Anticoagulation for Pregnant Women or Birthing People with Mechanical Heart Valves UHL Obstetric Guideline

University Hospitals of Leicester NHS
NHS Trust

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Contents

1. Introduction and who the guideline applies to:

This guideline covers the anticoagulation treatment of any pregnant woman or birthing person with mechanical heart valves and applies to any member of staff involved in their care.

Background:

The management of women on mechanical valves during pregnancy can be difficult due to the conflict between the optimal management for the mother to avoid valve thrombosis, versus the risk of anticoagulation to the embryo or fetus.

In non-pregnant women or birthing person with metallic valves, the incidence of valve thrombosis on warfarin is approximately 1% per year [(2)]. This risk is greater for tricuspid or mitral valves compared to the aortic position. Other risk factors include a history of previous thrombosis, atrial fibrillation and the presence of more than one prosthetic valves.

The risk of thrombosis during pregnancy is known to be to be higher due to pregnancy related haemostatic changes that cause hypercoagulability. There is also difficulty in INR control, which is known to be a major risk factor for valve thrombosis [(3)]. The physiological changes in cardiac output may also impact a woman's outcome.

It is clear that all women with metallic valves require therapeutic anticoagulation throughout pregnancy, but there is a lack of reliable data on the safety and efficacy of anticoagulation, which means that the optimal regime is uncertain. Conflict also exists in international guidelines. The American and European Cardiology societies favour continuing warfarin during the second and third trimesters [4, 5], whilst the American College of Chest physicians offers several alternative options [1]. The presence of therapeutic anticoagulation is associated with a risk of pregnancy-specific bleeding, with an increased risk of antepartum haemorrhage [6, 7].

2. General Recommendations;

1. Pre-pregnancy counselling should be clearly documented regarding the risks associated with anticoagulation, including warfarin embryopathy and maternal and fetal bleeding risks, as well as risk of valve thrombosis
2. Women should be managed in a cross-speciality team, with joint care involving Haematology, Obstetrics, Cardiology and Obstetric Anaesthetists. This includes pre-pregnancy discussions
3. An antenatal care plan should be discussed and agreed and should follow one of the recommended treatment regimens below. This should take patient preference regarding anticoagulation into account.
4. Regular cardiac monitoring is required, to include review by Cardiologist in each trimester and an echocardiogram in (at least) 1st and 3rd trimester
5. Regular anticoagulant monitoring is required dependent on treatment regimen (see below) and women or birthing people seen with the results in Haematology/Obstetric Clinic
6. A definitive intra-partum care plan should be discussed and agreed with all members of the joint team and distributed to relevant clinical areas/staff.
7. A paediatric alert form must be completed for all, and must identify if the woman or birthing person has been on warfarin in the pregnancy.
8. Maternal heart condition must be identified at the newborn examination.

2.1 Preconception evaluation and counselling

- All women or birthing people with prosthetic heart valves should receive preconception assessment including cardiological assessment with specific expertise in managing patients with valvular heart disease during pregnancy.
- For discussion of anticoagulation, women or birthing people should be referred to the Obstetric Haematology Clinic to counsel them on the maternal and fetal risks of continuing therapeutic anticoagulation. Women or birthing people should be aware of the life-threatening risk of thromboembolic events regardless of the anticoagulation regime chosen.
- Adherence has a significant impact on risks associated with anticoagulation and patient preference should therefore be taken into consideration when formulating an anticoagulation plan.
- Women or birthing people with regular periods who are attempting to conceive should be advised to continue warfarin until a positive pregnancy test. The risk of warfarin embryopathy is low in the first six weeks of gestation and it is following this time that women should be switched to an alternative anticoagulation.

2.2 Anticoagulation during pregnancy

Three options are primarily available for anticoagulation throughout pregnancy. Option 1 has historically been favoured within UHL in view of difficulty in INR stabilisation in pregnancy, along with the risks of teratogenicity and fetal complications with warfarin. Recent British Society of Haematology guidance has however recommended that option 2 is superior in terms of maternal outcomes and so should be considered in every case. Each woman or birthing persion should be counselled on all options and a care plan documented pre-conception (or in early antenatal period if this is not possible). Recommended regimens include:

1. Adjusted-dose twice daily low molecular weight heparin (LMWH) throughout pregnancy to achieve manufacturer's peak anti-Xa (Enoxaparin level taken 3 hours post dose, target range*)*
2. Oral anticoagulation substituted with low molecular weight heparin between 6-14 weeks with adjusted dose BD LMWH to achieve peak anti-Xa target as above. Maintain oral anticoagulation with warfarin between 14 and 36 weeks and substitute with adjusted dose BD LMWH from 36 weeks to delivery.
3. Continual warfarin throughout pregnancy

In high-risk patients, the addition of Aspirin 75mg OD can be considered to reduce thromboembolic complication rates. This can be increased to 150mg from 12 weeks' gestation if indicated for obstetric reasons.
Direct oral anticoagulants (Dabigatran, Rivaroxaban, Apixaban, Edoxaban) are contraindicated in both pregnancy and in use for prosthetic valves and **should not** be considered

Therapeutic anticoagulation with frequent monitoring is essential. Decisions are primarily based on prospective and retrospective cohort studies.

Warfarin:

- This is the safest anticoagulation for the birthing person as it is the most effective agent to prevent valve thrombosis. Pooled data of all reported pregnancies (N=1169) reported a 3.8% incidence of thromboembolic complications. There was a live birth rate of 66.6%, but an overall incidence of warfarin embropathy of 4.2% [(2)].
- Warfarin freely crosses the placenta and is thought to inhibit vitamin K dependent osteocalcins that play a role in calcification which occurs during embryogenesis [(8)]. Features of warfarin embryopathy include characteristic nasal hypoplasia and skeletal abnormalities (fetal warfarin syndrome). The critical time of exposure is weeks 6-9 of gestation.
- The risk of warfarin embryopathy may be higher in women with warfarin doses >5mg per day, which has led some international guidelines to differentiate management based on the woman's warfarin dose[(4,5)]. This is not widely practised in UHL.
- Warfarin exposure after the first trimester increases the risk of fetal bleeding with an increased rate of foetal loss and stillbirth. This is influenced by the foetal INR running at a higher level than that of the mother due to hepatic

immaturity.

- If warfarin is used during pregnancy, INR monitoring should occur on a weekly basis and may require referral to the UHL anticoagulation team for their expertise.
- If warfarin is used in pregnancy, this should be transitioned to LMWH by 36 weeks gestation.
- In the event of maternal bleeding, urgent reversal with 4-factor prothrombin complex concentrate may be required. This requires discussion with the on call haematology registrar or H&T consultant.

Heparin:

- Unfractionated heparin (UFH) does not cross the placenta and has no known harmful effects on the foetus. Thromboembolic complication rates are higher in women treated with SC UFH throughout pregnancy compared to warfarin (25-33%) [9]. Prolonged use causes bone density loss. It is therefore not recommended for prolonged use.
- LMWH is preferred to UFH due to apparent lower rate of valve thrombosis (rate 10.6% in pooled data of 104 pregnancies) ([2]. Fewest events are reported in those centres where therapeutic doses are used and regular anti-Xa monitoring is carried out. Active treatment failure in women taking LMWH with therapeutic anti-Xa levels is reported as 4.8% [2]. Therapeutic dose should be based on booking weight and given in split daily doses (see table below)
- Enoxaparin should be dosed at 2.5 mg/kg/day based on the most up to date weight available. This will be guided by the Obstetric Haematology team.
- Adjusted-dose twice daily low molecular weight heparin (LMWH) throughout pregnancy to achieve manufacturer's peak anti-Xa Enoxaparin is primarily used in UHL, with peak levels taken at 3-4 hours post dose. Data suggests that a peak target range of 1.0-1.4 IU/ml should be used, and some centres also advocate measuring trough levels in addition, although this is not advised routinely. Levels should be taken on a regular basis, and we advocate levels monthly. Women or birthing people should be seen with the results in the Haematology Obstetric Clinic to adjust treatment where necessary.

Role of aspirin:

- The rate of thromboembolic complications with single agent aspirin in women with metallic heart valves is reported to be as high as 25% [9]. It cannot therefore be used as single agent therapy but may be added to therapeutic anticoagulation in those high-risk patients.
- If indicated for obstetric reasons, such as pre-eclampsia prevention, aspirin can be increased to 150mg OD. This should be stopped in advance of planned delivery to reduce associated bleeding risk.

2.3 Treatment regimens throughout pregnancy
Based on reference 1: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278054/

2.4 Plan for delivery

- Obstetric Haematology Team should be informed of admission at earliest opportunity
- Mode of birth should be determined by maternal and obstetric indications
- Women or birthing people should be advised to omit fragmin when labour starts or on the day of a planned caesarean section/induction of labour if this is required
- Regional anaesthesia or analgesia techniques should not be undertaken until at least 24 hours after the last therapeutic dose of LMWH
- LMWH should not be given for 4 hours after the use of spinal anaesthesia or after the epidural catheter has been removed.
- The epidural catheter should not be removed within 12 hours of the most recent injection
- Maternal IM injections should be avoided
- Prophylactic antibiotics should be given in line with national guidance
- Women and birthing people should maintain hydration and mobilisation where possible
- IV unfractionated heparin 5000iu may be required if labour is prolonged and this should be discussed with the on call Haematology SpR or Haemostasis Consultant on call
- If urgent or emergency delivery is required, the management of anticoagulation reversal will depend on the regime chosen throughout pregnancy. 4 factor PCC will be required if warfarinis being taken. Full reversal of anticoagulation is not required for vaginal or caesarean delivery, but in the event of life-threatening bleeding or to protect the fetus, reversal may be required. Such cases should be urgently discussed with the Haematology SpR or Haemostasis Consultant on call.

2.5 Plan for 3rd stage of labour

- Active management of the 3rd stage with IV oxytocin infusion

2.6 Postpartum Care

- Restart fragmin at prophylactic dose 4 hours post-partum, .For the first 24-48 hours post-delivery, it may be pertinent to continue on prophylactic dose if bleeding risk is high or if a caesarean has been performed. An intermediate dose could be considered if bleeding risk is minimal, and the aim should be to restart full therapeutic dose by 48-72 hours post-delivery in the absence of bleeding. This will require further discussion with the obstetric haematology team.
- Anti-Xa level should be checked post 4th/5th dose (1 citrate sample taken 3

hours post dose and hand delivered to Special Haematology Lab, Level 2 Sandringham building). Please contact lab on 16619 when sample taken.
- Observe for excessive bleeding and consider if norethisterone is necessary
- Restart warfarin 5-7 days after delivery if there is a low risk of bleeding. Higher doses of Warfarin are frequently required in the early puerperium.
- Continue BD LMWH until INR within desired therapeutic range on 2 consecutive tests
- Advise breast feeding safe on both warfarin and LMWH

2.7 Neonatal Management

- Paediatric team should be informed of delivery and complete full assessment in view of bleeding risk and potential teratogen exposure
- Warfarin use in mother close to delivery (<4 weeks) will lead to risk of bleeding in baby and assessment for bleeding should be carried out. Neonatal Vitamin K should be given but the route should be discussed with Neonatologist (po/im). Repeat doses may be indicated.

2.8 Management of valve thrombosis

- This is associated with major morbidity or death and any women with suspected valve thrombosis require an urgent cardiology review and echocardiogram to assess the valve. Treatment is controversial, with approaches including intravenous UFH with strict APTT monitoring, thrombolysis or urgent cardiac surgery. Early involvement with the on-call Haematologist regarding anticoagulation in this setting is advised.

3. Education and Training:

None

4. Monitoring compliance:

None

5. Supporting References:

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Keywords:

Aspirin, Cardiology Enoxaparin, , Haematology, Low molecular weight heparin, LMWH, Thrombosis, Warfarin

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

DEVELOPMENT AND APPROVAL RECORD FOR THIS DOCUMENT	
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REVIEW RECORD			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
July 2017	V2	B Myers and A Bolger	
August 2020	V3	B Myers and A Bolger	Regional anaesthesia should not be taken until at least 24 hours after. Epidural catheter not to be removed within 12 hours. Fragmin not to be given for at least 4 hours following a spinal.
June 2023	V4	A Webster B Myers A Bolger Maternity guidelines group Maternity Governance group Neonatal Consultants Women's Quality & Safety Board	Anticoagulation options adjusted to reflect up to date BSH guidelines published 2023 Clarified neonatal notification and paed alert