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Management of Group B Streptococcal Bacteriuria in Pregnancy

This clinical practice guideline has been prepared by the Infectious Diseases Committee, reviewed by the Family Practice Advisory Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

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Abstract

Objective: To provide information regarding the management of group B streptococcal (GBS) bacteriuria to midwives, nurses, and physicians who are providing obstetrical care.

Outcomes: The outcomes considered were neonatal GBS disease, preterm birth, pyelonephritis, chorioamnionitis, and recurrence of GBS colonization.

Evidence: Medline, PubMed, and the Cochrane database were searched for articles published in English to December 2010 on the topic of GBS bacteriuria in pregnancy. Bacteriuria is defined in this clinical practice guideline as the presence of bacteria in urine, regardless of the number of colony-forming units per mL or L (CFU/mL or CFU/L). Low colony counts refer to $< 10^5$ CFU/mL or 10^8 CFU/L, and high (significant) colony counts refer to $\geq 10^5$ CFU/mL or 10^8 CFU/L. Results were restricted to systematic reviews, randomized controlled trials, and relevant observational studies. Searches were updated on a regular basis and incorporated in the guideline to February 2011. Grey (unpublished) literature was identified through searching the websites of health technology assessment and health technology assessment-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: Recommendations were quantified using the evaluation of evidence guidelines developed by the Canadian Task Force on Preventive Health Care (Table).

Benefits, Harms, and Costs: The recommendations in this guideline are designed to help clinicians identify pregnancies in which it is appropriate to treat GBS bacteriuria to optimize maternal and perinatal outcomes, to reduce the occurrences of antibiotic anaphylaxis, and to prevent increases in antibiotic resistance to GBS and non-GBS pathogens. No cost-benefit analysis is provided.

Recommendations

1. Treatment of any bacteriuria with colony counts $\geq 10^5$ CFU/mL or 10^8 CFU/L in pregnancy is an accepted and recommended strategy and includes treatment with appropriate antibiotics. (II-2A)
2. Women with documented group B streptococcal bacteriuria (regardless of level of colony-forming units per mL) in the current pregnancy should be treated at the time of labour or rupture of membranes with appropriate intravenous antibiotics for the prevention of early-onset neonatal group B streptococcal disease. (II-2A)

3. Asymptomatic women with urinary group B streptococcal colony counts < 10^5 CFU/mL or 10^8 CFU/L in pregnancy should not be treated with antibiotics for the prevention of adverse maternal and perinatal outcomes such as pyelonephritis, chorioamnionitis, or preterm birth. (II-2E)
4. Women with documented group B streptococcal bacteriuria should not be re-screened by genital tract culture or urinary culture in the third trimester, as they are presumed to be group B streptococcal colonized. (II-2D)

INTRODUCTION

Colonization with group B streptococcus in pregnancy is common,[1,2] and GBS infection is associated with significant neonatal morbidity and mortality.[3] Guidelines for the prevention of perinatal GBS disease by the Centers for Disease Control and Prevention,[3] the American Congress of Obstetricians and Gynecologists,[4] and the Society of Obstetricians and Gynaecologists of Canada[5] provide clear and consistent recommendations for intrapartum GBS prophylaxis in women with documented GBS bacteriuria in the current pregnancy. Although the incidence of early onset GBS disease has decreased significantly since the implementation of these preventive guidelines, the management of GBS bacteriuria before the intrapartum period for the prevention of adverse maternal and perinatal outcomes is less clear. This clinical practice guideline summarizes maternal and perinatal complications associated with any bacteriuria in general and with GBS bacteriuria in particular, and reviews the evidence for the management of GBS bacteriuria in pregnancy before labour or rupture of membranes, including treatment with antibiotics and ongoing infectious disease surveillance.

ASYMPTOMATIC BACTERIURIA IN PREGNANCY

Screening for asymptomatic bacteriuria (significant bacteriuria without the symptoms of an acute urinary tract infection) is a standard component of obstetrical care, and is a recommendation of most antenatal clinical practice guidelines. Asymptomatic bacteriuria occurs in 2% to 10% of all pregnancies.[6–9] Asymptomatic bacteriuria in non-pregnant women is diagnosed by quantitative culture using 2 consecutive voided urine specimens with isolation of the same bacterial strain in quantitative counts ≥ 10^5 CFU/mL or 10^8 CFU/L, or a single catheterized urine specimen with one bacterial species isolated in a quantitative count ≥ 10^2 CFU/mL or 10^5 CFU/L.[10] In pregnant women, however, a single quantitative culture in any trimester is sufficient.[11] *Escherichia coli* is the most common pathogen, identified in up to 80% of bacterial isolates. Other organisms include Gram-negative bacteria and GBS.[7,9] The American Congress of Obstetricians and Gynecologists recommends that if at any time during pregnancy GBS is present in urine in concentrations ≥ 10^5 CFU/mL or 10^8 CFU/L, antibiotics for asymptomatic bacteriuria or a symptomatic urinary infection should be administered as they would be for any other organism detected in significant concentrations.[4]

Although approximately 6% to 36% of pregnant women show vaginal-rectal GBS colonization, the reported incidence of GBS in quantities ≥ 10^5 CFU/mL or 10^8 CFU/L of urine is 0.4% to 5%,[12,13] and only 60% of pregnant women with GBS in quantities ≥ 10^5 CFU/mL or 10^8 CFU/L in urine specimens demonstrate GBS colonies by bladder tap (compared with 100% with *Escherichia coli*).[14] GBS colonization can be transient, chronic, or intermittent, and detection is dependent on the culture technique, the locations tested, the culture media, and the population studied.[8,11,13] Women with pre-gestational diabetes are at greater risk of asymptomatic bacteriuria, including GBS bacteriuria, than are pregnant women who do not have diabetes.[15]

MATERNAL AND PERINATAL RISKS ASSOCIATED WITH ANY ASYMPTOMATIC BACTERIURIA IN PREGNANCY

Asymptomatic bacteriuria in pregnancy has been associated with increased risks of pyelonephritis, low birth weight, and preterm birth.[7,12,16,17] Antibiotic treatment for asymptomatic bacteriuria has been shown to reduce the risk of pyelonephritis (RR 0.23; 95% CI 0.13 to 0.41) and low birth weight (RR 0.66; 95% CI 0.49 to 0.89), although no significant reduction in the rates of preterm birth has been demonstrated.[7] Women with recurrent bacteriuria (same strain with significant colony counts cultured within 2 weeks of completing initial treatment) or reinfection (same or different strain with significant colony counts more than 2 weeks after completing treatment), including GBS, should be re-treated and antibiotic sensitivities determined.[7,9,18]

Recommendation

1. Treatment of any bacteriuria with colony counts ≥ 10^5 CFU/mL or 10^8 CFU/L in pregnancy is an accepted and recommended strategy and includes treatment with appropriate antibiotics. (II-2A)

ABBREVIATIONS

CFU	colony-forming units
GBS	group B streptococcal

Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[26]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[26]

MATERNAL AND PERINATAL RISKS ASSOCIATED WITH ASYMPTOMATIC GBS BACTERIURIA IN PREGNANCY

Risk of Pyelonephritis

Urinary tract infectio ns are the most common bacterial infections during pregnancy, and GBS causes about 10% of cases of acute pyelonephritis, mainly in the second trimester.[17] Although it is recommended to treat asymptomatic bacteriuria in pregnancy ($\geq 10^5$ CFU/mL or 10^8 CFU/L) for the prevention of sequelae of urinary tract infections, there is no evidence to support the treatment of GBS bacteriuria with low colony counts for the prevention of pyelonephritis.[17]

Risk of Chorioamnionitis

A retrospective cohort study evaluated the risk of chorioamnionitis (defined as intrapartum fever, fetal tachycardia, and histologic inflammation of the membranes) in women with untreated asymptomatic GBS bacteriuria early in pregnancy compared with the risk in women with negative cultures.[19] Predictors of chorioamnionitis were found to be lack of therapy for GBS bacteriuria at any time in pregnancy (OR 7.2; 95% CI 2.4 to 21.2) and more than 8 vaginal examinations (OR 5.0; 95% CI 1.6 to 15.6). Although there was evidence of correlation between GBS colony count and severity (or grade) of chorioamnionitis ($P = 0.02$), 85% of women with GBS bacteriuria had colony counts $< 10^5$ CFU/mL or 10^8 CFU/L, and sample size was inadequate to determine a significant difference in risk of chorioamnionitis, by treatment or lack of treatment, stratified by colony counts.[19]

Risk of Preterm Birth

Early evidence suggested an association with GBS bacteriuria in the first trimester and subsequent preterm birth, even with low colony counts.[16] Subsequent retrospective and prospective studies with screening in the first trimester and at 28 weeks have shown no difference in preterm delivery rates.[12,17] A secondary analysis of a retrospective cohort study did not show an increased risk of preterm birth with asymptomatic GBS bacteriuria, although it did show an increased risk for preterm birth with GBS bacteriuria and additional antibiotics (administered for other urinary tract infections, sexually transmitted infections, or upper respiratory infections).[19] A systematic review of 20 studies demonstrated that preterm delivery was positively associated with GBS colonization at the time of delivery (case–control studies: OR 1.59; 95% CI 1.03 to 2.44; cross-sectional meta-analyses: OR 1.75; 95% CI 1.43 to 2.14), However, colonization during pregnancy was not associated with preterm delivery (cohort meta-analyses: OR 1.06; 95% CI 0.95 to 1.19). Several authors have postulated that antibiotic administration with GBS colonization may alter vaginal flora, allowing heavy growth of pathogenic organisms in the upper genital tract and leading to preterm birth.[12,19]

Recommendation

2. Women with documented group B streptococcal bacteriuria (regardless of level of colony-forming units per mL) in the current pregnancy should be treated at the time of labour or rupture of

membranes with appropriate intravenous antibiotics for the prevention of early-onset neonatal group B streptococcal disease. (II-2A)

Risk of Neonatal GBS Disease

Maternal GBS bacteriuria is considered a surrogate for heavy maternal colonization of the genital tract, with vertical transmission of GBS from mother to fetus occurring in most cases after the onset of labour or after membrane rupture. It is associated with a high risk for early-onset GBS disease, manifesting as sepsis and pneumonia in the newborn.[4,14] Third trimester vaginal-rectal culture is therefore considered unnecessary in women with documented GBS bacteriuria earlier in pregnancy,[4,5] even though these women may not have vaginal-rectal colonization detected at 35 to 37 weeks[20] or at delivery.[21] GBS bacteriuria, regardless of bacterial colony count, has been included among the indications for intrapartum antibiotic prophylaxis for the prevention of early-onset GBS neonatal disease.[3–5]

Although most senior obstetricians in the United States treat GBS bacteriuria with low colony counts,[22] there are inadequate data to guide decisions about antibiotic therapy for GBS bacteriuria at low colony counts. In fact, most women who receive antibiotics to suppress or eliminate GBS colonization are re-colonized 3 weeks after therapy is stopped.[23] The American Congress of Obstetricians and Gynecologists and Society of Obstetricians and Gynaecologists of Canada guidelines provide no recommendations regarding management of GBS bacteriuria before the intrapartum period.[4,5] The Centers for Disease Control and Prevention guidelines recommend against the use of antimicrobials before the intrapartum period because they are not effective in eliminating carriage or preventing neonatal disease, and they may have adverse consequences.

Recommendation

3. Asymptomatic women with urinary group B streptococcal colony counts $< 10^5$ CFU/mL or 10^8 CFU/L in pregnancy should not be treated with antibiotics for the prevention of adverse maternal and perinatal outcomes such as pyelonephritis, chorioamnionitis, or preterm birth. (II-2E)

NO INDICATION FOR THIRD TRIMESTER RE-SCREENING FOR GBS COLONIZATION

Current clinical practice guidelines do not support re-screening for GBS genital tract colonization in the third trimester with documentation of GBS bacteriuria, regardless of colony count.[3–5] Several studies have suggested that genital tract cultures at 35 to 37 weeks or at the time of labour correlate poorly with GBS bacteriuria in the first trimester, although these studies did not have the power to evaluate clinical outcomes associated with these findings.[20,21] An early study evaluating outcomes in women with asymptomatic GBS bacteriuria identified at 27 to 31 weeks' gestation showed a reduction in risk of preterm delivery in the antibiotic-treated group (5%) compared with the placebo group (38%).[24]

Recommendation

4. Women with documented group B streptococcal bacteriuria should not be re-screened by genital tract culture or urinary culture in the third trimester, as they are presumed to be group B streptococcal colonized. (II-2D)

SAFETY OF CHEMOPROPHYLAXIS

Antibiotic allergies, including anaphylaxis associated with GBS prophylaxis, occur but are rare, and morbidity associated with anaphylaxis is balanced by the reduction in adverse outcomes associated with GBS colonization. Penicillin continues to be the agent of choice for GBS prophylaxis, and resistance to penicillin has not yet been demonstrated. However, GBS strains are increasingly resistant to clindamycin and erythromycin.[3] There is also the potential for increasing incidence and increasing resistance of non-GBS pathogens. Some studies have suggested that the pattern of giving more doses of antibiotics—or longer duration of antibiotic administration—before deliveries has led to increased neonatal infection caused by an antibiotic-resistant organism; however, these studies were not designed to particularly address this issue.[3] Overall, there has been no evidence of an increase in the rates of early-onset neonatal sepsis due to antibiotic-resistant GBS.[25] Intrapartum antibiotic prophylaxis is still recommended for the prevention of GBS disease.[3]

SUMMARY

Heavy urinary colonization with GBS in pregnancy contributes to maternal pyelonephritis and preterm birth; therefore, treatment of asymptomatic bacteriuria with GBS colony count $\geq 10^5$ CFU/mL or 10^8 CFU/L is an accepted and recommended strategy for the prevention of adverse maternal and perinatal outcomes. Treatment for low urinary colony counts of $< 10^5$ CFU/mL or 10^8 CFU/L is not recommended. However, to prevent neonatal GBS disease, pregnant women in whom GBS bacteriuria has been diagnosed should still follow the current universal recommendations for intrapartum prophylaxis

for GBS bacteriuria at any colony count. Available studies are limited by inconsistencies in the definition of asymptomatic bacteriuria and maternal and perinatal outcomes, regional variation in the prevalence of group B streptococcus, incomplete information on follow-up, and adjustment of risk factors; therefore, ongoing surveillance and evaluation of outcomes in pregnancies complicated by GBS bacteriuria is required to optimize maternal and newborn care.

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