(3) In considering the dosage of pyridoxine used in treatment, in mg/kg, it is not valid to compare a healthy adult to a child with proved pyridoxine dependency, a condition requiring higher than physiological doses of pyridoxine to maintain normal concentrations.¹²

(4) There is no doubt that the minimum effective dose is best. We did not investigate the efficiency of maintenance doses of less than 75 mg pyridoxine/day because of evidence from the published reports that the effective dose is 40 to 100 mg/day.¹⁰⁻¹² Doses as high as 200 mg/day have been required⁹ to control seizures. In considering the optimal dosage, the potential hypoxic damage from recurrence of seizures cannot be ignored.

The conclusion of Dr Reynolds that our 'treatment may, in fact, have contributed substantially to the impaired mental development noted . . .' is not supported by our cases. The findings of others in man were of peripheral neuropathy, and 'the central nervous system was spared'¹ in man and in beagle dogs.⁵

We encourage the diagnostic use of pyridoxine in a baby with intractable seizures. Once a definite clinical response has been established treatment should be continued indefinitely: the optimal daily dosage, however, may need to be reviewed.

References

- Bankier A, Turner M, Hopkins JJ. Pyridoxine dependent seizures—a wider clinical spectrum. *Arch Dis Child* 1983;**58**:415–8.
- Schaumburg H, Kaplan J, Windebank A, et al. Sensory neuropathy from pyridoxine abuse. A new megavitamin syndrome. *N Engl J Med* 1983;**309**:445–8.
- Phillips WEJ, Mills JHL, Charbonneau SM, et al. Subacute toxicity of pyridoxine hydrochloride in the beagle dog. *Toxicol Appl Pharmacol* 1978;**44**:323–33.
- Krinke G, Schaumburg HH, Spencer PS, Suter J, Thomann P, Hess R. Pyridoxine megavitaminosis produces degeneration of peripheral sensory neurons (sensory neuronopathy) in the dog. *Neurotoxicology* 1980;**2**:13–24.
- Hoover DM, Carlton WW. The subacute neurotoxicity of excess pyridoxine. HCl and clioquinol (5-chloro-7-iodo-8-hydroxyquinoline) in beagle dogs. I. Clinical disease. *Vet Pathol* 1981;**18**:745–56.
- Hoover DM, Carlton WW. The subacute neurotoxicity of excess pyridoxine. HCl and clioquinol (5-chloro-7-iodo-8-hydroxyquinoline) in beagle dogs. II. Pathology. *Vet Pathol* 1981;**18**:757–68.
- Hoover DM, Carlton WW, Henrikson CK. Ultrastructural lesions of pyridoxine toxicity in beagle dogs. *Vet Pathol* 1981;**18**:769–77.
- Schaeppli U, Krinke G. Pyridoxine neuropathy: correlation of functional tests and neuropathology in beagle dogs treated with large doses of vitamin B-6. *Agents Actions* 1982;**12**:575–82.
- Clarke TA, Saunders BS, Feldman B. Pyridoxine-dependent seizures requiring high doses of pyridoxine for control. *Am J Dis Child* 1979;**133**:963–5.
- Bessey OA, Adam DJD, Hansen AE. Intake of vitamin B₆ and infantile convulsions: a first approximation of requirements of pyridoxine in infants. *Pediatrics* 1957;**20**:33–43.
- Gentz J, Hamfelt A, Johansson S, Lindstedt S, Persson B, Zetterstrom R. Vitamin B₆ metabolism in pyridoxine dependency with seizures. *Acta Paediatr Scand* 1967;**56**:17–26.
- Heeley A, Pugh RJP, Clayton BE, Shepherd J, Wilson J. Pyridoxol metabolism in vitamin B₆ responsive convulsions of early infancy. *Arch Dis Child* 1978;**53**:794–802.

Metabolic alkalosis in a neonate after frusemide

Sir,

Acute metabolic alkalosis is uncommon in newborns. When it occurs it is usually secondary to electrolyte imbalance, fluid depletion, chronic hypercapnoea or, more rarely, exchange transfusion with citrated blood.

We describe a term neonate of birthweight 2.52 kg who developed acute profound metabolic alkalosis after intravenous frusemide. At the time the baby was on nasal constant positive airways pressure for pulmonary hypoplasia secondary to chronic amniotic liquor loss during the pregnancy. Frusemide (1 mg/kg) was administered intravenously on two occasions (four hours apart) because of chest x ray changes suggestive of interstitial pulmonary oedema. After the second dose of frusemide the baby developed a metabolic alkalosis with pH 7.66, HCO₃ 58.5 mmol/l, base excess 28 mmol/l, Pco₂ 50 mm Hg. Her plasma electrolytes were urea 3.5 mmol/l, potassium 5.2 mmol/l, and sodium 135 mmol/l. The frusemide was stopped and the alkalosis corrected spontaneously in 14 hours. When a further dose of frusemide was administered two days later a similar episode of metabolic alkalosis occurred which again resolved spontaneously when the drug was stopped. Chlorthiazide was subsequently prescribed without side effects.

Frusemide is highly bound to albumin—more than 99% in adults and at least 95% in neonates. In the first week of life frusemide clearance is only 10% of the adult rate.¹ Thus, the prolonged half life may potentiate its action, particularly if doses are given less than 12 hours apart. De Rubentis *et al*² suggest three mechanisms that may contribute to its production of alkalosis, namely potassium depletion, renal loss of hydrogen ion, and extracellular fluid space contraction without accompanying bicarbonate loss. The latter, contraction alkalosis, may have played an important role in our patient. In patients at risk from a metabolic derangement it has been suggested that the dose of frusemide should be administered every other day or is combined with a potassium sparing agent.³

We suggest that metabolic alkalosis should be anticipated and looked for when neonates are given frusemide, particularly if the dosage interval is less than 12 hours.

References

- Peterson RG, Simmons MA, Rumack BH, Levine RL, Brooks JG. Pharmacology of frusemide in the premature newborn infant. *J Pediatr* 1980;**97**:139–43.
- De Rubentis FR, Michelis MF, Beck N, Davis BB. Complications of diuretic therapy: severe alkalosis and syndrome resembling inappropriate secretion of antidiuretic hormone. *Metabolism* 1970;**19**:709–19.
- Kreche HJ. Side effects and complications of diuretic therapy. *Internist (Berlin)* 1971;**12**:357–64.

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