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Ivermectin levels in human breastmilk

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Summary. Ivermectin levels were measured in breastmilk and plasma of 4 healthy mothers after an oral 150 μg/kg dose. Mean ± S.D. plasma and milk values were 37.9 ± 0.54 and 14.13 ± 0.43 (ng/ml) respectively. Steady-state ivermectin levels in milk were low. Our results suggest that exclusion of lactating mothers from mass chemotherapy with ivermectin may be unnecessary.

Key words: Ivermectin, Onchocerciasis, Milk, Chemotherapy

Ivermectin (Mectizan MSD) is now widely used for the chemotherapy of human onchocerciasis (Aziz et al. 1982) and lymphatic filariasis (Addis et al. 1991). It also enjoys wide acceptance as a successful broad-spectrum veterinary exo- and endoparasiticide (Wall and Strong 1987). When used in humans, it has the added advantage of expelling large worm loads including head lice in children (Whitworth 1992). Thus, the quality of life of rural dwellers in endemic communities is improved by ivermectin. However, lactating women are excluded in community wide distribution, within the first week of breastfeeding because of possible deleterious effects of ivermectin on their suckling newborns. Early research into ivermectin's antiparasitic activity against gut-dwelling nematodes in domestic animals led to the proposal that ivermectin mimics the action of gamma-aminobutyric acid, GABA, the nematode-inhibitory neurotransmitter (Pong et al. 1980).

In order to ascertain the rationale for excluding lactating mothers from the benefit of ivermectin therapy, we studied the plasma and breastmilk concentrations of the drug in four healthy mothers who had lost their babies at birth and had granted informed consent. Blood and breastmilk samples were obtained after an overnight fast followed by oral administration of 150 μg/kg ivermectin. Ivermectin was analysed by HPLC following derivatization and fluorescent detection as previously described (Klotz et al. 1990). Ivermectin was readily detected in the plasma and breastmilk of all mothers within 1 h of drug administration and throughout the 72 h of observation. Ivermectin plasma levels ranged from 6.8 ng/ml to 48.0 ng/ml, with a mean of 22.6 ± 0.22 ng/ml; and in breastmilk from 4.2–20.6 ng/ml, with a mean of 9.85 ± 0.38 ng/ml. Highest plasma concentrations, C_{max}, ranged from 27.5 to 48.0 ng/ml, with a mean of 37.9 ± 0.54 ng/ml. Breastmilk C_{max} ranged from 10.97 to 20.6 ng/ml, with a mean of 14.13 ± 0.43 ng/ml. The time to achieve highest concentrations, T_{max}, occurred at 4 h in the breastmilk of two subjects, at 6 h in one subject and at 12 h in the last subject. Generally there was a steady state ivermectin concentration in breastmilk of approximately 10 ng/ml over a 24-h period (see Fig. 1). The plasma time concentration profile in these women is similar to those in onchocerciasis patients (Okonkwo et al. 1993) and in healthy volunteers (Edwards et al. 1988).

Ivermectin is being distributed in some of the poorest countries of the developing world and in communities

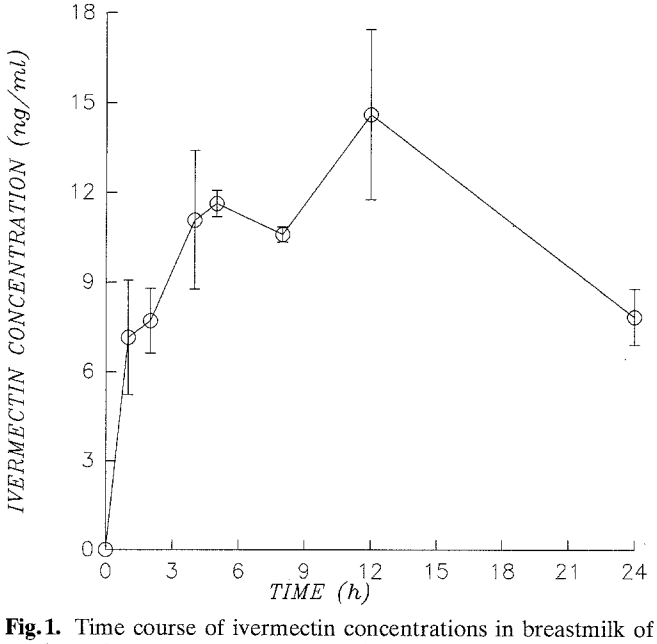

Fig. 1. Time course of ivermectin concentrations in breastmilk of mothers after an oral 150 μg/kg dose ($n = 4$)

where breastfeeding may be the only source of nutrition for newborn infants within the first and most critical weeks of life. For drugs with a relatively large margin of safety, a percentage of the adult dose may be applied to calculate the appropriate paediatric dose. Based on the 14.5 % of adult dose suggested for drugs such as ivermectin for infants at the age of 1 month (British National Formulary 1989), the following simple calculation can be used in the case of ivermectin:

1. Average daily consumption of milk at 1 month of life for African infants, A = 778 ml (Von Steenbergen et al. 1983).
2. Average weight of an African child at 1 month, W = 4 kg.
3. Mean ivermectin breastmilk concentration in our study, C = 14.13 ng/ml.
4. Total amount of ivermectin per day (A × C) = 778 ml × 14.13 ng/ml.
5. Dose $= \frac{A \times C}{W} = \frac{778 \text{ ml} \times 14.13 \text{ ng/ml}}{4 \text{ kg}} = 2.75 \text{ µg/kg}$

This amount of ivermectin is hardly more than one-tenth of the 14.5 % of the 150 µg/kg adult dose i. e. 21.75 µg/kg.

In our three years of experience in distributing ivermectin in a hyper-endemic area (Okonkwo et al. 1991) in which lactating mothers constituted 5–10 % of the population, there were no serious adverse effects, especially on the central nervous system (Chijioke and Okonkwo 1992). Instead, ivermectin, in addition to its microfilaricidal effects and its known effects on reproduction of adult worms (Larviere et al. 1985; Schulz-Key and Karam 1986), was found effective against ascariasis, strongyloidiasis and head and body lice infestations. The expulsion of these worms contributed greatly to the general health and well-being of the population.

Additionally, a large reservoir of women in our communities are either pregnant or lactating during each yearly treatment cycle and therefore this may vitiate the goals of mass treatment and break in disease transmission. In view of the additional benefits of ivermectin and of tolerably low levels in breastmilk we suggest that the exclusion of lactating mothers be discontinued.

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