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Hyperkalaemia, cardiac arrhythmias, and cerebral lesions in high risk neonates

D SHORTLAND,* J Q TROUNCE,† AND M I LEVENE*

Departments of Child Health, Leicester Royal Infirmary and Nottingham City Hospital†*

SUMMARY The case notes of 20 infants with hyperkalaemia (defined as two successive serum potassium measurements of >7·5 mmol/l) were reviewed. The incidence of hyperkalaemia was also looked at in an unselected population of 200 low birthweight infants. The mean gestational age of the 20 affected infants was 29 weeks and the mean birth weight 1235 g. The incidence of hyperkalaemia in the cohort of 200 infants weighing less than 1500 g at birth was 3·5%. Hyperkalaemia was associated with a high incidence of cardiac arrhythmia (60%), impaired renal function (50%), and changes on cerebral ultrasonography (88%). Hyperkalaemia responds slowly to conventional treatment with dextrose, insulin, and exchange resins. There is a close temporal relation in some infants between hyperkalaemia and cardiac arrhythmias and periventricular leukomalacia, suggesting a causal association.

There are little published data on the incidence and consequences of neonatal hyperkalaemia. It is known to cause cardiac arrythmias,[1–4] and recent evidence suggests that increased potassium concentrations in cerebrospinal fluid or brain parenchyma may cause spasm of the intracerebral arteries.[5] Both these factors could impair the neonatal cerebral circulation.

We looked at the incidence of hyperkalaemia in an unselected population of very low birthweight infants (n=200), and reviewed the case notes of 20 infants known to have had hyperkalaemia to estimate the incidence of cardiac arrhythmia, renal impairment, and cerebral abnormality.

Methods

A computer search for cases of hyperkalaemia among all admissions to the neonatal unit from April 1983 until May 1986 was undertaken. Hyperkalaemia was defined as two sequential serum potassium measurements of 7·5 mmol/l or more in non-haemolysed samples. In an earlier study at the Leicester Royal Infirmary and Nottingham City Hospital neonatal units 200 consecutive very low birthweight infants had had their neonatal complications documented prospectively. Serum potassium concentrations were recorded and from these data we calculated the incidence of hyperkalaemia in this group of very low birthweight infants.

The biochemical data were obtained in all the infants with hyperkalaemia. High serum urea or creatinine concentrations were defined as those above the normal range given in published reports.[6 7] Twelve hourly arterial pH measurements before and during the hyperkalaemic episodes were recorded to assess the degree of acidosis. We assessed the duration and severity of hyperkalaemia by calculating in mm^2 the area under the curve that

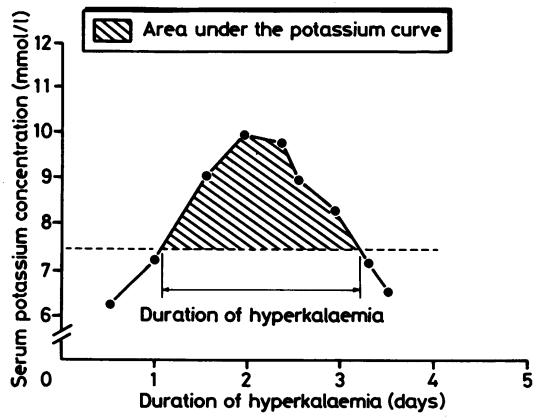

Fig 1 *Method of calculating duration and severity of hyperkalaemia (serum potassium concentration of >7·5 mmol/l).*

Table *Details of 20 infants with hyperkalaemia studied*

Case No	*Gestational age (weeks)*	*Birth weight (g)*	*Age at onset of hyperkalaemia (hours)*	*Severity of hyperkalaemia (mm^2)*	*Maximum potassium concentration (mmol/l)*	*Arrhythmia*	*Ultrasound findings*	*Outcome*
1	29	940	4	8	7·7	Bradycardia	Bilateral cystic periventricular leucomalacia	Died at six months (cot death)
2	33	2100	24	28	8·2	Supraventricular tachycardia; bradycardia	Not done	Survived
3	26	950	12	60	9·4	Supraventricular tachycardia	Germinal matrix haemorrhage	Survived
4	26	970	24	100	8·5	Supraventricular tachycardia	Germinal matrix haemorrhage	Died aged six days
5	31	1700	24	260	8·8	Supraventricular tachycardi	Normal	Died aged three days
6	26	780	28	325	9·9	Bradycardia	Intraventricular haemorrhage; periventricular leucomalacia	Died aged nine days
7	25	700	12	350	12·5	Supraventricular tachycardia	Intraventricular haemorrhage	Survived; development normal at 18 months
8	27	1000	36	360	8·6	Bradycardia	Germinal matrix haemorrhage; periventricular leucomalacia	Died aged seven days
9	26	740	48	375	9·1	Nodal arrhythmia	Germinal matrix haemorrhage; periventricular leucomalacia	Died aged twelve days
10	28	1300	42	520	9·9	Supraventricular tachycardia	Germinal matrix haemorrhage; periventricular leucomalacia	Survived
11	37	1420	46	1308	12·6	Supraventricular tachycardia	Transient flare	Died aged eight days
12	25	900	24	1733	12·2	Supraventricular tachycardia	Germinal matrix haemorrhage; periventricular leucomalacia	Died aged six days
13	29	1100	36	8	7·7	None	Intraventricular haemorrhage; periventricular leucomalacia	Survived; spastic cerebral palsy
14	38	2900	48	12	7·8	None	Normal	Died aged one day
15	29	1400	36	255	8·9	None	Transient flare	Survived
16	25	780	12	295	9·5	None	Not done	Survived
17	28	1000	24 & 108	330	8·7	None	Intraventricular haemorrhage	Survived
18	26	850	24	475	12	None	Intraventricular haemorrhage	Died aged one day
19	37	2180	12	885	11·3	None	Not done	Died aged three days
20	24	900	42	895	12·7	None	Intraventricular haemorrhage; venous infarction	Survived

related serum potassium concentration to time (fig 1). This method has been previously used to assess the severity of acidosis.[8] The number of episodes of cardiac arrhythmia and the treatment of hyperkalaemia were recorded and cerebral ultrasound scans of the hyperkalaemic infants were also reviewed.

Results

Seven of the 200 very low birthweight infants in the previously studied cohort developed hyperkalaemia in the neonatal period,[9] an incidence of 3·5%. We report the results from an additional 13 hyperkalaemic infants.

The mean birth weight of the 20 infants was 1230 g and the mean gestational age 29 weeks. In all the infants the hyperkalaemia became apparent within 48 hours of birth, and one infant had a second episode during the fifth day of life. The table gives details of the data on the infants. No infants had had prolonged seizures, and blood transfusions were not given in the first 48 hours of life, so these two possible causes of hyperkalaemia could be disregarded.

Serum urea concentrations were available for all 20 infants and creatinine concentrations were also available for 11 infants, of which five were abnormal. We used creatinine concentrations as an index of renal function when available, and the less reliable urea measurements in the rest. In the nine infants in whom only urea concentrations were available, five were above the normal range.

Arterial pH estimations were available before and during the hyperkalaemic episode in 10 infants, and these showed that there was no obvious trend towards acidosis when the serum potassium concentrations were at their highest.

Cardiac arrhythmias occurred in 12 (60%) of the infants; the most common was supraventricular tachycardia (n=7); three became bradycardic; one developed a nodal rhythm; and one had both supraventricular tachycardia and bradycardia. In four infants the arrhythmia preceded the diagnosis of hyperkalaemia. Five infants with cardiac arrhythmias had raised serum urea or creatinine concentrations, and therefore possible renal compromise. The mean peak potassium concentration in the group with arrhythmias was 9·8 mmol/l. This is the same as that found in the infants who did not have arrhythmias. The mean area under the curve in infants with an arrhythmia was 452 mm^2 compared with 394 mm^2 in those with no arrhythmia; this difference was not significant. In some infants with cardiac arrhythmia the blood pressure had been recorded continuously. In each infant with supraventricular tachycardia or nodal rhythm in whom continuous recordings of blood pressure were available there was a definite fall during the arrhythmia (fig 2).

The results of cerebral ultrasound scans were available in 17 of the infants. In two the scan remained normal throughout the neonatal period. The remaining 15 (88%), however, showed some abnormality; 11 had germinal matrix haemorrhage or intraventricular haemorrhage, and seven periventricular leucomalacia with or without germinal matrix haemorrhage or intraventricular haemorrhage. In a further two infants there were transient echodense areas in the parenchyma but these all resolved within two weeks of birth. In five infants with periventricular leucomalacia we determined the association between the diagnosis of hyperkalaemia and the onset of the lesion seen on the ultrasound scan. In three, parenchymal echodensity was first detected within 48 hours of the raised serum potassium concentration, and in another the next scan (performed four days after the onset of hyperkalaemia) showed periventricular leucomalacia for the first time. In one infant periventricular leucomalacia preceded the hyperkalaemia, and in three the ultrasound evidence of periventricular leucomalacia was seen within 24 hours of cardiac arrhythmia. The infant whose blood pressure trace is shown in fig 2 developed parenchymal echodensity within 12 hours of the documented arrhythmia. In only one infant was periventricular leucomalacia evident before the diagnosis of hyperkalaemia.

The hyperkalaemia was treated with insulin and infusion of 10% dextrose; calcium resonium enemas were given every four hours. Episodes of arrhythmia

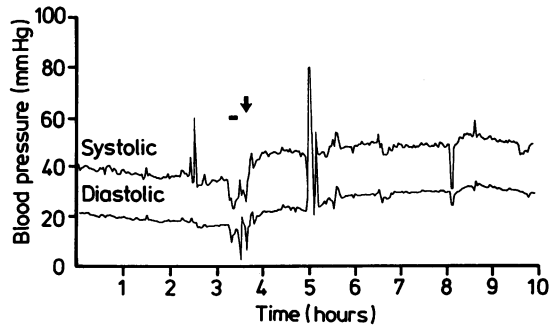

Fig 2 *Effects of supraventricular tachycardia on blood pressure in infant of 27 weeks' gestation when 24 hours old. Bar=duration of arrhythmia, terminated with 10% calcium gluconate (arrow). Systolic and diastolic blood pressures were recorded on disc every two minutes and displayed as a rolling average.*[14]

were treated with bolus injections of 0·2–0·5 ml of 10% calcium gluconate and cardioversion was not used. Case 10 (table) was treated by peritoneal dialysis.

Discussion

Despite the relatively high incidence of hyperkalaemia in the two neonatal units studied little seems to have been written about the condition in neonates. An infant is most likely to have raised serum potassium concentrations within the first 48 hours of life. At this time he or she will be receiving minimal amounts of oral or intravenous potassium, and so the likely cause of the condition is either leakage of intracellular potassium or diminished renal excretion. Potassium is predominantly an intracellular cation and any factor which causes it to move out of the cells (for example, acidosis) will result in an increased serum concentration. The rate of potassium excretion depends on the concentration gradient between the distal renal tubular cells and the luminal potassium concentration.[10] It follows that any factor increasing the intracellular potassium concentration (for example, insulin) or increasing luminal urine flow rates (for example, diuretics) will enhance potassium excretion.

The most important function of potassium is to maintain the normal membrane resting potential. An increase in extracellular potassium concentration will lower the resting potential and therefore a stimulus of lesser intensity will evoke an action potential. This will increase the 'excitability' of the cell membrane. An action potential is produced by the opening of sodium channels, thereby permitting the rapid entry of sodium into the cells. When potassium concentrations are extremely high these channels are inactivated and the stimulus cannot produce an electrical response.[11] This may account for the bradyarrhythmias associated with hyperkalaemia.

Therefore it is not surprising that so many of the infants (60%) developed cardiac arrhythmias. Two kinds of arrhythmia predominated in our study, supraventricular tachycardia and sinus bradycardia, but many different electrocardiographic changes have been previously reported.[2–4]

Hyperkalaemia seems primarily to affect very low birthweight infants and review of the case notes of these infants showed that the most likely to suffer from it are those with other problems. Guignard *et al* showed that renal function was impaired in infants with idiopathic respiratory distress syndrome and that the degree of impairment correlated with the severity of the respiratory illness.[12] They postulated that the hypoxaemia, hypotension, or intermittent positive pressure ventilation may have been responsible. Measurements of serum urea and creatinine concentrations were available for all the infants, and 10 (50%) of them had evidence of renal impairment. This was probably the cause of their hyperkalaemia, but we were unable to identify the cause in the remainder. There may have been a reduction in renal blood flow (and therefore in distal tubular luminal urine flow) that was sufficient to impair potassium excretion but not sufficient to be reflected in raised urea and creatinine concentrations. It is more likely, however, that there was a redistribution of potassium from the intracellular to the extracellular compartments. Acidosis causes such shifts in potassium, but we did not see appreciable decreases in arterial pH during periods of hyperkalaemia.

Edvinsson *et al* showed that human cerebral arteries in vitro contract when bathed by a potassium concentration of more than 10 mmol/l.[5] They postulated that this may be partly responsible for periventricular ischaemia in neonates. Abnormalities on ultrasound scan were seen in 15 of the 17 infants (88%), of whom eight (54%) had parenchymal changes. In a previous study of 200 very low birthweight infants parenchymal lesions were seen in only 14%.[9] In the present study, germinal matrix haemorrhage or intraventricular haemorrhage was seen in 70% of the infants. The close temporal relation between hyperkalaemia and periventricular leucomalacia that we found provides good circumstantial evidence of a direct association between them. In addition, three infants showed the first signs of periventricular leucomalacia within 24 hours of cardiac arrhythmia. In the case illustrated in fig 2 there was a period of acute hypotension lasting for over 20 minutes 12 hours before the first ultrasound changes of periventricular leucomalacia appeared, which supports a direct causal association between arrhythmia and cerebral infarction.

Our current policy is to treat any infant with a serum potassium concentration of >7·5 mmol/l, or a concentration of 6·5–7·5 mmol/l if it is associated with electrocardiographic abnormalities. Cardiac arrhythmias are treated with a bolus dose of 10% calcium gluconate intravenously. In the present study 13 of the infants were treated with insulin and dextrose infusions and calcium resonium exchange enemas. In these infants the mean duration of the hyperkalaemic episode was 47 hours. Because potassium concentrations decline slowly with conventional treatment we have begun to evaluate peritoneal dialysis; to date five infants have been treated in this way. Setzer *et al* reported the successful treatment of neonatal hyperkalaemia by an exchange transfusion of red blood cells washed in

saline.[13] Both these methods require further evaluation.

Hyperkalaemia may cause cerebral damage by reducing cerebral blood flow during episodes of cardiac arrhythmia or by inducing arteriolar spasm. In the absence of evidence to the contrary, we recommend that hyperkalaemia should be treated aggressively. Serum potassium concentrations should be checked regularly during the first 48 hours of life in very low birthweight infants, particularly in those with other problems.

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Correspondence to Dr MI Levene, Neonatal Unit, Department of Child Health, Leicester University School of Medicine, Leicester.

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