The female genital tract microbiota
Composition, relation to innate immune factors, and effects of contraceptives

Akademisk avhandling

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av

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Avhandlingen baseras på följande delarbeten:


The female genital tract microbiota
Composition, relation to innate immune factors, and effects of contraceptives

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ABSTRACT

Abnormal vaginal microbiota, as in bacterial vaginosis (BV), is associated with increased risk of obstetrical and gynaecologic complications and acquisition of sexually transmitted diseases. However, very little is known about the pathogenesis of BV. In BV, the normal vaginal Lactobacillus-dominated biota (LDB) is replaced by anaerobic bacteria. The diagnosis of BV is based on clinical symptoms (vaginal malodorous discharge) and/or microscopy of vaginal smears, methods that do not identify specific microorganisms. The aim was to analyse the composition of the vaginal microbiota in healthy, asymptomatic women of reproductive age, and investigate the relationship between the bacterial species and locally secreted proinflammatory cytokines and the antimicrobial secretory leucoprotease inhibitor (SLPI).

In the study of 37 women, a total of 42 bacterial species were found in vaginal secretions, by cultivation. In the women with asymptomatic BV, particularly, high numbers of the lesser-known Atopobium vaginae, Peptoniphilus harei, and Actinomyces urogenitalis were noted (exceeding 10^{11} bacteria per ml). The latter bacterium, together with Lactobacillus coleohominis, were both isolated from vaginal secretions and have been proposed as new species, based on phenotypic (biochemical testing, SDS-PAGE analysis of whole cell proteins) and phylogenetic results (16S rRNA gene sequencing).

The frequency of LDB in healthy asymptomatic women (n=313) was found to decrease with age, analysing age (years) cohorts 20-29, 30-39, and 40-49. Furthermore, the contraceptive methods used (oral hormone pills, copper- or hormone intrauterine device) were found to affect the frequency of LDB.

A non-cultivation-based, semi-quantitative, checkerboard DNA-DNA hybridisation technique (CDH), based on genomic probes from 13 selected bacterial species, was applied for analysis of vaginal and cervical secretions of 26 women. It was found that the anaerobic bacteria were more frequently detected by CDH, compared to cultivation. Correlations were found between specific bacterial species and cytokines or SLPI. For instance, the strict anaerobic species, B. ureolyticus and F. nucleatum, both correlated with vaginal IL-1α.

By identification and quantification of bacterial species of the lower genital tract, and analysis of their relationships to host-derived innate immune factors, it will be possible to define various types of abnormal microbiota, to develop ways of assessing the risk of specific bacterial species or groups of bacteria in various clinical settings, and to treat them. CDH will be a suitable tool for the quantitative analysis of as many as 40 specific bacterial species, making it possible to investigate large numbers of women. Both age and contraceptive method need to be considered when investigating the compositions of abnormal vaginal microbiota.

Key words: bacterial vaginosis, checkerboard DNA-DNA hybridisation, cytokines, SLPI, Lactobacillus coleohominis, Lactobacillus iners, Actinomyces urogenitalis