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The Effect of Treatment for Vaginal Yeast Infection on the Prevalence of Bacterial Vaginosis in Early Pregnancy

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SUMMARY Both bacterial vaginosis and candidiasis are commonly seen in pregnancy, with marked differences in pregnancy outcome. The aim of this study was to assess the effect of antifungal treatment on the prevalence of bacterial vaginosis in early pregnancy. This prospective randomized study included 126 women in early pregnancy with heavy vaginal yeast colonization and 88 healthy controls. Vaginal flora was evaluated on initial visit and on two check-ups for the presence of bacterial vaginosis. Half of the heavily colonized patients received an antimycotic agent (clotrimazole). The prevalence of vaginosis was compared among the three groups. χ^2-test and Fisher's exact test were used for statistical analysis. Three of 72 (4.2%) yeast-free controls, two of 79 (2.5%) yeast infected but not treated patients, and nine of 63 (14.3%) infected and treated patients presented with bacterial vaginosis 4 weeks after the initial visit. There was a statistically significant increase in the prevalence of bacterial vaginosis ($p<0.03$) in yeast infected and treated patients as compared to colonized and untreated patients. Treatment of candidiasis in early pregnancy may contribute to an increased rate of bacterial vaginosis.

KEY WORDS: bacterial vaginosis, candidiasis, therapy

INTRODUCTION

There is a continuous world-wide dilemma about the influence of sexually transmitted pathogens and vaginal commensals on the outcome of pregnancy. The majority of controversies have focused on the pathogens of endogenous origin, for instance bacterial vaginosis (BV), candidiasis and group B streptococcus, since those strictly related to sexual transmission (chlamydia, gonococci, viruses) have been documented to elicit a more clear effect on pregnancy outcome. A changing pattern of screening strategies is recommended in different countries evenly characterized by similar prevalence of particular pathogens and similar medical standards (1-4). For example, there is basic disagreement between the Centers for Disease Control and Prevention 2002 recommendations (1) for BV screening, and results of a recent meta-analysis of BV as a risk factor for preterm delivery published by authors from University of Vienna (5). With a huge impact of BV on the complication rate in early pregnancy, especially spontaneous abortions and preterm labor (odds ratio up to 7.55), is it reasonable to limit appropriate screening tests?

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Such confusion also applies to the understanding of yeast vaginal colonization, distinguishing between commensalism and infection, the need and effectiveness of treatment. The expected result of treating candidal infection is the renewal of normal vaginal flora, which ultimately leads to better pregnancy outcome by lowering the rate of ascending transmission, and decreasing chorioamniotic infections, thus improving the well-being of the baby after delivery. Generally, the negative influence of vaginal yeast colonization on pregnancy outcome is very doubtful. The question is whether antifungal therapy in early pregnancy has a positive or negative effect on the structure of vaginal flora. Such treatment could lead to the selection of potentially hazardous bacterial populations for pregnancy. We performed a prospective randomized study to assess the effect of vaginal yeast infection treatment on the incidence of BV in early pregnancy.

PATIENTS AND METHODS

The study included a population of 126 pregnant women aged 19-35, diagnosed with candidal vaginal infection, and 88 healthy pregnant controls aged 18-33 with vaginal flora estimated as normal. These pregnant patients were examined on initial check-up at University Department of Gynecology, Poznan University Medical School. The vaginal ecosystem was estimated after taking vaginal samples for microbiologic cultures and Gram stain testing. The inclusion criteria were 5 to 8 weeks of gestation, the lack of endocervical inflammatory reaction confirmed by microscopic examination of endocervical exudate, which showed all patients to have less than 10 polymorphonuclear leukocytes on HPF microscopy, and absence of any clinical signs of cervical inflammation (mucopurulent exudate, bleeding, edema). Patients with BV were excluded from the study. Women who exhibited redness of the exocervix and no other cervical inflammatory features were eligible to enter the study. According to mycologic (yeast colonization) and clinical status patients were classified as shown in Table 1.

A patient was described as free from yeast if presenting no subjective or objective clinical symptoms (speculum examination), along with negative microscopic tests and culture (n=72). If no clinical symptoms were present but a small number of yeast cells were seen on microscopy and/or a slight growth on Sabouraud medium was observed, the patient was considered healthy and described as “light to moderate colonization” (n=16). Pregnant women who were heavily colonized were characterized by vaginal exudate without itching or burning, while some only noticed a slight discharge. Microscopy revealed inflammatory vaginal exudate, presence of pseudohyphae and intense growth in culture (n=36). The symptomatic group (n=40) presented with all typical clinical symptoms and microbiologic features of inflammatory exudate. Every other patient with yeast inflammation (n=126) randomly received a standard 7-day vaginal treatment with antifungal agent (clotrimazole 2x100 mg) introduced within 3 days from initial examination.

In all groups, microbiologic and clinical studies were repeated 2 and 4 weeks after the first check-up, i.e. between the 9th and 12th week of gestation, using the same methods. All procedures were performed in accordance with ethical standards of the Committee on Human Experimentation.

Statistical analysis was made with the use of χ^2-test and Fisher’s exact test.

RESULTS

Three of 72 yeast-free controls (4.2%), two of 79 (2.5%) yeast infected but not treated patients, and nine of 63 (14.3%) infected and treated patients presented with BV 4 weeks after the initial visit (Table 2).

The prevalence of BV in the control group was relatively low as compared to what is seen in ado-

Table1. Pregnant patients yeast colonization status

	No yeast	Light to moderate Colonization	Heavy colonization No symptoms	Heavy colonization Symptomatic
Controls (n=88)	72	16		
Candidal infection (n=126)	-	-	76	50

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Table 2. Microbiologic status, antifungal treatment results and prevalence of bacterial vaginosis (BV) at 2 and 4 weeks of treatment

Status on initial visit	2 weeks of initial visit				4 weeks of initial visit			
	yeast negative	yeast positive	BV negative	BV positive	yeast negative	yeast positive	BV negative	BV positive
Controls with no yeast (72)*	72	0	70	2	64	8	69	3
Controls light/ moderate col. (16)*	1	15	16	0	2	14	15	1
Heavy colon, no symptoms (38)*	1	37	37	1	2	36	37	1
Heavy colon + symptoms (25)*	0	25	25	0	1	24	25	0
Heavy colon,no symptoms (38)	32	6	38	0	26	12	33	5
Heavy colon + symptoms (25)	21	4	25	0	7	18	21	4

*no antifungal treatment

lescents, while the prevalence recorded in the treated group corresponded to the rates often reported in Europe (6). There was no statistical significance in the prevalence of vaginosis in healthy controls and yeast infected untreated controls ($p=0.669$) at the end of the study. Yet, the number of BV positive pregnant women previously treated with antifungal agent increased during the second and at the last check-up. As a result, there was a statistically significant difference in BV prevalence ($p<0.03$) as compared with the yeast infected but untreated pregnant women. In addition, in all patients the onset of vaginosis after therapy started no sooner than two weeks of the treatment.

DISCUSSION

There is still some uncertainty in understanding the presence of *Candida* sp. in the female genital tract, but it is generally believed that, likewise the skin and gastrointestinal tract, yeast is an opportunistic, normal flora if limited in number and virulence. Candidiasis is detectable in vaginal flora of approximately 20% of the female population in Poland (7), with an increasing (iatrogenic?) tendency observed during the past twenty years. In pregnant women, an increased rate of yeast colonization is commonly observed. The symptoms are milder but there is a high recurrence rate of infection after treatment. Nature rarely works against the well-being of an organism it should protect, so why should it promote vaginal yeast growth if it were in fact harmful to pregnancy? The practical answer is known from a prospective American study (8): moderate and even heavy *Candida* vaginal colonization is not risky for pregnancy and the newborn. It is important to note, however, that some species other than *Candida albicans* may cause higher morbidity, most often during second trimester. Oral thrush in newborns is more often seen with a Candida infected mother. Fungi are occasionally isolated from amniotic fluid and are of medical concern in the presence of a foreign body such as cervical suture.

From the microbiologic point of view, normal vaginal flora and that contaminated by *Candida* sp. (with or without inflammation) is still free from domination by potentially more hazardous microorganisms, mainly anaerobic bacteria. In other words, if a woman has a yeast infection she cannot suffer from BV at the same time. As the results of the study show, eliminating yeast from vagina of pregnant women later increases the rate of BV. This phenomenon is difficult to explain, because clotrimazole, like many similar antifungal agents, is characterized by *in vitro* antibacterial activity against many bacterial species involved in the ori-

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gin of BV. In fact, MIC_{90} ranges from <0.03 mg/L for *Mobiluncus* spp., 0.125 mg/L for *Gardnerella vaginalis*, 8 mg/L for *Bacteroides fragilis* group to >16 mg/L for *Bacteroides urealyticus* (9). In many conditions, the achieved therapeutic level may not be sufficient for eradication of anaerobic species, especially those growing in the deeper layers of vaginal epithelium, where penetration of clotrimazole is poor as compared to, for example, fenticonazole (9). The other explanation is that clotrimazole (and many other medicines, mainly antibiotics) interferes with the delicate microbiologic balance in the vaginal exudate and promotes disturbances in antibiosis between several species of bacteria and antibacterial yeast activity. This antifungal may also leave too much space for the growth of selected populations of vaginal flora by eliminating several aerobic species including coryneforms and streptococci, and by a variable effect on *Lactobacillus sp*.

A study of the potential influence of candidiasis treatment and the incidence of BV with the use of other antifungal agents is obviously needed.

Since recent multi-center analyses have proved that vaginosis is related to abortion and other early pregnancy complications, they have prevented us from continuing the study to check pregnancy outcome in women with untreated BV.

CONCLUSION

The treatment of candidiasis in early pregnancy may contribute to an increased rate of BV. In order to avoid such a risk, a delayed routine screening test for BV should be implemented after such therapy.

References

1. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. MMWR CDC Surveill Summ 2002;51(RR6):1-79.
2. European STD guidelines. Int J STD AIDS 2001;12 (Suppl 3).
3. Stray-Pedersen B. Is screening for genital infections in pregnancy necessary? Acta Obstet Gynecol Scand 1997;76:116-20.
4. Glantz JC. Screening and treatment of bacterial vaginosis during pregnancy: a model for determining benefit. Am J Perinatol 1997;14:487-90.
5. Leitich H, Bodner-Adler B, Braunbauer M, Kaider A, Egarter C, Husseein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. Am J Obstet Gynecol 2003;189:139-47.
6. Pawlaczyk M, Grys E. Prevalence of bacterial vaginosis in adolescent girls. Acta Dermatovenerol Croat 2001;9:183-5.
7. Wlosinska J, Pawlaczyk M. Grzybica narzadow plciowych w ginekologii i poloznictwie. Post Dermatol Alergol 2001;93:189-93.
8. Cotch MF, Hillier SL, Gibbs RS, Eschenbach DA. Epidemiology and outcomes associated with moderate to heavy Candida colonisation during pregnancy. Am J Obstet Gynecol 1998;178:374-80.
9. Perti P, Cohen J, Gianotti B. Fenticonazole as antimicrobial chemotherapy of superficial fungal infections. J Chemother 1999; 11:3-42.