Hypernatraemia in Diarrhoeal Infants in Lagos

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Ahmed, I., and Agusto-Odutola, T. B. (1970). *Archives of Disease in Childhood*, 45, 97. **Hypernatraemia in diarrhoeal infants in Lagos.** Records of 48 patients with acute gastro-enteritis who had a serum sodium concentration of 148 mEq/l. or more have been reviewed. All except 3 were under 1 year of age and 62% were under 6 months. In the majority of patients no single cause for the hypertonicity of the body fluids could be identified, but general factors related to acute illness and continued feeding of the infants on powdered milk in addition to breast milk contributed. Excessive administration of saline was the probable cause in only 11 patients.

Twenty-two of the 48 patients had CNS manifestations; cerebral disturbances were commoner when the serum Na concentration was 158 mEq/l. or more. 14 of the 48 patients died; with one exception all deaths occurred among patients with CNS manifestations. In view of the high risk of brain damage and mortality, the importance of prevention of hypernatraemia has been emphasized.

Hypernatraemia has been recognized in Western countries as a frequently occurring phenomenon in the fluid and electrolyte imbalance which accompanies infantile diarrhoea (Weil and Wallace, 1956; Macaulay and Blackhall, 1961; Bruck, Abal, and Aceto, 1968), but this association is believed to be rare in the tropics and in malnourished children, and reports are few, there being none from West Africa. Our experience in Lagos with patients suffering from diarrhoea led us to suspect that hypernatraemia was not at all rare and in the present paper we describe the condition as it occurs here.

Subjects and Methods

We reviewed the records of 48 children (24 male, 24 female) with diarrhoea seen in our hospital from December 1966 to May 1968, who showed a serum sodium concentration of 148 mEq/l. or more. 30 were less than 6 months old; 13 were in the 6-9 month group; 2 were between 9 months and 1 year; and only 3 children were above 1 year. The oldest child was 3½ years of age. Body weight was recorded in 23 patients, and all of these were below the average weight of healthy children in social Class I (Institute of Child Health, Lagos Report 1963-68).

Of the 48 children, 39 presented as emergencies, and had been admitted to hospital earlier (Table I). All patients were from families of indigenous people.

In 41 patients blood was collected in a paraffin

bottle before the start of treatment for determination of serum sodium, potassium, chloride, and bicarbonate. In 7 patients blood samples were collected after they had received varying amounts of intravenous fluids (Cases 1-7, Table I).

Results

Most of the patients were brought to hospital between 3 and 7 days after the onset of illness. Gastro-enteritis was the most frequent provisional diagnosis, stools being watery and frequent: 5-10 times a day. Vomiting was frequent, especially after feeds. 3 patients were admitted with bronchopneumonia and diarrhoea; 4 had urinary tract infections; and 1 child, 3½ years old, had abdominal and pulmonary tuberculosis. Accurate records of fluid intake just before and during the illness were available in only 9 in-patients and these are summarized in Table I; of these, 4 patients were on intravenous fluids. One patient received 220 ml. Darrow's solution intraperitoneally. In Case 7 (Table I) the leakage of intravenous fluid was only discovered after 24 hours. 7 patients attended health centres and had received oral normal saline with glucose or Darrow's solution in unknown quantities. 34 patients, including Cases 8 and 9 (Table I), had received no fluids therapeutically, and during the illness had been fed on breast milk supplemented with milk recon-

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TABLE I
Fluid Intake in 9 Patients in First 24-48 Hours and During Illness

Case No.	Sex/Age	Weight (g.)	Immediate Cause of Dehydration	Initial Serum Na (mEq/l.)	Fluid Intake	Max. Serum Na Conc. (mEq/l.)
1	* 9 mth.	5443	Bronchopneumonia and diarrhoea	122	0.9% sodium chloride solution; 2740 ml. in 5 days	166
2	F 5 mth.	5443	Diarrhoea and vomiting		250 ml. 0.9% and 500 ml. N/2 NaCl solution	160
3	F 9 mth.		Diarrhoea and vomiting	115	1200 ml. 0.9% NaCl solution	160
4	F 1 yr.	4989	Diarrhoea and vomiting, kwashiorkor		1460 ml. 0.18% solution NaCl	162
5	F 5 mth.	4535	Diarrhoea and vomiting	150	220 ml. full strength Darrows solution intraperitoneally	162
6	F 1 mth.	4989	Diarrhoea and vomiting	150	610 ml. 0.18% saline	162
7	F 13 mth.	5443	Diarrhoea and vomiting	131	Intravenous fluid leaked; no oral fluids	148
8	F 1 mth.	2550	Diarrhoea and vomiting		F.S. Lactogen 720 ml./24 hr.	160
9	F 1 yr.	5556	Bronchopneumonia and diarrhoea	142	F.S. Lactogen 540 ml./24 hr.	160

* Sex not recorded.

stituted from powdered milk, in most cases Lactogen.

All except 5 children showed clear clinical signs of dehydration, often severe.

Thirty-one patients had fever of 37.8°C . or more; the temperature reached 40°C . in 11, and 41.1°C . in 2. Hyperirritability was present in 31 patients; of these, 16 were irritable when disturbed though lethargic otherwise. Thirst was present in all except those who were very sick and comatose. Only 5 patients were in shock with thin radial pulse and cold extremities. In 14 patients pulse volume and peripheral circulation were noted as good despite signs of severe dehydration.

Thirty-seven patients had hyperpnoea with acidotic breathing. In 3 respiration was depressed and breathing shallow, in spite of a very low bicarbonate concentration in blood.

Cerebral symptoms were present in 22 patients (46%). The salient features of these cases are summarized in Table II. Consciousness varied from hyperirritability to gross depression in 14 patients. 6 patients had generalized or focal convulsions. Involuntary movements, coarse tremors, and generalized hypertonia were present in 5. 6 patients showed signs of meningeal irritation such as neck stiffness, positive Kernig

sign, and a shrill cry. In only 2 patients was the anterior fontanelle found to be tense. Subarachnoid haemorrhage was found in 2 patients.

Fourteen (29%) out of the 48 patients died, all but one death occurring among patients with CNS signs. 7 necropsies were carried out; 3 (Cases 5, 13, 14, Table II) revealed petechial haemorrhages on the surface and in the substance of the brain, especially the cerebellum; numerous intravascular thrombi were found in 2 and massive intravascular haemorrhage in 1 of them (Case 5, Table II); in the remaining 4, cerebral oedema and extreme vascular congestion were the main findings. In 2 of them microscopy showed oedema and severe hyperaemia with marked stasis in blood vessels of meninges and extravasation of erythrocytes. These lesions were of the type known to be associated with hypernatraemia (Finberg, Lutterell, and Redd, 1959; Finberg, Kiley, and Lutterell, 1963).

Laboratory Investigation

The results are given in Table III. The serum sodium concentration ranged from 148-175 mEq/l. In 3 patients, the bicarbonate content of blood was above 20 mEq/l.; all others had significant metabolic

TABLE II
Clinical Features in 22 Patients with CNS Signs

Case No., Sex, and Age	Aetiology or Underlying Disease	Urea	Max. Serum Na(mEq/l.)	Clinical Features	Result of CSF	Outcome
1, F, 7 mth.	Diarrhoea and vomiting		153	Apathetic, irritable; anterior fontanelle tense; signs of meningeal irritation	Clear, normal biochemistry	Recovered
2, F, 2 mth.	Diarrhoea and vomiting treated at Gbaja with ? Darrow's orally		170	Hyperpyrexia, coma, gasping	Clear, normal biochemistry	Died; no necropsy
3, M, 3 mth.	Diarrhoea and vomiting	86	170	40 °C., unconscious, anterior fontanelle became tense, opisthotonos, tremor, convulsion, developed on 3rd day after admission	Uniformly blood-stained and xanthochromic; protein 800 mg./100 ml.	Recovered, but was spastic and mentally retarded
4, M, 15 mth.	Diarrhoea and vomiting	282	160	Hyperpyrexia, comatose, shrill cry, involuntary movements, convulsion	Protein 10 mg./100 ml. Cl 900 mg./100 ml.	Died, necropsy showed cerebral oedema and vascular congestion
5, M, 2 mth.	Diarrhoea		160	Hyperpyrexia, comatose, jittery, involuntary movements, and convulsion	Xanthochromic protein 860 mg.	Died, necropsy, intravascular thrombi, haemorrhage in brain and ventricular haemorrhage
6, F, 5½ mth.	Diarrhoea and vomiting		164	Hyperpyrexia, comatose, and depressed respiration		Died, necropsy, cerebral oedema and marked vascular congestion
7, F, 6 mth.	Diarrhoea and vomiting		150	Semiconscious, meningeal irritation, hypertonia	Clear, protein normal	Recovered
8, F, 4 mth.	Diarrhoea and vomiting; received 250 ml. normal saline subcutaneously		160	Irritable, restless, meningeal irritation	Clear, protein 140 mg./100 ml.	Recovered
9, M, 9 mth.	? Meningitis		160	Unconscious and gasping	Clear, protein not done, sugar 20 mg./100 ml. Cl 933 mg./100 ml.	Died, no necropsy
10, F, 2 mth.	Diarrhoea and vomiting	76	154	Irritable, signs of meningeal irritation	Clear, protein 30 mg./100 ml.	Recovered
11, M, 1½ mth.	Diarrhoea and vomiting	257	160	Restless, irritable, convulsion	Normal CSF	Died, no necropsy

TABLE II—*continued*

Case No., Sex, and Age	Aetiology or Underlying Disease	Urea	Max. Serum Na(mEq/l.)	Clinical Features	Result of CSF	Outcome
12, M, 4 mth.	Diarrhoea and vomiting, urinary infection, IVP non-functioning lt. kidney	252	160	Comatose, signs of meningeal irritation	Protein 100 mg./100 ml.	Recovered
13, F, 6 mth.	Diarrhoea and vomiting	114	150	Comatose, restless, convulsion	Protein 120 mg./100 ml.	Died; oedema of brain and petechial haemorrhage on the brain surface
14, M, 8 mth.	Diarrhoea and vomiting	42	158	Restless, irritable, neck retraction	CSF normal	Died; haemorrhage on surface and in brain; numerous intravascular thrombi
15, M, 1 mth.	Diarrhoea and vomiting		164	Semiconscious, hypertonic; brisk reflexes, bilateral ankle clonus		Recovered; CNS signs cleared up after recovery
16, F, 13 mth.	Diarrhoea and vomiting		148	Restless, thirst, tremor of hands		Died of hyperkalaemia
17, M, 3½ yr.	A case of primary TB; diarrhoea and vomiting		166	Semiconscious, hyperpyrexia, deep acidotic breathing		Died; tuberculous lesions in lungs and abdomen; cerebral oedema and hyperaemia
18, M, 1½ mth.	Diarrhoea and vomiting		158	Semiconscious, restless, head retraction, acidotic breathing	Protein 100 mg./100 ml.	Recovered
19, F, 1 yr.	Broncho-pneumonia; malnourished	54	160	Unconscious, hypertonic, convulsion	Protein 35 mg./100 ml.	Died, no necropsy
20, M, 3 mth.	Diarrhoea and vomiting	64	160	Irritable; slight hypertonia	Protein raised	Recovered
21, F, 9 mth.	Diarrhoea and vomiting	52	166	Comatose, hyperpyrexia, ? carpopedal spasm		Died, no necropsy
22, M, 8 mth.	Diarrhoea and vomiting		168	Comatose		Died, necropsy: cerebral oedema and congestion

acidosis. Potassium was above 6 mEq/l. in 4 patients and below 3 mEq/l. in 5 patients; none of the latter had signs of hypokalaemia.

Blood urea was estimated in 19 patients and ranged from 42 to 282 mg./100 ml.

Lumbar puncture was performed in 16 patients. CSF was uniformly blood stained and xantho-

chromic in 2 patients (Case 3 and 5, Table II); in others it was clear and under normal pressure. In 8 patients the protein content was high, ranging from 35 to 860 mg./100 ml. Sugar was normal or increased in all specimens. Chloride was increased in all and ranged from 800 to 933 mg./100 ml. (normal 750 mg./100 ml.).

TABLE III

Concentration of Electrolytes and Urea in Blood Serum

	Range	No. of Patients
Na (mEq/l.) ..	148-175	48
Cl (mEq/l.) ..	110-150	42
HCO ₃ (mEq/l.) ..	6-25	38
K (mEq/l.) ..	2.4-7.2	39
Blood urea (mg./100 ml.) ..	42-282	19

Discussion

Incidence. Hypernatraemic dehydration in diarrhoea is believed to be uncommon in the tropics. Ahmed and Webb (1963) found hypernatraemia in 1 single infant in a series of 65 infants presenting with diarrhoea at Vellore in South India and this infant had been given concentrated salt solution (500 mEq/l.) by mistake. A similar low incidence has been reported from Karachi (Zubeida *et al.*, 1968, personal communication).

By contrast, in our experience at Lagos, hypernatraemic dehydration in infants with gastroenteritis is not uncommon. Of 643 patients with diarrhoea who attended the Casualty Department from June 1967 to January 1968, 120 had their serum sodium measured. In 25 of these, serum sodium was 150 mEq/l. or more, an incidence of 20%. A similar incidence of hypernatraemic dehydration in diarrhoeal infants has been reported from the U.S.A. and other Western countries (Darrow *et al.*, 1949; Weil and Wallace, 1956; Finberg and Harrison, 1955; Bruck *et al.*, 1968).

Hypernatraemic dehydration is commoner in infants under 1 year and this is well illustrated in two recent studies on hypernatraemia (Morris-Jones, Houston, and Evans, 1967; Bruck *et al.*, 1968). In the present series also all infants except 3 were under 1 year, and of these, 30 (62%) were under 6 months.

Causes of hypernatraemic dehydration in infants. Hypernatraemia, i.e. serum sodium concentration of 150 mEq/l. or more, is due to excessive loss of water from body fluids or to reduced intake of water in relation to electrolytes. It is more often due to a total deficit of water than to an excess of sodium. The potential channels of excessive loss of water in infants are insensible water loss through skin and respiratory passages, diarrhoeal stools, and dilute urine. In normal infants more than 50% of daily water loss is from the surface of the skin and the lungs, and fever, hyperventila-

tion, and high environmental temperature tend to aggravate this loss. Heeley and Talbot (1955) observed average rates of insensible water loss of 1150 ml./m.² per day in sick infants, which is considerably higher than those for resting healthy infants. The average rate of insensible water loss in resting well infants is about 470-620 ml./m.² per day (Guest and Pettit, 1957).

Diarrhoeal stools are usually hypotonic when compared with blood. If the stools are large and frequent there is proportionately a greater loss of water than sodium (Skinner and Moll, 1956; Weil and Wallace, 1956; Bruck *et al.*, 1968).

Insufficient water intake. This is common in infants. In the present series, all patients except 4 (Table I, Cases 1, 2, 3, 4) had received insufficient quantities of water during the acute illness because of vomiting and anorexia.

Increased renal water requirement. Because of renal immaturity, dehydrated young infants are unable to form maximally concentrated urine. If they are fed on undiluted cow's milk and skimmed powder milk mixture which provides high protein intake, or given saline orally or parenterally, which gives a high solute load, the renal water requirement obligatory for excretion of electrolytes and urea is increased, thus increasing the water deficit (Pratt and Snyderman, 1953). 37 of 48 patients in the present series continued to be fed on powdered milk mixture in addition to breast feeding during the illness. It is possible that this could have contributed to the water deficit and to the hypertonicity of the blood.

In the majority of our patients no single cause could be identified as being responsible for the hypertonicity of the body fluids. A combination of several factors related to acute illness, i.e. water loss in a hypotonic diarrhoeal stool, excessive insensible water loss, insufficient water intake, and continued feeding of infants on powdered milk mixture in addition to breast-feeding accounted for or contributed to hypernatraemia. The rarity of this condition in India and Pakistan could be explained by the fact that mothers as a rule stop all feeds, including milk, and give only sugar and barley water to infants with diarrhoea.

Excessive administration of salt solution was the probable cause of hypernatraemia in only 11 of 48 patients. Of these, 4 patients (Cases 1, 2, 3, 4, Table I) had received large amounts of salt solution intravenously, while 7 patients, who were referred from Health Centres, had received orally unknown quantities of isotonic NaCl solution or Darrow's solution.

Cerebral manifestations in association with acute

hypernatraemia are common and well documented (Rapoport, 1947; Finberg and Harrison, 1955; Skinner and Moll, 1956; Weil and Wallace, 1956; Macaulay and Blackhall, 1961; Morris-Jones *et al.*, 1967), and subdural and subarachnoid haemorrhages have been observed in infants with hypernatraemia (Finberg, 1959). These clinical observations have been amply confirmed experimentally (Finberg *et al.*, 1959), and experimental studies have also shown that the osmolality of the extracellular fluid is the relevant factor rather than the sodium concentration alone (Finberg *et al.*, 1959). Thus, when a hypertonic solution, whether of sodium chloride, sodium bicarbonate, sucrose, mannitol, or urea, was injected into laboratory animals, cerebral lesions were produced which were closely akin to those found in human beings. Morris-Jones *et al.* (1967) showed a close relation between frequency of fits and serum sodium levels; thus the risk of fits was 10% when serum sodium was in the range of 140 to 158 mEq/l. but 71% at serum sodium levels above 158 mEq/l. The danger was further increased when high blood urea levels also contributed to extracellular osmolality.

Accepting the standard of Morris-Jones *et al.* (1967), that a serum Na concentration of 158 mEq/l. indicates severe hypernatraemia, 65% (17/26) of such patients in the present series had cerebral symptoms. 15 of these 17 had symptoms of severe cerebral disturbances, such as coma, convulsions, generalized hypertonia, gross involuntary movements, and neck retraction, whereas when the serum sodium level was below 158 mEq/l., 27% (5/22) of the patients had cerebral signs, and only one of them (Case 13, Table II) was unconscious and had convulsions. It is, therefore, clear that cerebral disturbances are correlated with high serum sodium concentration ($\chi^2=8.7$, $p<0.01$) (Fig.).

FIG.—Serum Na(mEq/l.) in 48 patients related to CNS signs and death.

Macaulay and Watson (1967) in a follow-up report on 100 hypernatraemic patients, who had no antecedent nervous disease, found that 16 patients had sustained permanent brain damage and of these only 8 patients were alive. Morris-Jones *et al.* (1967) reported neurological abnormalities in 37 (12/32) of the survivors; in several, however, abnormalities were unrelated to earlier hypernatraemia, and only 3 out of 32 (9%) had both related and symptomatically important lesions. Several other authors (Finberg, 1959; Weil and Wallace, 1956) have also reported permanent brain damage among survivors from acute hypernatraemic dehydration.

In the present series neurological signs were present in 22 (46%) of 48 patients, and of these, 13 died, though in one (Case 16, Table II) hyperkalaemia was the probable cause of death. 9 patients who, at the time of admission, had signs of severe brain damage, showed no improvement on treatment; coma deepened, respiration became irregular, and death followed. Of the 9 survivors, 1 child (Case 3, Table II) sustained permanent brain damage. 3 other children have been followed for one year and so far their physical and mental development have been normal.

Conclusions

This study shows that hypernatraemic dehydration is not infrequent in Lagos in infants suffering from diarrhoea. In our experience the clinical features that helped us to arrive at a diagnosis of this condition were: pyrexia, often high, hyperirritability, lethargy, increased thirst, absence of shock, good peripheral circulation in spite of moderate to severe dehydration, and presence of acidotic respiration.

In view of the high risk of brain damage and mortality attendant on this condition, it is important to prevent hypernatraemia. In the majority of patients hypernatraemia results from excessive loss of water in relation to sodium, and it can be prevented by ensuring an adequate fluid intake in an infant who has fever and is hyperventilating, especially when diarrhoea is also present. The daily fluid requirement of a normal infant is approximately 150 ml./kg. body weight in 24 hours. More may be needed in hot climates. During the diarrhoeal illness, twice the normal intake may be necessary. Injudicious administration of fluids with a high solute content such as 0.9% NaCl solution with 5% dextrose, or Darrow's solution should be discouraged. Mothers should be advised to stop milk feeds during the illness, and instead to offer the infant at frequent intervals a solution

containing sodium chloride 0.85 g., KHCO_3 1 g., and sugar 25 g. in a pint of water. If the diarrhoea continues and the child cannot take the fluids because of anorexia and vomiting, intravenous fluids will have to be given and this will necessitate admission to hospital.

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