Excretion of fluvoxamine in breast milk

Post-natal depression (PND) often requires antidepressive medication yet this poses problems for the clinician when considering patients who wish to breast feed their babies. Antidepressants (and often their metabolites, especially if pharmacologically active) are lipid-soluble and are excreted in breast milk. For this reason most manufacturers' data sheets carry warnings that antidepressants should not be given to nursing mothers. However, studies with antidepressants consistently give values for infant dose ingestion, corrected for weight, of less than 1% of the maternal dose (Buist *et al.*, 1990; Isenberg, 1990). Clinical experience has highlighted few problems and antidepressants are generally classed as drugs which may be used with caution when mother and baby are monitored (Golightly & Grant, 1988).

Data are reported from a case treated with the selective 5-hydroxytryptamine reuptake inhibitor fluvoxamine. The patient (23 years of age, 70 kg) was treated 12 weeks after delivery for PND with fluvoxamine maleate, 100 mg twice daily for 2 weeks before milk sampling. Since steady-state plasma concentrations are usually achieved within 10 days (Benfield & Ward, 1986) it may be assumed that steady-state conditions were achieved. On the day of sampling, the morning 100 mg dose was taken at 08.30 h and blood and milk samples were taken at 13.15 h.

Fluvoxamine was assayed by a gas chromatographic method (Dawling *et al.*, 1990). The plasma concentration of fluvoxamine base was 0.31 mg l^{-1} and the milk concentration was 0.09 mg l^{-1}. Obviously, the conclusions which can be drawn from a single case are limited but it does not appear that accumulation of fluvoxamine in breast milk occurred.

The following equation (Atkinson *et al.*, 1988) was used to calculate the dose to the infant.

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

where: D_{inf} = infant dose (mg kg^{-1} day^{-1})
$C_{ss(mother)}$ = maternal mean steady-state plasma drug concentration
M/P = ratio of milk/plasma drug concentrations
V_{milk} = daily volume of milk ingested (l kg^{-1})

The use of the milk to plasma-AUC ratio would give a better indication of the average milk to plasma concentration over a period of time because milk and plasma drug concentration curves are not parallel throughout the dosage period (Atkinson *et al.*, 1988). Unfortunately, in this case, serial plasma drug concentrations were not available for calculation of the AUC value. Nevertheless, the use of M/P ratio does provide an estimate of the infant dose.
Using this value and assuming

a $C_{ss(mother)}$ value of 0.24 mg l^{-1} (based on unpublished data from patients taking 200 mg day^{-1})

and a value of V_{milk} of 0.15 l kg^{-1}, the dose to infant was 0.0104 mg kg^{-1} day^{-1} fluvoxamine base.

The maternal dosage of fluvoxamine base was 2.09 mg kg^{-1} day^{-1} (equivalent to 2.86 mg kg^{-1} day^{-1} of the maleate). Therefore the baby would ingest only about 0.5% of the maternal intake. This can be considered as a total intake because fluvoxamine, unlike many antidepressants, is not metabolised to pharmacologically active products (Overmars *et al.*, 1983).

The infant suffered no unwanted effects as a result of this intake.

Thus, this case supports the notion that administration of fluvoxamine to nursing mothers poses little risk to the infant. Unfortunately, many women suffering with PND do not have the motivation to breast feed and worry over the risk to the infant of antidepressant medication can be a further negative influence. There is a need to establish how real the risks are.

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