

## TERBUTALINE EXCRETION INTO BREAST MILK

Oral treatment with the  $\beta_2$  adrenoceptor stimulating agent terbutaline produces bronchodilatation and relieves clinical symptoms in bronchial asthma (Legge *et al.*, 1971; Formgren, 1975). Since bronchodilating therapy might be necessary during the lactation period, there is an obvious need for data on the excretion of terbutaline into breast milk and the plasma levels reached in nursing infants. No such information seems to be available at present (Wilson *et al.*, 1980).

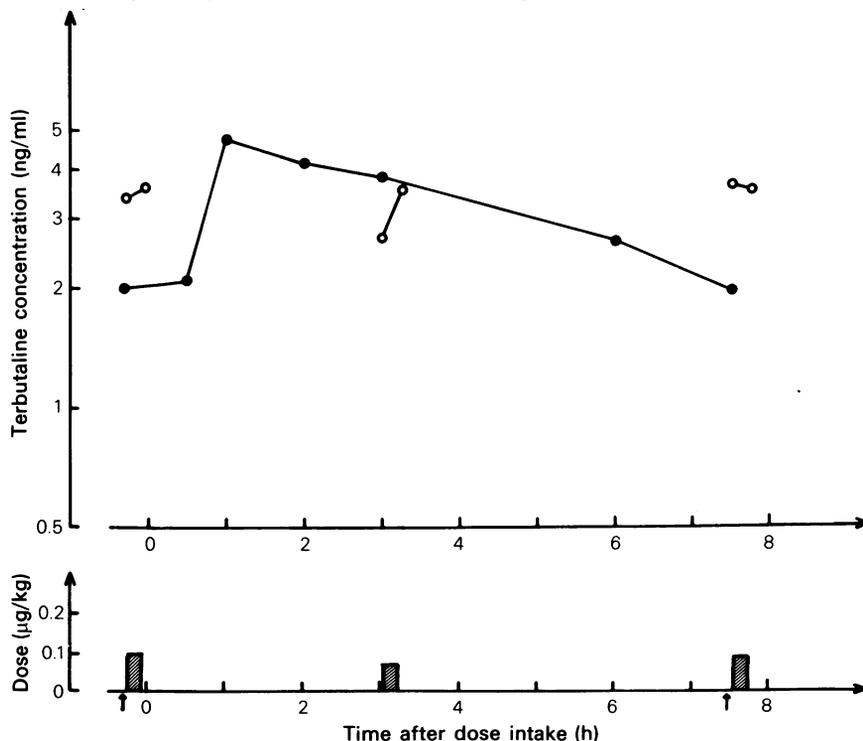
Breast milk and blood were collected from two nursing mothers suffering from chronic bronchial asthma, after informed consent. They were treated with oral terbutaline (Bricanyl<sup>®</sup>, AB Draco, Lund, Sweden), 5 mg three times daily, which is the dose recommended by the manufacturer. Inhaled  $\beta$ -adrenoceptor agonists were withheld during the test day. In one case blood samples were also drawn from the nursing infant.

Terbutaline concentrations in plasma and milk were determined in duplicate. Two ml samples of plasma and milk were extracted and derivatized according to the method of Jacobsson *et al.* (1980). Standardized cow milk (1% fat) was used for the

spiked samples when constructing the calibration graph for the milk samples. The gas chromatography-mass spectrometry measurements of the obtained terbutaline derivative were performed on Finnegan 4000 GC-MS equipment operated in a chemical ionization mode with methane as carrier and ionization gas as described by Leferink (1979), Leferink *et al.* (1976).

### Case 1

A 25 year old woman, who gave birth to a normal 3.7 kg female infant. The test was performed 8 weeks after delivery. The infant was fed only breast milk. On the day of the study, it weighed 5.2 kg, its development had been normal and there were no clinical signs of  $\beta$ -adrenoceptor stimulation (tachycardia, tremor, excitation). Before intake of the morning terbutaline dose, blood samples were drawn from the mother and the infant, and the infant was nursed. After dose intake, blood and milk were collected during the following 8 h dose interval (Figure 1). The child was weighed before and after nursing to determine the amount of milk ingested.



**Figure 1** Terbutaline concentrations in the plasma (●) and the breast milk (○) of a nursing woman treated with oral terbutaline, 5 mg three times daily. A 5 mg dose was ingested at time zero. Milk samples were collected at the beginning and at the end of each meal. The two plasma samples collected from the infant before the first and the last meal during the test period (arrows) did not contain detectable amounts of terbutaline ( $<0.1$  ng/ml).

The peak and trough concentrations of terbutaline in the maternal plasma were 4.8 and 2.0 ng/ml, respectively. The terbutaline concentrations in the milk were of the same order of magnitude as in the plasma, but varied less during the dose interval. For breast milk the area under the plasma concentration-time curve during the dose interval was 104% of that for plasma. There was no consistent difference between the terbutaline concentration in the first and the last milk portion of each meal. Using the mean milk terbutaline concentration values of 3.5, 3.2 and 3.7 ng/ml, the amounts of terbutaline ingested by the infant were calculated (Figure 1, lower panel). As the infant was nursed five times daily, the calculated daily dose of terbutaline was 0.4–0.5  $\mu\text{g}/\text{kg}$  body weight. Terbutaline was not detectable ( $<0.1$  ng/ml) in the two plasma samples from the infant (Figure 1).

#### Case 2

A 29 year old woman, tested 6 weeks after delivery. The concentrations of terbutaline in maternal plasma were 1.9 ng/ml before, and 2.5 and 3.7 ng/ml 2 and 4 h after dose intake, respectively. The milk concentrations were 2.5 ng/ml before and 3.8 ng/ml 4 h after dose intake. As the milk volumes were small and the infant was fed mainly artificial formulas, blood samples were not collected from this infant.

The terbutaline levels in the plasma of the two mothers were similar to those previously observed in healthy volunteers given the same dose of the drug (Leferink, 1979). The concentrations in the milk were

similar to or only slightly higher than in the plasma. Using the concentration values found and assuming a daily intake of 125–150 ml breast milk per kg body weight, yields an amount of terbutaline ingested by the infant not exceeding 0.5  $\mu\text{g}/\text{kg}$  body weight per day. This is only 0.2% of the dose taken by the mother. It is therefore not astonishing that terbutaline was not detectable in infant plasma, and that there were no clinical signs of  $\beta$ -adrenoceptor stimulation in the infant tested.

In summary, our data indicate that breast-feeding need not be interrupted due to maternal medication with terbutaline, since very small amounts are excreted into the breast milk and no accumulation of the drug in the infant seems to occur.

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