Background

Pregnancy increases the risk of venous thromboembolism (VTE) but the true incidence is unknown. The risk of VTE continues in the post-partum period and is probably higher than during pregnancy.

Anticoagulant therapy during pregnancy

The use of anticoagulants during pregnancy is problematic because of the potential side effects to the mother and the foetus. Warfarin crosses the placenta and can cause bleeding and embryopathy. Therefore, warfarin should generally be avoided during pregnancy. Unfractionated heparin (UFH) and low molecular weight heparin (LMWH) do not cross the placenta and appear safe for the foetus but must be administered parenterally. Side effects of heparin include bleeding, thrombocytopenia and osteoporosis. The potential for bleeding in the mother treated with UFH or LMWH is low and does not appear to be different from that reported in non-pregnant patients. LMWH probably causes less osteoporosis and thrombocytopenia than UFH. UFH, LMWH and warfarin are safe for the breast-fed infant when administered to the nursing mother.

Treatment of acute VTE during pregnancy

Women developing VTE during pregnancy require special attention and should be referred to a specialised care centre. There are two therapeutic options: UFH and LMWH.

LMWH is usually the preferred option and is initiated at a therapeutic dose and maintained throughout pregnancy. In non-pregnant patient, routine monitoring of LMWH, using anti-factor Xa levels, is not recommended. In pregnancy, the pharmacokinetics of heparin may differ, and monitoring of anti-factor Xa levels should be considered as the pregnancy progresses although supporting data are lacking about the utility of this approach.

UFH is usually initiated with an intravenous (I.V.) bolus of 5,000 U followed by a maintenance dose administered as a continuous I.V. infusion of 30,000 to 36,000 U per 24 hours in order to prolong the activated partial thromboplastin time (aPTT) into the therapeutic range. After initial I.V. treatment for 5-7 days, the patient should receive therapeutic doses of subcutaneous (s.c.) LMWH or s.c. UFH for the remainder of the pregnancy. If UFH is used, the total daily infusion dose is divided and given every 12 hours, with adjustment to maintain the aPTT (drawn 4 to 6 hours after injection) in the therapeutic range.

Anticoagulation should be continued for 4 to 6 weeks after delivery, and for a minimum duration of 3 to 6 months. Warfarin can be used after the delivery since it is safe for the breast-fed infant of a warfarin-treated mother. Screening for underlying thrombophilia is also suggested.

Previous VTE

Until recently the optimal management of pregnant patients with previous VTE was controversial because the true incidence and timing of recurrence during pregnancy were unknown. A recent study enrolled pregnant patients with one prior episode of VTE and demonstrated that the risk of recurrence was low in patients without thrombophilia if their previous VTE was associated with a transient risk factor. Routine prophylaxis during pregnancy is therefore not justified for these patients. For patients with either an idiopathic VTE or a secondary VTE associated with thrombophilia, the risk of recurrence is probably higher and management needs to be individualised until further studies are available. Women with a prior idiopathic VTE and thrombophilia should probably receive UFH or LMWH during pregnancy.

Asymptomatic thrombophilia

The prevention of thrombosis in patients with asymptomatic thrombophilia depends on the abnormality involved.
Prophylaxis is usually not required for heterozygous Factor V Leiden or heterozygous prothrombin mutation. For other thrombophilic conditions such as protein C, protein S, or antithrombin deficiency, and for “double heterozygotes” or patients who are homozygous for factor V Leiden, management is controversial and expert advice recommended.

Patients receiving long-term anticoagulant therapy prior to pregnancy

Women receiving long-term anticoagulants should be counselled before pregnancy.

Patients who are receiving warfarin prior to pregnancy for VTE or arterial thrombosis should be switched to therapeutic doses of UFH or LMWH, either at the earliest indication of pregnancy or prior to attempting to conceive, throughout pregnancy. Warfarin can be resumed after delivery.

For women with mechanical heart valves, concern exists about the efficacy of s.c. heparin in preventing thromboembolic complications. Warfarin poses risks to the foetus throughout pregnancy, with the highest risk of embryopathy during weeks 6 to 12 and the highest risk of bleeding near term. If UFH or LMWH is used, intense monitoring is advised to ensure a therapeutic level throughout pregnancy. The addition of low-dose aspirin should be considered. Alternatively, therapeutic dose heparin may be used during weeks 6 to 12 and after 35 to 36 weeks until term, and warfarin used during the remainder of pregnancy. The differential risks of these two approaches to both mother and foetus must be discussed with the patients and expert advice is recommended for such patients.

**Management during labour and delivery**

If patients are receiving prophylactic doses of UFH or LMWH, the treatment is usually discontinued when labour commences and resumed when haemostasis has been re-established after delivery. If patients are treated with therapeutic doses of UFH or LMWH, we recommend inducing labour and stopping UFH/LMWH 24 hours prior to induction. In high risk women (e.g. women with recent VTE), IV UFH can be given and stopped 6 hours before the anticipated time of delivery.

**References**

2. Sanson BJ et al., Thrombosis and Haemostasis 1999;81:668-72
5. Bates SN, Ginsberg JS. Blood 2002;100:3470-8