TROMBOSI VENOSA PROFONDA E EMBOLIA POLMONARE

Trombosi e gravidanza

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Thrombotic complications of pregnancy

1)

Venous thromboembolism (VTE)

→ **mother**

2)

Obstetrical complications

→ **fetus and mother**

VTE and pregnancy

- magnitude of the problem
- diagnosis
- treatment
- prophylaxis

VTE and pregnancy

- VTE is the leading cause of maternal mortality
- the incidence of VTE in pregnancy is 0.71-1.3 per 1,000 women
- in pregnancy the risk of VTE is increased approximately 10-fold

Relative distribution of VTE

- not substantially different in the three trimesters
- puerperium (6 weeks postpartum) is a particularly high risk period

Relative distribution of VTE

Martinelli et al, T&H 2002

- Duration: pregnancy: 280 days
  puerperium: 42 days
- Relative distribution of 100 VTE:
  pregnancy: 0.15 per day
  puerperium: 1.36 per day
- The probability of puerperium-VTE is 9 times higher than pregnancy-VTE

Thrombophilia and VTE in pregnancy

	odds ratio (95%CI)		
	Grandone, AJOG 1998	Gerhardt, NEJM 2000	Martinelli, T&H 2002
AT, PC, PS def.	-	6.0 (3.5-10.3)	13.1 (5.0-34.2)
factor V Leiden	16.3 (4.8-54.9)	6.9 (3.3-15.2)	10.6 (5.6-20.4)
PT G20210A	10.2 (4.0-25.9)	9.5 (2.1-66.7)	2.9 (1.0-8.6)

Leg of presentation

Martinelli et al, T&H 2002

	pregnancy DVT	puerperium DVT
left *	**90 %**	**63 %**
right	4 %	33 %
both	6 %	4 %

* compression on the left iliac vein by the right iliac artery where they cross.

VTE and pregnancy

- magnitude of the problem
- diagnosis
- treatment
- prophylaxis

Diagnosis of VTE in pregnancy

- In pregnancy symptoms such as leg swelling, dyspnea, chest pain due to nonthrombotic causes are common.
- Ionizing radiation are potentially oncogenic and teratogenic (> 5 rad).
- The potential risks associated with the radiologic tests used when VTE is suspected are minimal when compared with the consequences of misdiagnosis.

Diagnosis of **DVT** in pregnancy

- CUS is the objective testing of choice (less accurate in calf DVT)
- If CUS equivocal, or if isolated iliac vein thrombosis is suspected, consider venography shielding the fetus from radiation by placing a lead shield over the abdomen

Diagnosis of **PE** in pregnancy

- V/Q lung scan (if nondiagnostic + serial CUS)
- Helical CT scan
- Pulmonary angiography
- D-dimer levels are not specific since they increase with gestational age (NPV)

VTE and pregnancy

- magnitude of the problem
- diagnosis
- prophylaxis
- treatment

Treatment of acute VTE

- Low-molecular weight heparin (LMWH)
- Vitamin-K antagonist (VKA)
- Unfractionated heparin (UH)

- Heparinoids (danaparoid sodium, dermatan sulphate)
- Hirudin
- Other anticoagulants (idraparinux, fondaparinux, rivaroxaban, apixaban, edoxaban, dabigatran)

Drug of choice in pregnancy: LMWH

- **subcutaneous injection**
- **bid (preferable to od since the half-life of LMWH is decreased in pregnancy)**
- **does not cross the placenta**
- **less HIT and osteoporosis than UH**
- **to be discontinued 24h prior to elective induction of labor**
- **allergic skin reactions are common**

How much LMWH ?

- Full dose (eg, enoxaparin 100 UI/kg bid) for 4 weeks
- Then intermediate dose (70% of the full dose) bid

… HOWEVER … as pregnancy progresses and woman gain weight the potential volume of distribution for LMWH changes

Two options

- Change the dose in proportion to the weight change
- Perform regular anti-factor Xa levels 3 to 4 hours after the morning dose and adjust the dose of LMWH to achieve and anti-Xa level of 0.5-1.2 U/mL

… HOWEVER … clinical experience suggests that few dose adjustments are required and monitoring may not be necessary or need only be done infrequently

Drug of choice in puerperium

LMWH or warfarin

monitoring: NO ← PROS → oral

subcutaneous inj. ← CONS → monitoring: YES
(INR range: 2-3)

Use of anticoagulants in the nursing mother

UH and LMWH are not secreted into breast milk and can be safely administered to nursing mothers

Warfarin does not induce an anticoagulant effect in the breast-fed infant when the drug is given to a nursing mother.

VTE and pregnancy

- magnitude of the problem
- diagnosis
- Treatment
- prophylaxis
  - *primary*
  - *secondary*

Primary prophylaxis

1) Thrombophilia

2) Positive family history

Primary prophylaxis

Asymptomatic women

heterozygous factor V Leiden or prothrombin G20210A

- prophylaxis during 4-6 weeks postpartum
- watchful waiting during pregnancy
- extended prophylaxis in pregnancy can be considered in some cases (es. family history, obesity)

Primary prophylaxis

Asymptomatic women

homozygous factor V Leiden or prothrombin G20210A and combined heterozygous

- prophylaxis during 4-6 weeks postpartum
- extended prophylaxis throughout pregnancy

Primary prophylaxis

Asymptomatic women

Antithrombin, protein C, protein S deficiency

- prophylaxis during 4-6 weeks postpartum
- extended prophylaxis throughout pregnancy, particularly for antithrombin deficiency

Secondary prophylaxis

How shall we manage pregnant women with or without thrombophilia and previous VTE ?

Secondary prophylaxis

- prophylaxis during 4-6 weeks postpartum

  if previous VTE occurred for surgery or trauma risk factor

- extended prophylaxis throughout pregnancy

  if previous VTE was idiopathic, pill- or pregnancy-related

Drug of choice in pregnancy: LMWH

- **subcutaneous injection**
- **od**
- **does not cross the placenta**
- **less HIT and osteoporosis than UH**
- **to be discontinued 12h prior to elective induction of labor**
- **allergic skin reactions are common**

Patient 1: DP, 10.7.1980

- Storia familliare negativa per trombosi.
- 2000 TVP popliteo-femoro-iliaca sx + EP non massiva dopo 3 mesi di estroprogestinico (Mercilon, prima utilizzatrice). TAO per circa un anno.
- Screening → fattore V Leiden omozigote mutato
- G2, P2. 2008 parto vaginale a termine, F 3280g. Clexane 4000 UI/die in gravidanza e puerperio.
- 2009 recidiva di TVP femoro-iliaca dx alla 9na settimana di gestazione nonostante Clexane 4000 UI/die.
- Peso 63 kg, altezza 168 cm, BMI 22.6

Patient 2: TE, 5.5.1963

-Madre con tfs ricorrenti, safenectomizzata

- Mai estroprogestinici, interventi chirurgici, fratture.

-G5, P4. 1990 F 3100 g. 1994 M 2900 g. 1998 M 3500 g. 2000 aborto spontaneo precoce. 2001 M 3200 g.

- 2010 varicoflebite dorso del piede e VGS al III distale di gamba, trattata con LMWH per 2 settimane con risoluzione.

- Screening: AT 99%, PC 95%, PS funz 17%, PEG 14%, FVL e PT G20210A wild type, APA assenti, omo 12 µmol/ml, FVIII 105%

Patient 3: MN, 21.1.1988

- Storia familiare dubbia (padre?).
- 2008 TVP popliteo-femorale dx dopo 20 giorni di estroprogestinico (Yasmin, prima utilizzatrice). TAO x circa un anno.
- Screening → nella norma.
- G2, TC2. 2010 parto a termine, M 3200g. Clexane 2000 UIx2/die in gravidanza e puerperio.
- 2014 recidiva di TVP femoro-iliaca sx alla 10ma settimana di gestazione, non ancora in profilassi.
- Peso 51 kg, altezza 165 cm, BMI 18.7