Treatment of hyponatraemic seizures with intravenous 29·2% saline

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Abstract

Five patients with severe hyponatraemia and epileptiform seizures were given 50 ml of 29·2% saline (250 mmol) through a central venous catheter over 10 minutes to control seizures rapidly, reduce cerebral oedema, and diminish the incidence of permanent neuronal damage. The saline controlled seizures in all patients, increasing the mean serum sodium concentration by 7·4 (SD 1·14) mmol(mEq)/l and decreasing the mean serum potassium concentration by 0·62 (0·5) mmol(mEq)/l. Further saline and frusemide were then administered over 10 (2) hours, raising the serum sodium concentration by 2·14 (0·49) mmol/l/h until it reached 133 (2·35) mmol/l. A total of 790 (139) mmol saline was infused and a negative fluid balance of 3·34 (0·75) litres achieved. Four patients survived without neurological abnormality. One patient, who was not treated immediately and suffered a prolonged episode of status epilepticus, was left with a permanent neurological defect.

Introduction

Mild hyponatraemia, particularly if it develops over a long period, may be a biochemical abnormality of little clinical importance and may be corrected simply by restriction of water.[1] Severe hyponatraemia, however, may produce profound neurological disturbances requiring urgent correction.[2] Arieff and Guisado suggested that in patients with acute hyponatraemia hypertonic saline should be infused at 70 mmol(mEq)/h to raise the serum sodium concentration by 2-3 mmol(mEq)/l/h.[3] As permanent brain damage often follows hyponatraemic seizures,[4] however, the initial corrective phase may need to be more rapid in patients with convulsions to control the seizures, remove some of the excess cerebral water, and reduce the incidence of irreversible neuronal damage.

As the early pathological change found in patients with severe hyponatraemia is cerebral oedema,[3 5] it was reasoned that the initial treatment should be aimed at rapidly reducing this defect. To provide a blood-brain osmolar gradient of the 10-30 mmol (mosmol) needed to mobilise brain water rapidly[6 7] mannitol 1·0-1·5 g/kg (375-550 mmol/70 kg) administered over 10 minutes has been used to treat cerebral oedema.[8] In patients with hyponatraemic seizures 50 ml of 29·2% saline (500 mmol) was used to provide a similar osmotic gradient. A concentration of 29·2% (5 mmol/ml) was chosen as it approached saturation,[9] allowing a large amount of sodium chloride to be given in a small volume of fluid, and enabled amounts of sodium to be calculated easily.

Patients and methods

From 1978 to 1984 five patients were treated for hyponatraemic seizures. Plasma sodium, potassium, urea, and glucose concentrations were measured using a sequential multiple analyser with computer (Technicon Instruments Corporation, Tarrytown, New York), and osmolality was calculated from the formula P (mmol)=1·85×(sodium+potassium)+urea+glucose, where the concentrations of sodium, potassium, urea, and glucose were measured in mmol/l. Measurements were taken before and 30 minutes after 50 ml of 29·2% saline was given and every two to four hours thereafter. After the initial bolus of saline further saline and frusemide were administered, using calculations previously described,[10] in an attempt to raise the serum sodium concentration by 2-3 mmol/l/h until it reached 130-135 mmol/l. The time taken to correct the hyponatraemia (biochemical correction time) and the time taken before the patient would respond to command (clinical correction time) were recorded (see table II).

TABLE I—*Serum sodium (mmol/l) and potassium (mmol/l) concentrations and osmolality (mmol/kg) before and after infusion of 50 ml 29·2% saline*

Case No	Before saline			After saline			Final sodium	Total sodium	Negative fluid balance
	Sodium	Potassium	Osmolality	Sodium	Potassium	Osmolality			
1	109	3·5	220	116	3·3	231	134	750	2·9
2	109	3·9	219	117	3·5	232	135	650	3·5
3	100	5·1	203	109	3·8	219	131	700	4·2
4	106	3·6	214	112	2·6	223	130	850	2·3
5	99	2·8	197	106	2·4	207	135	1000	3·8
Mean (SD)	105 (4·83)	3·78 (0·84)	212 (10·2)	112 (4·64)	3·12 (0·6)	222 (10·2)	133 (2·35)	790 (139)	3·34 (0·75)

Conversion: SI to traditional units—Sodium and potassium: 1 mmol/l=1 mEq/l. Osmolality: 1 mmol/kg=1 mosmol/kg.

The 29·2% saline was prepared by dissolving 2·922 kg sodium chloride analytical reagent in freshly distilled water up to 10 litres. The solution was transferred aseptically through a 0·45 μm membrane filter into 50 ml type 1 glass containers and then autoclaved.

CASE 1

A 65 year old man weighing 73 kg with a history of diabetes and hypertension and a two year history of a leg ulcer overlying the right medial malleolus was admitted to hospital with an infected right ankle joint. Serum concentrations were: sodium 134 mmol/l, potassium 4·8 mmol(mEq)/l, urea 8·2 mmol/l (49 mg/100 ml), glucose 9·4 mmol/l (169 mg/100 ml), and creatinine 110 μmol/l (1·24 mg/100 ml). His right leg was amputated below the knee on the day after his admission. Postoperatively he received 3 litres of 4% dextrose and 0·18% saline and was allowed free oral fluids. On the third day after the operation he became disorientated and was given 10 mg intramuscular haloperidol. Seven hours later he had a grand mal seizure and received 10 mg diazepam intravenously. The fluid balance chart recorded a positive balance of roughly 7 litres for the first three days after the operation, and concentrations were sodium 109 mmol/l, potassium 3·5 mmol/l, urea 4·2 mmol/l (25·2 mg/100 ml), and glucose 7·4 mmol/l (133·3 mg/100 ml) and osmolality 220 mmol/kg.

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TABLE II—*Time taken to biochemical and clinical correction of hyponatraemia and increase in serum sodium concentration*

Case No	Biochemical correction time (h)	Clinical correction time (h)	Increase in serum sodium (mmol/l/h)
1	8	12	2·25
2	12	3 months	1·5
3	8	24	2·75
4	10	18	1·8
5	12	8	2·4
Mean (SD)	10 (2)		2·14 (0·49)

Conversion: SI to traditional units—Sodium: 1 mmol/l=1 mEq/l.

Thirty minutes after the first seizure he suffered two further grand mal seizures and 50 ml of 29·2% saline was administered over 10 minutes through a central venous line. Serum biochemical analysis 30 minutes after the saline was administered showed a sodium concentration of 116 mmol/l, potassium 3·3 mmol/l, and osmolality 231 mmol/kg. No further grand mal seizures occurred. He was given frusemide 40 mg and a further 100 ml of 29·2% saline (500 mmol) intravenously over the next eight hours. At this stage a negative fluid balance of 2·9 litres was achieved and serum concentrations were sodium 134 mmol/l and potassium 3·1 mmol/l and osmolality 263 mmol/kg. He responded purposefully to command 12 hours after the initial dose of hypertonic saline and two weeks later was discharged from hospital with no neurological defects.

CASE 2

A 47 year previously healthy woman weighing 67 kg had a bilateral mammary implantation performed at a district hospital. Postoperatively she received 3 litres of 5% dextrose and was allowed free oral fluids. On the fourth day after the operation she became very drowsy and was given naloxone 0·4 mg intravenously to reverse the narcotic effect of 75 mg pethidine, which had been given intramuscularly six hours earlier. One hour later she developed status epilepticus, which was unresponsive to a total of 60 mg diazepam and 1000 mg phenytoin administered intravenously over two hours. To control the fits she was intubated and paralysed and then transferred to this hospital for further treatment.

Three hours after the initial seizure her pupils were dilated and unresponsive to light and, although she was partially paralysed, generalised twitching indicated that the seizures had not been controlled. Her blood pressure was 60 mm Hg systolic and pulse 188 beats/minute, and serum concentrations were: sodium 109 mmol/l, potassium 3·9 mmol/l, urea 2·9 mmol/l (17·4 mg/100 ml), glucose 6·8 mmol/l (122·5 mg/100 ml), and osmolality 219 mmol/kg. Although accurate records of postoperative fluid balance were not kept, water intoxication from excess oral and intravenous fluids was diagnosed, 50 ml of 29·2% saline was infused over 10 minutes, and the seizures stopped after the first five minutes of the infusion. The serum concentrations after 30 minutes were sodium 117 mmol/l and potassium 3·5 mmol/l, and osmolality was 232 mmol/kg. Her blood pressure increased rapidly to 110/70 mm Hg after the intravenous administration of 10 ml of 10% calcium chloride, and her pupils became small and reactive to light two hours after the first dose of saline. She was given frusemide 80 mg and a further 80 ml of 29·2% saline (400 mmol) over eight hours. A negative fluid balance of 3·5 litres was obtained over the first 12 hours, at which time serum concentrations were sodium 135 mmol/l and potassium 3·8 mmol/l and osmolality was 265 mmol/kg. She slowly recovered consciousness and after three months began to respond purposefully to command. Two years later, however, she still needed to be managed in a nursing home and could not walk without help.

CASE 3

A 28 year old previously healthy woman weighing 52 kg received 2·5 litres of 4% dextrose and 0·18% saline daily after an appendicectomy. On the second day after the operation she drank an unknown amount of water, thinking that it would purify her body. During the evening of that day she became progressively more agitated and was given diazepam 10 mg intravenously. Three hours later she developed status epilepticus, which was unresponsive to intravenous diazepam 20 mg and phenobarbitone 200 mg. Her serum concentrations were sodium 100 mmol/l, potassium 5·1 mmol/l, urea 2 mmol/l (12 mg/100 ml), and glucose 6·2 mmol/l (111·7 mg/100 ml), and osmolality was 203 mmol/kg. Water intoxication was diagnosed. Over 10 minutes 50 ml of 29·2% saline was administered, during which time the seizures stopped. Thirty minutes later the serum sodium concentration was 109 mmol/l and potassium 3·8 mmol/l, and osmolality was 219 mmol/kg. She received frusemide 40 mg and a further 90 ml of 29·2% saline (450 mmol) over the next eight hours. A negative balance of 4·2 litres was obtained, and at this stage the serum concentrations were sodium 131 mmol/l and potassium 3·4 mmol/l and osmolality was 256 mmol/kg. She was responsive to commands 24 hours after the initial treatment with saline and was discharged from hospital eight days later with no neurological defect.

CASE 4

A 45 year old aboriginal man weighing 78·2 kg was admitted to hospital with 40% burns. He was resuscitated with blood and albumin and saline solutions, and after three days his serum concentrations were sodium 131 mmol/l, potassium 4·1 mmol/l, urea 4 mmol/l (24 mg/100 ml), and glucose 6·2 mmol/l (111·7 mg/100 ml), and osmolality was 260 mmol/kg. During the next two days he received 8 litres of 4% dextrose and 0·18% saline intravenously and was allowed free oral fluids. On the evening of the second day he had two grand mal seizures, which were treated with intravenous diazepam 10 mg and phenytoin 250 mg. Serum concentrations were sodium 106 mmol/l, potassium 3·6 mmol/l, urea 5·2 mmol/l (31·2 mg/100 ml), and glucose 5·7 mmol/l (102·7 mg/100 ml), and osmolality was 214 mmol/kg. As he had a positive fluid balance of 7·6 litres, 50 ml of 29·2% saline was administered over 10 minutes. Thirty minutes later the serum concentrations were sodium 112 mmol/l and potassium 2·6 mmol/l and osmolality was 223 mmol/kg. He had no more seizures and was given frusemide 20 mg and a further 120 ml of 29·2% saline (600 mmol) during the next 10 hours. At this stage a negative fluid balance of 2·3 litres was achieved and the serum concentrations were sodium 130 mmol/l and potassium 3·2 mmol/l and osmolality was 256 mmol/kg. Eighteen hours after his first seizure he was conscious and responding slowly to commands; 24 hours later he was fully alert. He was discharged from hospital three months after his admission with no neurological defect.

CASE 5

A 67 year old woman weighing 64 kg was admitted to hospital after taking an overdose of amitriptyline and diazepam. Her serum sodium concentration was 145 mmol/l and potassium 3·7 mmol/l, and osmolality was 275 mmol/kg. After an uneventful 24 hours of observation in the intensive care unit she was transferred to the psychiatric ward and underwent psychotherapy over the next four days. On the fifth day it was noticed that she was drinking frequently from a tap in the ward. Twenty four hours later she developed status epilepticus and was given diazepam 30 mg and phenytoin 750 mg intravenously. Serum concentrations were sodium 99 mmol/l, potassium 2·8 mmol/l, urea 1·3 mmol/l (7·8 mg/100 ml), and glucose 7·8 mmol/l (140·5 mg/100 ml), and osmolality was 197 mmol/kg. Fifty ml of 29·2% saline was administered over 10 minutes, and after 30 minutes her serum sodium concentration was 106 mmol/l and potassium 2·4 mmol/l, and osmolality was 207 mmol/kg. The seizures stopped during the infusion of saline. Frusemide 40 mg and a further 150 ml of 29·2% saline (750 mmol) were administered over the next 12 hours. At this stage a negative fluid balance of 3·8 litres had occurred and the serum concentrations were sodium 135 mmol/l and potassium 3·7 mmol/l, and osmolality was 264 mmol/kg. She became responsive to command eight hours after the first seizure and was discharged from hospital two weeks later with no neurological defect.

Discussion

Experimental studies have shown that severe hyponatraemia (plasma sodium concentration less than 125 mmol/l) is associated with cerebral oedema[11-13] and that the excess water content of the brain is important in influencing consciousness.[10] These observations have led many to use hypertonic saline solutions to correct hyponatraemia rapidly in patients with acute hypo-osmolar encephalopathy,[10 14 15] although reports of central pontine myelinolysis have led some workers to advise caution in the use of this form of treatment.[16 17] In a comprehensive review of all published cases of central pontine myelinolysis Arieff concluded that it was more likely to be seen in malnourished alcoholic patients and was not related to the speed of correction of the hyponatraemia.[2]

The ideal treatment for acute hyponatraemia has yet to be established,[3 14] but most would now agree that early diagnosis and rapid correction seem to reduce morbidity and mortality.[2-4] Arieff and Guisado recommended a treatment regimen of 70 mmol of saline/h or a negative balance of 600 ml of fluid/h until the plasma

sodium concentration reaches 130 mmol/l. In a study of seven patients Ayus *et al* used 3% hypertonic saline to increase the serum sodium concentration by 2·4 mmol/l/h without morbidity or mortality.[14] In patients with hyponatraemic seizures, however, we thought that an acute osmolar gradient at the beginning of treatment, to reduce cerebral oedema and control seizures rapidly, may also be necessary to reduce the incidence of irreversible neuronal damage. In our study all the patients survived, comparing favourably with the 50% mortality previously recorded,[3] but only four patients recovered completely. Although we thought that the prolonged episode of status epilepticus and hypotension that had occurred before treatment was responsible for the persistent neurological defect in the patient in case 2, we could not exclude an adverse effect of treatment as a possible cause.

In the five cases reported we thought that water intoxication from excess intravenous and oral fluids was the main cause of the hyponatraemia. With the initial infusion of 50 ml of 29·2% saline the mean serum sodium concentration increased from 105 (SD 4·8) mmol/l to 112 (4·64) mmol/l (table I). The increases in serum sodium concentration and osmolality were 7·4 (1·14) mmol/l and 11·8 (2·77) mmol/kg, respectively, and the reduction in serum potassium concentration was 0·62 (0·5) mmol/l. The fall in serum potassium concentration may have been caused by an increase in intracellular sodium, increasing the activity of the sodium-potassium adenosine triphosphatase.[18] The total amount of sodium administered was 790 (139) mmol, which increased the serum sodium concentration to 133 (2·35) mmol/l over 10 (2) hours. The rise in serum sodium concentration after the initial bolus of 29·2% saline was given was 2·14 mmol/l/h (table II), which was only slightly lower than the 2·4 mmol/l/h reported by Ayus *et al*.[14] The rapid administration of 500 mmol did not produce any discernible untoward clinical effects, which was not unexpected as similar osmotic amounts of mannitol and radiological contrast media have been rapidly infused in patients without complication.[8 19]

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(Accepted 28 October 1985)

SHORT REPORTS

Dietary practices of Asian diabetics

There is a widespread belief that Asian diabetics in Britain already follow a diet with a high carbohydrate, high fibre, and low fat content, which might be expected to help protect against diabetes and vascular disease. We investigated the dietary practices of a group of Asian diabetics living in the London Borough of Brent.

Patients, methods, and results

About 30% of patients attending this hospital's diabetic clinic are of Asian origin. About 70% of these are Gujarati, who have come either directly from India or from east Africa and are mostly Hindus. The remainder come from the Punjab and Pakistan, and many are Moslems. The Asian population covers all socioeconomic groups; 62% of men and 32% of women speak some English, usually as a second language. We randomly selected 48 patients (29 men and 19 women). Nine were treated with insulin and 39 by diet alone or with oral hypoglycaemic agents. Their mean age (range) was 53 (20-74) years, duration of diabetes 8 (2-23) years, and time in the United Kingdom 16 (2-36) years; in most cases the diagnosis had been made in the United Kingdom. The mean (SEM) body mass index was 25·1 (0·6) kg/m^2 in the men and 27·4 (0·6) kg/m^2 in the women.

A detailed dietary questionnaire was administered in the mother tongue by a nutritionist (JTD) during a home visit to each patient. Questions covered frequency of food consumption, methods of preparing and cooking food, and a 24 hour recall. Sizes of portions and daily intakes were calculated with the aid of food models and samples, graduated containers, and weighing scales. Any missing data were collected during a second interview in the clinic. Nutrient intakes were calculated from food composition tables.[1 2]

The basic traditional diet followed by most patients consisted of chapatis (made with 85% wheat flour), white rice, vegetables, pulses, beans, and fruit. Six men and 12 women were vegetarian, all being Hindus. The table gives an analysis of the diets. The high fat intake was accounted for mainly by ghee (clarified butter) and cooking oil. Most patients regularly ate fried snack foods such as chevda, ganthia, crisps, and nuts. Thirteen consumed more than one pint of whole milk daily. Intake of fibre is not reported as not all the relevant figures for Asian dishes are available in food tables, but it was unlikely to have been much higher than the national average for the United Kingdom. Rich sources of soluble fibre such as beans and lentils were consumed in only small amounts and were eaten daily by 20 patients. Chapati flour was the major source of cereal fibre; other sources such as bread and breakfast cereals were not popular.

Patterns of food consumption

	Mean (range) energy intake (MJ)	% Of daily energy intake obtained from:		
		Carbohydrate*	Fat†	Protein
Men	10·7 (5·1-17·3)	41	46	12
Women	6·8 (4·0-11·4)	43	45	11
Both	9·2	42	46	12

*Numbers of diabetics who regularly (that is, more than five times a week) ate various carbohydrates were: Asian sweets 11; confectionery 19; sweet biscuits and cakes 33; fizzy drinks 20; gur (unrefined sugar) 16; bread 11; and breakfast cereals 10.
†Numbers of diabetics who regularly ate various fats were: ghee 46 (those from Gujarat ate an average (range) of 245 (40-500) g/week; those from Kutch, a part of Gujarat, 424 (140-950) g/week; and others 188 (0-780) g/week; butter 36 (13 ate >120 g/week, 23 ate <120 g/week); unsaturated oil (<120 g/week) 15; and corn oil (<500 g/week) 21 and groundnut oil (<500 g/week) 13.
Conversion: SI to traditional units—Energy: 1 MJ=239 kcal.

Comment

This is the first detailed study of the diets of Asian diabetics in this country. It highlights the discrepancies between their dietary practices and current recommendations for diabetics.[3] Previous studies in India suggested that Asian diabetics there follow a diet close to these recommendations.[4 5] We found, however, that most Asian diabetics followed a diet with a low carbohydrate and high fat content and consumed sugar and refined carbohydrates regularly. There was widespread use of dairy products such as milk, ghee, and yoghourt, which are rich in saturated fats; this applied regardless of the patients' regional origins.

Diet has a central role in the management of diabetes. Many health workers lack the basic knowledge about the diets of Asians on which to base practical advice, and little educational material is available. There is a