

early treatment of the baby will be possible and it may also be possible to modify the drug regimen of the mother before delivery so as to delay the appearance of symptoms in the infant.

The management of the thyrotoxic neonate has usually included sedatives, potassium iodide, carbimazole, and digoxin, and recently propranolol has been used (Pemberton, McConnell, and Shanks, 1974). In view of the possibility of cardiac failure, many neonates may benefit from treatment with iodine and digoxin before propranolol is started. The long-term prognosis is good provided the initial thyroid crisis can be overcome, though Robinson, Hall, and Munro (1969) reported a baby who subsequently developed premature fusion of skull sutures. Long-term follow-up is therefore indicated.

The most important findings in this case were the high levels of HTSI in the mother and in cord blood. The level of HTSI has remained high in maternal serum, but the level in the baby has declined with time, with a half-life of approximately 10 days. In view of the results reported by Dirmikis and Munro (1975), HTSI should be estimated in the third trimester of a thyrotoxic pregnancy, or if there is a history of thyrotoxicosis. If the level of HTSI is high in the maternal serum, then the baby should be given propranolol from the time of delivery and the situation should be reviewed in the light of clinical progress and laboratory results obtained at the end of the first week of life.

Summary

A woman who developed thyrotoxicosis during pregnancy had a high level of HTSI at the time of delivery. The baby had high levels of HTSI initially but, unlike the mother, the levels fell, giving a half-life of HTSI of 10 days.

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Neonatal pyridoxine responsive convulsions due to isoniazid therapy

The control of neonatal fits after pyridoxine administration is well recognized. These may be either pyridoxine dependent (Hunt *et al.*, 1954; Robins, 1966), or secondary to pyridoxine deficiency. We report an infant born to a mother on anti-tuberculous therapy, who was started on isoniazid therapy at birth. On the 13th day of life convulsions began which persisted for 4 days and only ceased after starting pyridoxine therapy. The pyridoxine deficiency was presumed secondary to the isoniazid medication.

Case report

An infant aged 17 days was referred with a 4-day history of frequent generalized convulsions. He was the first child of unrelated Indian parents. Active pulmonary tuberculosis was diagnosed in his 35-year-old mother by chest x-ray during the 19th week of pregnancy. She was treated with ethambutol 200 mg and isoniazid 100 mg three times daily, but stopped taking the drugs after 2 weeks because of nausea. The same therapy was started again 3 weeks before delivery. The pregnancy was otherwise uncomplicated; the infant was delivered by forceps under epidural block and weighed 2.9 kg at term. He was inoculated with isoniazid-resistant BCG after birth and started on oral isoniazid 20 mg twice a day. He was bottle fed (Cow and Gate full cream) and remained well, making normal progress until the onset of convulsions.

On admission he was convulsing. He had generalized, multifocal clonic fits that lasted for 60 to 90 seconds and occurred every 15 to 30 minutes. Between convulsions no abnormalities were detected on examination. Investigations for an infective or biochemical cause were

negative. Hb 17.4 g/dl, WBC 18 700/mm³ normal differential. Blood: urea 4 mmol/l, electrolytes normal; glucose 3.6 mmol/l; calcium 2.0 mmol/l; magnesium 0.66 mmol/l. Cerebrospinal fluid glucose, protein, Gram's stain and culture normal. Plasma amino acids normal. Skull x-rays normal. Rubella HAI and cytomegalovirus complement-fixation titre normal.

He was treated with phenobarbitone 7.5 mg intramuscularly on admission and calcium gluconate 200 mg intravenously when blood was taken for the above investigations, with no effect on the pattern of convulsions and over the next 2 hours the frequency of the fits increased. At this point intramuscular pyridoxine 50 mg was given. Over the next 4 hours the frequency and duration of the fits decreased dramatically and no further seizures occurred. Pyridoxine was continued in an oral dose of 10 mg per day for the next 2 weeks, phenobarbitone was discontinued after 48 hours, and no isoniazid was given from the time of his admission. Subsequently, on review of his mother's x-rays, no further antituberculous therapy was advised for the infant. An electroencephalogram 9 days after admission was normal and now 4 months later the infant is off pyridoxine, fit free, and neurologically and developmentally normal.

Discussion

During the neonatal period 90% of convulsions occur before the second week of life (Keen and Lee, 1973). The majority of these are secondary to perinatal brain damage or hypocalcaemia. In the infant reported fits occurred with increasing frequency between the 15th and 17th days of life; no infective or biochemical cause was found and they ceased permanently within 4 hours of administering pyridoxine 50 mg intramuscularly.

The relationship between pyridoxine deficiency and convulsions in infants was reported by Coursin in 1954. The deficiency was ascribed to a low pyridoxine content in the milk formula fed to the group of infants studied. One infant aged 28 days who developed status epilepticus was given pyridoxine 100 mg intramuscularly with dramatic results, the electroencephalogram becoming normal within 3 minutes and the infant clinically normal after 48 hours. The association between isoniazid-induced pyridoxine deficiency and neurotoxicity is well recognized, with peripheral neuritis as the commonest presentation (*British Medical Journal*, 1958). Biehl and Vilter (1954) showed a dose relationship in adults, a larger dose of isoniazid resulting in the earlier appearance of toxicity. In doses greater than 10 mg/kg daily peripheral neuritis can be expected to appear in 40% of adults within 8 weeks unless pyridoxine is administered concurrently. In a group of 20 children receiving isoniazid no signs of pyridoxine deficiency

could be shown by Morales and Lincoln (1957), but in only 2 cases was the dose greater than 10 mg/kg daily.

Assuming that the action of isoniazid on pyridoxine metabolism is not significantly different in infants and adults, the low convulsive threshold of neonates could explain why the first manifestation of pyridoxine-deficient neurotoxicity in this group is convulsions. The case presented here and the data of Snyderman *et al.* (1953) and Coursin (1954) support this. Though pyridoxine levels were not measured before treatment, we believe that the history of isoniazid medication, its recognized effect on pyridoxine metabolism, the lack of another biochemical or infective cause, and the rapid and complete response to pyridoxine injection strongly suggest a diagnosis of pyridoxine deficiency secondary to the isoniazid therapy. We recommend that neonates treated with isoniazid should not receive a dose greater than 10 mg/kg daily and that all should receive additionally pyridoxine supplements.

Summary

A 17-day-old infant on isoniazid therapy 13 mg/kg daily from birth because of maternal tuberculosis was admitted after 4 days of clonic fits. No underlying infective or biochemical cause could be found. The fits ceased within 4 hours of administering intramuscular pyridoxine, suggesting an aetiology of pyridoxine deficiency secondary to isoniazid medication.

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