Thromboprophylaxis in Pregnancy

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KEYWORDS

• Thromboembolism • Prophylaxis • Pregnancy • Thromboprophylaxis

KEY POINTS

- Venous thromboembolism is a significant contributor to maternal morbidity and mortality. Thromboprophylaxis for patients at highest risk of venous thromboembolism should be part of standard obstetric practice.
- Measures to mitigate the risk of venous thromboembolism after cesarean delivery should be used, including early ambulation and mechanical or pharmacologic thromboprophylaxis based on individual risk factors.
- Low-molecular-weight heparin and unfractionated heparin are safe and effective for use in pregnancy.
- Neither prophylactic nor intermediate dosing of low-molecular-weight heparin or unfractionated heparin requires monitoring of anti-Xa levels or activated partial thromboplastin time.
- Standard doses of low-molecular-weight heparin and unfractionated heparin may be inadequate in the obese population. Higher or weight-based dosing should be considered for severely obese patients.

BACKGROUND

Venous thromboembolism (VTE) is one of the leading causes of maternal death in the United States and the world. VTE includes deep vein thrombosis and pulmonary embolism (PE) as well as other more rare forms such as mesenteric vein thrombosis and intracranial venous thrombosis. The overall incidence is 2- to 4-fold higher than the rate in the nonpregnant population.[1] The risk is increased throughout pregnancy, but greatest in the postpartum period.[2] The incidence of VTE ranges from 1 to 2 per 1000 with up to 80% being DVTs in the antepartum period and 20% to 25% being PE.[3,4] In contrast, the incidence of PE is much higher postpartum, with 40% to 60% of all PEs occurring after delivery.[2] Recent efforts to address maternal mortality in the United States led to the development of strategies to help identify patients at

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greatest risk of VTE, and to implement practices focused on prevention. The relatively low incidence of VTE makes prospective studies difficult. Recommendations for practice are, therefore, based largely on small retrospective studies, epidemiologic studies, and expert opinion.[5]

Pregnancy is considered a thrombogenic state, owing to venous stasis, an increase in coagulation factors, and relative immobility. Plasma levels of coagulation factors, fibrinogen, Von Willebrand factor, and other markers of thrombin generation are increased during pregnancy, theoretically to protect the mother from excessive bleeding during delivery.[5] Compression of the vena cava and pelvic vessels by the gravid uterus is another contributing factor. Universal prophylaxis is not recommended during pregnancy. Instead, efforts in prevention of VTE have focused on interventions for those patients with risk factors in addition to pregnancy.[6,7] Risk factors may be preexisting, such as a personal history of VTE or known thrombophilia, or may emerge during pregnancy, such as hospital admission or a need for surgery. In this article, we review the current recommendations for thromboprophylaxis in pregnancy, including outpatient antepartum, inpatient, perioperative, and postpartum thromboprophylaxis. We do not address therapeutic anticoagulation for VTE diagnosed in pregnancy, mechanical heart valve, atrial fibrillation, or other conditions requiring therapeutic anticoagulation.

DEFINITION, RISKS, AND GUIDING PRINCIPLES

Prophylaxis is an action taken to prevent disease, especially by specified means or against a specified disease. Thrombosis prevention can be achieved via mechanical or pharmacologic methods. The benefits of pharmacologic thromboprophylaxis in preventing the occurrence of VTE must be balanced by the increased risk of bleeding during pregnancy, delivery, and the postpartum period. There is wide variation among recommendations regarding indications, dosing, and duration of thromboprophylaxis for the pregnant patient.

Mechanical strategies to prevent VTE include early ambulation after surgery, graduated venous compression stockings, or sequential compression devices (SCD), all aimed at decreasing venous stasis. Several models of SCD have been developed. None are superior over the others in terms of preventing VTE[8]; however, all mechanical methods have been found to reduce the risk of deep vein thrombosis by two-thirds in general surgical patients.[9] There is little evidence for the efficacy of these methods in pregnancy because there are no large-scale studies. The American Congress of Obstetricians and Gynecologists (ACOG) recommends SCD for all women undergoing cesarean section who are not already on pharmacologic thromboprophylaxis.[6]

Pharmacologic thromboprophylaxis has been used for many decades to prevent VTE. The most common forms used include heparins and warfarin. Heparins act indirectly by binding to antithrombin, which then inhibits thrombin, and inactivates factor Xa.[10] Coumadin reduces the synthesis of active clotting factors by depleting the levels of functional vitamin K.[11] The use of any medication in pregnancy requires weighing the risks and benefits to the woman and her fetus. Anticoagulants are associated with an increased risk of bleeding, including placental abruption, postpartum hemorrhage, and perioperative bleeding.[11] The goal of thromboprophylaxis is to administer a dose of medication that reduces VTE risk while minimizing the risk of bleeding.

Warfarin has long been used in the nonpregnant population for prophylaxis against recurrent VTE. Warfarin crosses the placenta and has been associated with fetal anomalies, such as midface hypoplasia, stippled chondral calcification, scoliosis, and short proximal limbs when exposure occurs in the first trimester.