excessive sodium in the form of incorrectly prepared formula or oral rehydration solution prior to hospital admission. In the earlier part of the study period, sodium bicarbonate was given frequently to correct acid-base imbalance, a practice which would have increased the amount of sodium administered, but which was shown not to significantly affect outcome. Furthermore, neurological deficits recorded in the ward medical record notes were elicited on gross neurological examination only and it is possible that more subtle neuro-developmental problems

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may have gone undetected. There was also no longer-term neurological follow-up which might have identified these subtle problems.

Conclusion

This study demonstrates that the majority of critically ill children with moderate to severe hypernatraemia, associated with gastroenteritis, survived to hospital discharge without significant neurological sequelae. The occurrence of seizures in these children post PICU admission was not associated with either the serum sodium level or the rate of fall of sodium, but was associated with subsequent outcome. Intravenous solutions containing 61 mmol/l sodium may be used for the rehydration of children with hypernatraemic gastroenteritis in order to correct the serum sodium at a rate of approximately 0.6 mmol/l/hour. Moreover, a fall in serum sodium > 0.6 mmol/l/hour was not independently associated with acquisition of neurological deficit or death.

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Table 1: Biochemical and clinical data (n = 57).

Parameter	**median (range) or n (%)**	
Clinical degree of dehydration:		
0 %	5	(9 %)
5 %	13	(23 %)
>/= 10 %	37	(65 %)
Not recorded	2	(4 %)
Admission potassium (mmol/l)	3.1	(1.2 – 7)
Admission pH	7.1	(6.8 – 7.5)
Admission chloride (mmol/l)	141	(106 – 176)
Admission sodium (mmol/l)	165	(145 – 199)
Highest sodium (mmol/l)	169	(151 – 199)
Sodium at 24 hours (mmol/l)	151	(134 – 171)
Hours to normal sodium	43	(8 – 115)
Rate of fall to normal sodium (mmol/l/hr)	0.5	(0.0 – 1.7)
Rate of fall of sodium over 24 hours (mmol/l/hr)	0.6	(-0.5 to 2)
Rate of fall of sodium > 0.6 mmol/l/hr	24	(42%)
Shock on admission	46	(81%)
Volume of resuscitation fluid (ml/kg)	39	(0 – 180)
Volume of total IV infusion (ml/kg/hr)	6	(2 – 18)
Sodium content of total IV infusion (mmol/l)	61	(0 – 154)
Sodium content of total IV infusion < 61 mmol/l	12	(21%)
8.4% Sodium bicarbonate administered	28	(49%)
Excess salt administration prior to admission	12	(21%)
Co-morbid neurological condition	9	(16%)
Mechanical ventilation	35	(61%)
Seizures pre PICU admission	15	(26%)
Seizures post fluid therapy in ICU	14	(25%)
Newly acquired neurological deficit	5	(9%)
Survived	53	(93%)
Adverse outcome	23	(40%)

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Table 2: Co-morbid neurological conditions and complications (n = 10)

Condition	Outcome
Pneumococcal meningitis	Died
Hypoxic-ischaemic brain injury without oedema	Cerebral palsy
Aseptic meningitis	Good
Right caudate infarct, hydrocephalus	Cerebral palsy
Multi-organ failure, brain death	Died
Right parietal infarct, cerebral vein thrombosis	Good
Aseptic meningitis	Good
Encephalopathy, brain death	Died
Craniosynostosis, cerebral oedema	Good
Previous left internal capsule infarct	Hearing and visual defects

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Table 3: Fall of sodium over the first 24 hours in PICU, divided into children with a rate of fall of sodium < 0.6 mmol/l/hr (n= 33) and those with a rate of fall of sodium > 0.6 mmol/l/hr (n=23)*. Data are median (range) and n (%).

	< 0.6 mmol/l/hr	**> 0.6 mmol/l/hr**	**p**
Admission sodium (mmol/l)	161 (145 – 181)	174 (151 – 199)	0.0002
Highest sodium (mmol/l)	166 (153 – 193)	179 (151 – 199)	0.004
Admission potassium (mmol/l)	3.2 (1.2 – 7)	3.1 (1.6 – 7.5)	0.39
Admission pH	7.1 (6.8 – 7.5)	7.2 (6.9 – 7.5)	0.51
Salt administration	5 (15%)	7 (30%)	0.34
Resuscitation fluid (ml/kg)	41 (0 – 180)	38 (0 – 170)	0.81
8.4% $NaHCO_3$ given	20 (67%)	8 (35%)	0.1
Sodium content of total IV infusion (mmol/l)			
< 61 mmol/l	5 (15%)	6 (26%)	0.49
0 mmol/l	3 (9%)	4 (17%)	
20 mmol/l	1 (3%)	0	
40 mmol/l	1 (3%)	2 (9%)	
= / > 61 mmol/l	28 (85%)	17 (74%)	
61 mmol/l	25 (76%)	15 (65%)	
77 mmol/l	1 (3%)	2 (9%)	
154 mmol/l	2 (6%)	0	
Co-morbid condition	2 (6%)	7 (30%)	0.04
Mechanical ventilation	21 (64%)	13 (57%)	1.0
Seizures post PICU admission	7(21%)	7 (30%)	0.43
New neurological deficit	4 (12%)	2 (9%)	0.7
Survived	32 (97%)	21 (91%)	0.73
Adverse outcome	9 (26%)	9 (41%)	0.31

*1 child who died before 24 hours excluded from analysis.

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Table 4: Sodium content of intravenous rehydration solution, divided into those children receiving at least 61 mmol/l sodium (n=45), and those receiving < 61 mmol/l sodium (n=12). Data are median (range) and n (%).

	Sodium = / > 61 mmol/l	**Sodium< 61 mmol/l**	**p value**
Admission sodium (mmol/l)	164 (145 – 196)	165 (153 – 199)	0.46
Highest sodium (mmol/l)	171 (151 – 196)	166 (153 – 199)	0.75
Sodium at 24 hr (mmol/l)	151 (135 – 171)	151 (134 – 171)	0.53
Rate of fall of sodium over 24 hr	0.5 (-0.5 – 1.33)	0.9 (0.4 – 2.0)	0.06
Adverse outcome	14 (32%)	4 (33%)	1.0

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Table 5: Comparison of children with seizures post PICU admission (n=14) and those without seizures or with seizures pre PICU admission (n=43). Data are median (range) and n (%).

	Seizures post PICU	**No seizures/ pre PICU**	**p value**
Admission sodium (mmol/l)	168 (153 – 196)	164 (145 – 199)	0.19
Highest sodium (mmol/l)	172 (153 – 196)	168 (151 – 199)	0.82
Admission pH	7.13 (6.96 – 7.49)	7.11 (6.79 – 7.45)	0.56
Sodium in IV infusion ≥61 mmol/l	11 (79%)	34 (79%)	1.0
Rate of fall of sodium over 24 hr	0.63 (0.17– 1.29)	0.50 (-0.54 – 1.96)	0.11
Rate of fall > 0.6mmol/l/hour	7 (54%)	16 (37%)	0.43
Mechanical ventilation	10 (71%)	25 (58%)	0.57
Co-morbid neurological condition	5 (36%)	5 (12%)	0.11

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Table 6: Comparison of children with good outcome (n=38) and adverse outcome (n=18)*. Data are median (range) and n (%).

	Good outcome	Adverse outcome	p
Admission sodium (mmol/l)	163 (145 – 199)	172 (153 – 196)	0.068
Highest sodium (mmol/l)	167 (151 – 199)	175 (153 – 196)	0.40
Admission potassium (mmol/l)	3.0 (1.2 – 5.9)	4.0 (1.7 – 7)	0.017
Admission pH	7.11 (6.79 – 7.32)	7.13 (6.84 – 7.49)	0.62
Excess salt administration	9 (26%)	3 (17%)	0.71
Resuscitation fluid (ml/kg)	43 (0 – 180)	38 (0 – 136)	0.75
8.4% $NaHCO_3$ given	20 (53%)	7 (39%)	0.5
Sodium in total IV infusion (mmol/l)	61 (0 – 154)	61 (0 – 77)	0.68
< 61 mmol/l	8 (21%)	4 (22%)	1.0
= / > 61 mmol/l	30 (79%)	14 (78%)	
0 mmol/l	5 (13%)	2 (11%)	0.68
20 – 40	3 (8%)	2 (11%)	
61	26 (69%)	13 (72%)	
77	2 (5%)	1 (6%)	
154	2 (5%)	0	
Sodium at 24 hr (mmol/l)	151 (134 – 171)	151 (139 – 171)	0.49
Rate of fall of sodium 24hr (mmol/l/hr)	0.48 (-0.54 – 1.75)	0.63 (0.17 – 1.96)	0.083
Rate of fall of Na > 0.6 mmol/l/hr	13 (34%)	9 (53%)	0.31
Co-morbid condition	2 (5%)	7 (39%)	0.006
Mechanical ventilation	21 (55%)	13 (72%)	0.36

*One child with pre-existing cerebral infarct excluded from outcome analysis.

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Table 7: Details of the children who died (n = 4)

Patient	**1**	**2**	**3**	**4**
Admission pH	7.29	7.15	7.08	6.84
Admission Na (mmol/l)	194	179	153	173
Rate of fall to normal (mmol/l/hr)	1.73	0.55	1.13	N/A*
Sodium in IV infusion (mmol/l)	0	61	35	61
Resuscitation fluid (ml/kg)	10	26	24	58
8.4% $NaHCO_3$ given	No	Yes	No	Yes
Cause of death	Brain death	Klebsiella sepsis	Pneumococcal meningitis	Brain death
Other details	Encephalopathy	MOF **	/	cardiac arrest
Time to death	60 hrs	5 days	23 hrs	42hrs
Scan	perfusion scan	none	none	none

* Sodium did not reach normal levels before death
** MOF: multi-organ failure

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