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Use of sodium aurothiomalate during lactation

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The report concerns a mother who breast fed her infant whilst receiving sodium aurothiomalate for the treatment of rheumatoid arthritis. The milk : serum concentration ratio was not constant, reflecting the non-concurrence of the concentration-time profiles of gold in milk and maternal serum after i.m. injection. Gold was detected in the infant's serum. Calculations indicate that the weight-adjusted dose to the infant exceeded that received by the mother.

Keywords gold sodium aurothiomalate breast milk human milk infant plasma concentrations

Introduction

Gold salts are important agents for the treatment of rheumatoid arthritis and may be considered for postpartum exacerbations of the disease. Evidence on exposure of the suckling infant to gold has been slow to accumulate and subject to different interpretations in respect of the quantity of drug to which the infant is exposed (Ostensen *et al.*, 1986; Rooney *et al.*, 1987). We recently had the opportunity to study a mother who breast fed her baby while receiving sodium aurothiomalate. These data together with information from the literature now permits a more accurate assessment of risk to the infant.

Methods

Gold was assayed by electrothermal atomisation atomic absorption spectrometry (Kamel *et al.*, 1977). From analysis of samples supplemented with known amounts of gold, the method was shown to be accurate to within 5% of the expected value. Milk was collected by an electrically-driven breast pump, not at feeding times, and the whole sample obtained was used for the assay.

Case report

The mother, a Caucasian, was aged 38 years at the time of the study. She had developed seronegative arthritis 3 years before, in July 1983, commenced gold injections 8 months later and continued this therapy up to and throughout her third pregnancy in 1986, receiving a total of 190 mg during the pregnancy. The birth was normal, the female infant weighed 3.92 kg and was well. The patient indicated a strong desire to nurse her baby because both of her other infants had developed allergy to artificial milk. A decision was therefore taken to breast feed but to monitor serum gold concentrations. The data obtained appear in Table 1.

The infant's haematological profile was normal on day 72 and her biochemical profile was normal on day 111. No gold was detected in her urine on day 90. Breast feeding ceased on day 100. Her serum immunoprotein profile was normal on day 364 (IgG 7.7, IgM 0.9, IgA <0.4 g l^{-1}). She received the full complement of vaccinations without adverse reaction. The infant's growth record has been normal. She has had episodes of otitis media but not in excess of that which might be expected in an atopic child,

Table 1 Gold in maternal serum, milk and infant serum

		Gold ($\mu g\ l^{-1}$)			
	Na aurothiomalate	*Maternal serum*	*Milk*	*Milk/serum ratio*	*Infant serum*
Days before birth					
6	10 mg	–	–	–	–
Days after birth					
7	–	302	93	0.3	–
22	10 mg	–	–	–	–
27	–	1133	21	0.02	–
34	–	541	21	0.04	–
41	–	459	30	0.07	–
51	10 mg	–	–	–	–
72	–	–	15	–	51
85	10 mg	–	–	–	–

and three episodes of cutaneous *Candida* infection; these apart, her health record has been good.

Discussion

Exacerbation of rheumatoid inflammation in the postpartum period occasionally justifies the use of gold compounds, but in the breast feeding woman any therapeutic advantage must be balanced against the degree of risk to her infant. The decision to breast feed appeared justifiable because the mother wished to, her other infants had developed allergy to artificial milk, the dose of gold was low, the infant was well despite exposure throughout pregnancy, and was closely monitored. Gold injected as thiomalate is cleaved from the parent molecule, distributes to body tissues and fluids, and is known to cross the placenta (Cohen *et al.*, 1981). Published data suggest that the concentration-time profiles are not concurrent in serum and milk (Ostensen *et al.*, 1988; Rooney *et al.*, 1987), a finding which is borne out in the present case. Between days 7 and 27 serum concentration rose while the milk concentration fell; thereafter to day 41 serum concentration fell while that in milk rose (Table 1). These changes are reflected in the milk to serum ratios which ranged from 0.02 to 0.07 over this period. Lag of the milk concentration behind that in serum would lead to continued exposure of a suckling infant to gold despite cessation of gold therapy.

Milk gold concentrations of 22–65 $\mu g\ l^{-1}$ were reported after repeated administration of gold compounds in doses ranging from 10–50 mg (Bell & Dale, 1976; Rooney *et al.*, 1987). After aurothiomalate 10 mg i.m. monthly, we found milk gold concentrations of 15–30 $\mu g\ l^{-1}$ which were similar to those recorded by Ostensen *et al.* (1988) in mothers who also received this dose. Assuming a daily milk intake of 150 ml kg^{-1} day^{-1} and taking the highest milk concentration recorded, an infant would ingest $30 \times 0.15 = 4.5$ $\mu g\ kg^{-1}\ day^{-1}$ of gold. If it is further assumed that this rate applied over the 29 days between injections then a total of 130.5 $\mu g\ kg^{-1}$ would have been ingested by the infant. Sodium aurothiomalate contains 46% of elemental gold (Martindale, 1989) and a 60 kg mother would have received $10000 \times 0.46/60 = 76.6$ $\mu g\ kg^{-1}$ over this time, allowing the estimate that the infant would have been exposed to $130.5/76.6 \times 100 = 170.4\%$ of the weight-adjusted maternal dose. Alternatively, the lowest milk concentration recorded in this time, 21 $\mu g\ l^{-1}$, corresponds to 119.2% of the weight-adjusted maternal dose. There are no data on systemic availability of gold ingested in milk but our finding of 51 $\mu g\ l^{-1}$ of gold in the infant's serum suggests that alimentary absorption may be significant. Others have suggested a lesser exposure of the suckling infant to gold. Ostensen *et al.* (1986), without stating their method of calculation, considered that the infant was exposed to 20% of the maternal dose and Rooney *et al.* (1987) gave a value of 0.71%, but did not correct for differences in maternal

and infant body weight. Even using the most favourable interpretation of the data (the lowest recorded milk concentration), our calculation indicates that the infant dose exceeds that to the mother. Indeed, the dose greatly exceeds those generally found for drugs in milk (Atkinson *et al.*, 1988; Bennett, 1988). Despite this, the infant we report exhibited no adverse clinical, biochemical or haematological effects and developed normally during exposure to gold throughout pregnancy and 100 days of lactation. During pregnancy, furthermore, fetal serum gold concentrations may approach those in maternal serum (Cohen *et al.*, 1981) and indicate an exposure greater than that during lactation. The normality to date of the present case therefore suggests that an infant can tolerate gold received *in utero* and in milk in the doses quoted. Nevertheless, the relatively high exposure must demand close monitoring of any infant exposed to maternal gold during pregnancy or lactation.

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