

Prevention and management of venous thromboembolism in pregnancy

Venous thromboembolism, including deep vein thrombosis, pulmonary embolism and cerebral venous sinus thrombosis, is a major cause of morbidity and mortality in pregnancy and the postpartum period (Greer, 2015). The most recent Confidential Enquiries into Maternal Deaths identified 48 deaths from venous thromboembolism during pregnancy or up to 6 weeks postpartum in the period 2009–13. The mortality rate from venous thromboembolism is 1 in 100 000 maternities, which makes it the leading direct (pregnancy-specific) cause of maternal death in the UK (Nelson-Piercy, 2015). For every death, there are 100–200 pregnancies complicated by a non-fatal venous thromboembolism, so the overall maternal incidence of venous thromboembolism is 1–2 cases per 1000 pregnancies (Greer, 2015).

The relative risk of antenatal venous thromboembolism is approximately 5-fold higher than non-pregnant age-matched women, and 20-fold higher in the postpartum period (Greer, 2012).

Pregnancy increases the risk of venous thromboembolism because of a combination of the following factors (Hunt and Greaves, 2011):

- Raised intra-abdominal pressure and vascular compression from the gravid uterus
- Physiological changes in coagulation factors (increased levels of factor VIII and fibrinogen, reduced levels of protein S)
- Suppressed systemic fibrinolytic capacity
- Tissue damage at the time of delivery (increased risk related to caesarean section).

Additional risk factors increase the likelihood of venous thromboembolism for particular women and this forms the basis for risk stratification. The Confidential Enquiries into Maternal Deaths found that >80% of the women who died from venous thromboembolism in 2009–13 had recognizable risk factors for venous thromboembolism (Nelson-Piercy, 2015). The risk for venous thromboembolism increases with gestational age, reaching a maximum just after delivery. However, a significant proportion of fatal antenatal events occur in the first trimester, so appropriate thromboprophylaxis should begin early in pregnancy (Royal College of Obstetricians and Gynaecologists, 2015a).

This article summarizes the current evidence-based guidelines (Green-top guidelines) from the Royal College of Obstetricians and Gynaecologists for prevention and management of venous thromboembolism in pregnancy and the puerperium (2015a,b).

Prevention of venous thromboembolism in pregnancy and the postpartum period

The keys to prevention of venous thromboembolism in pregnancy are (Nelson-Piercy, 2015; Royal College of Obstetricians and Gynaecologists, 2015a):

1. Risk assessment: documentation of risk factors for venous thromboembolism for all women pre-pregnancy or in early pregnancy, repeated if the woman is admitted to hospital or develops intercurrent problems. It is very important that the risk assessment is repeated again intrapartum or immediately postpartum

2. Thromboprophylaxis: administration of low molecular weight heparin for women at risk of venous thromboembolism. Prescriptions for the full treatment course should be provided by secondary care
3. Specialist antenatal clinics: review of selected high risk women throughout pregnancy.

Who is at risk of venous thromboembolism and should receive thromboprophylaxis?

Tables 1 and 2 summarize the risk factors considered in the Royal College of Obstetricians and Gynaecologists (2015a) guideline for women during pregnancy (*Table 1*) and the postpartum period (*Table 2*). These stratify women into high, intermediate and low risk groups, with subsequent recommendations for thromboprophylaxis. An assessment must be performed and documented at booking, again if new problems develop or on admission to hospital and then again on the delivery suite. A numerical scoring checklist in the guideline can assist.

Following the decision to use thromboprophylaxis, refer to hospital guidelines for which low molecular weight heparin preparation to use. *Table 3* gives a guide to dosing. Remember, doses should be reduced in women with renal impairment.

What about thrombophilia?

Thrombophilia refers to laboratory-detected abnormalities of the haemostatic system that predispose to thrombosis. Certain inherited and acquired conditions have been identified, which can be tested for in a 'thrombophilia screen' (*Table 4*). The British Committee for Standards in Haematology guidelines recommend that most women with a previous unprovoked, pregnancy or combined oral contraceptive-related venous thromboembolism should receive thromboprophylaxis on clinical risk alone, so testing for heritable thrombophilia is not required (Baglin et al, 2010).

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Table 1. Antenatal risk assessment and management with thromboprophylaxis

Risk factor	Risk category	Management
Previous venous thromboembolism (except single venous thromboembolism provoked by major surgery)	High risk	Requires low molecular weight heparin prophylaxis throughout pregnancy
Any one of the following risk factors: <ul style="list-style-type: none"> ■ Hospital admission ■ Single venous thromboembolism provoked by major surgery ■ High risk thrombophilia ■ Medical comorbidities* ■ Any surgical procedure ■ Ovarian hyperstimulation syndrome 	Intermediate risk	Consider low molecular weight heparin prophylaxis throughout pregnancy
Consider the following risk factors: <ul style="list-style-type: none"> ■ Obesity (body mass index >30 kg/m²) ■ Age >35 years ■ Parity ≥ 3 ■ Smoker ■ Symptomatic varicose veins ■ Pre-eclampsia ■ Significant immobility, e.g. as a result of pelvic girdle pain ■ Family history of either unprovoked venous thromboembolism or oestrogen-provoked venous thromboembolism in first-degree relative ■ Low-risk thrombophilia ■ Multiple pregnancy ■ In vitro fertilisation (IVF) or assisted reproductive technology 	Four or more risk factors from this list manage like intermediate risk	Consider low molecular weight heparin prophylaxis throughout pregnancy
	Three risk factors from this list – manage like intermediate risk but delayed start to thromboprophylaxis	Low molecular weight heparin prophylaxis from 28 weeks gestation
	Fewer than three risk factors from this list = lower risk	Advise keep mobile and avoid dehydration
Transient risk factors <ul style="list-style-type: none"> ■ Admission with dehydration/hyperemesis/systemic infection ■ Ovarian hyperstimulation syndrome ■ Long-distance travel (>4 hours) if additional risk factors 	Transient venous thromboembolism risk	Transient low molecular weight heparin prophylaxis for duration of risk factor; for ovarian hyperstimulation syndrome duration first trimester

*Adapted from Royal College of Obstetricians and Gynaecologists (2015a) Green-top guideline number 37a. *including: cancer, heart failure, inflammatory bowel disease, systemic lupus erythematosus, inflammatory polyarthropathy, nephrotic syndrome, type 1 diabetes with nephropathy, sickle cell disease, intravenous drug use*

In the circumstances below, specific investigation is recommended because the results change clinical management in pregnancy:

1. Personal history of unprovoked venous thromboembolism – test for antiphospholipid antibodies
2. Personal and family history of venous thromboembolism – test for antithrombin deficiency.

The identification of antiphospholipid antibodies or antithrombin deficiency in women with a previous venous thromboembolism should guide an increased dose of thromboprophylaxis to 50–75% of the full treatment dose of low molecular weight heparin (Royal College of Obstetricians and Gynaecologists, 2015a).

In addition, the British Committee for Standards in Haematology guidelines recommend consideration of heritable

thrombophilia screening in pregnant women with no personal history of venous thromboembolism but a family history of either unprovoked, pregnancy, combined oral contraceptive or minor risk factor-provoked venous thromboembolism in a first-degree relative under 50 years of age (considering the result will be more informative if the affected relative has a known thrombophilia) (Baglin et al, 2010). *Table 4* can be used in conjunction with *Tables 1* and *2* to guide which of these women should receive thromboprophylaxis.

How should women on long-term anticoagulation be treated during pregnancy?

The Royal College of Obstetricians and Gynaecologists guidelines state that women already on long-term oral anticoagulation for previous venous thromboembolism

should be counselled about the risks of these medications to the fetus and changed to treatment with low molecular weight heparin as soon as possible and before 6 weeks’ gestation. Warfarin should not be used in pregnancy because it crosses the placenta and is associated with adverse pregnancy outcomes, but can be used in the postpartum period and is safe when breastfeeding. The direct oral anticoagulants (e.g. rivaroxaban) are not recommended in pregnancy or when breastfeeding (Royal College of Obstetricians and Gynaecologists, 2015a).

Women receiving anticoagulation for venous thromboembolism and known to have antithrombin deficiency should also be considered for antithrombin replacement at initiation of labour or before caesarean section (Rogenhofer et al, 2014). These decisions should be made in collaboration with a haematologist.

Table 2. Postnatal risk assessment and management with thromboprophylaxis

Risk factor	Risk category	Management
Any one of the following risk factors: <ul style="list-style-type: none"> ■ Any previous venous thromboembolism ■ Any woman requiring antenatal low molecular weight heparin (see Table 1) ■ High risk thrombophilia ■ Low-risk thrombophilia and family history of venous thromboembolism 	High risk	At least 6 weeks postnatal low molecular weight heparin prophylaxis
Any one of the following risk factors: <ul style="list-style-type: none"> ■ Emergency caesarean section ■ Body mass index >40 kg/m² ■ Readmission or prolonged admission (≥3 days) in the puerperium ■ Any surgical procedure in the puerperium except immediate repair of the perineum ■ Medical comorbidities* 	Intermediate risk	At least 10 days postnatal low molecular weight heparin prophylaxis If persisting or more than three risk factors consider 6 weeks low molecular weight heparin prophylaxis
Considering the following risk factors: <ul style="list-style-type: none"> ■ Elective caesarean section ■ Preterm delivery (<37 weeks) ■ Mid-cavity rotational or operative delivery ■ Prolonged labour (>24 hours) ■ Postpartum haemorrhage >1 litre or blood transfusion required ■ Stillbirth ■ Obesity (body mass index >30 kg/m²) ■ Age >35 years ■ Parity ≥ 3 ■ Smoker ■ Symptomatic varicose veins ■ Pre-eclampsia ■ Family history of venous thromboembolism ■ Significant immobility, e.g. as a result of pelvic girdle pain, long-distance travel (>4 hours) ■ Low-risk thrombophilia ■ Multiple pregnancy ■ Systemic infection 	Two or more risk factors from this list = intermediate risk	At least 10 days postnatal low molecular weight heparin prophylaxis If persisting or more than three risk factors consider 6 weeks low molecular weight heparin prophylaxis
	One risk factor from this list = lower risk	Advise early mobilization and avoidance of dehydration

*Adapted from Royal College of Obstetricians and Gynaecologists (2015a) Green-top guideline number 37a. *including: cancer, heart failure, inflammatory bowel disease, systemic lupus erythematosus, inflammatory polyarthropathy, nephrotic syndrome, type 1 diabetes with nephropathy, sickle cell disease, intravenous drug use*

Acute management of venous thromboembolism in pregnancy and the postpartum period

Suspect an acute venous thromboembolism in women who present with any of the following clinical symptoms or signs

during pregnancy or the postpartum period (Nelson-Piercy, 2015).

Deep vein thrombosis

■ Unilateral leg pain or swelling (85% of cases affect the left leg; Greer, 2015)

- Unilateral leg erythema or oedema
- Iliac fossa, groin or buttock pain (may occur along with whole leg swelling in iliac vein thrombosis)
- Lower abdominal pain (as a result of extension of thrombus into pelvic vessels and/or development of collateral circulation).

Table 3. Low molecular weight heparin thromboprophylaxis – guide to dosing

Type of low molecular weight heparin	Weight				
	<50 kg	50–90 kg	91–130 kg	131–170 kg	>170 kg
Enoxaparin	20 mg	40 mg	60 mg	80 mg	0.6 mg/kg/day
Tinzaparin	3500 units	4500 units	7000 units	9000 units	75 units/kg/day
Dalteparin	2500 units	5000 units	75 000 units	10 000 units	75 units/kg/day

Reproduced from Royal College of Obstetricians and Gynaecologists (2015a) Green-top guideline number 37a.

Pulmonary embolism

- Dyspnoea (typically sudden onset)
- Chest pain (typically sudden onset)
- Haemoptysis
- Dizziness
- Syncope
- Collapse
- Tachycardia
- Hypoxia.

Table 4. 'High risk' and 'low risk' heritable and acquired thrombophilia

	High risk	Low risk
Heritable thrombophilia	Antithrombin deficiency	Heterozygous factor V Leiden
	Protein C deficiency	Heterozygous prothrombin gene mutation
	Protein S deficiency	
	Compound or homozygous for low risk thrombophilia	
Acquired thrombophilia	Antiphospholipid syndrome (previous venous thromboembolism with persistent antiphospholipid antibodies)	Asymptomatic antiphospholipid antibodies

Adapted from Royal College of Obstetricians and Gynaecologists (2015a) Green-top guideline number 37a.

It can be difficult to distinguish symptoms of venous thromboembolism from those related to pregnancy itself (e.g. increased shortness of breath). Pregnant and postpartum women presenting to accident and emergency with medical problems should be discussed with a member of the obstetrics team (Nelson-Piercy, 2015). It is preferable to have a high index of suspicion and rule out or confirm venous thromboembolism by objective measurements than to miss the diagnosis.

Cerebral venous sinus thrombosis

Consider cerebral venous sinus thrombosis in a pregnant woman presenting with clinical features of raised intracranial pressure (including headache, vomiting, visual disturbance, impaired consciousness), focal neurological signs or seizures. Additionally, a pregnancy test is crucial in the diagnostic work-up of any woman of child-bearing age presenting with cerebral venous sinus thrombosis. Investigation for cerebral venous sinus thrombosis is by brain imaging (magnetic resonance imaging or computed tomography venogram) decided in conjunction with a radiologist (Sapoznik et al, 2011).

What should you do if you suspect an acute venous thromboembolism?

Massive pulmonary embolism

If a pregnant woman presents with hypotension or refractory hypoxaemia, a massive life-threatening pulmonary embolism may be implicated and immediate action must be taken to establish the diagnosis and treat. Call for help from the experienced senior medical and anaesthetic teams and the on-call consultant obstetrician. An urgent computed tomography

pulmonary angiogram (CTPA) or portable echocardiogram is needed to look for right ventricular dysfunction. In a peri-arrest situation, consider thrombolysis before confirming the diagnosis on imaging. A case-by-case decision should be made about the treatment options for massive pulmonary embolism (Royal College of Obstetricians and Gynaecologists, 2015b):

Intravenous unfractionated heparin: This is the preferred initial treatment in massive pulmonary embolism (without hypotension) because of its rapid onset of action, and the ability to adjust around thrombolysis if required.

- Dose: bolus intravenous dose (80 units/kg) followed by continuous infusion (18 units/kg/hour) (Royal College of Obstetricians and Gynaecologists, 2015b).
- Follow your hospital protocol, and monitor the activated partial thromboplastin time (APTT) ratio.

Thrombolysis: This is needed if there is haemodynamic compromise (hypotension) because anticoagulation alone will not reduce circulatory obstruction (Royal College of Obstetricians and Gynaecologists, 2015b). There is a risk of maternal haemorrhage, a theoretical risk of fetal haemorrhage, and the possibility of premature separation of the placenta in the first 18 weeks of pregnancy (Joint Formulary Committee, 2016). After thrombolysis start an unfractionated heparin infusion (without the loading dose) (Royal College of Obstetricians and Gynaecologists, 2015b).

- Dose: refer to local trust protocol and the British National Formulary for dosing of individual thrombolytic agents. For example – alteplase: 10 mg by intravenous

injection over 1–2 minutes, followed by intravenous infusion of 90 mg over 2 hours (maximum 1.5 mg/kg in patients <65 kg) (Joint Formulary Committee, 2016).

Thrombolysis should also be considered for life- or limb-threatening ischaemic complications from extensive iliofemoral vein thrombosis (Royal College of Obstetricians and Gynaecologists, 2015b).

Thoracotomy and surgical embolectomy: These should be considered if the patient is not suitable for thrombolysis (Royal College of Obstetricians and Gynaecologists, 2015b).

Non-massive pulmonary embolism and deep vein thrombosis

The Royal College of Obstetricians and Gynaecologists guidelines (2015b) recommend treatment of a suspected non-massive pulmonary embolism or deep vein thrombosis with therapeutic dose low molecular weight heparin until the diagnosis is excluded by objective investigation, unless there is a strong contraindication to anticoagulation.

The diagnostic test for deep vein thrombosis is compression duplex ultrasound (Royal College of Obstetricians and Gynaecologists, 2015b). If there is a high clinical suspicion of a deep vein thrombosis but the ultrasound is negative, stop low molecular weight heparin and perform serial compression ultrasound on days 3 and 7 to safely exclude deep vein thrombosis (Chan et al, 2013; Royal College of Obstetricians and Gynaecologists, 2015b). Owing to the extensive nature, iliac vein thrombosis can often be diagnosed on compression ultrasound; however, if clinically suspected and ultrasound is negative, further investigation by Doppler ultrasound of the iliac vein or magnetic resonance venography should be considered (Bates et al, 2012).

If a pulmonary embolism is suspected, the following investigations should be carried out urgently (Royal College of Obstetricians and Gynaecologists, 2015b):

- Electrocardiogram – look for T wave inversion, S1Q3T3 pattern, right bundle-branch block
- Chest X-ray – to establish an alternative diagnosis and direct the most appropriate further chest imaging
- Bilateral compression duplex ultrasound (particularly if clinical features of deep vein thrombosis)

Table 5. Radiation dose to fetus and pregnant breast tissue of CT pulmonary angiogram and ventilation/perfusion scans

	CT pulmonary angiogram	Ventilation/perfusion (V/Q) scan
Effects on the fetus*	Radiation dose 0.1 mGy Childhood cancer risk low (estimated 1 in 170 000)	Radiation dose 0.5 mGy Childhood cancer risk low but higher than CT pulmonary angiogram (estimated 1 in 34 000) The ventilation component can be omitted (Q scan), which minimizes the radiation dose
Effects on the pregnant woman	Radiation dose 20 mGy Increased risk of breast cancer (absolute increased risk 0.01–0.02%); higher in younger women Reduce dose by use of bismuth shields	Radiation dose 0.2–1 mGy Consider as first-line investigation if chest X-ray normal and particularly if the patient has had a previous CT scan or there is a family history of breast cancer

*Radiation exposure from both scans is well below threshold for teratogenicity, fetal death and growth restriction. Adapted from Royal College of Obstetricians and Gynaecologists (2015b) Green-top guideline 37b. CT = computed tomography.

Table 6. Low molecular weight heparin treatment – guide to dosing

Type of low molecular weight heparin	Early pregnancy weight				
	<50 kg	50–69 kg	70–89 kg	90–109 kg	110–125 kg
Enoxaparin (OD)	60 mg	90 mg	120 mg	150 mg	180 mg
Enoxaparin (BD)	40 mg BD	60 mg BD	80 mg BD	100 mg BD	120 mg BD
Tinzaparin (OD)	175 units/kg	175 units/kg	175 units/kg	175 units/kg	175 units/kg
Dalteparin (OD)	10000 units	12000 units	16000 units	20000 units	24000 units
Dalteparin (BD)	5000 units BD	6000 units BD	8000 units BD	10000 units BD	12000 units BD

BD = twice daily; OD = once daily. Reproduced from Royal College of Obstetricians and Gynaecologists (2015b) Green-top guideline number 37b.

should be considered, and discussed with the patient. Computed tomography pulmonary angiogram is often more readily available and can detect alternative lung pathology, whereas V/Q scanning has a higher negative predictive value (Royal College of Obstetricians and Gynaecologists, 2015b). The radiation doses of both scans and the associated risks are shown in *Table 5*. Be honest about the risks but provide reassurance that these are low so appropriate investigation can take place. If the initial computed tomography pulmonary angiogram or V/Q scan is normal but there is a high clinical suspicion of a pulmonary embolism, continue anticoagulation while pulmonary embolism is excluded by repeat or alternative V/Q scanning or computed tomography pulmonary angiogram.

What is the treatment of venous thromboembolism in pregnancy?

Low molecular weight heparin is the treatment of choice for anticoagulation during pregnancy (Royal College of Obstetricians and Gynaecologists, 2015b). Refer to your hospital guidelines for the low molecular weight heparin preparation to use in your trust (*Table 6* can be used for guidance). There is insufficient evidence to recommend twice daily over once daily dosing (Royal College of Obstetricians and Gynaecologists, 2015b). Calculate the dose with the booking or early pregnancy weight, and adjust in the case of renal impairment.

Anti-Xa level monitoring is not routine, but is recommended in the following circumstances (Royal College of Obstetricians and Gynaecologists, 2015b):

- Weight <50 kg or >90 kg
- Renal impairment
- Recurrent venous thromboembolism despite anticoagulation.

If indicated, a ‘peak’ anti-Xa level should be taken 4 hours after low molecular weight heparin. Discuss the results with a haematologist for advice on dose adjustments.

For cerebral venous sinus thrombosis, the British Committee for Standards in Haematology guidelines recommend commencing therapeutic dose low molecular weight heparin, unless anticoagulation is contraindicated. Importantly, intracranial haemorrhage associated with cerebral venous sinus thrombosis is not a contraindication to anticoagulation, based on a systematic review that showed treatment benefit and no new symptomatic intracranial haemorrhage in

- Ventilation/perfusion (V/Q) scan (if chest X-ray normal) or computed tomography pulmonary angiogram.

If a deep vein thrombosis is identified, diagnosis of pulmonary embolism can be assumed based on clinical features, avoiding V/Q or computed tomography pulmonary angiogram scanning with higher associated radiation risks, because these additional tests will not change anticoagulation management. A negative ultrasound does not rule out a diagnosis of pulmonary embolism, and a V/Q scan or computed tomography pulmonary angiogram will be required (Royal College of Obstetricians and Gynaecologists, 2015b).

What are the risks of chest imaging for a pregnant woman and the fetus?

It is important to note the low rates of pulmonary embolism diagnosis (of 1.4–4.2%) in women investigated by computed

tomography pulmonary angiogram or V/Q scanning (Goodacre et al, 2015). Standard methods of venous thromboembolism exclusion in non-pregnant patients (e.g. with a pre-test Wells score and D-dimer assay) have not been validated in pregnancy, so radiological investigation is needed in all suspected cases (Nelson-Piercy, 2015). Clinical judgement is crucial so that investigation in unselected low risk women does not result in more harm than benefit.

The estimated individual background radiation exposure in the UK over a 1-year period is 2.7 mSv (Public Health England, 2011), which is the equivalent of a dose of radiation of 2.7 mGy. A chest X-ray exposes a fetus to a negligible level of radiation (0.01 mSv) (Royal College of Obstetricians and Gynaecologists, 2015b). The radiation exposure of computed tomography pulmonary angiogram and V/Q scanning are higher and the advantages and disadvantages

anticoagulated patients. In a patient with extensive cerebral venous sinus thrombosis that is likely to be fatal or not responding to anticoagulation, thrombolysis should be considered, and if there is impending cerebral herniation surgical decompression should be considered (Tait et al, 2012).

What is the duration of anticoagulation?

The Royal College of Obstetricians and Gynaecologists (2015b) guidelines recommend the following:

- Treatment with low molecular weight heparin should continue for the remainder of pregnancy and at least 6 weeks postnatally or 3 months in total, whichever is longer
- Offer the choice of continuing low molecular weight heparin or switching to warfarin after day 5 postpartum (or longer in women at increased risk of postpartum haemorrhage)
- Assess the continuing risk of thrombosis before anticoagulation is stopped, ideally at a postnatal review, where the need for thromboprophylaxis in any future pregnancy should also be discussed.

Is there a role for inferior vena cava filters?

The purpose of inferior vena cava filter insertion is prevention of pulmonary embolism in a patient with a venous thrombosis and contraindication to anticoagulation (Baglin et al, 2006). Consider in the following situations, in line with Royal College of Obstetricians and Gynaecologists and British Committee for Standards in Haematology guidelines (Baglin et al, 2006; Royal College of Obstetricians and Gynaecologists, 2015b):

1. Acute extensive deep vein thrombosis or iliac vein thrombosis diagnosed within 2 weeks of delivery (meaning anticoagulation will need to be interrupted)
2. Absolute contraindication to anticoagulation (e.g. significant bleeding complications)
3. Recurrent pulmonary embolism and proven deep vein thrombosis despite adequate anticoagulation (see previous section on treatment of venous thromboembolism for guidance on anti-Xa monitoring to ensure adequate anticoagulation). Continue low molecular weight heparin after inferior vena cava filter insertion if there is no contraindication.

Discuss each case with a haematologist and ensure there is a plan for filter retrieval when no longer required, preferably within 3 months. The potential adverse effects of inferior vena cava filters, including filter migration, increased risk of lower limb and vena cava thrombosis, and infection (Baglin et al, 2006) need to be taken into account when weighing up benefits and risks on a case-by-case basis.

Managing thromboprophylaxis and anticoagulation at the time of delivery

At the time of delivery the benefit of thromboprophylaxis and anticoagulation for prevention and treatment of venous thromboembolism must be weighed up against the risk of haemorrhage. The Royal College of Obstetricians and Gynaecologists (2015b) guidelines include the following recommendations.

When should low molecular weight heparin thromboprophylaxis be stopped?

- Advise women not to inject any further doses if they have any vaginal bleeding or once labour begins
- In cases of elective caesarean section, thromboprophylaxis should be continued until the day before delivery
- Avoid regional anaesthesia until ≥ 12 hours after the last dose of prophylactic low molecular weight heparin.

When should low molecular weight heparin thromboprophylaxis be restarted after delivery?

The puerperium is the time of highest risk of venous thromboembolism (20-fold relative risk compared to age-matched controls), therefore appropriate re-commencement of thromboprophylaxis is imperative.

- The first dose of prophylactic low molecular weight heparin should be given as soon as possible after delivery provided there is no postpartum haemorrhage
- Low molecular weight heparin should not be given for 4 hours after regional anaesthesia or removal of an epidural catheter
- Women at high risk of haemorrhage should be managed initially with mechanical thromboprophylaxis (e.g. anti-embolism stockings) and low molecular weight heparin restarted when the risk of haemorrhage has reduced.

KEY POINTS

- Venous thromboembolism remains the leading cause of direct maternal death in the UK.
- The risk of venous thromboembolism is highest in the postpartum period.
- The aim of risk assessment and appropriate use of thromboprophylaxis is to reduce maternal morbidity and mortality from venous thromboembolism.
- Antenatal risk assessment should be dynamic and repeated at time of delivery.
- If symptoms and signs are concerning for deep vein thrombosis or pulmonary embolism, treat with low molecular weight heparin while objective investigations are urgently organized.
- Clinical presentation with a possible massive pulmonary embolism needs urgent investigation and treatment with immediate involvement of the senior medical team, anaesthetists and consultant obstetrician.
- A clear birth plan should be agreed including advice to stop low molecular weight heparin injections once labour begins.
- Thromboprophylaxis should be restarted as soon as possible after delivery (special consideration is needed in cases of postpartum haemorrhage and epidural/regional anaesthesia).

How should therapeutic anticoagulation be managed during labour and delivery?

- Women should be advised not to inject any further doses when labour commences
- Treatment dose low molecular weight heparin should be stopped 24 hours before elective caesarean section or induction of labour
- If venous thromboembolism occurs at term, use of intravenous unfractionated heparin should be considered, because of the shorter half-life and reversibility with protamine sulphate. This should be stopped 6 hours before induction of labour or regional anaesthesia
- Regional anaesthesia should not be given until ≥ 24 hours after the last treatment dose of low molecular weight heparin
- Removal of an epidural catheter should be ≥ 12 hours after low molecular weight heparin and anticoagulation not restarted until ≥ 4 hours after epidural catheter removal or spinal anaesthesia

■ Following caesarean section, a prophylactic dose of low molecular weight heparin should be given 4 hours postoperatively (taking into account regional anaesthesia as above) and treatment dose restarted 8–12 hours later

Conclusions

Venous thromboembolism is a largely preventable principal cause of pregnancy-related maternal death. Key factors that will reduce morbidity and mortality are recognition of the risk of venous thromboembolism, administration of low molecular weight heparin thromboprophylaxis for women who are at risk and timely acute management of women during pregnancy and the postpartum period who present with symptoms of a possible venous thromboembolism. **BJHM**

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