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LETTER TO THE EDITOR

Infliximab concentrations in the milk of nursing mothers with inflammatory bowel disease

Dear Sir,

Female patients with inflammatory bowel disease (IBD) may require treatment with infliximab (IFX) during pregnancy and lactation to maintain remission. Reports on the excretion of IFX in breast milk during lactation are conflicting and sample collection has been sporadic.[1–4] To assess the infant's exposure to IFX, we measured the concentration of IFX in milk from nursing mothers with IBD who continued breastfeeding during treatment.

Patients 1 and 2 were diagnosed with Crohn's disease and received IFX treatments before and during pregnancy. They both resumed IFX treatment postpartum due to a flare-up. Patient 3 experienced an onset of severe ulcerative colitis during pregnancy, and was treated with IFX postpartum due to only a partial response to steroids. We systematically collected milk samples during IFX treatment and over the following five days. Milk samples from two healthy breastfeeding mothers never exposed to IFX were used for spiking experiments. The IFX levels were measured using the enzyme-linked immunosorbent assay (SHIKARI, QS-INFLIXI, Matriks Biotek Laboratories). To validate the assay for the analysis of breast milk, exogenous IFX was added to milk from the healthy donors. The assay performed well between 0.125 and 0.25 μg/mL, with acceptable recovery (42%–93%). However, for values below 0.100 μg/mL, the assay had a tendency to underestimate (recovery 30%) the spiked IFX, and for values above 0.25 μg/mL, the assay overestimated the spiked IFX.

For patient 1, after the first infusion, IFX was not detected in the breast milk until days four and six (Fig. 1). Following the second infusion, IFX was detected with fluctuating levels, never exceeding 130 ng/mL. For patient 2 the highest level measured was 300 ng/mL. Patient 3 only had minimal amounts of IFX in the milk on days two and four. Considering the performance of the assay, it is possible that some of the samples with undetectable IFX may have contained minute amounts of IFX.

If the highest IFX concentration measured in any of the samples (300 ng/mL) is multiplied by the amount of milk ingested by the infant, approximately 150 mL·kg bodyweight^{-1}·day^{-1}, the infant is estimated to receive 0.045 mg IFX·kg bodyweight^{-1}·day^{-1}.[5] If the variation in the recovery rate is taken into account, the absolute infant dose is 0.15 mg·kg bodyweight^{-1}·day^{-1}. At the time of follow-up, all the children were healthy, and no adverse events had been observed.

This is the first study to evaluate the overall infant exposure during IFX treatment. The infant's exposition to IFX through breast milk seems minimal. However, further studies are warranted to elucidate the local effects in the infant's gut of continued exposure to even very small amounts of IFX. Additional studies should use other types of validated assays to confirm the results.

Conflict of interests

Declaration of personal interests: Lisbet Ambrosius Christensen has served as a speaker for Ferring A/S, MSD A/S, and AbbVie A/S, and she is a member of the advisory board for MSD A/S and AbbVie A/S. Mette Julsgaard has served as a speaker for Ferring A/S, AbbVie A/S, and MSD A/S. The remaining authors have nothing to declare.

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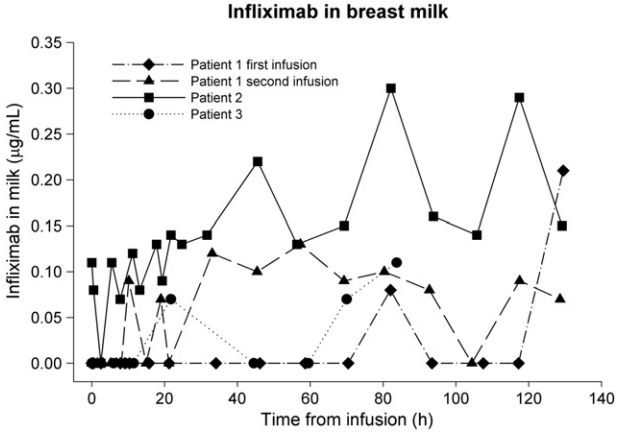

Figure 1 Infliximab concentrations in breast milk from lactating women before and after infliximab infusion.

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