Q&A 261.4

Can mothers breastfeed after a medical termination of pregnancy?

Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals

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Background

Lactation provides some protection from conception; however the duration varies and is influenced partially by the degree of breastfeeding. Between 9 and 30% of mothers exclusively breastfeeding their infants will experience a return of menses within 3 months, and between 19 and 53% within 180 days of delivery. The first menstrual cycle is often anovulatory, but ovulation before menses does occur and an unplanned pregnancy in a breastfeeding mother is possible (1).

A single oral dose of mifepristone, followed 36 to 48 hours later by a prostaglandin E1 analogue, misoprostol or gemeprost, are effective for termination of pregnancy at various stages, including the first trimester (2, 3). Misoprostol can be given via a variety of routes (orally, intravaginally, bucally or sublingually), and gemeprost is administered intravaginally.

Answer

Mifepristone

Based on its lipophilic properties, molecular weight of 429.6 Dalton, and protein binding of 98%, only small amounts of mifepristone would be expected to pass into breast milk (4, 5, 6). This is supported by the single published study of mifepristone use with breastfeeding, in which milk samples were collected from 12 women who had undergone a medical abortion during the first 7 days after intake of either 200 mg (n=2) or 600 mg (n=10) of mifepristone (6). Additionally, serum samples were collected from four mothers on day 3. Milk levels of mifepristone were highest in the samples collected during the first 6 hours following drug intake, and ranged from 0.063 micromol/L to 0.913 micromol/L. Thereafter, mifepristone levels declined for up to 7 days. The lowest levels of mifepristone in milk were measured following ingestion of the 200 mg dose. The milk:serum ratio of mifepristone ranged from < 0.013 to 0.042 on day 3. The calculated infant dose was 0.5–1.5% of a weight-adjusted maternal dose. The authors concluded that the levels of mifepristone in milk are low, especially when using the 200 mg dose, and that breastfeeding can be safely continued in an uninterrupted manner during medical abortion of this kind (6).

The elimination of mifepristone is biphasic with an initial half-life of between 12 and 72 hours, and a terminal half-life (including all active metabolites) of up to 90 hours (4, 5). Taking the half-life of all active metabolites into consideration, the manufacturer recommends that a 26 day interval is left between mifepristone administration and recommencing breastfeeding (7). This would necessitate discontinuing breastfeeding as lactation cannot, in practice, be maintained for this long. Although there is limited evidence, it does not support the manufacturer's recommendation (8).

Misoprostol

Mispoprostol is a prostaglandin E1 analogue. Naturally occurring prostaglandin E1, and other naturally occurring prostaglandins, appear normally in colostrum and milk (9). Misoprostol is rapidly and almost completely absorbed after oral administration, although it undergoes extensive first pass metabolism to its active metabolite, misoprostol acid (MPA). Absorption after vaginal administration is slower and more variable, but the area-under-the-curve is higher than after oral administration. Sublingual administration is reported to have the greatest bioavailability when compared to other routes (10). After buccal administration, the area-under-the-curve is just half that of vaginal administration (10).

There is no information regarding the pharmacokinetics of misoprostol in breast milk for non-oral routes of administration (10). After oral administration, the active metabolite, MPA passes into breast milk in small amounts and levels rapidly decline. Drug levels are undetectable after 5 hours (10).

There are only two published studies of misoprostol secretion into breast milk. In the first, 20 women were given 600 micrograms misoprostol orally either immediately or within 2 to 4 days after delivery. Maternal plasma levels were measured in all 20 women, but milk colostrum levels were measured in only 12 due to inadequate colostrum supply immediately after birth of the infant. Mean misoprostol acid (MPA) colostrum levels peaked one hour after administration at 20.9 picograms/mL and gradually declined to less than 1 picogram/mL after 5 hours (detection limit). These levels were significantly below maternal plasma levels (mean at 2 minutes of 91.5 picogram/mL, peak at 20 minutes of 344.6 picogram/mL, falling to 27.8 picogram/mL at 120 minutes) (11). As this study measured misoprostol in colostrum, the levels of MPA may not be the same in lipid-rich mature milk.

In the second study of 10 lactating mothers given 200 micrograms misoprostol orally for uterine atony, mean MPA milk levels of 7.6 picograms/mL were seen at 1.1 hours. Levels rapidly declined to a median of 0.2 picograms/mL at 5 hours. The milk half-life was calculated as 1.1 hours. Milk:plasma ratios were 0.04 at 30 minutes, and 0.06 at 1 hour respectively. The infants were not reported to be breastfed during this study, and the effect, if any, of the small amounts of MPA on a breastfed infant is therefore unknown (12).

Due to the low levels of oral misoprostol found in breast milk, no interruption of breastfeeding is necessary (8). However, if a mother wished to further reduce any risk, breastfeeding could be interrupted for 5 hours after oral administration of misoprostol (11).

There is no information regarding the level of misoprostol after other routes of administration, but based on pharmacokinetics, the levels in milk are also likely to be low and no break in breastfeeding is required.

Gemeprost

There are no data on the effects of gemeprost on lactation or on a breastfed infant. Bioavailability is limited to between 12 and 28% after vaginal administration (13). However, based on its low molecular weight (394.5 Dalton), passage into breast milk would be expected, although only in very small amounts (5).

There are no further pharmacokinetic data to advise whether any period of suspending breastfeeding could further reduce risk, and therefore, based on the assumption that only small amounts would be present in breast milk, suspension of breastfeeding would not be required after vaginal gemeprost administration.

Summary

- There are no data on the effect of mifepristone, misoprostol or gemeprost on lactation or on a breastfed infant.
- Such interventions are usually only given as one-off doses, and therefore any risk of accumulation in the infant, from exposure via the breast milk, is limited.
- Limited data suggests that the levels of mifepristone in milk are low, especially when using the 200 mg dose, and that breastfeeding can be safely continued in an uninterrupted manner during medical abortion. This overrides the manufacturer's recommendation to withhold breastfeeding for 26 days after administration.
- Oral misoprostol is excreted into human breast milk in small amounts which are rapidly eliminated. No interruption of breastfeeding is necessary, although the mother could interrupt breastfeeding for 5 hours after an oral dose, to reduce any risk.
- Gemeprost would be expected to pass into breast milk in small amounts, although there is no data to support this. However, breastfeeding can continue in an uninterrupted manner.
- Where a surgical method is being offered, the effects of local or general anaesthetics must be considered when advising on the safety of breastfeeding.

Limitations

- The above recommendations are based on pharmacokinetic observations only, and not supported by clinical evidence. Any effect on a breastfed infant is unknown.
- The information above applies to full-term and healthy infants. If the infant has been born prematurely, or is unwell, further advice can be sought from the UK Drugs in Lactation Advisory Service provided jointly by the Trent Medicines Information Service (0116 258 6491) and the West Midlands Information Service (0121 311 1974).

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- NHS choices. Available at www.nhs.uk. Accessed on 04/12/15
- British Pregnancy Advisory Service. Available at www.bpas.org. Accessed on 04/12/15
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