Two-Drug BV Regimen May Be Best for Pregnant Women

BY JANE SALODOF MACNEIL
Southwest Bureau

HOUSTON — Bacterial vaginosis in pregnant women requires a two-drug regimen to reduce the incidence of low-birth-weight and preterm babies, Dale Brown Jr., M.D., said at a conference on vulvovaginal diseases sponsored by Baylor College of Medicine.

Dr. Brown, chair of clinical affairs in the obstetrics and gynecology department at Baylor, said clinical studies involving single-drug therapy have failed to show a reduction in the incidence of low birth-weight and preterm babies, because such therapy is not aggressive enough to prevent recurrence of bacterial vaginosis (BV).

"I just don't think that the single drug treatment … is eradicating the organisms appropriately, because we know this vaginosis itself is a coterie of several types of organisms," Dr. Brown said.

"If we allow any options for gram-negative organisms to take hold, that's why we continue to see" low-birth-weight babies and preterm deliveries, he said.

Dr. Brown estimated that 15%-20% of pregnant women are diagnosed with BV. They face a fivefold increased risk of late miscarriage in the second trimester, he said. While more than 30% of infections will spontaneously resolve, there is a high recurrence rate.

Recurrence can be up to 30% in 3 months and 80% in 9-12 months in nonpregnant patients.

The American College of Obstetricians and Gynecologists has taken the position (in a practice bulletin) that "there are insufficient data to suggest screening and treating women at either low or high risk will reduce the overall rate of preterm birth" (Obstet. Gynecol. 2001;98:709-16).

For its part, the Centers for Disease Control and Prevention recommends BV screening in symptomatic pregnant women and asymptomatic pregnant women who are at high risk because they have previously delivered a premature infant.

Treatment can be given to pregnant women who test positive for BV, the CDC says.

In contrast with the ACOG and CDC positions, Dr. Brown called for aggressive screening for BV in pregnant women regardless of their risk.

All pregnant women should be screened early in pregnancy, Dr. Brown said.

For those who test positive, he endorsed treatment before 20 weeks with an oral regimen recommended by the CDC.

In addition, he advocated reevaluating high-risk women at every visit up to 32 weeks.

Dr. Brown said the ACOG and CDC guidelines were driven by evidence-based studies that tested one-drug treatments, whereas his opinion derived from clinical practice. He also cited the hypothesis that BV is an inflammatory condition as evidenced by increased levels of proinflammatory cytokines in women with BV (Obstet. Gynecol. 2003: 102;527-34).

Symptomatic women may be hyperresponders to BV, and asymptomatic women may be hyporesponders and also would benefit from aggressive treatment, according to Dr. Brown.

In contrast with the ACOG and CDC positions, Dr. Brown called for aggressive screening for BV in pregnant women regardless of their risk.

The CDC recommends pregnant women be treated with 250 mg of metronidazole orally three times a day or 300 mg of clindamycin orally twice a day, both for 7 days, according to Dr. Brown.

In addition, he advocated using a second agent, probably erythromycin or azithromycin. "*Gardnerella vaginalis* is not really attacked by metronidazole," he said.

If BV recurs, he recommended switching medications and treating with the new regimen for a longer period of time.

Though randomized studies have not shown improvement with treatment of the male partner, he advocated treating the partner as well. "You may have that rare situation where it is passed back by the male," Dr. Brown said. "I would treat the partner."

Among other management strategies for treating recurrent BV, he listed use of condoms, intravaginal use of *Lactobacillus crispatus*, oral or vaginal use of yogurt containing *L. acidophilus*, povidone iodine suppositories, hydrogen peroxide douches, lactate gel/acid preparation, boric acid suppositories, and tea tree oil vaginal pessaries.

The underlying physiologic and pathologic conditions are not well understood, he said.

He speculated that "some unknown factor involving interaction between vaginal bacteria" might be behind the perseverance of BV. "We really don't understand it very well," he said. ■

DRUGS, PREGNANCY, AND LACTATION

Ginger for Nausea and Vomiting

BY GIDEON KOREN, M.D.

Ginger in many forms is taken by pregnant women, with the hopes of alleviating the nausea and vomiting of pregnancy. These forms range from ginger tea, cookies, crystals, and sugars to inhaled powder and capsules containing ginger, as well as fresh ginger.

In a recently published metaanalysis of studies on ginger's use as an antiemetic during pregnancy published last month, the authors concluded that the cumulative experience suggests that the herbal supplement may be safe and effective for managing the nausea and vomiting of pregnancy (NVP).

They noted, however, that more observational studies and larger randomized trials were needed before any definitive statement on safety could be made (Obstet. Gynecol. 2005; 105:849-56).

The metaanalysis included six double-blind randomized controlled clinical trials of almost 700 women and an observational study that my colleagues and I conducted on 187 women taking ginger (Am. J. Obstet. Gynecol. 2003;189:1374-7).

This is the first metaanalysis of studies on the use of ginger as an antiemetic during pregnancy.

In the six randomized controlled trials, 500-1,500 mg daily of ginger were used for 3 days to 3 weeks in women who were at less than 20 weeks' gestation.

In four trials, ginger was more effective than placebo in controlling symptoms of NVP, and in the two remaining trials, ginger was as effective as vitamin B_6 although I would add that vitamin B_6—when used alone—is effective mostly for mild cases of NVP, as the authors also note.

No serious adverse effects or pregnancy-related problems were detected in the five studies that looked at safety.

The outcomes evaluated in the randomized trials included prepartum hemorrhage, preeclampsia, preterm birth, congential abnormalities, major malformations, perinatal and neonatal death, birth weights, and gestational age.

In the prospective observational study, we looked primarily at fetal safety, comparing outcomes in 187 pregnant women who took ginger in the first trimester with another 187 women who during the first trimester took drugs known to be nonteratogenic. With one exception, we found no significant differences in adverse pregnancy outcomes between the two groups.

The exception was that there were significantly more infants with birth weights of less than 2,500 g in the comparison group (6.4% compared with 1.6% in the ginger group), even though there were eight pairs of twins in the ginger group.

There were two major malformations in the comparison group, and three in the ginger group (a ventricular septal defect, right lung abnormality, and a kidney abnormality). At age 2, the daughter of a mother who took 1,000 mg of ginger a day from weeks 11 to 20 of gestation, as well as doxylamine/vitamin B_6 in the first trimester, was diagnosed with idiopathic central precocious puberty. This may be a random finding.

In a subgroup of 66 women, we evaluated the effectiveness of ginger by asking them to rank from 0 to 10 how well ginger controlled NVP, with 0 as no effect and 10 as a maximal effect.

The mean score was 3.3, not a very strong effect. Moreover, when we considered response by the form of ginger used (teas, lozenges, and other preparations), only the capsules containing ginger were associated with an effect significantly greater than zero.

Thus, our observational study put effectiveness against placebo into context: While it is helpful to show in randomized controlled trials that ginger has a better antiemetic effect than placebo, the effect is very mild.

There are other options for managing NVP. In Canada, those include Diclectin (the combination of the antihistamine/anticholinergic doxylamine and vitamin B_6, equivalent to Bendectin), which results in higher scores of about 5-6 on this scale. Clinicians should understand that ginger is a very mild antiemetic, and that only certain formulations seem to be better than placebo, and that the teas, lozenges, and other sources of ginger are likely no better than placebo.

Needless to say, many pregnant women are much more comfortable taking a natural product than a medication because of the perception that natural products are safer. But they should be aware that these products are not necessarily as effective as medicinal products, which in the United States and Canada, include ondansetron and metoclopramide.

At Motherisk, we advise women who call about ginger that it is probably safe and may help ease mild NVP, but it is unlikely to help with moderate to severe NVP.

A precautionary note: Women should also be aware that since there are many formulations of ginger, the amount of ginger in a given form is almost never certain. This is because natural products are not regulated with the same scrutiny as drugs. At this point, more studies comparing ginger with placebo probably are not needed. What would make sense now is to compare the safety and effectiveness of ginger and drugs, such as ondansetron and doxylamine and vitamin B_6, medicinal products that have been proved to be safe and effective for nausea and vomiting in pregnant women.

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