

What is the preferred triptan for the treatment of migraine in breastfeeding mothers?

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Background

Triptans (5-hydroxytryptamine-1-like receptor agonists or 5-HT₁ agonists) are effective drugs for the treatment of migraine. Migraines are common in women, with an incidence of 4 in 10, and can be very debilitating (1). A study of 60 migraine sufferers found that more than 50% of patients experience recurrence during the first month after delivery (2). A mother should not be discouraged from breastfeeding over concerns of worsening migraine (3). For women who suffer from migraine during lactation, analgesics such as paracetamol and ibuprofen, which are compatible with breastfeeding (4,5), may not provide adequate pain relief. A triptan may be considered appropriate especially if this has been used with previous success.

The 5HT₁ agonists available are almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan.

Answer

Sumatriptan

One study looked at the excretion of 6 mg of sumatriptan administered subcutaneously to five lactating women. Milk and plasma samples were collected at regular intervals over an 8 hour period. The mean maximum plasma concentration, 80.2 nanograms/mL, occurred 16 minutes post dose while the mean peak milk concentration, 87.2 nanograms/mL, occurred approximately 2.6 hours after the dose. The mean milk:plasma ratio was calculated to be 4.9, showing a significant transfer of sumatriptan into milk. The mean total recovery of drug from milk was estimated to be only 14.4 micrograms which is 0.24% of the administered dose. On a weight adjusted basis this corresponded to a mean infant exposure of 3.5% of the maternal dose. If oral bioavailability in the infant is presumed to be the same as in adults (i.e. 14%) the weight adjusted infant dose decreases to 0.49%. If reduced drug clearance is taken into account for a premature infant, exposure could vary from 4.9% for a very premature baby to 0.7% in a 30 week old infant. The authors concluded that, since sumatriptan is usually only administered acutely as one off doses, the drug will not pose a significant risk to the infant. Expressing and discarding all milk for 8 hours after the dose, could further reduce this minor exposure (6). Although sumatriptan is concentrated in breast milk, absolute breast milk levels still remain low as maternal plasma levels are low.

In an unpublished study 3 women used sumatriptan during breastfeeding with no adverse effects reported in the infants. Another woman who had a single injection of sumatriptan had a cessation of milk production (7). However, this report has not been verified.

An assessment of the Intensive Medicines Monitoring Programme (IMMP), a national postmarketing surveillance system in New Zealand, states that there have been 29 reports of outcomes following exposure to sumatriptan during lactation. There were no adverse effects reported in the infants (8).

The manufacturers state that infant exposure can be minimised by avoiding breastfeeding for 12 hours after treatment, during which time any breast milk expressed should be discarded (9).

Eletriptan

In a small study, 8 lactating women were given a single 80 mg oral dose of eletriptan. The mean concentration in breast milk was about a quarter of the plasma eletriptan concentration. Specific breast milk levels were not quoted in this paper. The elimination half life in breast milk was found to be 3.6 hours. The mean total amount of the drug excreted into breast milk over 24 hours was

12.9 micrograms which is 0.02% of the 80mg dose administered. The author considered however that even though the total amount of eletriptan excreted in milk is low it could still pose a risk to the infant considering the smaller volume of distribution in a child and therefore higher plasma concentration, immaturity of drug clearance systems and the potential for the active metabolite to be excreted into breast milk. The author advised avoiding exposure of breastfeeding mothers to eletriptan due to the lack of data (10).

The bioavailability of eletriptan is 50%, which is greater than that of sumatriptan. It is commented that it is unlikely that the dose delivered in the study above would harm a breastfed infant (11).

The manufacturers state that caution should be exercised when considering administration of eletriptan to women who are breastfeeding. Infant exposure can be minimised by avoiding breastfeeding for 24 hours after treatment (12).

Almotriptan

No published data are available on the transfer of almotriptan into human milk. It has an oral bioavailability of 80% which is greater than that of sumatriptan, suggesting that infant exposure to almotriptan could potentially be higher than with sumatriptan (11). The manufacturers recommend caution should be exercised when prescribing during lactation. Infant exposure may be minimised by avoiding breastfeeding for 24 hours after treatment (13).

Frovatriptan

No published data are available on the transfer of frovatriptan into human milk. It has a long half life of 26 hours and so a shorter acting triptan with more data (i.e. sumatriptan) would be preferred (11). The manufacturers state that, although it is not known whether frovatriptan or its metabolites are excreted in human breast milk, the administration of frovatriptan to women who are breastfeeding is not recommended, unless it is clearly needed. In which case, a 24 hour interval must be observed (14).

Naratriptan

No published data are available on the transfer of naratriptan into human milk. It has an oral bioavailability of 70%, which is greater than that of sumatriptan (11). The manufacturers state that no studies have been conducted to determine the level of transference of naratriptan into breast milk of nursing women. It is recommended that infant exposure be minimised by avoiding breastfeeding for 24 hours after treatment (15).

Rizatriptan

No published data are available on the transfer of rizatriptan into human milk. The manufacturers advise that caution should be exercised when administering rizatriptan to women who are breastfeeding. Infant exposure should be minimised by avoiding breastfeeding for 24 hours after treatment (16).

Zolmitriptan

No published data are available about the transfer of zolmitriptan into human milk. The manufacturers advise that caution should be exercised when administering to women who are breastfeeding (17).

The safety of triptans in breastfeeding mothers has been further supported in additional evidence-based reviews (18,19). Adverse effects in breastfed infants would not be expected with triptans, especially considering their short term use (20).

Summary

- ◆ There is limited data about the safety of triptans in breastfeeding.
- ◆ Sumatriptan is the drug of choice from this class as there are more data available. It is transferred into breast milk but with a short half life and low oral bioavailability, infant exposure and the risks of adverse effects are expected to be low.
- ◆ Almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan and zolmitriptan should be used with more caution since data is lacking.
- ◆ Adverse effects in breastfed infants would not be expected with triptans, especially considering their short term use. If the mother or clinicians wish to be more cautious a

post dose wash out period of 8 hours after sumatriptan or 24 hours after other triptans could be observed before the mother resumes breastfeeding. However this is usually considered to be over-cautious.

Limitations

- There is a lack of data about transfer of the triptans into human breast milk particularly for almotriptan, frovatriptan, naratriptan, rizatriptan and zolmitriptan. For sumatriptan and eletriptan data is limited to small studies.
- The information relates to full-term and healthy infants. Evidence in pre-term infants is largely lacking. If the infant is pre-term, of low birth weight or has other concomitant pathology or medical problems, then specialist advice should be sought as this answer may not apply. *Contact the UK Drugs in Lactation Advisory Service (UKDILAS) provided by the Trent and West Midlands Medicines Information Services.*

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