COMPLICATIONS OF PREGNANCY

VENOUS THROMBOEMBOLISM (VTE): IN PREGNANCY & PUERPERIUM

VTE PROPHYLAXIS: PRIOR THROMBOTIC EVENT PLUS THROMBOPHILIA

Keywords: Venous thromboembolism, VTE, thrombophilia, thromboprophylaxis, pulmonary embolus, anticoagulants, low molecular weight heparin, LMWH, antithrombin deficiency

AIM

To recognise the need for thromboprophylaxis in women at high risk of thromboembolism in pregnancy and the postpartum period.

BACKGROUND

In pregnancy and the postpartum period, VTE is uncommon (1-2 per 1000) but clinically important.[1, 2] The risk of VTE is increased in pregnancy (4-6 fold), and further increased postpartum,[1] with VTE being the second most common cause of direct maternal mortality in Australia,[3] and one of the leading causes worldwide[4]. Previous VTE is one of the most significant risk factors (odds ratio 24.8) for pregnancy associated VTE,[1, 2] with a pregnancy / postpartum recurrence of 2-11% (relative risk 3.5).[1] Additionally, heritable thrombophilia has also been identified in 20-50% of pregnancy- associated VTE.[1] The risk of recurrence is higher following previous unprovoked (no identified risk factors) than provoked (associated with a risk factor) event.[2]

MANAGEMENT

PREVIOUS VTE

- If the original VTE was unprovoked / idiopathic or related to oestrogen (oestrogen containing contraception / pregnancy) or related to a transient risk factor (other than major surgery) or who have other risk factors, should be offered thromboprophylaxis throughout the antenatal period[1] and 6 weeks postnatally.[2]

  - If single VTE associated with the combined oral contraceptive pill, antenatal prophylaxis is recommended if other risk factors present, or prior pulmonary embolus (PE) +/- proximal deep vein thrombosis (DVT).[2]
- For women with prior single provoked VTE (not associated either with the combined oral contraceptive pill or pregnancy), antenatal thromboprophylaxis should only be considered if other risk factors are present.[2]
- If the original VTE was provoked by major surgery (and the woman has now recovered) and the woman has no other risk factors, antenatal thromboprophylaxis can be withheld as long as no other risk factors are present. Provide close surveillance to identify any other risk factors that may develop.[1]
- Antenatal thromboprophylaxis should begin as early as practical for each case.[1]
- Postpartum thromboprophylaxis is recommended for all women with prior VTE.[1]
- Testing for thrombophilia including antiphospholipid antibodies (if previous VTE):
  - Preferably done pre-pregnancy, to provide early thromboprohylaxis planning and because pregnancy can affect protein S estimation.
  - As all women with prior VTE are considered for thromboprophylaxis, testing is not done routinely. If finding of thrombophilia will affect management then screening can be performed.
  - Counsel prior regarding implications of positive or negative results.
  - Results to be interpreted by clinician with expertise in the area.

Previous single VTE

1. Pre-conception counselling (or early pregnancy referral if already pregnant) and prospective management plan for antenatal thromboprophylaxis with an expert in pregnancy thrombosis.[1]
2. Women with previous VTE (except if single VTE related to major surgery & no other factors) should be thoroughly assessed and offered thromboprophylaxis throughout pregnancy with low molecular weight heparin (LMWH).[1]
   There are no randomised trials on measures to prevent antenatal VTE in women with prior VTE and decisions are made from observational studies. Recurrence risk of VTE antenatally is very low if the prior VTE was provoked by a transient major risk factor that is no longer current.[1]
3. All women with previous VTE should receive postnatal thromboprophylaxis.[1]
4. See also Clinical Guideline, O&M, Complications of Pregnancy, VTE Prophylaxis for women with a Prior Thrombotic Event with NO Thrombophilia identified.

Previous recurrent VTE's- extra advice:

1. Doses of LMWH should be managed by clinicians with expertise in haemostasis and pregnancy. Some of these women require higher doses of LMWH.[1]

2. Pre-conception counselling for women on long term warfarin or other oral anticoagulants is recommended to counsel women on the risks of these medications to the fetus, and advise women to change to LMWH as soon as pregnancy confirmed (ideally within 2 weeks of the missed period).[1]
3. Women not on warfarin or other anticoagulants should commence LMWH as soon as they have a positive pregnancy test.[1]
4. If previous recurrent provoked VTE's, antenatal prophylaxis is recommended and prophylaxis for 6 weeks postnatally.[2]
5. If recurrent unprovoked VTE's, use therapeutic anticoagulation in the antenatal period and 6 weeks postnatal.[2]

Thrombophilia-associated VTE

Previous VTE & Heritable thrombophilia / antithrombin deficiency

1. Women with prior VTE and antithrombin deficiency (who are often on long term oral anticoagulation) should have thromboprophylaxis antenatally and 6 weeks postpartum[2] (or until returned to oral anticoagulant therapy) with higher dose (either 50%, 75% or full therapeutic dose) LMWH.[1]
2. Involve a haematologist with expertise in pregnancy thrombosis in the woman's management, and consider antenatal anti-Xa monitoring and potential for antithrombin replacement at labour onset or prior to caesarean birth.[1]
    - If anti-Xa levels are measured, use a test that does not use exogenous antithrombin, and 4-hour peak levels of 0.5-1.0 iu/ml aimed for.[1]
3. Other heritable thrombophilic defects can be managed with standard doses of thromboprophylaxis as they are lower risk.[1]
4. Family history of VTE, but no personal history of VTE:
    - With or without weak laboratory thrombophilia: Antenatal observation (no thromboprophylaxis) unless other risk factors; consider postnatal prophylaxis especially if other risk factors.[2]
    - With significant thrombophilia (excluding antithrombin deficiency): Antenatal & 6 weeks postnatal prophylaxis, especially if other risk factors present.[2]
    - With antithrombin deficiency: Require antenatal (intermediate or therapeutic dose) and 6 weeks postpartum (therapeutic dose) thromboprophylaxis with LMWH.[2]

Previous VTE & Acquired thrombophilia/ Antiphospholipid syndrome (APS)

1. These women (who are often on oral anticoagulation) are considered to be high risk and require intermediate (50%, 75%) or full therapeutic doses of LMWH during pregnancy and for 6 weeks postpartum (or until return to oral anticoagulation).[1]

2. Antenatal women with APS and previous VTE or arterial thrombosis should receive collaborative management involving a haematologist and/or rheumatologist with experience in this area.[1]
3. Women on therapeutic dose / long term anticoagulation before pregnancy should receive therapeutic dose LMWH during pregnancy, returning to pre-pregnancy anticoagulation in the postpartum period.[2]
4. Persistent antiphospholipid antibodies (lupus anticoagulant, anticardiolipin or β_2-glycoprotein 1 antibodies) in women with previous VTE are considered a risk factor, and if other risk factors are present, antenatal and postnatal thromboprophylaxis can be considered.[1]

ASYMPTOMATIC HERITABLE THROMBOPHILIA

1. Assess risk associated with thrombophilia, family history and other risk factors.[1]
2. Women with asymptomatic antithrombin, protein C or S deficiency or ≥1 thrombophilic defect (including homozygous factor V Leiden, homozygous prothrombin gene mutation & compound heterozygotes) should be referred to an expert clinician and antenatal prophylaxis considered. Postnatal prophylaxis for 6 weeks is recommended, even in the absence of additional risk factors.[1]
3. Heterozygosity for factor V Leiden or prothrombin gene mutation or antiphospholipid antibodies are considered risk factors for thrombosis in asymptomatic women. If other risk factors also present, such women may be considered for antenatal thromboprophylaxis.
4. Testing for thrombophilia (if no personal history or risk factors for VTE): Consider for thrombophilia testing if there is family history of a first degree relative, under 50 years old, having an unprovoked or oestrogen provoked VTE.[1]

INTRAPARTUM / BIRTH

- Planned birth where possible. Liaise with the multidisciplinary team regarding timing of cessation and recommencement of anticoagulation and document a plan of care.
- If receiving intermediate or high risk anticoagulation:
  - Discontinue LMWH 24 hours before planned birth.[5, 6] Planned birth assists necessary preparations.[4, 7] Inform women to stop antenatal LMWH if any vaginal bleeding or if labour commences. Reassess on hospital admission and prescribe LMWH as required.[1]
  - Elective caesarean birth: Stop prophylactic LMWH the day prior to the birth. On caesarean day, perform morning caesarean and restart LMWH soon after the birth (if no postpartum haemorrhage and no regional analgesia used).[1]
- Regional pain relief should be avoided until ≥12 hours after the last dose of prophylactic LMWH or ≥24 hours after the last therapeutic dose. Any epidural catheters should be removed at least 12 hours after last LMWH dose.[1] LMWH

should not be given within 4 hours after using spinal anaesthesia or after removing an epidural catheter.[1]

- If high risk of haemorrhage, use graduated compression stockings and intermittent pneumatic compression devices and consider heparin.[1]
- LMWH is safe with breastfeeding.[1]

REFERENCES / STANDARDS

1. Royal College of Obstetricians and Gynaecologists. Green-top guideline No. 37a: Reducing the risk of venous thromboembolism during pregnancy and the puerperium. **RCOG**. 2015. Available from: https://www.rcog.org.uk/globalassets/documents/guidelines/gtg-37a.pdf.
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National Standards- 1-Care Provided by Clinical Workforce is Guided by Current Best Practice; 4-Medication Safety
Legislation -
Related Policies -
Other related documents – KEMH Clinical Guidelines:

- O&M: Complications of Pregnancy: VTE: Occurring in Present Pregnancy; Prophylaxis for Women with Prior Thrombotic Event in Whom NO Thrombophilia Identified; Cardiac Conditions: Anticoagulation
- O&M: Caesarean Section: Thromboprophylaxis After Caesarean Birth
- Anaesthetics: Epidural Catheter Removal

RESPONSIBILITY	
Policy Sponsor	**Nursing & Midwifery Director OGCCU**
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