Short reports

Plasma terbutaline levels in asthma

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SUMMARY Plasma terbutaline levels and peak expiratory flow rates were measured in 5 asthmatic children using doses of 0.25 and 0.075 mg/kg. The higher dose resulted in safe, non-toxic plasma levels and returned the peak expiratory flow rate to normal. This dose (maximum 5 mg) is safe in children.

Terbutaline is known to be an effective drug in the treatment of asthma which acts by β_2 receptor stimulation in the lung.¹ If given in large doses this agent may produce side effects—such as tremor, headache, and tachycardia. Children seem to be fairly tolerant of such side effects and therefore may continue to obtain benefit at doses higher than currently recommended. The present study was undertaken to evaluate the pharmacokinetics of terbutaline at two different dose levels.

Patients and methods

Five children (4 boys and 1 girl) recovering in hospital from an acute asthmatic attack were studied while convalescent. Their ages ranged from 7 to 11½ years; each was of normal height and weight. Parental consent was obtained before the study.

On two consecutive days each patient was given an oral dose of terbutaline* on an empty stomach. Dosage was either 0.075 (low dose) or 0.25 mg/kg (high dose) allocated randomly. Other bronchodilators—such as salbutamol or oral theophylline—were stopped for 8 hours before the study, although agents such as sodium cromoglycate or steroids were continued.

In each case an intravenous cannula was inserted and blood samples were taken before the dose and at 1, 2, 3, and 5 hours after it. Plasma (2.5 ml) thus obtained was then stored at -20°C until analysis using a non-radioactive technique with gas chromatography and mass spectrometry.² Immediately before

sampling the peak expiratory flow rate (PEFR),³ heart rate, respiratory rate, and blood pressure were measured. Subjective comments regarding side effects were also noted.

Results

The higher dose of terbutaline (0.25 mg/kg) produced a significant improvement ($P < 0.01$) in PEFR up to 5 hours after administration (Fig. 1). This was associated with a steady increase in plasma levels reaching a peak 2 hours after ingestion (Fig. 2). Although the low dose also resulted in improved PEFR at all times, none was significant. Plasma levels were lower and more variable. Neither dose produced any significant change in pulse rate, respiratory rate, or blood pressure. Only one patient on high dosage complained of slight headache.

Fig. 1 Peak expiratory flow rate (% predicted) expressed as mean $\pm$ SEM ($n=5$) for low dose and high dose terbutaline. All levels after the high dose are statistically significant, $P < 0.01$.

*Bricanyl syrup—Astra Pharmaceuticals Ltd.

Fig. 2 Plasma terbutaline levels (ng/ml) expressed as mean $\pm$ SEM ($n=5$) for low dose and high dose terbutaline.

Discussion

This study demonstrates a highly significant improvement in peak flow rate when terbutaline is given in a higher dose adjusted for weight than that used in adults. Peak plasma levels within a range known to be non-toxic in adults⁴ were reached 2 hours after the dose and only one patient complained of slight headache during this part of the study.

The lower dose also improved PEFR but not significantly. This is contrary to the findings of Leegaard and Fjulsrud⁵ who used this dosage in a larger number of children. The failure to show significance in the present study may be related to the few children taking part and the fact that they were studied within 24 hours of stopping intravenous therapy for severe wheeze. Further studies are

required to assess the optimum absorption of the drug in such conditions.

Maximum bronchodilatation as measured by PEFR did not correspond directly to maximal plasma levels; this is not surprising since the response in the lung will relate more directly to the amount of free drug present locally and the state of reactivity of the β receptors, in addition to other mucosal factors within the airways.

This study demonstrates that it is safe and effective to give children terbutaline in a dose of 0.25 mg/kg (maximum 5 mg) in asthma.

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Chloride deficiency syndrome due to chloride-deficient breast milk

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SUMMARY A case of dietary chloride deficiency syndrome in a fully breast-fed infant is described. The mother's milk was found to be deficient in chloride and the infant's symptoms resolved on cows' milk formula.

The dietary chloride deficiency syndrome in infants is characterised by anorexia, failure to thrive, and hypokalaemic metabolic alkalosis.¹ First described

in 1979² the condition resulted from the ingestion of Neo-Mull-Soy subsequently found to be deficient in chloride. Recently a single case was reported in a breast-fed infant; the mother's milk was found to be deficient in chloride.³

This report describes a further case of dietary chloride deficiency syndrome in a fully breast-fed infant. The mother's milk was found to be deficient in chloride and the infant's symptoms resolved completely once the feeds were changed to cows' milk formula.