### PROJECT DETAILS

**Title of project**  
Predicting infant exposure to novel oral anticoagulants through breastfeeding – population pharmacokinetic modelling and simulation of the novel oral anticoagulants

**Supervisor 1**  
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**Project description (max 500 words)**

Venous thromboembolism (VTE) is a significant complication during the puerperium and is a leading cause of both maternal morbidity and mortality in the Western world. Women identified at significant risk of VTE are prescribed low molecular weight heparin (LMWH), in order to reduce this risk, and are required to inject LMWH by subcutaneous injection daily for up to 6 weeks post-partum. For many women, this is the first time they have been asked to inject themselves, with research demonstrating that adherence to LMWH being extremely variable during this period. The use of the oral vitamin K antagonists, e.g. warfarin, is not appropriate in this setting, as the need for frequent monitoring of the international normalised ratio (INR) and subsequent dose adjustments, impacts negatively on the mother for the short time they are required.

More recently the novel oral anticoagulants (NOACs) have become available for use in clinical practice. NOACs have the significant advantage of being orally active and exerting a predictable anticoagulant effect, requiring minimal monitoring. They potentially provide a convenient alternative to the use of LMWH as thromboprophylactic agents during the post-partum period. However, it is not however known whether NOACs transfer into breast milk and if they do, what infant exposure is likely to be.

This study aims to investigate whether the different NOACs available in the UK (apixaban, dabigatran and rivaroxaban) transfer into breast milk, by how much and determine whether it would be safe for mothers to breastfeed whilst prescribed a NOAC. The study will utilise the method of population pharmacokinetic modelling and simulation.

**Skills training and over-arching objectives:**

**YEAR 1:** i) assessment of the physiochemical properties of the NOACs and predicting their transfer into breast milk, ii) *in-vitro* measurement of NOACs in breast-milk using liquid chromatography-mass spectrometry and assay validation.
YEAR 2 and 3: iii) ethics application, iv) complete in-vivo work in volunteer nursing mothers.

YEAR 4: v) population pharmacokinetic modelling and simulation of the absolute infant dose (AID) and the milk to maternal plasma ratio (M/P) using NONMEM and ‘R’, vi) feedback results for clinical practice.

Representative publications


Please indicate the type of programme
4 years