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Deep vein thrombosis in pregnancy

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Abstract

Venous thrombotic events (VTE) prevalence is estimated to be 1-2 for every 10,000 pregnancies, making it one of main causes of maternal mortality in developed countries. VTE's leading risk factors are history of the condition and hereditary thrombophilia. D-dimer tests conducted during pregnancies have in many cases led to false positive results while a few false negatives have also been found. For pregnant women, it is important for evaluation to begin with compression ultrasound before magnetic resonance imaging, which seeks a negative test and focuses on the pelvis. On the other hand, a chest x-ray should be done for pulmonary embolism, which helps in deciding between a CT pulmonary angiogram and perfusion study for normal and abnormal x-ray, respectively. Generally, treatment is composed of heparin of low molecular weight for at least six weeks after childbirth. Thrombolysis can be significant for life-threatening and serious thrombolysis. For populations at high risk, VTE prophylaxis still faces a lot of uncertainty. In fact, there is still little evidence to support the essence of mechanical prophylaxis for all women who have delivered through cesarean.

Key words: Pregnancy, obstetrics, DVT, PE

Introduction

Pregnancy is associated with 5 times higher risk of DVT compared to non-pregnant women. The absolute risk of VTE is 1-2/ 1000 deliveries.[1] Frequency is the same in all trimesters and extends up to 6 weeks postpartum. The risk is highest in certain conditions, inherited or acquired thrombofilias, the previous history of thrombosis, antiphospholipid syndrome, SLE, heart disease and sickle cell disease. Other independent risk factors, which increase the risk by 1,5-2 fold, include maternal age > 35, null parity, multiple gestations, BMI> 30 and immobility. In addition, gestational diabetes and assisted reproduction are also considered risk factors, although data is limited.[2]

Pathophysiology

Pregnancy meets all three criteria of Virchow's triad: venous stasis, hypercoagulability and en-

dothelial damage. This procoagulant state acts as protection against excessive haemorrhage from the placental bed following delivery and miscarriage.[3]

The growing gravid uterus causes mechanical obstruction of the venous outflow, leading to venous stasis in the lower extremities. DVT is more common in the left lower extremity (82%). Furthermore, anatomic reasons, such as May-Thurner syndrome (compression of the left common iliac vein by the right common iliac artery which is accentuated by the enlarging uterus) predispose pregnant women to venous thrombosis. In addition, hormonic changes in pregnancy, including increase in circulating progesterone and relaxine, cause a decrease in venous tone and a reduction of the venous flow velocity of 50% by 25- 29 weeks of gestation, which last until approximately 6 weeks postpartum.[4]

Endothelial damage can occur during delivery or from venous hypertension, especially in pelvic veins. As a result, pelvic vein thrombosis which is uncommon in non-pregnant women, contributes to 6-11% of DVT in pregnancy and puerperium.[5]

Hypercoagulability is the major cause of venous thrombosis in pregnancy. The concentrations of the clotting factors fibrinogen, VII, VIII, von Willebrand factor, IX, X, XII are increased, in addition to the progressive decrease in protein S levels and the acquired resistance in activated protein C. These homeostatic changes contribute to the preparation of hemostasis during delivery, as indicated by the increased levels of D- dimer and prothrombin fragments.[6]

Deep Vein Thrombosis

The signs and symptoms of DVT during pregnancy is a diagnostic challenge. Atypical symptoms, swelling of the lower extremities, shortness of breath and chest pain are common in normal pregnancy due to physiological changes, often mimicking DVT. Nonetheless, DVT in pregnancy can be presented with oedema and erythema of the limbs, extremity discomfort and pain, calf swelling and difficulty walking, with 85% localized in the left side. The LEFt rule can be also used, which includes left lower extremity symptoms, difference in calf circumference of more than 2 cm and first trimester of presentation. The incidence of pelvic vein thrombosis is also higher, presenting with abdominal pain, back pain and swelling of the entire lower extremity. Most importantly, isolated pelvic vein thrombosis counts for 12% of all DVT in pregnancy, compared to 1% in general population.[1,7,8]

Pregnancy is also a risk factor for May- Thurner syndrome, which occurs when compression of the right common iliac artery against the fifth lumbar vertebra causes left common iliac vein obstruction and thrombosis. The syndrome is diagnosed in patients with chronic lower extremity swelling and left lateral abdominal pain which extends to the left thigh.[1]

Acute massive PTE

Acute massive PTE during puerperium can characterize itself as collapsed shocked person, and should be treated with urgency. For such a case, the most recommended initial intervention is UFH because of its fast onset of action. Also, dose can be adjusted in case thrombolytic therapy is used. Thrombolysis can also be considered for patients that have pulmonary embolism that is life threatening or hemodynamic compromise.[3] The intravenous need to be done early enough after thrombolysis, which can later be changed to LMWH after achievement of stability. There is a risk of bleeding complication of 2-3% for not only the mother and their fetus but also for non-expectant women.[6]

Diagnosis

During pregnancy, investigation of pulmonary embolism should begin with a chest radiograph before conducting objective diagnostic testing. The former test is important because it can rule out

some conditions like pneumonia and pneumothorax, which are conditions that have symptoms which mimic those of pulmonary embolism. For pulmonary embolism that have been proven objectively, the investigation is considered normal for more than half of the patients, however, the abnormal features associated with the condition include focal opacities, basal atelectasis, pleural effusions, and pulmonary oedema. In case abnormal features are established on chest radiography, objective testing becomes necessary, which is conducted through computed tomography pulmonary angiogram (CTPA).[9] CTPA is preferred over ventilation perfusion scanning that is more reliable in such circumstances. Fears over fetal malformations should not be an issue for concern since it has been established that the radiation dose from procedure (chest radiography) is less than 0.1mGy, which does not affect the fetus. Apart from measuring saturation of oxygen through sampling of arterial blood gas, electrogram is another important preliminary investigation that should be done. According to one research study, for about 40% of expectant mothers with acute pulmonary embolism, there were electrocardiogram abnormalities presented like T-wave inversion, S1Q3T3 pattern, and right heart strain evidence. In the same group, analysis of arterial blood gas showed that only 10% of the women had less than 60mmHg and less than 90% levels of oxygen levels and saturation, respectively. The sampling or analysis method has reduced diagnostic value for that particular cohort of women with results being normal when there is no pulmonary embolism.[9]

Management

Before starting an anticoagulant therapy, it is important to conduct initial investigations such as full blood count, test on liver functions, coagulation screen. Tests should also be done on electrolytes and urea; however, thrombophilia screen is not always advised since its results are inconsequential in the management and interpretation of outcomes because of pro-thrombotic alterations in various coagulation factors as well as the effect of a developing or recent thrombus.[10]

During pregnancy, VTE treatment usually entails LMWH for at lest 3 months and until a minimum of 6 weeks after delivery. The treatment intervention is appropriate during pregnancy because it does not pass into breast milk via the placenta unlike the warfarin and other coumarin derivatives, which can cross the placenta and lead to embryopathy when administered later on. Conversely, warfarin is recommended for lactating mothers after childbirth since it crosses in very small amounts into the breast milk. Unless the prevailing case is serious, such as a mother who has artificial valves of the heart, coumarins are generally avoided during pregnancy.[5] For the aforementioned case, coumarin are administer during the first trimester after embryogenesis. Other new anticoagulants, which are capable of crossing the placenta that should also not be used during pregnancy include rivaroxaban, edoxaban, dabigatran, and apixaban. However, there are no apparent dangers if used postnatally for non-breastfeeding mothers. Additionally, fondaparinux has been found to be safe for use during pregnancy with evidence also suggesting that it should only be used under severe cases of allergy to heparin or thrombocytopenia that has been induced by heparin. However, if it used during pregnancy, it is critical to be aware that it has a more extended half-life compared to LMWH of the same dosage.[7]

For patients with serious DVT but no heightened progression of clot risks as well as pulmonary embolism, graduated elastic compression stockings are effective in reducing both swelling and pain. National guidelines recommend and stipulate that compression hosiery coupled with an over 23mmHg ankle pressure need to be put on the leg that is affected for

a minimum of 2 years in order to decrease the risks of post-thrombotic syndrome development. However, according to the SOX randomized controlled trial (RCT), which sampled 800 non-expectant women with proximal DVT, class II compression stockings with a pressure of 30-40mmHg were neither effective for preventing of post-thrombotic syndrome nor decrease recurrent DVT risks when comparisons were made with placebo stockings that were worn each day for 2 years after an occurrence. Thus, compression stocking is not recommended at present as a way of preventing the condition.[11]

The inferior vena cava (IVC) filters have a particular role in managing acute PTE during pregnancy. However, these filters are not widely used because of the inherent risked linked with insertion and removal. They include 0.12-0.3% rate of fatality, 5% filter fracture, over 20% filter migration, and IVC perforation that affects 5% of people. In necessary cases, the retrievable IVC filter, also referred to as temporary caval filter is deemed suitable for mothers with recurring VTE with acceptable treatment or those where anticoagulation is contraindicated.[7]

Conclusion

Evidence from research studies conducted on non-expectant populations are critical for both the diagnosis and management of VTE during pregnancy since they inform the suitable recommendations and guidelines. This leads to a lot of contention regarding multiple areas of management as well as reluctance by practitioners to pursue a diagnosis that is considered objective. While LMWH has been predominantly substituted UFH in managing VTE in pregnancy, the right schedule for dosing is yet to be established. Also, anti Xa activity, which entails the value of assessing LMWH activity is yet to be determined. Concerning diagnosis, there is inadequate data to inform the risks for the mother or fetus linked with V`/Q` and CTPA screening for detection of pulmonary embolism during expectancy. As a result of this, it is still not clear on the best wat of managing an expectant mother who has undergone an transitional probability V`/Q` scan and consequently fails to have a supplemental CTPA for follow-up. These concerns are best addressed with evidence from sufficiently powered RCTs among pregnant women.

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