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Methylphenidate and Breast-Feeding

TO THE EDITOR: As there are no data on the use of methylphenidate in women who are breast-feeding, our aim was to measure its concentration in milk versus its concentration in plasma, estimate the amount the infant is receiving, and assess the infant's progress.

A 26-year-old lactating mother (68 kg) prescribed methylphenidate 40 mg 2 times daily usually for 5 days each week for attention deficit disorder gave informed consent to participate in a study approved by the local ethics committee. Her breast-fed son (6.4 mo, 7.75 kg) was included in the study. She had been taking methylphenidate for 5.5 weeks and for 7 consecutive days before the study began.

Methods. Samples of breast milk were collected by electric pump immediately before the woman's first morning dose of methylphenidate (40 mg) and at each of the 7 times her infant was breast-fed over the following 24 hours. Heparinized blood samples were taken by venipuncture immediately before the first morning dose and at 2.2, 4, 6.2, and 24 hours thereafter. Methylphenidate in plasma and milk was extracted into hexane from alkalinized samples, it was back-extracted into HCl, and aliquots were analyzed by HPLC (RP Select B column, 250 mm × 4.6 mm id, E Merck, Damstadt, Germany, mobile phase 20% v/v CH_3CN in 45 mM phosphate buffer [pH 3] at 1.5 mL/min, with detection at 210 nm).

Intra- and interday relative standard deviations (plasma 5 μg/L and 160 μg/L; milk 5 μg/L and 265 μg/L, respectively) were less than 8.2% and less than 10.7%, respectively. The limit of detection was 1 μg/L. Areas under the milk and plasma concentration-time curves calculated by the log-linear trapezoidal rule[1] were divided by the total time of sampling to give average concentrations (C_{avg}). Milk-to-plasma ratio was calculated from the C_{avg} data. Absolute and relative infant doses were calculated as previously described.[2]

Results. The methylphenidate concentration–time profiles are shown in Figure 1. C_{avg} values were 15.4 μg/L for milk and 5.8 μg/L for plasma, giving a milk-to-plasma ratio of 2.7. Absolute and relative infant doses were 2.3 μg/kg/day and 0.2% of the weight-adjusted maternal dose, respectively. The hind- to fore-milk concentration ratios of methylphenidate were 0.9, 0.8, and 1 in samples taken at approximately 4, 6, and 23 hours, respectively, when absorption was unlikely to be a confounding factor.

The infant derived his primary daily sustenance from breast milk, together with 1–3 cans of solid baby food. His birth weight was 3.025 kg, and he was at the 50th percentile for weight at the time of the study. The mother reported that the infant was feeding well, sleeping well, and gaining weight satisfactorily. Methylphenidate was not detected in a plasma sample taken from the infant 5.3 hours after the first maternal dose.

Discussion. The maternal plasma C_{avg} data were consistent with the manufacturers' product information.[3] Although the milk-to-plasma ratio was high, the relative infant dose of 0.2% was very low. Given that methylphenidate was not detected in the infant's plasma and he was progressing satisfactorily, the overall findings are consistent with minimal exposure. However, the infant had been exposed for only 5.5 weeks, and this may not have been long enough for adverse effects to be apparent. In addition, at the age of 6 months, the infant would be protected by having well-developed hepatic drug-metabolizing enzymes.[4]

For most drugs in breast milk, a relative infant dose of not more than 10% exposure is considered safe.[5] Nevertheless, we studied only one case of an older infant with a relatively short drug exposure. Therefore, each decision regarding breast-feeding while a woman is taking methylphenidate should be the subject of an individual risk/benefit analysis.

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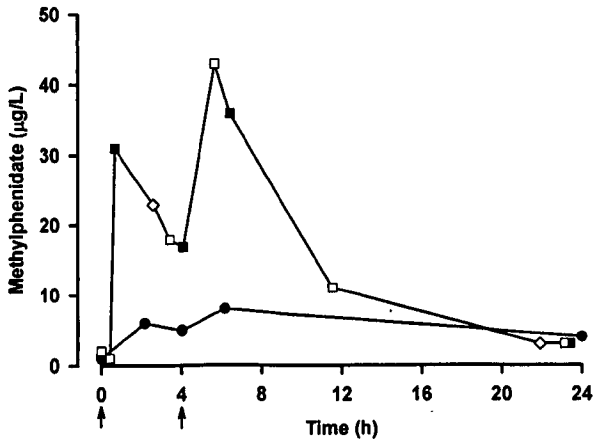

Figure 1. Methylphenidate concentration–time plots for plasma (filled circles) and milk (squares; open squares show fore-milk, closed squares show hind-milk, and the open diamonds are an equal mix of fore- and hind-milk). Methylphenidate 40 mg was taken at each arrow.

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Letters are subject to review prior to acceptance. They should address areas related to pharmacy practice, research, or education, or articles recently published. Corrections of previously published material also are accepted. Letters are limited to no more than five authors. In cases where adverse drug effects are described, the Naranjo ADR probability scale should be used to determine the likelihood that the adverse effect was drug-related (Clin Pharmacol Ther 1981;30:239-45). Text: limit 500 words. References: limit 5. Art: limit 1 table or figure.