Oseltamivir and breastfeeding

Oseltamivir is a selective inhibitor of influenza virus neuraminidase enzymes. In the case of an avian influenza pandemic, many breastfeeding women will potentially be prescribed oseltamivir.[1] Following oral administration, oseltamivir is absorbed and rapidly converted into the active metabolite oseltamivir carboxylate.

We were consulted on the case of a healthy laboratory assistant who had stung herself with an influenza H5N1 virus-contaminated needle. She was treated with oseltamivir 75 mg bid for 5 days. At the time of the incident she was breastfeeding her 9-month-old child twice a day. Since it was unknown whether or not oseltamivir transfers into breast milk, and that adverse effects to the suckling infant could not be ruled out, we advised her to discontinue breastfeeding during treatment.

To obtain information on the transfer of oseltamivir into breast milk we asked the patient to collect samples during her treatment period. These breast milk samples were collected twice a day over the 5-day period, giving a total of 11 samples. She was instructed to completely empty her breasts. The samples were analyzed by Roche.[2]

Figure 1 shows the concentration profiles of oseltamivir and oseltamivir carboxylate in breast milk over the five consecutive days of sampling. Oseltamivir concentrations fluctuated over time. The active carboxylate metabolite was not measurable in the first sample and reached steady-state concentrations of 37 to 39 ng/ml after 3 days. At steady-state, concentrations of metabolite were higher than those of oseltamivir, consistent with the reported higher metabolite than oseltamivir plasma concentrations in healthy volunteers.[3] After reaching a steady state, no continued accumulation of oseltamivir carboxylate occurred in breast milk.

Internationally, the relative infant dose (RID), expressed as a percentage of the weight-adjusted maternal dose, is regarded as the most accurate tool to get an impression of the infant's daily dose as a result of exposure via breastfeeding.[4]

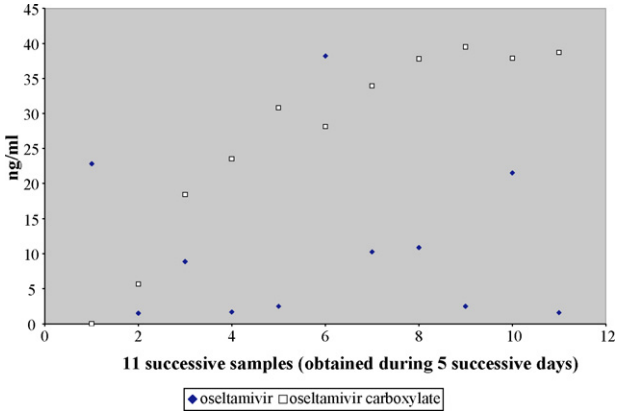

Figure 1 The first oseltamivir tablet was taken one hour before milk sampling. Thereafter oseltamivir was taken eight times within 30 minutes before or after the time of milk sampling. The last two milk samples were taken 4.5 and 13.5 hours, respectively, after the last oseltamivir intake.

A RID of less than 10% is generally considered safe for continuing breastfeeding.

Based on our data of breast milk levels, the maximum concentration of oseltamivir (38.2 ng/ml) and the maximum concentration of oseltamivir carboxylate expressed as equivalent of oseltamivir (the molecular weight of oseltamivir divided by the molecular weight of oseltamivir carboxylate times the maximum concentration of oseltamivir carboxylate in the breast milk: $312.4/284.4 \times 39.5 = 43.4$ ng/ml) give a total exposure of 81.6 ng/ml to the infant at maximum. This means that a fully breastfed infant would drink at maximum 0.012 mg/kg/day (81.6 ng/ml times 150 ml/kg/day). If the mother's weight is assumed to be 60 kg, she was treated with oseltamivir 2.5 mg/kg/day. Therefore the RID at a maximum is 0.5% of the maternal weight-adjusted dose. Since the maximum concentration of oseltamivir is exceptionally high (see Figure 1), this can be regarded as the 'worst case scenario'.

Based on this case report, oseltamivir or oseltamivir carboxylate exposure via breast milk is not expected to cause clinically significant concentrations in the suckling infant. Further studies in more nursing mothers are required to verify the safety of oseltamivir during breastfeeding.

Conflict of interest: No conflict of interest to declare.

References

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