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SAFETY OF ENOXAPARIN AND DALTEPARIN IN BREASTFEEDING

Question:
What is the safety of enoxaparin and dalteparin in breastfeeding? The manufacturer of enoxaparin advises against its use in lactation.

Answer:
In general, we regard dalteparin and enoxaparin as 'safe' during breastfeeding because they are very large molecules with average molecular weights of 5,000 and 4,500 daltons, respectively[1,2] (compare with an average drug size of approximately 300 daltons). This is a feature that markedly limits the ability of low molecular weight heparins to cross the biological membranes that separate maternal blood and milk. In addition, these agents are very poorly absorbed from the gastrointestinal tract, therefore any drug that is ingested via breast milk is unlikely to be appreciably absorbed from the infant's gut. A major reference text supports our view[3].

In an extensive literature review[1-7], we located one report that documented the transfer of dalteparin into breast milk[8]. This study measured anti-Xa activity in the blood and breast milk of 15 mothers, 3 to 4 hours after administration of dalteparin SC 2,500 IU. (Anti-Xa activity is used as a measure of low molecular weight heparin activity.) Anti-Xa activity in milk ranged from < 0.005 (limit of quantification) to 0.037 IU/mL. Using the mean and highest value (worst-case), the infant dose is approximately 5 - 13% of the maternal dose, after correcting for the difference in body weight. For most drugs, an infant dose that is less than 10% of the maternal dose (weight-adjusted) would be considered compatible with breastfeeding if the baby is healthy and born at term[5]. Assuming the oral availability of low molecular weight heparins is the same in infants as it is in adults, infant exposure would be expected to be negligible.
There are a number of issues regarding methodology of this study that warrant consideration. These include the possibility of assay error (as reported by the authors of this paper); sampling of immature milk at 4 to 8 days post-partum which may fail to adequately describe transfer into mature milk (> 14 days post-partum); measurement of single pairs of plasma and milk anti-Xa activity rather than area under the concentration-time curve; measurement of anti-Xa activity without consideration of the impact on other factors eg. anti-IIa.
However, the authors concluded that *"based on the present data and the very low bioavailability of heparin ingested orally, it appears highly unlikely that the puerperal thromboprophylaxis with low molecular weight heparin has any clinically relevant effect on the nursing infant"*[8].
These authors also cited another study where no anti-Xa activity was detected in breast milk following a 5,000 IU dose of low molecular weight heparin (specific agent not stated)[9]. Further details are lacking[6,9].

Conclusions:
Although data documenting the risks associated with maternal use of dalteparin and enoxaparin in lactation are limited, we would generally regard both of these agents as compatible with breastfeeding. We do not particularly have a preference for which agent is used in lactation. The availability of clinical data for dalteparin may suggest an advantage. However, both of these agents are extensively used in clinical practice, both in pregnancy and in the immediate post-partum period

(when breastfeeding would be expected to occur). The lack of reports in the literature of adverse effects in the suckling infant is reassuring.

References:

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