Sultanate of Oman
Ministry of Health
The Royal Hospital
Department of Obstetrics and Gynecology

Code: OBG-CLN-GUD-39-Vers.2.0

Effective Date: 31/05/2022
Target Review Date: 31/05/2025

Title: THROMBOEMBOLISM IN PREGNANCY

1.0 Venous thromboembolism (VTE) remains one of the main direct causes of maternal death.

The risk of antenatal VTE is four to five folds higher in pregnant women than in non-pregnant women of the same age.

Venous thromboembolism can occur at any stage of pregnancy but the puerperium is the time of highest risk, with estimates of relative risk of approximately 20-fold **Diagnosis of Venous Thromboembolism in Pregnancy**

· Any woman with symptoms or signs suggestive of VTE should have objective testing immediately. Treatment with low-molecular-weight heparin (LMWH) should be given until the diagnosis is excluded by tests, unless treatment is strongly contraindicated.

· If Deep Vein thrombosis (DVT)remains untreated, 15–24% of these patients will develop Pulmonary embolism (PE).

· PE during pregnancy may be fatal in almost 15% of patients.

1.1 Investigations to diagnose Deep vein thrombosis (DVT)

· Compression duplex ultrasound should be undertaken where there is clinical suspicion of DVT

· If ultrasound is negative and there is a low level of clinical suspicion, anticoagulant treatment can be discontinued.

· If ultrasound is negative and a high level of clinical suspicion exists, anticoagulant treatment should be discontinued but the ultrasound should be repeated after 3- 7 days. If repeat testing is negative, no further treatment is required.

· When iliac vein thrombosis is suspected (back and buttock pain and swelling of the entire limb), Doppler ultrasound of the iliac vein, magnetic resonance venography or conventional contrast venography may be considered.

1.2 Investigations to diagnose acute pulmonary embolism (PE)

· Electrocardiogram (ECG) - the most common abnormalities are T wave inversion and right bundle branch block.

· Chest X-ray may be normal in 50% of the cases; however it may identify other pulmonary diseases like pneumonia or pneumothorax. Abnormal features caused by PE include atelectasis, effusion, focal opacities or pulmonary edema

· If the chest X-ray is abnormal with a clinical suspicion of PE, CT pulmonary angiography (CTPA) should be done in preference to a ventilation /perfusion (V/Q) scan.

· In the absence of symptoms and signs of DVT, a ventilation/perfusion (V/Q) lung scan or a computerized tomography pulmonary angiogram (CTPA) should be done.

· Alternative or repeat testing should be carried out where V/Q scan or CTPA is normal but the clinical suspicion of PE remains. Anticoagulant treatment should be continued until PE is definitively excluded.

· Compared with CTPA, V/Q scanning may carry a slightly increased risk of childhood cancer but is associated with a lower risk of maternal breast cancer; in both situations, the absolute risk is very small.

Ideally, informed consent should be obtained before these tests are undertaken.

· In women with suspected PE who also have symptoms and signs of DVT, compression duplex ultrasound should be performed. If compression ultrasonography confirms the presence of DVT, no further investigation is necessary and treatment for VTE should continue as anticoagulant therapy is the same for both.

· D-dimer testing should not be performed in the investigation of acute VTE in pregnancy. In pregnancy, there is a progressive rise in D-dimer levels with advancing gestational age. D-dimer levels are increased further in multiple pregnancies after caesarean section and in major postpartum haemorrhage and pre-eclampsia.

· Baseline blood investigations should be performed before initiating anticoagulant therapy - full blood count, coagulation screen, urea and electrolytes, and liver function tests.

2.0 Pregnant women diagnosed with acute venous thromboembolism should be hospitalized. In pregnant women with acute proximal leg deep vein thrombosis, the use of graded compression stockings can be considered for relief of symptoms

Treatment with low-molecular-weight heparin (LMWH) should be started immediately

LMWH should be given in doses based on the woman's booking or early pregnancy weight. This can be given once daily or in two divided doses. As a rough guide the dose can be calculated - (enoxaparin 1 mg/kg twice daily; dalteparin 100 units/kg twice daily)

Therapeutic dose of enoxaparin (clexane) -

Booking or early pregnancy weight	Initial dose of enoxaparin
< 50 kg	40 mg twice daily or 60 mg once daily
50–69 kg	60 mgms twice daily or 90 mg once daily
70–89 kg	80 mgms twice daily or 120 mg once daily
90–109 kg	100 mgms twice daily or 150 mg once daily
110–125 kg	120 twice daily or 180 mg once daily
> 125 kg	Discuss with haematologist

Therapeutic dose of dalteparin -

Booking or early pregnancy weight	Initial dose of dalteparin
< 50 kg	5000 iu twice daily or 10, 000 iu once daily
50–69 kg	6000 iu twice daily or 12, 000 iu once daily
70–89 kg	8000 iu twice daily or 16 000 iu once daily
90–109 kg	10 000 iu twice daily or 20 000 iu once daily
110–125 kg	12 000 iu twice daily or 24 000 iu daily
> 125 kg	Discuss with haematologist

Dose of tinzaparin (based on booking or early pregnancy weight): 175 units/kg once daily.

2.1 Monitoring while on LMWH

· Lower doses of LMWH should be employed if the creatinine clearance is less than 30 ml/min
· Routine measurement of peak anti-Xa activity for patients on LMWH for treatment of acute VTE in pregnancy or postpartum is not recommended except in women at extremes of body weight (less than 50 kg and 120 kg or more) or with renal impairment or recurrent VTE.
· Routine platelet count monitoring should not be carried out as the risk of HIT is low
· Obstetric patients who are postoperative and receiving unfractionated heparin should have platelet count monitoring performed every 2–3 days from days 4 to 14 or until heparin is stopped

2.2 Additional therapies

· In the initial management of DVT, the leg should be elevated and a graduated elastic compression stocking applied to reduce edema.
· Mobilization with graduated elastic compression stockings should be encouraged. Trials have shown that early ambulation, with leg compression, does not increase the risk of PE, does not increase thrombus propagation, and that pain and swelling improved faster compared to those patients who had their mobility restricted.
· Consideration should be given to the use of a temporary inferior vena cava filter in the peripartum period for patients with iliac vein VTE to reduce the risk of PE or in patients with proven DVT and who have recurrent PE despite adequate anticoagulation.

2.3 Maintenance treatment of VTE

· Treatment with therapeutic doses of subcutaneous LMWH should be continued during the remainder of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total.
· Women should be taught to self-inject LMWH and then can be managed as out - patients
· Pregnant women who have heparin allergy and require continuing anticoagulant therapy should be managed with an alternative anticoagulant after discussion with the hematologist, though the cross reactivity rate is 33%
· Because of their adverse effects on the fetus, vitamin K antagonists, such as warfarin, should not be used for antenatal VTE treatment
· Consideration can be given to the use of newer anticoagulants (fondaparinux, argatroban or hirudin) in women who are unable to tolerate heparin, though these drugs are not yet licensed for use in pregnancy.

3.0 Management of massive life-threatening PE in pregnancy and the puerperium

(Refer to guideline on maternal collapse)

Massive PE may present with collapse, shock, refractory hypoxaemia and/or right ventricular dysfunction on echocardiogram and is a medical emergency

Management should involve a multidisciplinary team including senior physicians, obstetricians and

radiologists

Women should be managed on an individual basis regarding intravenous unfractionated heparin, thrombolytic therapy, Thoracotomy and surgical embolectomy.

3.1 Immediate treatment in massive PE

· Intravenous unfractionated heparin is the preferred initial treatment in massive PE because of its rapid effect and since it can be adjusted more readily if thrombolytic therapy is administered.
· An urgent portable echocardiogram and CTPA within 1 hour of presentation should be arranged. If massive PE is confirmed, or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered.
· Maternal resuscitation should commence following the principles of ABC and if cardiac arrest occurs, cardiopulmonary resuscitation should be performed with the woman in a left lateral tilt.
· In massive life-threatening PE with haemodynamic compromise (or with limb- or life-threatening ischaemic complications from extensive iliofemoral vein thrombosis), thrombolytic therapy should be considered as anticoagulant therapy alone will not reduce the obstruction in the circulation.
· If the patient is not suitable for thrombolysis or is moribund, a discussion with the cardiothoracic surgeons with a view to urgent thoracotomy should be had

4.0 Anticoagulant therapy during labour and delivery

· When VTE occurs at term, consideration should be given to the use of intravenous unfractionated heparin which is more easily manipulated.
· Patients who are on LMWH should be advised that once she is in labor, she should not inject any further heparin.
· Where delivery is planned, either by elective caesarean section or induction of labour, LMWH maintenance therapy should be discontinued 24 hours prior to planned delivery.
· Subcutaneous unfractionated heparin should be discontinued 12 hours before and intravenous unfractionated heparin stopped 6 hours before induction of labour or regional anaesthesia.
· Regional anaesthetic or analgesic techniques should not be undertaken until at least 24 hours after the last dose of therapeutic LMWH.
· LMWH should not be given for at least 4 hours after the use of spinal anaesthesia or after the epidural catheter has been removed, and the epidural catheter should not be removed within 12 hours of the most recent injection.
· One option is to give a prophylactic dose of LMWH 4 hours postoperatively and the treatment dose recommenced 8 to 12 hours later.
· In patients receiving therapeutic doses of LMWH, wound drains (abdominal and rectus sheath) should be considered at caesarean section and closure of the skin incision with interrupted sutures to allow drainage of any haematoma.
· Any woman, who is considered to be at high risk of haemorrhage or may require a repeat surgical procedure, can be managed with intravenous unfractionated heparin until the risk factors for haemorrhage have resolved, as unfractionated heparin has a shorter half-life than LMWH and its activity is more completely reversed with protamine sulfate.

5.0 Postnatal anticoagulation

· Therapeutic anticoagulant therapy should be continued for the duration of the pregnancy and for at least 6 weeks postnatally and until at least 3 months of treatment has been given in total.
· Women should be offered a choice of LMWH or oral anticoagulant for postnatal therapy after discussion about the need for regular blood tests for monitoring of warfarin, particularly during the first 10 days of treatment.
· Postpartum warfarin should be avoided until at least the fifth day and for longer in women at increased risk of postpartum haemorrhage.
· Testing of the international normalized ratio (INR) is recommended during the transfer from LMWH to warfarin to avoid over-anticoagulation.
· The INR should be checked on day three of warfarin treatment and subsequent warfarin doses titrated to maintain the INR between 2.0 and 3.0; heparin treatment should be continued until the INR is greater than 2.0

for at least 24 hours.
· Women should be reassured that neither heparin nor warfarin is contraindicated in breastfeeding.
· Following a DVT, graduated elastic compression stockings should be worn on the affected leg to reduce pain and swelling.

6.0 Postnatal review and follow up

Patients who develop VTE during pregnancy or the puerperium should be given a follow up appointment with Hematologists at the time of discharge

Thrombophilia testing should be performed once anticoagulant therapy has been discontinued only if it is considered that the results would influence the woman's future management**.**

Referances

- Thromboembolic Disease in Pregnancy and the Puerperium: Acute Management RCOG, Green-top Guideline No. 37b April 2015**.**
- ACOG practice bulletin No 196, Thromboembolism in Pregnancy - 2018

Written By: DR CHITRA JHA
Checked By: OBG PROTOCOL GROUP
Authorized by: ALYA YOUSUF ABDULLAH AL MADHANI