Increased concentration of aluminium in the brain of a parenterally fed preterm infant

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SUMMARY Parenteral feeding solutions currently used for preterm infants are contaminated with aluminium. We report the case of an infant who was fed parenterally for 45 days, who died aged 3 months, and who had a considerably increased concentration of aluminium in his brain tissue at necropsy.

Aluminium toxicity occurs in patients with renal failure who require haemodialysis[1] or who receive aluminium hydroxide as a phosphate binding agent.[2] It presents as anaemia, poor bone mineralisation and encephalopathy ('dialysis dementia'). Preterm infants receiving parenteral nutrition are at risk of toxicity because of reduced renal function, and reported high levels of contamination of their parenteral feeding solutions.[3]

We describe the case of a preterm infant who received parenteral nutrition for 45 days, and who had repeated unexplained convulsions.

Case report

The baby boy was born at 24 weeks' gestation, weighing 630 g. Intermittent positive pressure ventilation was started at the age of 6 hours, initially for respiratory distress and subsequently for apnoea during episodes of sepsis. Bilateral intraventricular haemorrhages with right sided periventricular leucomalacia were diagnosed by ultrasound scan on day 7.

Parenteral nutrition was given from days 1 to 25 and days 47 to 68 because of respiratory distress, sepsis, and intolerance of enteral feeds. The solutions used were Vamin 9 glucose with mineral, trace element, and water soluble vitamin additives, and Intralipid 10% with fat soluble vitamins.

Convulsions first occurred on day 10. Full investigations to diagnose metabolic abnormalities and the presence of sepsis were carried out, including lumbar puncture, which showed an excess of leucocytes in the cerebrospinal fluid. Benzylpenicillin and chloramphenicol were given for 10 days, although no organism was cultured. Phenobarbitone was given until day 37 when because there had been no further convulsions it was reduced, and then discontinued.

Convulsions recurred on day 69. No evidence of sepsis or metabolic disturbance was found. Ultrasound scanning showed moderate bilateral ventricular dilation, more obvious on the right side, but no other structural abnormality. Phenobarbitone was recommenced, and a 24 hour electroencephalogram one week later showed no abnormal activity. The anticonvulsant treatment was reduced, and discontinued on day 86.

The absence of a convincing explanation for the convulsions (other than structural damage from intraventricular haemorrhages and periventricular leucomalacia) led us to consider the possibility of aluminium toxicity as a result of parenteral feeding. Before investigations could be instituted, however, the infant had further convulsions; again, no cause was found. The infant died two days later aged 93 days.

At necropsy samples of temporoparietal grey matter were taken for analysis for the presence of aluminium. The avoidance of contamination is of paramount importance in aluminium estimations, and attention was paid to avoiding potential hazards; the pathologist removed glove dust by careful washing before handling samples, specimens were taken by sectioning with an unused scalpel, and placed immediately in plastic containers. No processing of samples was done, other than freezing; they were thawed immediately before being digested by nitric acid. Analysis was by direct injection into a Perkin Elmer Zeeman 3030 atomic absorption spectrophotometer.

Samples of temporoparietal grey matter from 12 infants who had died suddenly and unexpectedly in the first year of life were analysed for comparison. The aluminium contents of parenteral nutrition solutions have been previously published.[3] Aluminium intake was calculated as the mean aluminium content of each component solution multiplied by the volume given for each day during periods of parenteral feeding.

RESULTS OF ANALYSIS

The average aluminium intake was 14 μg/day. Total intake of aluminium from intravenous feeding solutions was 645 μg. Additional aluminium may have been given with intravenous drugs and plasma, and with oral feeds.[3]

The aluminium content of the subject's grey matter was 40·1 μg/g wet weight of tissue; the mean (SD) value for 12 infants dying unexpectedly within the first year of life was 2·4 (1·6) μg/g wet weight of tissue. The fat content of the brain doubles during the first year of life; this would not however, account for the 20 fold difference in brain aluminium concentrations observed. In addition, aluminium accumulates specifically in cortical grey matter, the fat content of which is less likely to vary with age.

Discussion

The preterm infant studied here had a brain aluminium content of 40 μg/g wet weight of tissue. In 'dialysis dementia', corresponding cortical aluminium concentrations are reported to be 20–30 μg/g in adults,[1] and even lower in infants.[2 4]

Toxicity is not proved by the finding of a high brain aluminium content. Nevertheless, with a history of unexplained convulsions and prolonged intravenous feeding, there is a strong possibility that high aluminium intake was at least a large contributory factor.

Parenterally administered aluminium is poorly excreted by preterm infants, who retain up to 80% of an intravenous load.[5] Calcium gluconate, potassium acid phosphate, and the trace element solution (Ped-El) together accounted for 90% of the contamination. The substitution of calcium chloride for calcium gluconate reduces delivery of aluminium by 70% from an average intake of 30 μg/kg/day when on full intravenous feeding at 150 ml/kg/day to 8 μg/kg/day. The lower value of 14 μg/kg/day for the index case was due to partial enteral feeding.

The signs of aluminium toxicity, which include encephalopathy, anaemia, and poor bone mineralisation, are common complications of many diseases in sick premature babies. Nevertheless, we suggest that when conventional therapeutic manoeuvres fail, aluminium toxicity should be considered.

References

1 Van de Vyver FL, De Broe ME. Aluminium in tissues. *Clin Nephrol* 1985;**24**(suppl 1):S37–S57.
2 Randell ME. Aluminium toxicity in an infant not on dialysis. *Lancet* 1983;**i**:1328–9.
3 McGraw M, Bishop N, Jameson R, *et al.* Aluminium content of milk formulae and intravenous fluids used in infants. *Lancet* 1986;**i**:157.
4 Freundlich M, Zillervelo G, Faugere MC, Abitbol C, Strauss J, Malluche HH. Infant formulae as a cause of aluminium toxicity in neonatal uraemia. *Lancet* 1985;**ii**:527–9.
5 Sedman AB, Klein GL, Merritt RJ, *et al.* Evidence of aluminium loading in infants receiving intravenous therapy. *N Engl J Med* 1985;**312**:1337–43.

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Gowers' sign revisited

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SUMMARY We studied the patterns of standing in children with neuromuscular disorders and central hypotonia for Gowers' sign, and compared these two groups with healthy controls. More children with central hypotonia than controls rolled prone before standing at 36 months; at this age all children with neuromuscular disorders rolled prone. Neurological assessment is indicated in children continuing to roll prone before standing at 3 years.

In 1879 Gowers first described the pattern of standing in 21 boys with pseudohypertrophic muscular paralysis in a clinical lecture to the students of University College.[1] He initially thought this pattern of standing was pathognomonic for children with this condition as it was present in all his ambulatory cases. It has subsequently been shown to be present in other children with proximal muscle weakness.

Dr Gowers' eloquent description of the pattern of standing, which now bears his name, emphasised two important features (figure): (i) the children adopting a prone position on all fours before attempting to stand and (ii) the children 'walking up their legs'. It is the second feature that is often quoted in textbooks and remembered by physicians as Gowers' sign.

The Muscular Dystrophy Group report that the