

RECURRENT PREGNANCY LOSS: FIRST TRIMESTER

BACKGROUND

- defined as 3 or more **consecutive** early trimester losses (or >2 **consecutive** losses if age over 35)
- most occur at less than 10 weeks gestation
- incidence 0.4-1% of couples overall, 5% in women over age 35
- associations with nicotine, alcohol, caffeine, non-steroidal anti-inflammatory agents, insulin resistance, uncertain
- significant emotionally traumatic experience similar to stillbirth or neonatal death

EVALUATION

HISTORY:

- pre-embryonic or embryonic loss at <10 wks gestation (but often present later)
- document evidence of each first trimester loss, e. g. pathology, decreasing quantitative HCGs.
(Do not include second trimester losses, which suggest cervical insufficiency)
- later fetal death, h/o autoimmune disease, thrombocytopenia, venous thromboembolism (suggests antiphospholipid syndrome – 5-15%)
- prior preterm birth, malpresentation (suggests mullerian abnormality – 10-15%)
- prior infant with congenital anomalies (suggest parental karyotype abnormality – 3-6%)

PHYSICAL:

- cervical or vaginal malformation
- evidence of thyroid disease or uncontrolled diabetes
- hirsutism, significant acne, e. g., hyperandrogenism

RECOMMENDED LABORATORY TESTING:

- lupus anticoagulant, anticardiolipin antibody, Beta-2 Glycoprotein 1 Antibodies: IgG, IgM, and IgA (antiphospholipid antibody)
- sonohysterography (mullerian abnormality)
- parental karyotypes (balanced parental translocations)
- karyotyping of products of conception
- prolactin (if suggested by history or physical)

LABORATORY TESTING NOT RECOMMENDED:

- thyroid stimulating hormone, thyroxine (T4), thyroid peroxide antibody, 2-h glucose tolerance test
- screening for sexually transmitted infections (ureaplasma, mycoplasma, Chlamydia)
- measurement of progesterone levels
- general hereditary thrombophilia work up (Factor V Leiden, Prothrombin Gene Mutation 20210A, Protein C and S, antithrombin III, methylenetetrahydrofolate reductase (MHTFR))
- human leukocyte antigen testing

MANAGEMENT:

- If antiphospholipid syndrome documented, then prophylactic low molecular weight heparin and low dose aspirin (81 mg) are indicated
- if unexplained recurrent (3) **consecutive** losses, empiric progesterone supplement may be tried. Start three days after the luteinizing hormone surge, so as not to inhibit ovulation, and continue until 10 weeks of gestation, when placental progesterone production should be fully functional. The Cochrane Review does not differentiate the various progesterone modalities by success rate, but elsewhere oral micronized progesterone has been found not to be effective and the micronized progesterone gel was not approved by the FDA, so consider this agent which is on formulary:
- Progesterone vaginal suppositories, 100 mg twice daily

- If uterine septum, hysteroscopic resection may be considered (only evidence is observational)
- If balanced translocation carrier, 70% chance of live birth with no intervention
- Genetic Counseling

MANAGEMENT OF NO PROVEN BENEFIT:

- if unexplained recurrent early losses, no benefit from empiric heparin and/or low dose aspirin
- for other (non-septal) mullerian abnormalities, repair is not generally advised
- myomectomy for fibroids is of unproven benefit/subsequent risks
- pre-implantation screening/invitro fertilization does not increase chance of live birth/not recommended
- metformin has not been shown to reduce miscarriage in women with PCOS
- micronized oral progesterone

OUTCOMES:

- after 3 early losses -→32% risk of another loss
- after 2 early losses -→26% chance of another
- after 1 early loss -→24% chance of another
- no treatment of women with unexplained recurrent losses results in a 65% live birth rate

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