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HERPES SIMPLEX VIRUS (HSV) INFECTIONS DURING PREGNANCY

A. Background

1. Twenty five to 65 per cent of pregnant women in the U.S. have genital infection with herpes simplex virus type I or 2 (HSV-1 or HSV-2).
2. Vertical transmission to the newborn is accompanied by devastating consequences (30-60% mortality rate, 20-90% neurologic damage in survivors).
3. There are 3 forms of HSV-associated neonatal disease: disseminated (25%), central nervous system (30%), and cutaneous (45%), in decreasing order of adverse neonatal outcomes.
4. The frequency of neonatal HSV infection in the U.S. varies between 8 to 60 cases per 100,000 live births by population studied and is the result of exposure to HSV in the genital tract during delivery.
5. The neonatal risk is greatest in women who acquire HSV for the first time during the pregnancy, as compared to women with longstanding HSV whose infection is reactivated during the pregnancy (risk 25-50% vs. <1%).
6. Newly acquired HSV infection accounts for 80% of neonatal cases, and is usually the associated with asymptomatic cervical viral shedding.
7. Up to 50-80% of new genital infections in women, and 30-50% of neonatal infections, may be caused by HSV-1, so the former distinction between HSV-1 and HSV-2 has become less meaningful at present; either viral type may be associated with severe neonatal disease.

B. Diagnosis

1. A diagnosis of genital HSV infection based on physical examination unfortunately has a sensitivity of only 40% and a false positive rate of 20%, but is what must most commonly be relied upon in clinical decision making.
2. Viral culture for HSV, once considered the 'gold standard', is limited by stage of the lesion at the time of specimen collection (vesicle>ulcer>crusted lesion), and by viral inoculum (80% positive for primary lesions, 40% positive for recurrent lesions).
3. Polymerase chain reaction techniques (PCR) have superior sensitivity compared to culture, but unfortunately are not yet currently standardized or FDA approved. They are most likely to become the standard of care soon, and should be sufficiently sensitive to detect asymptomatic viral shedding.
4. Second generation type-specific glycoprotein-G HSV serologic assays are available and have sensitivities and specificities of 80-98%, but first-generation tests still abound, and percentage of false negatives and positives is much higher.

5. There is no current evidence that screening asymptomatic patients is cost-effective, and such a strategy is not recommended by American College of Obstetricians and Gynecologist, (ACOG), the Center for Disease Control and Prevention (CDC), or the US Preventative Services Task Force (USPSTF).
6. IgM testing for HSV is likewise neither sensitive nor specific, and is not clinically useful.
7. Differentiation of primary HSV infection from a non-primary first episode during pregnancy (secondary or recurrent infection) can only be made by positive viral detection and a negative second generation serologic test result.

C. Management

1. Primary HSV infection: All primary HSV outbreaks during pregnancy should be treated at presentation to reduce the severity of the symptoms, shorten the duration of the outbreak, and reduce the duration of viral shedding.
2. The following regimens are recommended:

    a. Acyclovir 400 mg po 3x daily x 7-10 days -OR-
    b. Valacyclovir 1000 mg po 2x daily x 7-10 days

3. Topical therapy with acyclovir cream is ineffectual, but many women may have severe symptoms with fever and urinary retention and require local symptomatic treatment, oral analgesics, and/or urinary drainage until the lesions crust over and the pain is relieved.
4. Women with complications that require hospitalization should receive:

    Acyclovir 5-10 mg/kg IV q8h x 2-7 days, followed by 10 days of oral therapy

5. Recurrent HSV infections:
    A. Episodic treatment of recurrences: The following treatment regimens are recommended:

        a. Acyclovir 400 mg po 3x daily x 5 days -OR-
        b. Valacyclovir 1000 mg po 2x daily x 5 day

    B. Suppressive therapy for recurrent HSV: Women who have had active genital recurrences will benefit from suppressive treatment at 36 weeks as it can reduce the frequency of recurrences by 75%, reduce the incidence of cesarean delivery by 40%, and reduce the rate of shedding (as determined by PCR) by 90%. Nevertheless, none of the current evidence is able to demonstrate that suppressive treatment near term is able to decrease the incidence of neonatal infection.

        The suggested regimen is:

        a. Acyclovir 400 mg po 3x daily from 36 weeks gestation

b. Valacyclovir 500 mg po 2x daily from 36 weeks gestation

c. While treatment of discordant heterosexual couples decreases transmission to the uninfected partner, unfortunately, there is no current evidence that treating the partners of women with known HSV infection is effective in the prevention of neonatal HSV infection.
d. Consistent condom use and abstinence during acute episodes should be encouraged, but likewise has not been demonstrated to prevent neonatal infection.
e. Acyclovir has not been demonstrated to be teratogenic, and is considered safe in all trimesters. The drug only becomes active in viral infected cells. It has been associated with transient neonatal leukopenia in up to 20% of the infants of mothers taking the drug, but no long term adverse effects have been observed.
f. Valacyclovir is costlier, but have better bioavailability compared to acyclovir, and are metabolized to acyclovir in vivo. (The ANMC pharmacy will only provide valacyclovir to transplant patients.)
g. Please note that women at risk are begun on suppressive therapy at 36 weeks gestation, not earlier in the pregnancy.

6. Intrapartum Care

a. Cesarean delivery is indicated for women with active genital HSV lesions or significant prodromal symptoms (vulvodynia) at the time of active labor. Nevertheless, neonatal infection may occur in 1.2% of women delivered abdominally, and cesarean is not able to prevent all vertical transmission.
b. There is no evidence that there is a duration of ruptured membranes beyond which cesarean delivery is not beneficial or not recommended in women with active HSV infection.
c. Women with preterm premature rupture of membranes prior to 34 weeks who have active disease do not present a contraindication to antenatal corticosteroid therapy for fetal lung maturation. Treatment with an antiviral agent may also be considered.
d. Invasive fetal monitoring (scalp electrodes) is associated with a 6-fold increase in the vertical transmission of HSV, and should be avoided in at risk women.
e. Women with recurrent HSV *nongenital* lesions (e.g., on the face, buttocks or thigh) do not require cesarean delivery, but the lesions should be isolated with an occlusive dressing.
f. Breastfeeding is not contraindicated in women with active genital lesions, but good hand-washing is counseled before handling the infant.

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