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Multi-Gyn Gel in the Prevention and Treatment of Bacterial Vaginosis

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Summary: The Leiden Cytology and Pathology Laboratory (LCPL) evaluates some 60,000 smears per year and is covering 17% of the routine GP cervical smears in the Netherlands for screening. The LCPL has developed a special line of interest for the vaginal ecology and its relationship to pathogenic conditions. In this study the smears of a total of 128 patients could be evaluated. 69 of the patients reported complaints of BV. These were itching, burning, excessive discharge and fishy odour of the discharge. 59 told the GP that they had not experienced any discomfort at the time of the routine PAP smear. In 74 % of the control smears a lactobacilli flora was observed and in 26% smears a mixed flora consisting of lactobacilli and cocci. No coccoid overgrowth was found. The control smears of the patients with Trichomonas in the original smear, 4 showed exclusively lactobacilli and 3 a mixed flora. In none Trichomonas was found back. Of the 69 patients that reported complaints of BV, 78% had experienced relief of itch and burning by the application of Multi-Gyn gel. The other 22 % still had complaints of excessive discharge. They all had a mixed flora in the control smear. No side effects were reported of the use of Multi-Gyn gel.

Key words: vaginal ecosystem, bakterial vaginosis, Multi-Gyn gel

Introduction

1. Cervical cytology and vaginal microbiology.

The Leiden Cytology and Pathology Laboratory (LCPL) services 900 General Practitioners (GPs). With the evaluation of some 60,000 smears per year it is covering 17% of the routine GP cervical smears in the Netherlands for screening. Microbiologic changes have long been associated with alterations in vaginal health (1,2,3,4). Therefore the vaginal flora in these smears is evaluated as well and the GP is informed of any abnormal observation. The LCPL has developed a special line of interest for the vaginal ecology and its relationship to pathogenic conditions, resulting in several research programs and publications. The advantage of studying the vaginal flora in smears as opposed to cultivation of these microorganisms is that the microorganisms can be observed in their natural habitat.

The vaginal environment can be divided in three ecosystems (1):

a. The Döderlein flora that is represented by lactobacilli and a low pH < 4.5 established by the lactate production of the lactobacilli. The low pH of the lactobacilli flora inhibits the growth of most (possible) pathogenic organisms. Candidiasis is observed in association with this flora. Trichomonas is seldomly seen in this flora. Recently it has become evident that an overgrowth of lactobacilli is in itself a possible cause of complaints. This new diagnosis is called lactobacillosis. Actinomyces is seldomly observed.

b. The mixed flora that is represented by lactobacilli and cocci and a pH 4.5 - 5. In this flora lactobacilli and cocci are in equilibrium. It may show the presence of candida and trichomonas. Actinomyces is most often observed. With this flora complaints are however rarely reported.

c. The coccoïd flora that is associated with the clinical presentation of bacterial vaginosis (BV) and a pH > 5. In this flora there are few or no lactobacilli.This flora is often associated with trichomoniasis. Actinomyces is also observed but in this flora candida is never seen.

In the context of the vaginal ecosystem, it is of interest to investigate the association of vaginal microbiology with abnormal cytology; CIN I-II (= PAP I-II) versus CIN III (= PAP III).

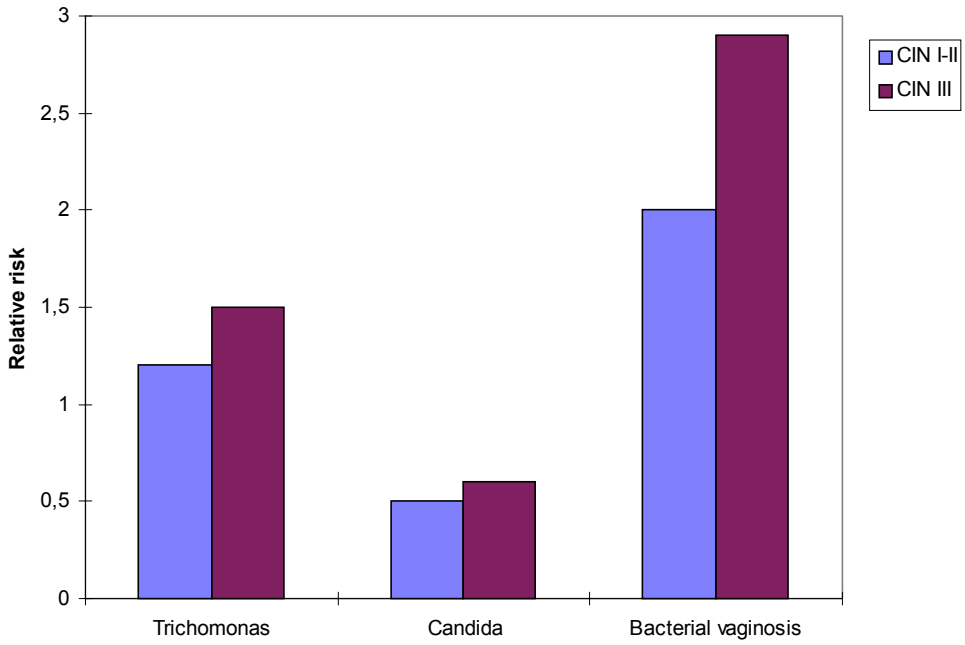
The vaginal microbiology of 666 CIN I-II cases and 293 CIN III cases is shown in Table 1. It is clear that bacterial vaginosis is quite prominent in CIN I-II and the CIN III group.

Table 1. Vaginal microbiology of 666 CIN I-II cases and 293 CIN III cases.

	CIN I-II %	CIN III %
Trichomonas	0.75	1.02
Candida	1.25	1.2
Bacterial vaginosis	13.21	19.11

The relative risk for CIN (RR) in the three types of vaginal microbiology (trichomonas, Candida, bacterial vaginosis) is shown in Figure 1. The relative risk is calculated as the incidence of the type of vaginal microbiology in CIN smears versus its incidence in negative smears. A RR of I implies that there is no association between CIN and the vaginal microbiology values < = 1 mean that there is a negative relationship and values > 1 mean a positive relationship. It is clear that Candida women have less CIN and women with bacterial vaginosis have more CIN. Trichomonas (also associated with an alkaline pH of the vagina) has also a higher RR.

Fig. 1. Relative risk for CIN I-II and CIN III related to three types of vaginal microbiology



2. Bacterial vaginosis and the vaginal ecosystem.

In view of the pathogenecity of microorganisms the preferable ecosystem is that with a pH of < 5. The relationship between the vaginal pH and bacterial vaginosis (BV) has been well established and can be considered as a first observation of the existence of a vaginal ecosystem. Bacterial vaginosis is a very common disorder affecting many women. BV affects approximately 15 to 20% of pregnant women and it has been associated with preterm labor. It is caused by several anaerobic bacteria such as Gardnerella vaginalis, Bacteroides, beta-Streptococci and Mobiluncus/Falcivibrio sp. Trichomonas vaginalis is a STD that is closely related to BV (5). In smears no determination can be made of the species. They are observed as roundish coccoid organisms as opposed to the rod shaped lactobacilli. A typical overgrowth of cocci shows

"clue cells", an abundance of coccoid bacteria glued to epithelial cells. This condition is most often associated with the complaints of BV such as excessive discharge, pain, itch and fishy odor.
Several types of antibiotics are used to treat this condition. Metronidazole, an anti-microbial agent with activity against protozoa and anaerobic bacteria, was found to be the most effective but none was completely successful either in cure or prevention (6, 7). Medication with Metronidazole also has reported side effects of stomatitis, headaches, vertigo and gastrointestinal problems and alcohol consumption is prohibited.

It is obvious that medication by which microorganism are erased for instance for (non gynecological) sore throat, will influence the ecosystem of the vagina. Antibiotics for non gynecological complaints that kill lactobacilli often give rise to symptoms of bacterial vaginosis. Local general disinfectants such as chlorhexidine and povidone iodine are also detrimental for lactobacilli and the vaginal pH. (5)
Other disruptive influences on the vaginal pH are coitus and hygiene (5). Semen is alkaline (pH 7) and many women have postcoital complaints due to the elevated vaginal pH that creates a condition for the overgrowth of cocci. These complaints usually start with a fishy odor. Alkaline soap is also of influence on the local vaginal pH.
Because attachment is the first step in infection and because clue cells are such a prominent feature of BV the adherence characteristics of the anaerobic bacteria have been studied. G. vaginosis adheres better to vaginal epithelial cells at between pH 5 and 6 and all other bacteria involved in BV at a pH of >5.5! (6,7).
The corrective manipulation of a pH > 5 seems to be a tool for the treatment of complaints that are caused by the overgrowth of the coccoid flora (BV) and for the prevention of the growth of these organisms.
Alternative treatments have indeed been proven to be useful and efficacious. There are several clinical situations such as pregnancy or in patients with recurrent BV in which they are the treatment of choice. Some authors claim that lactate-gel is the most promising of all alternative substances. The only effects of this gel are to re-establish a normal acid environment in the vagina and to facilitate recolonization with lactobacilli (8, 9,10,11).

3. Multi-Gyn Gel.
Multi-Gyn Gel combines a low pH of 4.1 with the therapeutic properties of Aloe barbadensis Gel for the relief of pain and itch. The gel adheres well to mucous.
The LCPL has participated by the evaluation of vaginal smears in a previous study of women using Multi-Gyn for the treatment of atypical vulvitis and vaginitis. The results of that study have been the reason to pursue a follow-up study with Multi-Gyn on the monitoring of BV by the principle of the correction of the vaginal pH in combination with the relief of the complaints of pain and itch.
Multi-Gyn gel is commercially available in drugstore and pharmacy. It comes in a 50 ml. aluminum tube with a 5 cm. nozzle for internal application. Application is described on the information leaflet and advised twice per day. In cases of vaginal discomforts such as itch or burning, application can be as often as relief is needed, because the product is non toxic.
Multi-Gyn gel consists of Aloe barbadensis gel (83%) with an analyzed high amount of acytelated polymannose (acemannose). This component has proven to be immunomodulatory and effective in cell processes that are involved in inflammation. (13) Acemannan also seems to be responsible for the inhibition of adhesion of certain anaerobic bacteria and the improvement of phagocytosis of macrophages.(14, 15) Aloe gel appears to have pain killing and itch stopping properties. (13, 16) The thickener of the gel is Xanthan gum that promotes adhesion of the product to mucous. MIC tests have shown that this gel does not affect growth of lactobacilli. The product is buffered to a pH of 4.1.

Study design

Patients come to the GP's office for a regular PAP smear for the early detection of cervical dysplasia. The materials (slide, brush, tempex slide-box and expedition envelope) are provided by the LCPL to the GP's of its client group and the smear is sent to the LCPL. In these routine PAP smears the LCPL also evaluates the vaginal flora. Any special observation is reported to the GP. Coccoid overgrowth is observed in approximately 7% of the smears.
In this study the smears of patients of a group of 40 participating GP's were selected for coccoid overgrowth with and without clue cells. When the LCPL informed the GP on the coccoid overgrowth of a patient, the GP would contact the patient and advise application of Multi-Gyn gel. The patient was asked to come back to the GP's office after one week treatment with Multi-Gyn for a control smear of the vagina. Small questionnaires were provided to the GP to collect the relevant information on the vaginal discomforts of the patient with coccoid overgrowth and the comments on the application of Multi-Gyn gel.
During the control visit the questionnaire was completed and afterwards returned to the LCPL together with the control smear.

Results

At the LCPL a total of some 2100 (7%) smears with coccoid overgrowth are observed in a total of 30,000 routine PAP smears over a period of 6 months. Of the group of 40 GPs who were to cooperate in this study 159 smears were diagnosed for significant coccoid overgrowth; cocci +++. In seven cases Trichomonas was also present.
A response of 80% control smears was received after treatment with Multi-Gyn gel together with the comments of the GP and the patient in the questionnaire. A total of 128 patients could be evaluated in this study. Patients had used the Multi-Gyn gel 5-10 days before their follow-up appointment with the GP.
69 = 54% of the patients reported complaints of BV. These were itching, burning, excessive discharge and fishy odor of the discharge (Figure 2). 59 = 46% told the GP that they had not experienced any discomfort at the time of the routine PAP smear (Figure 2).
In 74% = 95 of the control smears a lactobacilli flora was observed and in 26% = 33 smears a mixed flora consisting of lactobacilli and cocci. No coccoid overgrowth was found (Figure 3). The control smears of the patients with Trichomonas in the original smear, 4 showed exclusively lactobacilli and 3 a mixed flora. In none Trichomonas was found back.
Of the 69 patients that reported complaints of BV, 78% = 54 had experienced relief of itch and burning by the application of Multi-Gyn gel (Figure 4). They had applied the gel externally and internally with an average of 5 times per day for 3 days. After the disappearance of the complaints they continued with the application of two times per day. The other 15 patients still had complaints of excessive discharge. They all had a mixed flora in the control smear. Because no indication of BV could be detected in their smears, it is possible that this discharge is physiological for these individual women. None reported malodorous discharge (Figure 4).

No side effects were reported of the use of Multi-Gyn gel. Because of the acidity of the gel some women had complained about a transient stinging effect directly after application during the first days of use.

Fig. 2. Complaints in women with coccoid overgrowth

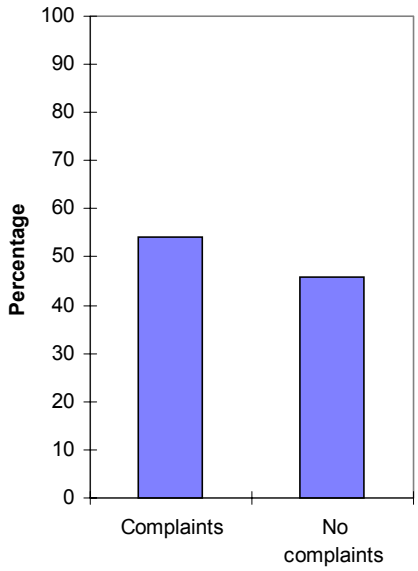


Fig. 3. Flora of control smears after use of Multi-Gyn gel

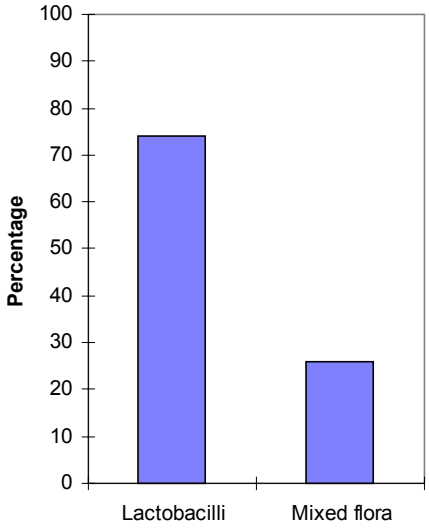
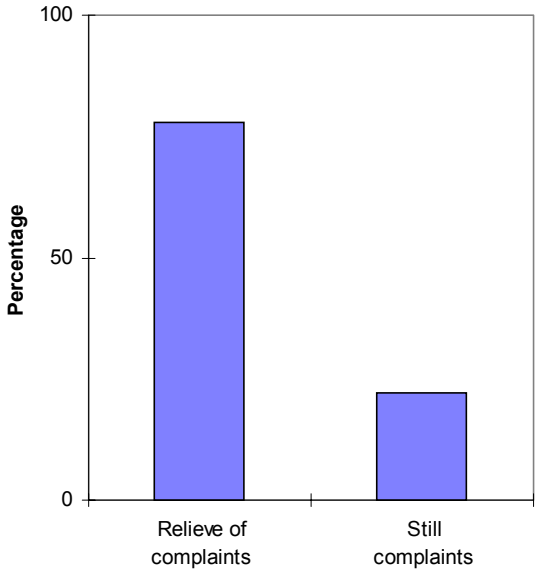


Fig. 4. Relieve of complaints after use of Multi-Gyn gel



Discussion

This study was performed with the microscopic observation of the vaginal flora in Papanicolaou-stained smears. Rod-shaped lactobacilli, and roundish coccoid micro-organisms can be observed in their natural habitat. No effort was made to isolate and determine the anaerobes. In previous studies it has been established that the occurrence of exclusively lactobacilli is associated with a pH < 4.5 as a result of the lactate production of these lactobacilli, a combination of lactobacilli and cocci is associated with a pH 4.5 to 5 and a coccoid overgrowth without presence of lactobacilli is associate with a pH > 5. We have found that both extremes of this scale are related to clinical symptoms. A pH of 3.8 and an overgrowth of lactobacilli may show candida-mimicking complaints. This condition has only recently been recognized as Lactobacillosis (12). On the other side of the scale a pH of > 5.5 and a coccoid overgrowth often shows the clinical signs of BV. Contrary to what is frequently said about the presence of coccoid micro-organisms we find that a mixed flora is seldomly associated with clinical symptoms. Only disbalances of the vaginal flora may be associated with clinical symptoms. In this study the microscopic observation of the coccoid overgrowth was matched only after the receipt of the control smears with the clinical signs of BV as reported by the patients in the questionnaires. 69 reported clinical signs as expressed in irritation of the vaginal area (itch, burning) , excessive discharge and a foul smell of the discharge. Patients had not visited the GP for these complaints in the first place. 59 patients did not report any complaints. This shows that a vaginal ecological disbalance of coccoid overgrowth is not necessarily related to clinical symptoms of BV.
The results of this study show that the manipulation of the vaginal pH into an acidity that is unfavourable for the habitat of anaerobic coccoid vaginal flora appears to be both clinically and microbiologically effective. Previous results of a study on the treatment of BV with an acid lactate cream are in agreement with the effects of the acid Multi-Gyn gel. As coccoid overgrowth is a frequent vaginal ecological disbalance, application of Multi-Gyn gel seems to be a suitable tool for the treatment and prevention of bacterial vaginosis.
Moreover, in Multi-Gyn gel the combination of an optimal vaginal pH and the aloe components seems to be effective for the relief of the vaginal discomforts (such as itch and burning) in clinical BV. Regular application of Multi-Gyn gel is an effective tool in the prevention of coccoid overgrowth and the recurrence of BV.

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