Excretion of centchroman in breast milk

Centchroman, a nonsteroidal oral contraceptive [1], is being marketed in India with a recommended dose of 30 mg twice weekly for 12 weeks followed by 30 mg once-a-week. Infrequently it may be used by nursing mothers and hence the question of how much drug is excreted into the milk and ingested by the child arises. The pharmacokinetics of centchroman after single dose have been reported in two normal females [2]. The drug has a long elimination half-life of 7 days and attains peak plasma concentrations at 4 h [2]. However, no studies of its transfer into breast milk have been reported. Therefore, we have measured centchroman concentrations in three nursing mothers who were receiving the drug for more than 16 weeks. We assumed that at this time, steady-state serum drug concentrations had been achieved. On the day of sampling a 30 mg oral dose was administered at 08.30 h and samples of blood and milk were collected at 12.30 h.

The concentrations of centchroman in serum and milk were determined by h.p.l.c. [3] and are shown in Table 1. Although it is possible to determine a milk plasma (M/P) drug concentration ratio from these data, such ratios are best calculated from serial samples as the final course of drug in milk may not parallel that in serum [4]. Nevertheless, the M/P ratio may be used as an approximation for calculating infant dose [4] from:

\[ D_{inf} = C_{ss} \text{(mother)} \times M/P \text{ ratio} \times V_{milk} \]

The percent of maternal dose excreted in milk was calculated [4] from:

\[ \% \text{ maternal dose} = C_{milk} \times V_{milk} \times 100/D_{maternal} \]

where \( D_{inf} \) = dose to the infant (mg kg\(^{-1}\) day\(^{-1}\)); \( C_{ss} \) (mother) = maternal steady state plasma drug concentration = 0.0326 mg l\(^{-1}\) (based on unpublished data from volunteers taking 30 mg week\(^{-1}\)); \( V_{milk} \) = daily volume of milk ingested (assumed to be 0.15 l kg\(^{-1}\) day\(^{-1}\)); \( C_{milk} \) = drug concentration in milk (mg l\(^{-1}\)); \( D_{maternal} \) = maternal dose (mg kg\(^{-1}\) day\(^{-1}\)).

The M/P ratio in subject 1 was 2.4, which gave a \( D_{inf} \) of 0.012 mg kg\(^{-1}\) day\(^{-1}\); in subject 2 the M/P ratio was 1.2 and dose was 0.006 mg kg\(^{-1}\) day\(^{-1}\), while in subject 3 the M/P ratio was 2.4 and \( D_{inf} \) was 0.012 mg kg\(^{-1}\) day\(^{-1}\). The estimated percentages of maternal dose excreted in milk were 3.1%, 1.6% and 2.8% respectively.

These data show that centchroman passes into breast milk. However, the infant is likely to be exposed to only a small percentage of the maternal dose. Moreover the ratio between the plasma drug concentration (0.0655 mg l\(^{-1}\), s.d. ± 7.09) in the mothers 4 h after drug administration and the oral dose to the mother was 0.002 and only 2.5% (s.d. ± 0.8) of maternal dose (30 mg oral, once a week) was excreted in milk. Thus, assuming that absorption of the drug in the baby is similar to that in the mother, the concentrations of centchroman present in breast milk are unlikely to be of any physiological consequence to suckling babies. However, further studies are necessary to establish the long term safety of centchroman in breast fed babies. The M/P ratios reported here were based on only a single time point and, therefore, are subject to inaccuracy. A more detailed study with serial sampling would be required to confirm our initial findings.

J. K. PALIWAL\(^1\), P. K. GROVER\(^1\), O. P. ASTHANA\(^2\), S. NITYANAND & R. C. GUPTA\(^1\)
\(^1\)Pharmacokinetics and Metabolism Division and 
\(^2\)Clinical and Experimental Medicine Division, Central Drug Research Institute, Chattar Manzil, P.O. Box No. 173, Lucknow-226001, India.

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<th>Sex</th>
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Correspondence: Dr R. C. Gupta, Pharmacokinetics and Metabolism Division, Central Drug Research Institute, Chattar Manzil, P.O. Box No. 173, Lucknow-226001, India
References