Worcestershire Acute Hospitals NHS Trust

Treatment of venous thromboembolism occurring in pregnancy

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Key Amendments

Date	Amendments	Approved by

Introduction

Venous thromboembolism (VTE) remains the leading cause of direct maternal death in the UK.

A national matched case–control study using the UK Obstetric Surveillance System (UKOSS) reported a total of 143 antenatal pulmonary embolisms between February 2005 and August 2006. This represents an estimated incidence of 1.3 per 10,000 maternities. Seventy per cent of women had identifiable classical risk factors for thromboembolic disease.

Clinical diagnosis of VTE in pregnancy is often difficult and only a small percentage of those suspected of having a VTE will actually have one when investigations are performed. However, since VTE is ten times more common in pregnancy and especially in the puerperium than out of pregnancy, it should always be suspected in women with symptoms and signs until proven otherwise.

Acute symptoms suggestive of thromboembolism in known high-risk women are an emergency and anticoagulation may be indicated before the diagnosis is clear.

NOTE: In any pregnant or post partum woman with a suspected diagnosis of VTE, treatment should be commenced prior to confirmation of the diagnosis unless the use of anti-coagulation is strongly contraindicated. In this situation immediate consultation with the consultant obstetrician and haematologist is necessary.

Diagnosis Of Deep Venous Thrombosis (DVT)

Clinical symptoms and signs

- Leg discomfort or pain (especially left leg)
- Increased temperature and oedema of affected leg
- Lower abdominal pain (iliac vein thrombosis)

Initial treatment

- Start anticoagulation (unless strongly contra-indicated: see above)
- Legs must be elevated to reduce the oedema.
- Fit graduated elastic compression stockings (TEDs).Encourage mobilisation with stockings

Investigations

- Blood tests- FBC, U & Es, LFTs, coagulation screen
  - Do not perform a thrombophilia screen: interpretation in pregnancy is difficult and is unlikely to affect the immediate management.
  - D-dimer testing should not be performed to diagnose acute VTE in pregnancy.
    In pregnancy, D-dimer can be elevated because of the physiological changes in the coagulation system and levels become ‘abnormal’ at term and in the postnatal period in most healthy pregnant women

- Compression duplex ultrasound
  - If ultrasound is positive: continue anticoagulation
  - If ultrasound is negative and clinical suspicion low: stop anticoagulation
  - If ultrasound is negative and clinical suspicion high: continue anticoagulation and repeat ultrasound in one week.
  - If repeat testing is negative, anticoagulant treatment should be discontinued.
- Magnetic resonance venography or conventional venography should be considered in cases of suspected iliac vein thrombosis. (Abdominal pain, back pain and swelling of the entire limb).

Diagnosis of Pulmonary Embolism (PE)

Clinical symptoms and signs

- The clinical features of PE encompass a spectrum from cardiovascular collapse to small emboli with few or no haemodynamic consequences.
- Symptoms: Faintness or collapse, central chest pain, severe dyspnoea, haemoptysis Exertional dyspnoea.
- Signs: Tachycardia, hypotension, ↑ JVP, cyanosis, On auscultation: Pleural rub, crackles

Initial treatment

Women with suspected PE emboli must be admitted and be commenced on anticoagulation before the diagnostic tests.

The management of women with life threatening massive PE is discussed separately

Investigations

- Blood tests- As discussed above with DVT.
- ECG
  - The commonest findings are - sinus tachycardia and anterior T-wave inversion
  - Larger emboli may cause right heart strain revealed by an $S_1Q_3T_3$ pattern And right bundle branch block
- Arterial blood gases
  - Arterial blood gases typically show a reduced PaO_2 and a normal or low $PaCO_2$, but are normal in a significant minority.
  - A metabolic acidosis may be seen in acute massive PE with cardiovascular collapse.
- Imaging techniques:
  - CXR **-** The radiation dose to the foetus at any stage of pregnancy is negligible Normal in over 50% of cases of PE. May demonstrate atelectasis, effusion, focal opacities or pulmonary oedema. May identify other disease processes (pneumonia, pneumothorax, cardiomyopathy. If the CXR is normal, decision for further imaging depends upon clinical suspision of PE.
  - The choice of technique for definitive diagnosis (V/Q scan or CTPA) will depend on local availability and should be made after discussion with a radiologist. If feasible, women should be involved in the decision making.
  - Women should be advised that V/Q scanning carries a slightly increased risk of childhood cancer (1 in 280,000) compared with CTPA (<1 in a million) but a lower risk of maternal breast cancer. There is an electronic consent form outlining in details the risks and benefits of both imaging techniques.
  - The advantages of CTPA- Better sensitivity and specificity; Lower radiation dose to the foetus. May identify other pathology (e.g. aortic dissection). The disadvantages are increased radiation dose to maternal breasts and missing of small peripheral PE.

- **If iodinated contrast media used during the pregnancy, neonatal thyroid function should be checked.** (Complete Antenatal paediatric referral.)
- If V/Q scan reported as "medium or high probability of PE": +/- leg Doppler studies are positive continue anticoagulation
- If V/Q scan reported as "low probability of PE" and leg Dopplers are negative: stop anticoagulation **unless there is a high clinical suspicion of PE.** In this situation, either continue anticoagulation and repeat V/Q and leg Dopplers in one week or perform a CTPA.

Treatment of VTE In Pregnancy

Inform the Consultant Obstetrician in cases of suspected or proven VTE in pregnancy and the puerperium.

In any pregnant or post partum woman with a suspected diagnosis of VTE, treatment should be commenced prior to confirmation of the diagnosis unless the use of anti-coagulation is strongly contraindicated. In this situation immediate consultation with the consultant obstetrician and haematologist is necessary.

First line treatment of choice is Low Molecular Weight Heparin (LMWH)

- LMWH does not cross the placenta. Compared with unfractionated heparin, LMWH less risk of thrombocytopenia, osteoporosis and haemorrhagic complications
- LMWH should be given in two subcutaneous divided doses with dosage titrated against the woman's booking (or most recent weight).
- The initial dose of enoxaparin (Clexane) is 1mg/kg sc TWICE DAILY

Table 1: Dose of Clexane

Weight	Dose
<50Kg	Yellow syringe 40mg sc b.d.
50 – 69Kg	Orange syringe 60mg sc b.d.
70 – 89 kg	Brown syringe 80mg sc b.d.
90 – 100 kg	Black syringe 100mg sc b.d.
>100kg	Discuss with Haematologist

- Routine measurement of peak anti-Xa activity for patients on LMWH is NOT necessary except in women at extremes of body weight (less than 50Kg or more than 90Kg) or with other complicating factors (eg renal impairment)
  - If LMWH requires monitoring, aim to achieve a peak anti-Xa level 3 hours post injection of 0.5-1.2 units/ml.
- In the event of an antenatal VTE, treatment with therapeutic doses of LMWH should be continued for the remainder of the pregnancy.
- Oral anticoagulants (eg warfarin) should be avoided antenatally as they cross the placenta.
- An individual management plan for the antenatal and postnatal period should be documented in the health records.

Management of labour and delivery

- Women should be advised that if they think they are in labour they should omit the next dose of LMWH and present to hospital to be assessed. (This should be documented in patient's handheld notes under management plan.)

  - If in labour, omit heparin until delivered and inform anaesthetist and obstetric consultant on call.
  - Epidural/spinal anaesthesia should not be administered within **24** hours of **treatment** doses of LMWH.

- If elective LSCS planned:
  - Stop **treatment** dose of LMWH 24 hours prior to LSCS and give **prophylactic** dose of LMWH (40mg) at 18:00 on the day prior to LSCS.
  - Inform anaesthetist
  - Inform consultant obstetrician on call
  - Check FBC and clotting on morning of LSCS (send urgently)
  - Regional analgesia/anaesthesia should not be administered within **24** hours of **treatment** doses of LMWH.
  - Consider placement of pelvic and rectus sheath wound drains and the use of interrupted skin sutures or staples for skin closure.
  - Low threshold for oxytocin infusion (40 units oxytocin in 500mls Sodium Chloride 0.9% over 4 hours) post delivery.
  - If IOL is planned:
    - Stop **treatment** dose of LMWH 24 hours prior to first prostin.
    - Give prophylactic dose of LMWH daily during IOL, ideally aiming to give last dose 12 hours prior to ARM.
    - Inform consultant obstetrician on call
    - Low threshold for oxytocin infusion (40 units oxytocin in 500mls Sodium Chloride 0.9%over 4 hours) post delivery.
- Regional analgesia/anaesthesia should not be administered within **24** hours of **treatment** doses of LMWH.
- Regional analgesia/anaesthesia should not be administered within **12** hours of **prophylactic** doses of LMWH.
- No LMWH should be given for at least 6 hours following siting or removal of epidural catheters or spinal analgesia.
- **Restarting treatment post delivery:**
  - Post LSCS/ vaginal delivery:
    - Give **thromboprophylactic dose** of LMWH 3 hours post operatively (6 hours after removal of epidural catheter or siting of spinal analgesia)
    - Re start **treatment dose** of LMWH that evening.
  - In patients at high risk of haemorrhage like placenta praevia, caesarean section after prolonged labour it is the consultant obstetrician's decision to change the treatment to unfractionated heparin after discussing with the haematologist.

Duration of Treatment and Follow Up

- The postnatal plan for treatment should be clearly documented in the hospital and handheld antenatal notes after liaising with the Haematologist.
- Any woman with an antenatal VTE should continue therapeutic dose anticoagulant therapy for the duration of the pregnancy and for at least 6 weeks postnatally and until at least 6 months treatment in total has been given.
- Women can be offered a choice of either continuing postnatal LMWH (at the antenatal dose) or commencing warfarin postnatally.
  - If commencing warfarin, the LMWH should be continued until the INR is greater than 2.0 on two successive days.
  - Must be made aware of the need for regular blood tests if on warfarin, aiming for an INR of 2.0-3.0. Refer to Trust Warfarin guideline (WAHT-HAE-002).
- Warfarin should not be commenced until at least three days after delivery in women at increased risk of postpartum haemorrhage.
- Neither warfarin nor LMWH are contraindicated in breast feeding.

- Any woman suffering from a DVT should be advised that the wearing of graduated elastic stockings for two years after the event will reduce the incidence of post-thrombotic syndrome.
- All women who have been diagnosed with VTE during pregnancy or postnatal period should have a follow up appointment 8-10 weeks by the Haematologist

Treatment of Massive Life Threatening Pulmonary Embolism

- Collapsed, shocked patients need immediate review by a team of experienced clinicians which should include the on call consultant obstetrician.
- Urgent involvement of the anaesthetic and medical teams should also be sought.
- **IV unfractionated heparin is the treatment of choice in massive PE with cardiovascular compromise. Refer to trust guidelines on unfractionated heparin infusion- WAHT-HAE-010**
- An urgent portable echocardiogram or CTPA within one hour of presentation should be arranged. If massive PE is confirmed, **immediate thrombolysis should be considered.**
- A multi-disciplinary approach to management should be made: Decisions regarding IV unfractionated heparin, thrombolysis, thoracotomy and surgical embolectomy require multi-speciality team management.

Alternatives to Clexane in special circumstances:

All unfractionated and low molecular weight heparins in the UK are derived from pigs. There are other alternatives if women can't accept the drugs derived from animal products.

For more information, see guideline (WAHT-PHA-015) - Animal derived medical products – trust guideline for patients who do not wish to receive medicines containing animal extracts.

Alternative to Clexane is Fondaparinux. This is not licensed for use in pregnancy. This can only be used after detailed discussion between the patient and the obstetrician. It is contra indicated in breast feeding.