Pulmonary Embolism in Pregnancy

Overview
1. Pulmonary embolism (PE) during pregnancy is associated with increased mortality compared to non-gravid state
2. PE causes approximately 20% of pregnancy-related mortality surpassing pre-eclampsia and eclampsia
3. Embolism can be:
   - Venous thromboembolism (VTE)
   - Venous air embolism (VAE)
   - Amniotic fluid embolism (AFE)

VENOUS-THROMBOEMBOLISM (VTE)
1. Epidemiology/risk factors
   - VTE is 5-10x more common in pregnant women than non-pregnant women of the same age
   - Many of the classical signs and symptoms of VTE in non-pregnant women are also present in normal pregnancy
   - Risk factors for VTE in pregnancy
     - Maternal age > 35 yo
     - Multiparity (at least 3)
     - Weight of > 165 lbs
     - Personal or family history of VTE is the highest risk factor
     - Prolonged bed rest
     - Surgical delivery
     - Hemorrhage or sepsis
     - Pre-eclampsia
   - Post-partum period has 10-20x increase in risk of VTE compared to that during pregnancy
   - VTE encompasses both deep venous thrombosis (DVT) and pulmonary embolus (PE)
   - It is estimated that DVT occurs in 0.5-2.0/1000 pregnancies
   - About 15-24% of undiagnosed and untreated DVT will develop PE
   - 15% mortality rate in those who develop PE
   - Majority of pts with fatal PE die within 30 mins of onset of symptoms
   - Due to risk of sudden death, treatment should be initiated immediately and not delayed while patient is being evaluated

2. Pathophysiology of VTE
   - Hypercoagulable state
     - Multifactorial, and persists for 6 weeks after delivery
       - Venous stasis (e.g. post delivery immobility)
       - Altered coagulation factors (decrease in protein S level, increase in the factor I, II, VII, VIII, IX, no change in protein C level)
       - Increase in fibrin level and decrease in fibrinolytic activity
       - Increase in platelet activation
   - Hormonal and anatomical changes:
     - Progesterone mediates venous distensibility in early pregnancy which leads to increase in venous stasis
- DVTs more common in left lower extremity (iliac more than calf region) as high as 90% during pregnancy because of compression effect of common and right iliac artery on left iliac vein
- Damage to vessels during vaginal or operative delivery

3. Diagnosis of VTE
   o Challenges
   - Clinical signs and symptoms
     - Leg swelling, and tachycardia
     - Have lower accuracy in pregnant women since these signs and symptoms can exist in normal pregnancies without VTE
   - Most large and well-designed clinical trials evaluating diagnostic and therapeutic approaches to VTE, excluded pregnant women
   - Important to consider different hormonal and anatomical risks in pregnant women

   o Diagnosis of DVT
     - See Dx of PE
     - D-Dimer
       - Because D-dimer is normally increased in pregnant women, a normal D-dimer is useful to rule out a PE in pregnant woman and look for alternative source for respiratory symptoms Elevated D-dimer not sufficient to establish diagnosis of DVT
     - Compression ultrasound:
       - Non-invasive, no risk of radiation, most used
       - 97% sensitive, 94% specific in diagnosing symptomatic proximal DVT.
       - Less accurate in isolated calf DVT
       - Less accurate in isolated DVTs that involve ilio-femoral area
       - Because risk of PE is increased in pregnancy, further testing is indicated if PE is suspected clinically even with normal ultrasound

   o Diagnosis of PE
     - See Dx of DVT
     - Start with bilateral lower extremity ultrasound
       - Positive-> treat for PE
       - Negative-> perform Ventilation-perfusion V/Q scan
     - VQ scan
       - Can be performed safely during pregnancy
       - Low probability VQ scan and normal D-dimer rules out PE
       - Start with perfusion test to minimize radiation exposure
       - If perfusion defect is present -> treat for PE
       - If perfusion scan is not clear, then ventilation scan is done
       - Non-diagnostic test indicates the need to pursue different modalities, such as CT scan
       - Pt should be informed about risks and benefits of such controversial studies

   - Helical CT
     - Safety in pregnant women is controversial
     - Large variation in its specificity and sensitivity
   - Pulmonary angiography
     - Gold standard
4. Treatment of VTE
   o Heparin
     • Does not cross placenta
     • No risk of teratogenesis or fetal hemorrhage
     • Major complications
       ▪ Maternal hemorrhage: no significant increased risk than non-pregnant women
       ▪ Thrombocytopenia (HIT I, II)
       ▪ Osteopenia: inhibition of the activation of 1, 25 hydroxy-Vit D, but long term risk is not known
     • Heparin requirement during pregnancy increases due to:
       ▪ Increase in level of heparin-binding proteins
       ▪ Increase in plasma volume
       ▪ Increase in renal clearance of heparin
       ▪ Placenta enhances degradation of heparin
     • Recommended dose
       ▪ 7,500-10,000 UI of IV bolus heparin followed by IV infusion of 1300 units/hr to achieve an aPTT that twice the normal aPTT, for 5-10 days
       ▪ Then, 5,000-10,000 Units/12 hrs is given subQ for the rest of pregnancy
   o LMWH
     • Does not cross placenta
     • No risk of teratogenesis or fetal hemorrhage
     • Controversial in terms of the decrease in the major complications vs. heparin
     • Dosing more difficult in pregnant women since it binds less to proteins and has longer half life
     • Optimal LMWH dosing not established for pregnant patients
     • Some authors recommend measurement of anti-factor Xa levels q6 weeks
     • Dose for LMWH should titrated to 1-2 IU/ml if administered once daily
   o Warfarin
     • Crosses placenta-> high risk of teratogenesis and fetal hemorrhage
     • Can be used post delivery with heparin overlap to obtain INR of 2-3
   o Breastfeeding
     • Heparin, LMWH, and warfarin safe during breastfeeding
   o Duration of anticoagulation
     • No clinical trials
     • Some authors recommend 3-6 months after delivery or during pregnancy followed by another 6 weeks after delivery
   o Life threatening PE
     • Challenge in pregnant women
     • Supportive care and IV anticoagulation should be started without any delay
     • Supportive care:
       ▪ Support BP > 90 mmHg
Position: Patient should be positioned on lateral decubitus position to displace uterus off the IVC to increase preload and cardiac output

Volume resuscitation

Vasopressor role:
- Not well studied
- Balance between effects of maternal hypotension vs. vasoconstrictive effect of vasopressors on blood flow to uterus
  - Dopamine shown to be safe in animal studies

IVC filter:
- Same indications as nonpregnant population

Thrombolytic therapy:
- No large clinical trials are available that assert safety and effectiveness
- Thrombolytics are relatively contraindicated during pregnancy
- Streptokinase is teratogenic, tPA is safer
- Lower risk of fetal loss than embolectomy

VENOUS AIR EMBOLISM (VAE)
1. Most common during intraoperative period for patients undergoing C-sections
2. Pathophysiology:
   - Air entrapment in right ventricle leading to hemodynamic compromise
   - Increase in coagulopathy due to air contact with endothelial cells
   - End-organ damage due to low blood perfusion in case of paradoxical embolus
   - Paradoxical embolus is a venous clot that passes from right side of heart through defect in heart such as ventricular septal defect to left side of heart and then to general circulatory system
3. Clinical manifestation:
   - Similar to PE that results from VTE
4. Diagnosis of VAE
   - Sharp decline in end-tidal carbon dioxide and low peripheral oxygen saturation (PaO₂, 60 mmHg)
   - Significant V-Q mismatch
5. Treatment of VAE
   - Stabilize pt hemodynamically
   - Position patient so that surgical site is lower than heart
     - If pt develops cerebral hypoperfusion or neurological Sx, position patient so the heart is lower than the head
   - FIO₂ of 1.0, hyperbaric O₂ (2 atm) Tx is the only proven therapy
   - IV fluids to displace air bubble from right ventricular to distal pulmonary vasculatures

AMNIOTIC FLUID EMBOLISM (AFE)
1. Increased awareness led to more reported cases since 1950
2. Incidence
   - 1/20,000-80,000 deliveries
3. Significant cause of maternal mortality in USA
4. Risk factors:
   - Increase in maternal age
   - Multiparity
   - Fetal death
   - Trauma
   - Uterine over distention

5. Pathophysiology and clinical manifestation
   - Immediate phase:
     - Respiratory distress, hemodynamic compromise, cerebral hypoperfusion or coma
   - Second phase:
     - Increase in coagulopathy
   - Third phase:
     - Sequelae of first phase, such as long-term brain damage

6. Diagnosis of AFE
   - No tests specific for amniotic fluid embolus currently available
   - Clinical diagnosis

7. Treatment of AFE
   - Stabilize vital signs:
     - PaO2 > 60 mmHg
     - Systolic BP > 90 mmHg
     - Urine output > 25 ml/hr
   - Correct coagulation abnormality
   - Massage lower abdomen to reduce uterine tone

References

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