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FROM THE FAMILY PRACTICE INQUIRIES NETWORK

Should we screen for bacterial vaginosis in those at risk for preterm labor?

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EVIDENCE-BASED ANSWER

Bacterial vaginosis (BV) is associated with preterm delivery (strength of recommendation [SOR]: **A**, meta-analysis). However, treating asymptomatic, low-risk women with BV does not always prevent preterm delivery (SOR: **A**, randomized controlled trials [RCTs]). There is some benefit to early screening by Gram stain using Nugent's criteria[1] (**Table**) and treating BV-positive women with a history of preterm delivery, premature rupture of membranes, low birth weight infants, or spontaneous abortion. In this group, treatment has been associated with decreased rates of preterm labor, preterm prelabor rupture of membranes, and low birth weight infants (SOR: **B**, conflicting RCTs).

Empirically treating high-risk women without documented infection has been associated with an increase in preterm deliveries and neonatal infections (SOR: **B**, single RCT).

Nugent's Criteria

Score	Lactobacillus morphotypes	Gardnerella and Bacteroides spp. morphotypes	Curved gram-variable rods
0	4+	0	0
1	3+	1+	1+ or 2+

2	2+	2+	3+ or 4+
3	1+	3+	
4	0	4+	

1+, <1 morphotype present; 2+, 1 to 4 morphotypes present; 3+, 5 to 30 morphotypes present; 4+, >30 morphotypes present. The diagnosis of bacterial vaginosis is present with a score of 7 or greater. From Nugent 1991.[1]

EVIDENCE SUMMARY

Bacterial vaginosis in early pregnancy is a risk factor for preterm delivery.[2] The role of BV in preterm labor is not well understood, but it has been consistently associated with preterm labor and delivery. The detection of BV in early pregnancy seems to be a stronger risk factor for preterm delivery than BV in later pregnancy.

Studies evaluating the screening and treatment of BV in women at risk for preterm delivery have demonstrated varying results. Most treatment studies have excluded women who are in the first trimester. A meta-analysis of 7 RCTs reviewed the evidence of screening for BV in pregnancy.[3] In this meta-analysis, 5 of the trials specified that women were asymptomatic, and the other 2 did not comment on whether the women were symptomatic or not. In general, there was no benefit to routine screening and treatment of BV.

However, a subgroup of high-risk women seems to benefit from screening and treatment. They defined high-risk women as those have had a preterm delivery, premature rupture of membranes, birth weight <2500 g, or spontaneous abortion. Treating BV in women with a high-risk pregnancy decreased preterm delivery (absolute risk reduction [ARR]=0.22; 90% confidence interval [CI], 0.13–0.31; number needed to treat [NNT]=4.5) regardless of antibiotic choice. However, 2 trials of high-risk women who were empirically treated for BV, but did not have BV, showed an increase in preterm delivery less than 34 weeks (number needed to harm [NNH]=11).

A new study evaluating screening for vaginal infections in pregnancy has demonstrated a reduction in preterm delivery.[4] In this study, looking at a general obstetrical population in Austria, 4429 asymptomatic pregnant women between 15 and 19.6 weeks gestation had a vaginal screen for bacterial vaginosis, candidiasis and trichomoniasis. The 2048 women in the intervention group were given the results of the screen from their maternity care provider. The 2097 women in the control group and their providers did not receive the results of the vaginal screen. There were 447 women in the intervention group and 441 women in the control group with positive screens. Using the Nugent criteria, women who were diagnosed with BV received a 6-day course of intravaginal clindamycin 2% cream. Those with positive test results for *Candida* were treated with intravaginal clotrimazole 0.1 g; those with positive results for trichomonas received intravaginal metronidazole 500 mg for 7 days. After treatment, women with a positive test result in the intervention group had a second vaginal smear between 24 and 28 weeks. Persistent BV was treated with oral clindamycin 300 mg twice daily for 7 days. If *Candida* or trichomonas were noted, women were treated with the intravaginal clotrimazole or metronidazole. A statistically significant reduction was seen in preterm births in the intervention group(3.0% vs 5.3%, 95% CI,

1.2–3.6; *P*=.0001; number needed to screen=44).

A large study in 2000 that looked at the use of metronidazole in the treatment of asymptomatic women for BV did not demonstrate any reduction in preterm birth.[5] In this study, 21,965 asymptomatic women between 8 and 22 weeks gestation were screened for BV with Gram stain using Nugent's criteria. Then, 1953 women with BV were randomized to receive either 1 g of metronidazole orally for 2 days or placebo. Between 24 and 29 weeks, all of the women were then rescreened for BV by Gram stain. Even if the results were negative, women received another course of the metronidazole or placebo. In this study, preterm delivery rates did not improve for either low- or high-risk women. Specifically, a subgroup analysis of 213 women with previous preterm delivery did not show any benefit to treatment with metronidazole.

In 2003, a Cochrane meta-analysis of 5 studies involving 622 women with previous preterm birth showed a decrease in the risk of low birth weight infants born to women receiving antibiotics vs placebo for the treatment of BV (odds ratio [OR]=0.31; 95% CI, 0.13–0.75).[6] Treatment also decreased the risk of preterm-prelabor rupture of membranes (OR=0.14; 95% CI, 0.05–0.38) compared with placebo. Unfortunately, these studies did not always specify whether women were asymptomatic for BV infection. In many of the trials, symptomatic women were excluded as they were automatically treated with antibiotics.

In 2003, 2 RCTs evaluating the early treatment of asymptomatic BV in low- and high-risk patients showed a decrease in preterm labor. The first RCT included 494 asymptomatic pregnant women who presented for prenatal care between 12 and 22 weeks gestation. If women had BV detected by Gram stain using Nugent's criteria, they were randomized to receive either 300 mg oral clindamycin twice daily for 5 days or placebo. In the general population, treatment with clindamycin reduced the rate of late miscarriage and spontaneous preterm delivery by 10.4% (95% CI, 5.0–15.8). In women with a previous preterm delivery or a late miscarriage the proportion of preterm delivery or late miscarriage was reduced (16.6% vs 42%).[7]

The second RCT included 409 asymptomatic women between 13 and 20 weeks gestation with BV by Gram stain using Nugent's criteria. Investigators randomized women to intravaginal clindamycin each night for 3 days. At a second visit, 20 to 24 days after treatment, women were retested for BV and if they were positive, they received a 7-day course of intravaginal clindamycin or placebo based on the previous randomization. In this study, the incidence of preterm birth was reduced from 10% to 4% (relative risk [RR]=0.38; 95% CI, 0.16–0.90; NNT=17). This study only included 21 women with previous preterm delivery and a subgroup analysis was not performed.[8]

Intravaginal clindamycin has been associated with worse pregnancy outcomes for patients who do not have bacterial vaginosis. A randomized trial of the prophylactic intravaginal clindamycin 2% cream to prevent preterm birth in high-risk women showed an increase in spontaneous preterm delivery in women who actually used all of the medication and did not have BV (NNH=12.3; *P*<.05).[9]

RECOMMENDATIONS FROM OTHERS

The US Preventive Services Task Force concludes that the evidence is insufficient to recommend for or against routinely screening for BV for high-risk pregnant women. Furthermore, they recommend against screening for average risk women.[10]

The Centers for Disease Control and Prevention recommends that high-risk pregnant women (eg, those women who have had a previous preterm delivery) with asymptomatic BV may be evaluated for treatment. The recommended treatment regimens are metronidazole 500 mg orally twice a day for 5 days, metronidazole gel intravaginally for 5 days, or clindamycin cream intravaginally for 7 days.[11]

The Cochrane Pregnancy and Childbirth Group finds no evidence supporting routine screening and treatment for asymptomatic bacterial vaginosis in pregnancy, except possibly for women with a history of preterm birth.[6]

The American College of Obstetrics and Gynecology summarizes no data supports screening for BV to prevent preterm birth. Their bulletin references a subgroup of women with previous preterm birth who did show benefit from treatment for BV, but the authors speculated that reanalysis with the inclusion of the largest trial to date, which did not show a benefit for this subgroup, might nullify these results.[12]

CLINICAL COMMENTARY

Until there's more research, only screen women who are high-risk or symptomatic

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Although the association of BV and chorioamnionitis and preterm labor is strong, the RCTs do not show any change in outcomes by screening and treating asymptomatic BV in pregnancy except in women who already have a history of preterm labor or premature rupture of membranes. Our practice was screening and treating all pregnant women at the first prenatal visit until about 3 years ago when the RCTs failed to show an impact. The studies that brought BV to the forefront of this discussion show that the inflammatory response caused by BV start in the first trimester or before and treatment is most effective when done early. Perhaps these RCTs are not treating enough women early in pregnancy to see a difference in outcome.

The study we need to have (and which may never be done) would test the treatment of women with BV, either just before conception or early in the first trimester. I am awaiting the next round of information, but for now, I only screen women who are high risk or women who are symptomatic.

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