Correlation of Innate Immune Response with IgA against *Gardnerella vaginalis* Cytolysin in Women with Bacterial Vaginosis

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INTRODUCTION

Bacterial vaginosis (BV) is the main vaginal disorder in non-pregnant and pregnant women and is associated with several adverse outcomes, such as increased susceptibility to HIV sexual transmission, upper genital tract infections, post-surgical infections, and adverse pregnancy outcomes.[1,2] BV is a complex polymicrobial alteration of the vaginal ecology, characterized by decreased lactobacilli flora and largely increased colonization of several facultative and strictly anaerobic microorganisms. *Gardnerella vaginalis* is almost always present. Thus far, the only vaginal-specific IgA response characterized in women with BV is the IgA against the hemolysin produced by *G. vaginalis* (anti-Gvh IgA).[3] The anti-Gvh IgA appears to be a critical host response in vaginal fluid of BV-positive women.[3–5] Interestingly, preliminary observations show that high anti-Gvh IgA levels are protective, whereas low levels of anti-Gvh IgA and high levels of microbial hydrolytic enzymes are cor-

related with an increased risk of adverse pregnancy outcomes, including early pre-term birth (<34 weeks' gestation).[6,7]

The present study was performed to assess the correlation between levels of neu-trophils, interleukin (IL)-8, IL-1β, and anti-Gvh IgA in vaginal fluid of healthy and BV-positive women.

PATIENTS AND METHODS

Non-pregnant white women aged 18–45 years were recruited during routine gy-necologic examinations to undergo the Papanicolau exam, which was administered in Italy from May 2001 to March 2002. Women were enrolled after informed consent according to local Ethics Committee. Inclusion and exclusion criteria were analo-gous to those previously adopted.[4] Anti-Gvh IgA, IL-8, IL-1β, and neutrophils were quantified in the vaginal fluid as previously described.[3–5]

Informed Consent

Appropriate informed consent was obtained, and clinical research was conducted in accordance with guidelines for human experimentation that had been adopted by the authors' institutions.

Statistical Analysis

Two-tailed significance of Spearman's ρ coefficient was reported to assess corre-lation. The Mann-Whitney U-test was used to compare factors levels between groups. A *P* value <0.05 was considered statistically significant.

RESULTS

Levels of IL-8 and of neutrophils were not statistically increased in 40 BV-posi-tive women with respect to 40 healthy controls, whereas IL-1β levels were elevated 15-fold ($P < 0.001$), and anti-Gvh IgA levels were twofold higher ($P < 0.05$).

The number of neutrophils was strongly associated with IL-8 and IL-1β in all 80 enrolled women ($P < 0.001$), in healthy controls ($P < 0.001$), and in BV-positive women ($P < 0.001$).

Overall, the women's vaginal IL-8 and IL-1β levels were positively correlated ($P < 0.001$). In the group of women positive for BV, the level of anti-Gvh IgA was positively associated with the vaginal IL-8 and IL-1β levels and neutrophil counts ($P < 0.001$).

DISCUSSION

BV status causes a dramatic increase of IL-1β levels (15-fold). This finding shows that the innate immune system is strongly reacting to abnormal microbial col-onization, although most BV-positive women do not show any signs of inflamma-tion. In fact, IL-8 levels and neutrophil counts are not statistically increased in BV-

positive women. These last findings suggest that the BV microbial consortium produce virulence factors specific to inhibit IL-8 rather than IL-1β. The scarcity of IL-8 may be responsible for the clinically observed absence of inflammatory symptoms and poor counts of vaginal leukocytes in most women with BV. Local adaptive immune levels were correlated with vaginal innate immune factors. Further studies on innate and acquired immunity in BV-positive women are ongoing.

ACKNOWLEDGMENTS

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