# Warfarin in Pregnancy

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<th><strong>Full Title of Guideline:</strong></th>
<th>Guideline for the use of warfarin in pregnancy</th>
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<td>National and international guidelines, literature on the effects of warfarin in pregnancy</td>
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*This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt contact a senior colleague or expert. Caution is advised when using guidelines after the review date or outside of the Trust.*
Guideline for the use of warfarin in pregnancy

Introduction

Indications for warfarin use

Warfarin is an oral anticoagulant agent (vitamin K antagonist). Indications for its use include (NICE 2015; SIGN 2013):

- Prosthetic heart valves
  - Mechanical
  - Bioprosthetic with another risk factor (e.g. atrial fibrillation)
- Short term treatment of venous thromboembolism
- Long term prophylaxis for recurrent venous thromboembolism
- Persistent atrial fibrillation

Risks to the fetus with warfarin use in pregnancy

Use of warfarin in the first trimester, particularly in the 6th – 9th week, is teratogenic. Fetal warfarin syndrome is associated with exposure during this period. The features of this embryopathy are as follows (Briggs & Freeman 2015):

- Nasal hypoplasia
- Birth weight <10th percentile for gestational age
- Hypoplasia of the extremities (ranging from severe rhizomelic dwarfing to dystrophic nails and shortened fingers)
- Developmental retardation
- Seizures
- Scoliosis
- Deafness/hearing loss
- Congenital heart disease
- Eye defects (blindness, optic atrophy, microphthalmia) when drug also used in 2nd and 3rd trimesters

The incidence is low (2.6%) when the dose is <5mg of warfarin daily, but higher where the dose is >5mg (8%)(ESC guideline). Exposure after the first trimester carries a risk of central nervous system defects, possibly due to the risk of scarring and subsequent haemorrhage. The risk of late fetal loss is approximately 10% with ongoing warfarin use, which is dose dependent.
In the late second and third trimester there is a risk of fetal intracranial haemorrhage. This is because when a mother is adequately anti-coagulated, the fetus will be severely over anti-coagulated as the vitamin K levels in the fetus are approximately 1/10th of those of the mother. (McLintock 2010).

**Indications for continuing warfarin in pregnancy**

Due to the fetal risks, women should only continue taking warfarin during pregnancy if the risks of thrombosis outweigh the risks. For women on warfarin for recurrent venous thromboembolism, conversion to low molecular weight heparin (LMWH) within 2 weeks of a positive pregnancy test provides adequate anti-coagulation and is safe for the fetus.

**In the vast majority of women taking warfarin for venous thromboembolism or thrombophilia, conversion to LMWH will provide adequate anti-coagulation. This therapy is safe for the fetus and therefore preferred to warfarin unless there are maternal risks with converting to heparin as outlined below.**

See ‘Short guideline on the management of thromboprophylaxis in pregnancy’ for guidance on the management of women at risk of venous thromboembolism.

Women with prosthetic heart valves are at particular risk of thrombotic complications in pregnancy and therefore LMWH may not provide adequate thromboprophylaxis.

**Thrombotic complications associated with mechanical heart valves in pregnancy**

Valve thrombosis is associated with significant morbidity and mortality. Outside of pregnancy, the risk is approximately 1% in patients on warfarin. In pregnancy, the risk has been quoted as 3.9% with warfarin used throughout, and 4 - 9% with LMWH throughout (ESC guideline). There is also a risk of systemic thrombosis, including cerebrovascular accident (CVA) and peripheral emboli in women who are inadequately anti-coagulated.

Options therefore include:
1. Therapeutic dose LMWH throughout pregnancy
2. LMWH from 6-12 weeks then warfarin from week 13
3. LMWH from 6-12 weeks, warfarin for the second trimester, LMWH third trimester
4. Warfarin throughout

In options 2 and 4 consideration should be given to conversion to LMWH or unfractionated heparin prior to delivery. The timing should be individualised depending on the thrombosis risk and planned mode of birth.

Recommendations

Women on warfarin pre-pregnancy/ up to 6 weeks gestation

- Women on warfarin who attend for pre-pregnancy counselling, should have an individualised plan for anti-coagulation made after discussion of the risks and benefits of warfarin and LMWH. The GP should also be made aware of the plan of care. Women should be advised to do regular home pregnancy tests when trying to conceive and inform the GP when they have a positive result. A plan for early referral to the combined haematology-obstetric clinic (QMC Tues am, City Thurs pm, weekly) and/or the obstetric cardiology clinic (City campus, alternate Tuesdays) for women with an artificial valve should be put in place.
- Women presenting early in the first trimester, should be referred urgently (ideally to be seen within 1 week) to the combined obstetric haematology clinic.
- Each anti-coagulation plan should include:
  - Whether the woman plans to continue on warfarin or LMWH in the first trimester
  - If warfarin: target INR and recommended frequency of testing. Aim for tight control to minimise the risks to the fetus
  - If LMWH: starting dose. Often 1mg/kg twice daily but higher may be indicated.
  - Schedule for anti Xa monitoring (if required) and therapeutic target. Please note that if this is performed, the timing of the test post dose is critical in interpreting the results. If levels are outside the therapeutic target, please discuss with the haematology, ideally the consultant involved in the woman’s care, before altering the dose.
Plan for conversion back to warfarin: timing (e.g. 13+0 weeks gestation, postnatal), starting dose, schedule for INR monitoring, therapeutic level at which LMWH can be discontinued

Women on warfarin throughout the first trimester

- Women taking warfarin at 6-12 weeks gestation should be counselled about the risk of fetal complications including embryopathy
- Referral to a fetal medicine specialist for evaluation at 18-21 weeks gestation is indicated, although women should be advised that ultrasound may not detect all of the features of warfarin embryopathy and the risk of fetal intracranial haemorrhage persists beyond this gestation.
- A neonatal alert should be completed
- If aspirin is indicated for other reasons e.g. pre-eclampsia prophylaxis, there is no contraindication to using this alongside warfarin.

Women on warfarin in the second and third trimester

- Regular scans for monitoring fetal growth are indicated due to the risk of growth restriction associated with warfarin.
- Timing and mode of delivery should take into account obstetric indications and maternal morbidity
- Ideally, delivery should be timed (e.g. induction of labour at 39 weeks) to facilitate planning of anti-coagulation
- Vaginal birth is contraindicated in a woman currently anticoagulated with warfarin due to the risk of fetal intracranial haemorrhage
- Caesarean section in a woman who is fully anticoagulated carries significant risk of secondary PPH, intra-abdominal collection and wound haematoma
  - The risk of wound haematoma with therapeutic LMWH or unfractionated heparin is approximately 2%. (NICE 2010)
- An individualised plan for delivery and anti-coagulation should be put in place with input from: an obstetrician, anaesthetist, haematologist and neonatologist (cardiologist if cardiac indication for warfarin)
- Consideration should be given to converting to LMWH 3-4 weeks prior scheduled delivery to allow ‘washout’ of warfarin from the fetal system when vaginal birth is planned
Even if an adequate period without warfarin has ensued, if a woman has been treated with warfarin in the third trimester, precautions should be taken to avoid fetal trauma including:
  - Avoid fetal blood sampling/ fetal scalp electrode
  - Avoid ventouse
  - Avoid rotational/ difficult forceps

A shorter washout period may be considered if a caesarean section is planned, but conversion to LMWH or IV unfractionated heparin in the peri-delivery period may reduce the risk of haemorrhage for the mother.

Anticoagulation will affect the safety of regional anaesthetic for birth. An obstetric anaesthetist should be involved in writing the birth plan. When emergency delivery is required in someone who is fully anticoagulated, the on call anaesthetic and obstetric consultants should be informed.

Neonatal alert should be completed.

Postnatal management

- Precautions should be taken to minimise maternal bleeding, including active management of the third stage of labour.
- The neonatal team should attend delivery.
  - Site IV cannula for the baby and take clotting screen
  - Administer IV vitamin K via cannula
  - Further management depending on clotting screen result
- Warfarin treatment may be recommenced when bleeding risk has subsided.
  - See NUH ‘Guideline on warfarin dosing in adults’

Important points/ In an Emergency

- Compliance and timely administration of medication is vital. The likelihood of missing/ late doses increasing the risk of valve thrombosis must be highlighted to patients and ward staff.

- Symptoms and signs of valve thrombosis include:
  - Neurological symptoms
  - Chest pain
Symptoms of heart failure (shortness of breath, peripheral or pulmonary oedema)
Detection of a new cardiac murmur

This is a life-threatening emergency and the cardiology team must review the patient as soon as possible if valve thrombosis is suspected. A transthoracic/ transoesophageal echo is indicated.

- In a patient who is bleeding, check INR urgently and discuss ASAP with haematology and cardiology on- call teams.

References


