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SAFETY OF 'STATINS' IN BREASTFEEDING

Question:
What is the safety of the 'statins' in breastfeeding?

Answer:
We are not aware of any data describing the transfer of atorvastatin or simvastatin into human breast milk (these are the two statins that are available in New Zealand)[1-5]. Limited manufacturer's data is available on other statins. For example, pravastatin is reported to appear in milk in *"small amounts"*[1]. However, all drugs should be considered to transfer into breast milk to some extent, and may pose risk to a suckling infant. Therefore, this information offers little in terms of risk assessment.

In general, it is recommended that these agents are avoided during breastfeeding[1,2]. This is because there are insufficient data to ascertain their safety in lactation. Furthermore, the use of lipid lowering drugs is for long-term maternal benefits and temporary interruption of therapy is not usually considered to significantly impact on maternal morbidity or mortality[1,6].

In situations where clinical data in humans are lacking, we can use predictive models to estimate the transfer of a drug into breast milk from known physicochemical properties (eg. plasma protein binding):
Simvastatin: We could not find sufficient published physicochemical data for simvastatin, its major active metabolite (simvastatin acid) and other active metabolites to predict transfer[6,7]. The major active metabolite, simvastatin acid, is highly bound to plasma proteins (95-98%) and is an acid[7,8]. These are two physicochemical properties that markedly limit transfer into milk. Parameters for other metabolites could not be found (the majority of metabolites are suggested to be inactive)[6]. A reasonable approach might be to administer the daily dose of simvastatin at the time of the last breastfeed for the night. Delaying breastfeeding for six hours post-dosing would be expected to reduce plasma and milk concentrations to < 25% of peak concentrations (peak HMG-CoA reductase inhibitor concentrations occur at 1.3-2.4 h post-dose[6]; half-life of simvastatin acid is 2 h[8]). Problems with this method include the inability to account for the transfer of other metabolites into milk and the possibility that milk concentrations may not mimic plasma concentrations.

Atorvastatin: As with simvastatin, atorvastatin has active metabolites with insufficient physicochemical data to predict transfer into milk[6,9].

Alternatives:
We are not aware of any data describing the transfer of the fibrates, nicotinic acid or bile acid sequestrants into human breast milk[1-4]. However, the bile acid sequestrants, cholestyramine and colestipol are expected to be safe in breastfeeding because they are not absorbed from the maternal gastrointestinal tract[1,2]. These would be the preferred options for breastfeeding mothers. However, the possibility of maternal (and infant) deficiencies in fat-soluble vitamins should be considered.

Conclusions:

We are not aware of any published data describing the transfer of simvastatin or atorvastatin into breast milk and these agents are generally avoided in breastfeeding mothers. Physicochemical properties for simvastatin and its major metabolite suggest that transfer may be low. However, it is not known whether low exposure to simvastatin/metabolites in milk may have an adverse effect on infant cholesterol synthesis, and therefore growth and development. Ideally, statins should be avoided in breastfeeding in favour of safer options such as cholestyramine. If the latter option is used, watch for maternal nutrient deficiencies.

References:

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