Thromboprophylaxis during pregnancy, Labour and after vaginal delivery

Introduction

Pulmonary thromboembolism is the most common direct cause of maternal death in the UK. Confidential enquiries into maternal deaths have highlighted the hitherto unappreciated risk of venous thromboembolism (VTE) in the first trimester and after non operative vaginal delivery and failures in identifying risk factors. The recently updated RCOG guideline on VTE thromboprophylaxis highlights important changes including; increased number of risk factors, focus on admitted patients and extended duration of Low Molecular Weight Heparin (LMWH) post partum from 3-5 days to 7 days. This guideline addresses these issues.

Assessment of risk

Pregnancy is associated with a ten fold increase in risk of VTE. Therefore all women should undergo a documented assessment of risk factors for VTE as follows:

- At booking, the midwife should identify whether there are any risks factors present for VTE and discuss with the Consultant Obstetrician whether a referral is required.

- Risk assessment and documentation ( see proforma: appendix 1) at every hospital admission.

- Risk assessment and documentation after every delivery irrespective of the mode of delivery.

- After a Spontaneous Vaginal Delivery (SVD) the assessment of risk factors for VTE to be performed on delivery suite by the responsible midwife who then communicates this with Obstetric Middle grade or Consultant on call.

- After an Assisted or a Caesarean section delivery, the assessment of risk factors for VTE to be performed by the responsible Obstetric doctor on delivery suite ( SHO, Middle grade or Consultant – who ever performs it )

- Women with previous VTE should be screened for inherited and acquired thrombophilia, ideally before pregnancy and referred to the joint Obstetrics – Haematology Clinic for pre-pregnancy counselling
Table 1. Risk factors for VTE in pregnancy and the puerperium

<table>
<thead>
<tr>
<th>Pre-existing</th>
<th>New onset or transient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age over 35 years</td>
<td>Surgery in pregnancy or puerperium</td>
</tr>
<tr>
<td>BMI &gt; 30 Pre-pregnancy or at booking</td>
<td>Hyperemesis, dehydration</td>
</tr>
<tr>
<td>Parity &gt; 3</td>
<td>Caesarean section</td>
</tr>
<tr>
<td>Congenital thrombophilia</td>
<td>Severe infection e.g. pyelonephritis</td>
</tr>
<tr>
<td>Acquired thrombophilia</td>
<td>Immobility (&gt; 4 days bed rest)</td>
</tr>
<tr>
<td>Previous VTE</td>
<td>Pre-eclampsia</td>
</tr>
<tr>
<td>Smoking</td>
<td>Multiple pregnancy</td>
</tr>
<tr>
<td>Gross varicose veins</td>
<td>Excessive blood loss (PPH&gt;1litre)</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>All Long-distance travel (&gt;4 hours)</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>Prolonged labour</td>
</tr>
<tr>
<td>Inflammatory disorders</td>
<td>Midcavity instrumental delivery</td>
</tr>
<tr>
<td>Myeloproliferative disorders</td>
<td>Immobility after delivery</td>
</tr>
<tr>
<td>Some medical disorders e.g. cardiac, nephrotic syndrome, SLE, Cancer</td>
<td>Ovarian hyperstimulation syndrome</td>
</tr>
</tbody>
</table>

Thromboprophylaxis during pregnancy and the puerperium

- Patients with risk factors for thromboembolism should be referred early in pregnancy to a Consultant Obstetrician.
- Seek consultant haematological advice when there is any obstetric uncertainty as to the need for, timing of, and type of thromboprophylaxis
- If therapy is indicated in pregnancy or the puerperium, Delivery Suite should be informed for the ‘High Risk’ folder and Lead Consultant Obstetric Anaesthetist should be informed of any woman requiring antenatal therapy
- LWMH are the agents of choice for antenatal thromboprophylaxis. These are as effective and safer than unfractionated heparin.
- Antenatal thromboprophylaxis should begin as early in pregnancy as possible.

1. Previous VTE and no thrombophilia²

- Postpartum prophylaxis with low molecular weight heparin (LMWH) for at least 6 weeks
- No antenatal thromboprophylaxis if past history of only a single previous VTE that was associated with a temporary risk factor
- Advice can be sought from the Haematologist (email/telephone)

- Antenatal thromboprophylaxis if:
  - Previous recurrent VTE
  - Estrogen – provoked VTE
- Consider antenatal thromboprophylaxis if:
  - Family history of VTE in first degree relative
2. Previous VTE and an inherited thrombophilia\(^2\)

- Although risk varies according to the specific thrombophilia, current evidence supports antenatal LMWH thromboprophylaxis and for 6 weeks postpartum.
- Seek haematological advice because specific thrombophilias, e.g. antithrombin deficiency, merit higher doses of LMWH. See table 2.

### Table 2. Antenatal prophylactic and therapeutic doses of LMWH

<table>
<thead>
<tr>
<th>Prophylaxis</th>
<th>Dalteparin dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight 50-90 kg</td>
<td>5000 units daily</td>
</tr>
<tr>
<td>Body weight &lt;50kg</td>
<td>2500 units daily</td>
</tr>
<tr>
<td>&gt; 90kg or booking BMI &gt;30</td>
<td>5000 units 12 hourly</td>
</tr>
<tr>
<td>Higher prophylactic dose</td>
<td>5000 units 12 hourly</td>
</tr>
<tr>
<td>Therapeutic dose</td>
<td>90 units/kg 12 hourly</td>
</tr>
</tbody>
</table>

3. Women with inherited thrombophilia without previous VTE\(^2\)

- Risk varies depending upon the specific thrombophilia so a haematological opinion should be obtained.
- Postnatal thromboprophylaxis should be considered, especially in the presence of other risk factors even if antenatal prophylaxis has not been given.
- Antenatal and postnatal thromboprophylaxis should be given if:
  - Combined defects
  - Homozygous for defects
  - Antithrombin deficiency

4. Women with acquired thrombophilia (antiphospholipid syndrome, APS)\(^2\)

- A diagnosis of APS requires the presence of lupus anticoagulant or elevated anticardiolipin antibodies on 2 occasions 8 weeks apart combined with at least one of arterial or venous thrombosis, recurrent first trimester miscarriage, a later pregnancy loss or PET/IUGR requiring delivery before 35 weeks\(^3\)
- Women with APS and a past history of thrombosis should receive antenatal and postnatal thromboprophylaxis.
- Women with APS and an adverse past obstetric history should receive low dose aspirin from early pregnancy/prepregnancy.\(^4\) The value of LMWH is not yet clear and care should be individualised.
5. Women without previous VTE or thrombophilia²

- Women with two or more persisting risk factors should be considered for prophylactic LMWH for 7 days postnatally. (see Table 1)
- Women with three or more persisting risk factors should be considered for an extension of prophylaxis postnatally and possibly into the antenatal period. (see Table 1)
- All women with a BMI > 40 should be considered for LMWH thromboprophylaxis for 7 days after delivery, irrespective of mode of delivery.
- All women who have had an emergency caesarean section should be considered for 7 days of LMWH thromboprophylaxis.
- All women who have had an elective caesarean section, who have one or more additional risk factors should be considered for 7 days of LMWH thromboprophylaxis.

Timing and duration of thromboprophylaxis²

Antenatal

VTE has an equal distribution throughout pregnancy⁵ so if a decision is made for antenatal thromboprophylaxis this should start in early pregnancy unless the decision to treat is initiated by a new risk factor developing in later pregnancy. Those patients on once daily LMWH prophylaxis should continue once daily dosage until delivery. Higher prophylactic or therapeutic LMWH doses are given twice daily (due to increased metabolism in pregnancy) and should remain so until delivery (see Delivery section) All should be referred to the Combined Obstetric – Haematology Clinic or seek advice from Haematologist (email or telephone)
Check platelet count on Day 7 after starting thromboprophylaxis.

Delivery

- Standard once daily LMWH thromboprophylaxis:
  - Withhold at the onset of spontaneous labour
  - continue during prostaglandin induction of labour but withhold on the day of ARM or the onset of labour
  - Withhold on the day of elective caesarean section
- Therapeutic / higher prophylaxis twice daily LMWH:
  - withhold at the onset of spontaneous labour
  - halve the dose (continuing BD) the day before elective caesarean section and withhold on the morning of the operation
  - halve the dose (continuing BD) during prostaglandin induction of labour and withhold on the day of ARM or the onset of labour
- For women at high risk of both VTE and haemorrhage, switching to intravenous unfractionated heparin should be considered (5000 IU bolus, then infusion of 32000 IU in 24 hours with APTT at 4-6 hours, adjusting dose to ratio of 1.5-2.5 according to chart in RCH Anticoagulation Policy) Seek Haematologist advice.

Anaesthetic Issues

- Regional anaesthesia should not be administered until 12 hours after the previous prophylactic dose of LMWH or 24 hours after a therapeutic dose⁶
- Withhold first LMWH dose until 4 hours after insertion or removal of epidural or spinal. Remove catheter 12 hours after LMWH⁷
Postpartum

- Initiate thromboprophylaxis once the risk of bleeding has subsided (class 2 compression stockings or flowtron boots until then)
- Six weeks of thromboprophylaxis should be considered for high risk cases (three or more persisting risk factors)
- Early postpartum thromboprophylaxis should be considered for:
  - two current risk factors
  - Congenital thrombophilia (as a single risk factor) such as heterozygous factor V Leiden or heterozygous prothrombin gene variant where there is no past history of VTE
- All women should be counselled appropriately regarding ongoing increased risk for VTE up to 7 weeks post partum (increase hydration, encourage mobilisation and reporting any signs/symptoms of VTE to Community Midwife/Nurse or GP

Agents for thromboprophylaxis

1. Heparin

- LMWH is drug of choice although patients should be informed that it is not licensed for use in pregnancy
- Only use pre-filled syringes
- Anti-Xa levels are only required in highest risk women (eg antithrombin deficiency)
- Measure platelet count one week after initiating therapy
- Switch LMWH preparation or change to a heparinoid if allergic skin reactions occur
- LMWH is safe for breastfeeding and is usually preferred to warfarin in the puerperium

2. Aspirin

- Evidence for 75 mg aspirin as thromboprophylaxis is weak but should be considered when VTE risk is increased but insufficient for antenatal LMWH e.g. previous provoked VTE and no thrombophilia

3. Warfarin

- Avoid antenatally except for patients with metal heart valves and in some cases of antithrombin deficiency
- Safe for breastfeeding and a possible alternative for 6 week postpartum thromboprophylaxis. Initiate on 2nd or 3rd day post delivery and continue LMWH until INR > 2.0

4. Graduated elastic below knee compression stockings

- Class II: Antenatal and postpartum (6-12 weeks) if previous VTE or thrombophilia (obtain through the patient's primary care team). These are higher compression than class I (TEDS)
- Class I (TEDS): hospital inpatients and Long distance travel in pregnancy
RISK ASSESSMENT FOR VTE AND TREATMENT ALGORITHM. Adapted from RCOG guideline (2)

A) ANTENATAL ASSESSMENT AND MANAGEMENT

**HIGH RISK**
- Requires antenatal thromboprophylaxis with LMWH
- Refer to Obstetric Consultant and or Combined Obstetric-Haematology clinic

**INTERMEDIATE RISK**
- Consider antenatal thromboprophylaxis with LMWH.
- Refer to Obstetric Consultant and or Combined Obstetric-Haematology clinic for advice

**LOWER RISK**
- Mobilisation and avoidance of dehydration

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**RISK FACTORS**

**High Risk**
- Single previous VTE +
  - Thrombophilia or family history
  - Unprovoked/estrogen-related previous recurrent VTE (>1)
- Medical Comorbidities eg. Heart lung disease, SLE, cancer, surgical procedures, inflammatory conditions, nephritic syndrome, sickle cell disease etc.

**Intermediate Risk**
- Age > 35 years
- Obesity (BMI > 30)
- Parity >3
- Smoker
- Gross Varicose veins
- Current systemic infection
- Immobility (SPD/ Paraplegia, Long distance travel
- Pre-eclampsia
- Dehydration, hyperemesis,OHSS
- Multiple pregnancy or ART

**Lower Risk**
- 3 or more risk factors
- 2 or more if admitted
- < 3 risk factors
RISK ASSESSMENT FOR VTE AND TREATMENT ALGORITHM . Adapted from RCOG guideline (2)

B) POSTNATAL ASSESSMENT AND MANAGEMENT

- Any previous VTE +
- Anyone requiring antenatal LMWH

HIGH RISK
- Requires at least 6 weeks postnatal prophylactic LMWH
- Refer to Obstetric Consultant and or Combined Obstetric-Haematology clinic for postnatal follow up

INTERMEDIATE RISK
- At least 7 days postnatal prophylactic LMWH
- Consider extending thromboprophylaxis beyond 7 days if persisting or > 3 risk factors

- Caesarean section in labour
- Asymptomatic thrombophilia
- BMI > 40
- Prolonged hospital admission
- Medical Comorbidities eg. Heart lung disease, SLE, Cancer, inflammatory conditions, sickle cell disease, nephritic syndrome etc

- Age > 35 years
- Obesity (BMI > 30)
- Parity >3
- Smoker
- Elective Caesarean section
- Any surgical procedure in the puerperium
- Gross Varicose veins
- Current systemic infection
- Immobility (SPD/ Paraplegia, Long distance travel
- Pre-eclampsia
- Mid-cavity rotational operative delivery
- Prolonged labour (>24 hours)
- PPH > 1 litre or blood transfusion

LOWER RISK
- Mobilisation and avoidance of dehydration

2 or more risk factors

< 2 risk factors
References


