Can low dose aspirin be used in breastfeeding mothers as an antiplatelet agent?

Prepared by UK Medicines Information (UKMi) pharmacists (or other as appropriate) for NHS healthcare professionals

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Summary

- Limited data and pharmacokinetics indicate that low dose aspirin (defined here as 75 – 150mg daily) passes into breast milk in small amounts.
- There have been no adverse events described in infants exposed to aspirin via breast milk when used as an antiplatelet agent. However, the data available for the use of aspirin whilst breastfeeding are limited and therefore it should be used with caution. Infants exposed to aspirin via breastmilk should be monitored for side effects described in children when used in directly.
- It is unknown whether the small amounts of aspirin present in breast milk following an antiplatelet dose could cause Reye's syndrome in a breastfed infant. To minimise the risk, breastfeeding should be withheld if the infant develops a fever, or consider temporarily discontinuing the aspirin if clinically justified.

Background

In the UK, aspirin is licensed as an oral antiplatelet agent. It is also licensed for use as an analgesic or anti-inflammatory at higher doses (1). The focus of this Q&A is antiplatelet low doses of aspirin defined as 75 – 150mg daily. There are only limited data available for the excretion of aspirin into breast milk when used at low doses. Therefore, an assessment of risk in breastfeeding mothers can be made by taking account of the pharmacokinetics of aspirin, the pharmacological action and potential adverse reaction profile.

Answer

Pharmacokinetics

Aspirin (also called acetylsalicylic acid) is rapidly metabolised into its main active metabolite, salicylic acid, in the maternal plasma. Although aspirin is completely absorbed from the gastrointestinal tract, it has an oral bioavailability of 50-75% and is 88-93% protein bound. The half-life of the active metabolite (salicylic acid) is approximately 2-3 hours (3, 4). Much of the evidence relating to the excretion of salicylic acid into breast milk relates to maternal usage of aspirin at analgesic or anti-inflammatory doses, and there is only very limited evidence relating to mothers taking low dose aspirin as an antiplatelet agent.

The molecular weight of salicylic acid is small enough to expect it to pass into breast milk. However, salicylic acid is highly protein bound and almost completely ionised at a serum pH of 7.4, therefore only very small amounts are free to pass into breast milk (5). A higher pKa means a greater amount of the drug being ionised at an acidic pH resulting in higher levels in milk. As the pKa of salicylic acid is low it would not be expected to accumulate in milk, which is slightly more acidic than plasma (5). Based on its pharmacokinetics, the transfer of aspirin into breast milk when used at low doses is likely to be low. There is a significant variation however in the amount of salicylic acid reported to pass into the breast milk with analgesic doses (6).

Excretion into breastmilk

There is a published study on the use of low dose aspirin in breastfeeding mothers (7). Six lactating women were taking aspirin 81 mg daily and one mother 325 mg daily. Milk samples were taken from mothers six times throughout a 24-hour period. Aspirin was undetectable in all samples. The average concentration for salicylic acid in milk samples was estimated to be 24 ng/ml and the peak observed concentration was 114.9 ng/ml at 4 hours. The relative infant dose (RID) is the weight-adjusted maternal dose expressed as a percentage to indicate infant drug exposure. In this study, the estimated RID was reported as 0.4%. The RID for the mother taking 325mg/day was 0.45%. No adverse effects were noted in the infants. The authors conclude that the two doses used in the study should be 'quite safe' for breastfed infants (7).

A more recent case report describes the use of aspirin in a 30 year old breastfeeding mother with aspirin exacerbated respiratory disease (AERD). The patient underwent a two day protocol for aspirin desensitisation starting with 40.5mg aspirin increasing to 325mg and then maintained on 81mg aspirin daily whilst breastfeeding. The patient responded well after desensitisation and was followed up for 12 months. No adverse effects were reported in the infant (8).

Adverse reactions

Infants exposed to aspirin via breastmilk should be monitored for adverse effects described with therapeutic doses of aspirin when used in children directly. In particular, signs of bruising and bleeding, which may be prolonged (7–10 days). Other possible adverse effects include tachycardia, hypersensitivity reactions such as rash, urticaria, dyspnoea, severe bronchospasm, angioedema, increased bleeding during or after surgery, and thrombocytopenia.

No reports describing adverse effects in infants of mothers taking low dose aspirin as an antiplatelet agent could be identified.

Several case reports have described serious adverse effects in infants exposed to aspirin via breast milk in mothers taking analgesic or anti-inflammatory doses, including metabolic acidosis (9), thrombocytopenia, fever, anorexia and petechiae (10), and haemolysis in a G6PD deficient infant (11). However, the case report describing metabolic acidosis could not rule out direct administration of aspirin to the infant (9). In contrast, a prospective follow-up to detect adverse reactions in 15 breastfed infants exposed to aspirin not find any adverse effects, although aspirin doses were unspecified. (12).

Aspirin has been definitively associated with Reye's syndrome when administered to children with fever. Reye's syndrome is a disorder characterised by acute encephalopathy and fatty degeneration of the liver. It occurs most commonly in young children although cases have been seen in patients over the age of 12. Many factors may be involved in its aetiology but it typically occurs after a viral infection such as chickenpox or influenza and may be precipitated by a chemical trigger (13). A definitive dose-related relationship between aspirin and Reye's syndrome has not been established (14) and it is unknown whether the small amounts present in breast milk following an antiplatelet dose would be clinically significant. To minimise the risk of developing Reye's syndrome, breastfeeding should be withheld if the infant develops a fever and the mother is taking aspirin. In some cases it may be clinically appropriate to withhold the aspirin for short periods instead in order to avoid disrupting breastfeeding.

Other antiplatelet agents

Information on the use of other antiplatelet agents in breastfeeding mothers, including dipyridamole, clopidogrel, prasugrel and ticagrelor is available via the SPS website.

Limitations

- Evidence for the transfer of aspirin into breast milk and its safety in breastfed infants is limited to relatively small studies and a few case reports. Long-term safety data are lacking.
- The above information applies to maternal monotherapy and a full-term, fit and healthy infant only. Should the infant be premature, unwell, or the mother taking multiple medications, an individual risk assessment is required. Please contact the UK Drugs in Lactation Advisory Service for advice on 0116 258 6491**/**0121 424 7298 or ukdilas.enquiries@nhs.net.

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Search strategy

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