when the patients with hypoparathyroidism were treated.

Tabaee-Zadeh *et al.* (1972) reported a patient with paroxysmal kinesogenic choreoathetosis and basal ganglia calcification due to idiopathic hypoparathyroidism, in whom the extrapyramidal motor features improved when normocalcaemia was restored. They suggested that the movement disorder might be due to a direct effect of hypocalcaemia on already damaged neurones.

Hower *et al.* (1974) described a child with myopathy and idiopathic hypoparathyroidism with increased CPK activity which returned to normal with treatment. They suggested that hypocalcaemia led to lowered cell membrane potentials resulting in increased cell membrane permeability allowing the escape of cytoplasmic proteins.

The findings in this patient suggest that the extrapyramidal motor features were not due directly to the basal ganglia calcification, but that both they and the increased CPK activity resulted from the

effects of hypocalcaemia on cell membrane potentials of neurones and muscle.

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Half life of theophylline in the preterm baby with apnoeic attacks

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SUMMARY Plasma theophylline levels were measured by an enzyme immunoassay method in 6 preterm babies. The method gave accurate and rapid results. The study showed a considerably prolonged half life of an oral preparation.

Xanthine derivatives have become established as a method of treatment of recurrent apnoeic attacks in the preterm baby (Lucey, 1975). However, because of the interpatient variation and prolonged half-life of theophylline in such babies (Giacioia *et al.*, 1976), it is essential that plasma levels be estimated frequently so that adequate doses of the drug can be maintained and serious side effects avoided.

We used an enzyme immunoassay method (EMIT, Syva) for determining plasma theophylline levels on as little as 10 µl plasma. It was known that plasma concentrations measured by either high pressure liquid chromatography or EMIT showed excellent agreement (Chang and Bastiani, 1977).

Patients and methods

Six preterm babies were studied. Details of gestation periods and birthweights are given in the Table. After one attack of apnoea lasting at least 25 seconds, a single oral theophylline preparation was given by a nasogastric tube (theophylline BP as sodium glyconate salt 5 mg/kg). Plasma theophylline levels (µg/ml) were measured at 0, 2, 4, 8, 12, 24, and 48 hours. If a baby had a second attack of apnoea during the period he was withdrawn from the study.

Plasma theophylline levels were estimated by enzyme immunoassay using the EMIT-aad kit

Table *Details of the 6 preterm babies*

Case	Age (days)	Birthweight (g)	Gestation (weeks)	Theophylline half life (hours)
1	3	1370	31	35
2	5	2500	36	33
3	11	1400	31	25
4	2	1030	28	64
5	3	2240	37	32
6	12	1950	34	24

(Syva). Volumes of 10 μ l plasma were pipetted into microsample cups and thereafter dilutions, reagent additions, and reaction kinetics were performed on the Gilford 3500 analyser in accordance with the manufacturer's instructions for this assay. Under these conditions, neonatal plasma, to which known amounts of theophylline were added, gave coefficients of variation between expected and measured concentrations ranging from 6.5% at 2 μ g/ml to 5.5% at 10 μ g/ml; values which are compatible with the reported between-run precision of the assay itself.

Results

Peak plasma levels occurred between 4 and 8 hours after the single oral administration of theophylline. The slope of the log of the plasma concentration in the postabsorptive phase plotted against time was used to determine the half-life of the drug. The theophylline half-life for each baby is shown in the Table. The range was 24–64 hours.

Comment

The enzyme immunoassay method for measuring

plasma theophylline levels by using microsamples in this group of preterm babies was found to give accurate, reproducible, and rapid (within 10 min) results, thus allowing theophylline dosage to be regulated as often as is clinically indicated. The study showed the prolonged half life of an oral theophylline preparation and the wide interpatient and within-patient variations.

EMIT reagents were kindly donated by Syva Corp. and the 3500 analyser lent for laboratory evaluation by Gilford Instruments Ltd. The oral theophylline was prepared by McCarthy's Pharmaceuticals.

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