Pregnancy and Thrombosis: Is Thromboprophylaxis Necessary?

Winnie W. Sia, MD, FRCPC

Helen's case

Helen, is a 35-year-old gravida 0 (G0) at seven weeks. She presents for her first prenatal checkup.

Medical history

Helen's medical history reveals the following:

- She had a pulmonary embolism three years ago and was treated with anticoagulants for six months
- She used oral contraceptives
- She was a smoker
- Her mother had postpartum deep vein thrombosis

Look to page 59 for more on Helen.

Table 1

Common thrombophilia tests performed in pregnancy

- Protein C
- Protein S (lowered by pregnancy)
- Antithrombin
- Activated protein C resistance (may increase in pregnancy)
- Factor V Leiden
- Prothrombin 20210 mutation
- Anticardiolipin antibodies
- Lupus anticoagulant

Does Helen need to be on thromboprophylaxis during pregnancy?

Pregnancy increases the risk of thromboembolism (TE) six-fold. The overall risk of thrombosis in pregnancy is 0.5 to 3 per 1000 women.[1] The risk of TE recurrence in pregnancy for women with a history of thrombosis is 0% to 56% and depends on two factors:

1) Whether the thrombosis was idiopathic or associated with precipitating factors
2) Whether or not thrombophilia is present (Table 1)

If the previous thrombosis was associated with a precipitating factor (*i.e.*, immobility, oral contraceptive use, *etc.*) and if the thrombophilia screen is negative, then the risk of TE recurrence in pregnancy is 0% to 8%. If the previous thrombosis was idiopathic or if the thrombophilia screen is positive, then the risk of TE recurrence in pregnancy is generally much higher.[2]

Dr. Sia is an Assistant Professor, Department of Medicine and Obstetrics and Gynecology, Univeristy of Alberta, Edmonton, Alberta.

Helen's case cont'd...

Helen has heterozygous factor V Leiden. Her risk is 13% and you recommend the use of low-dose anticoagulants during the entire pregnancy and six weeks postpartum.

Turn to page 60 for the conclusion to this case.

It is important to start thromboprophylaxis as soon as pregnancy is confirmed, since venous thromboembolsim presents equally in all three trimesters and postpartum.

What are thromboprophylaxis options in pregnancy?

In general, low molecular weight heparin (LMWH) (Table 2 and Table 3) is a better choice in pregnancy over unfractionated heparin (UFH), if affordability is not an issue.

Helen doesn't like injecting herself. Are there any other options of anticoagulation in pregnancy?

No. Oral anticoagulants (*i.e.*, warfarin) cross the placenta and so their use is contraindicated in pregnancy because of teratogenicity and the risk of fetal bleeding.[3]

What should you advise Helen to do while taking LMWH or UFH?

I would advise Helen to take adequate calcium and vitamin D q.d. and to have her platelets monitored. LMWH cannot be given for at least 24 hours prior to regional anesthesia due to the risk of epidural hematoma.

Table 2

Low molecular weight heparin vs. unfractionated heparin

Low molecular weight heparin (LMWH)	Unfractionated heparin (UFH)
• Expensive • Lower risk of osteopenia • Lower risk of heparin-induced thrombocytopenia (< 1%) • Bleeding risk is < 1% for major bleed	• Cheap • Higher risk of osteopenia • Higher risk of heparin-induced thrombocytopenia (approximately 3%) • Slightly higher bleeding risk than LMWH

Table 3

Different regimens for thromboprophylaxis

Enoxaparin	Dalteparin	UFH*
• 40 mg q.d. subcutaneous (SC) • Consider increasing to 30 mg b.i.d. SC after 20 weeks • Switch to heparin near term if epidural is desired	• 5,000 units q.d. SC • Consider increasing to 5,000 units b.i.d., SC after 20 weeks • Switch to heparin near term if epidural is desired	• 5,000 U b.i.d. first 12 weeks • 7,500 U b.i.d. until 24 weeks • 10,000 U b.i.d. until delivery

*Use the formulation without the preservative benzyl alcohol. (Case reports exist documenting neonatal gasping syndrome in premature infants).

More on Helen

Helen was started on enoxaparin. Her injections are going well in her abdomen and thighs. Her platelets remain normal. At 36 weeks, you switch her to heparin. You tell Helen to stop further heparin doses with any regular contractions suggestive of labor, or if there is a scheduled induction of labour or cesarean delivery date (for obstetric indications). She is to stop the morning heparin dose if this is the case.

The first dose of UFH or of LMWH for postpartum management, assuming hemostasis is achieved, can be given either six hours to 12 hours after a vaginal delivery, or 12 hours to 24 hours after cesarean delivery, depending on the physician's discretion.

Oral anticoagulants (*i.e.*, warfarin) can be started the first day postpartum, if there is no increased bleeding. Titrate the dose up to the international normalized ratio (INR) 1.8 to 2.5 (prophylaxis). The use of warfarin does not interfere and is safe for breastfeeding. Helen can also decide to continue subcutaneous injections of UFH or LMWH for six weeks, if going out to the lab for INR testing during her course on anticoagulants is a problem. The risk is osteopenia on LMWH must be explained to Helen.

Helen returns for a postpartum visit. She asks what birth control is safe to use, given that she has had a clot before.

Estrogen is contraindicated, but progesterone is not. Be careful with prescribing intramuscular injections for those already on therapeutic anticoagulation.

Take-home message

- The risk of venous thromboembolism (VTE) in pregnancy with previous VTE can be estimated based on the presence of precipitating factors for VTE and any abnormal thrombophilia
- Enoxaparin and dalteparin are a good choice of anticoagulants to use in pregnancy. UFH is a good alternative
- LMWH cannot be given for at least 24 hours prior to regional anesthesia
- It is important for women with a history of thrombosis to seek preconception counseling

Helen's contaceptive options include:

1. Progestin-only pills
2. Intrauterine device
3. Medroxyprogesterone acetate (if not currently taking anticoagulation medication. Patients should be cautioned about the risk of osteopenia)
4. Surgical (*i.e.*, tubal ligation) Dx

References

1. Rosene-Montella K, Barbour L: Thromboembolic Disease and Hypercoagulable States. Chapter 8 Hemtalogy. In: *Medical Care of the Pregnant Patient. ACP Women's Health Series 2000.* Philadelphia, 2000, pp. 423-48.
2. Brill-Edwards P, Ginsberg J, Gent M, et al: Safety of withholding heparn in pregnant women with a history of venous thromboembolism. NEJM 2000; 343(20):1439-44.
3. REPRORISK®, MICROMEDEX® Healthcare Series [Database on Internet]. Thomson Healthcare; circa 1974-present.