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Effect on Vaginal pH of a Polycarbophil Vaginal Gel Compared with an Acidic Douche in Women with Suspected Bacterial Vaginosis: A Randomized, Controlled Study

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ABSTRACT

Background: **Vaginal pH is a key factor in maintaining a healthy vaginal ecosystem. An increase in vaginal pH is commonly observed during bacterial vaginosis.**

Objective: **This study was undertaken to compare the effects of polycarbophil, a new bioadhesive polymer in gel form, with those of an acidic vaginal douche on restoration of physiologic vaginal pH in women with a vaginal pH ≥4.5 and suspected bacterial vaginosis. We also assessed the pH-lowering effect of a single application of polycarbophil compared with that of a single application of acidic vaginal douche in an additional group of women.**

Methods: **In this controlled, randomized, investigator-blinded study, women aged between 18 and 60 years with a vaginal pH ≥4.5 and suspected bacterial vaginosis who were attending a gynecologic outpatient clinic for a routine visit were randomly allocated to receive polycarbophil gel 2.5 g or an acidic vaginal douche twice a week for 6 weeks. We determined vaginal pH by means of a pH meter and the presence of a fishy vaginal odor using a potassium hydroxide (whiff) test at baseline and after each treatment. Vaginal pH was measured in the lateral vaginal fornix at baseline and at weeks 3 and 6 by an investigator who was blinded to treatment. In an additional group of women with a baseline vaginal pH >5.0, we assessed the effect of treatment after a single application of polycarbophil or douche on vaginal pH at baseline and at 8, 32, 56, and 80 hours.**

Results: **Of 45 women screened, 30 women, 2 of whom were pregnant, participated. All completed the study. An additional 8 postmenopausal women (mean age 56 ± 5 years) received a single application of polycarbophil (n = 4) or vaginal douche (n = 4). Polycarbophil significantly ($P < 0.001$) reduced vaginal pH from 5.4 to 4.7 ± 0.6 at week 3 and 4.6 ± 0.7 at week 6 compared with baseline and with the vaginal douche group (5.4 ± 0.5 at week 3 and 5.3 ± 0.8 at week 6; not statistically significant). At the end of the study, vaginal pH was significantly ($P < 0.04$) lower in the polycarbophil**

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group than in the vaginal douche group (4.6 ± 0.7 vs 5.3 ± 0.8, respectively). Physical and microbiologic signs of bacterial vaginosis were also improved in the polycarbophil group. Both treatments were well tolerated, with no adverse events as determined by the primary investigator. The pH-lowering effect of a single application of polycarbophil gel lasted significantly ($P < 0.01$) longer than that of vaginal douche, decreasing from 5.5 at baseline to 4.5 after 80 hours.

Conclusions: **Our findings show that polycarbophil vaginal gel appears to reduce elevated vaginal pH to physiologic levels for 80 hours compared with acidic vaginal douche and to reduce vaginal pH in women with suspected bacterial vaginosis. Such reduction may help prevent the clinical complications associated with an altered vaginal pH. Randomized, controlled, clinical trials are needed to assess the role of polycarbophil vaginal gel in the long-term treatment of acute and recurrent bacterial vaginosis.**

Key words: **polycarbophil, vaginal pH, bacterial vaginosis, randomized trial. (*Curr Ther Res Clin Exp.* 2000;61:781–788)**

INTRODUCTION

Acidity of the vagina has long been thought to be a protective mechanism.[1] Alkalinization of vaginal pH (ie, >4.5) may be linked to alterations in the vaginal ecosystem. The mild acidity of the healthy vagina has been shown to correlate with decreased risk for *Chlamydia* and *Trichomonas* infections as well as urinary tract infections.[2] More recently, 2 studies have shown that an acidic vaginal pH significantly increases the ability of lactobacilli to bind to the vaginal epithelium[3] and reduces the activity of several pathogenic bacterial enzymes such as sialidase.[4] Adhesion of *Gardnerella,* the probable causative agent of bacterial vaginosis, to vaginal epithelial cells is pH dependent, with maximum attachment occurring between pH 5 and 6.[5]

In a normal, properly estrogenized vagina, the characteristic acidity of vaginal secretions is maintained by the high levels of lactic acid produced by *Lactobacillus*-dominated flora.[6] However, factors such as ovarian hormones,[7] aging,[8] and sexual activity[9] can affect vaginal pH, which can also be elevated during bacterial vaginosis and vaginal infections.[10] Vaginal pH is thus recognized to be the most significant predictor of the status of the vaginal ecosystem, and an increased pH is an important tool in the diagnosis of several vaginal disorders, particularly bacterial vaginosis.

Despite its mild clinical presentation, bacterial vaginosis, both symptomatic and asymptomatic, appears to be associated with obstetric and serious gynecologic complications.[11,12] Therefore, whenever an increase in vaginal pH is observed in routine clinical practice, vaginal acidity should be restored to normal levels to prevent clinical complications.

Recently, polycarbophil,* a new bioadhesive polymer in gel form, became available. This drug reduces vaginal pH to the physiologic range,

* Trademark: Miphil™ (Mipharm SpA, Milan, Italy).

thereby preventing the volatilization of amines and promoting the restoration of acidophilic lactobacilli. Polycarbophil, a weak polyacid, is a large molecule that is neither absorbed nor immunogenic. Because of its multiple carboxyl radicals, polycarbophil adheres to the vaginal epithelial cells until they turn over (3 to 5 days)[13] and buffers vaginal secretions near its pKA (dissociation constant) (4.3).

This study was undertaken to compare the effects of polycarbophil with those of an acidic vaginal douche† on restoration of physiologic vaginal pH in women with a vaginal pH ≥4.5 and suspected bacterial vaginosis. We also assessed the pH-lowering effect of a single application of polycarbophil compared with that of a single application of acidic vaginal douche in an additional group of women.

PATIENTS AND METHODS

Study Design

Women attending the gynecologic outpatient unit at "Borella" General Hospital, Giussano, Italy, between May and June 1999 for a routine visit were enrolled in this randomized, controlled study after written informed consent was obtained; vaginal pH was then determined. The study protocol was approved by the local institutional review board.

Patients were eligible for the study if they were aged between 18 and 60 years and had a vaginal pH ≥4.5, whether or not they were pregnant. In addition, they had to meet ≥1 of the following criteria: presence of vaginal discharge, positive potassium hydroxide (KOH) (whiff) test, presence of clue cells on a wet mount, and a Gram's stain score ≥4 according to Nugent et al.[14]

Patients with suspected *Candida* species or *Trichomonas* infection and those who tested positive for human immunodeficiency virus were excluded from the study. Patients were also excluded if they had undergone hysterectomy, had vaginal bleeding, were currently using a female barrier method of contraception, or had used any vaginal antifungal or antibiotic preparations in the previous month.

Patients were randomly allocated by a computer-generated randomization list (Quickstat® Software, Arcus, Cambridge, United Kingdom), to receive polycarbophil vaginal gel 2.5 g or an acidic vaginal douche twice a week for 6 weeks.

To assess the pH-lowering effect of polycarbophil over time, a second group of women with a baseline vaginal pH >5.0 were randomized by the same method to receive a single application of polycarbophil vaginal gel 2.5 g or acidic vaginal douche. Vaginal pH was measured at baseline and at 8, 32, 56, and 80 hours.

† Trademark: Unigyn® (Uniderm, Casalpalocco, Italy).

Vaginal pH Measurements

Vaginal pH was measured at baseline and at weeks 3 and 6 using an electronic pH meter (Krison PIA-KO1, Medisal, Salerno, Italy) in the lateral vaginal fornix by an investigator who was blinded to treatment. Wet mount and Gram's stain examination of the vaginal flora and KOH testing were performed at each visit. All vaginal specimens were collected 8 hours after the last gel or douche application, ≥7 days after the end of the last menstrual period, and ≥48 hours after the last sexual intercourse (to avoid interference from the alkalinizing effect of semen). The pH-lowering effect over time was assessed in an additional group of women with a baseline vaginal pH >5.0 at baseline and 8, 32, 56, and 80 hours after a single vaginal application of polycarbophil vaginal gel or vaginal douche using the same electronic pH meter.

Statistical Analysis

A previous trial[15] showed that polycarbophil vaginal gel can reduce vaginal pH by 1 ± 0.5. The pH-lowering effect of acidic vaginal douche was hypothesized to be 0.3 to 0.4. Therefore, we assumed that at the end of the 6-week treatment period a clinically significant difference in mean vaginal pH values of 0.7 ± 0.5 could be found between the 2 groups. With an alpha error of 5% and a power of 95% (beta error), there should have been ≥28 assessable patients in the trial.

Statistical analysis was performed using analysis of variance. A two-tailed P value <0.05 was considered statistically significant.

RESULTS

Of 45 patients screened during May and June 1999, 30 women, 2 of whom were pregnant, met the inclusion criteria. All 30 women completed the 6-week study. An additional 8 postmenopausal women (mean age 56 ± 5 years) received a single application of polycarbophil vaginal gel (n = 4) or vaginal douche (n = 4). No adverse events were reported during the trial in any patient as assessed by the principal investigator (B.M.). Patient characteristics at baseline are shown in the table.

Compared with baseline, polycarbophil gel significantly ($P < 0.001$) reduced vaginal pH from 5.4 to 4.7 ± 0.6 at week 3 and to 4.6 ± 0.7 at week 6. The corresponding pH values in the group that received vaginal douche were 5.4 ± 0.5 at week 3 and 5.3 ± 0.8 at week 6. This comparison was not statistically significant. At the end of the study, vaginal pH in the polycarbophil-treated group was significantly lower ($P < 0.04$) than in the vaginal douche group (4.6 ± 0.7 vs 5.3 ± 0.8, respectively). At week 6 the extent

Table. Baseline characteristics of the study patients.

	Polycarbophil Gel (n = 15)	Vaginal Douche (n = 15)
Age (y), mean ± SD	37 ± 9	38 ± 10
Menopause		
Yes	2	3
No	13	12
HRT		
Yes	1	0
No	14	15
pH (mean ± SD)	5.4 ± 0.8	5.6 ± 0.8

HRT = hormone replacement therapy.

of pH reduction correlated significantly with the baseline values ($P < 0.01$; $r = .56$) in polycarbophil-treated patients but not in those who received douche; the higher the baseline pH values, the greater the reduction (Figure 1).

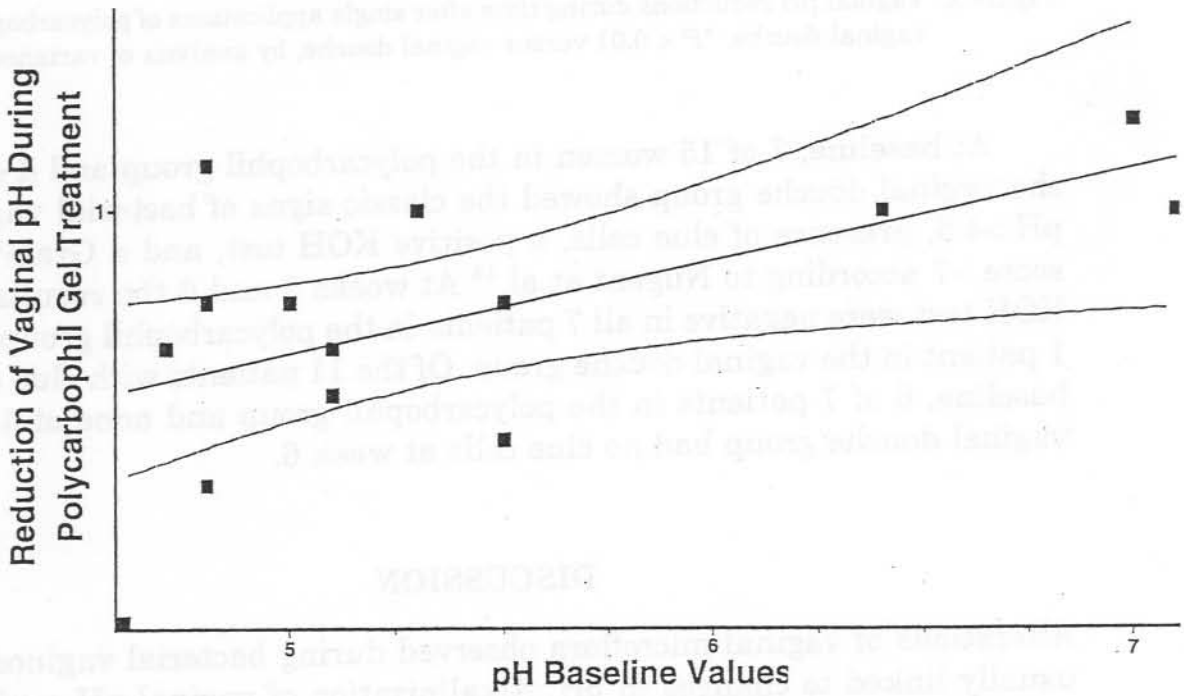

Figure 1. Correlation between baseline pH values and absolute reduction after therapy in polycarbophil-treated patients (n = 15).

In the polycarbophil group at the end of the treatment period, 10 of the 15 patients (67%) had a vaginal pH <4.5 compared with 4 of 15 patients (27%) in the vaginal douche group. In the additional 8 women who received a single application of polycarbophil or vaginal douche, patients in the polycarbophil group had significantly ($P < 0.01$) reduced vaginal pH up to 80 hours compared with patients in the vaginal douche group (Figure 2).

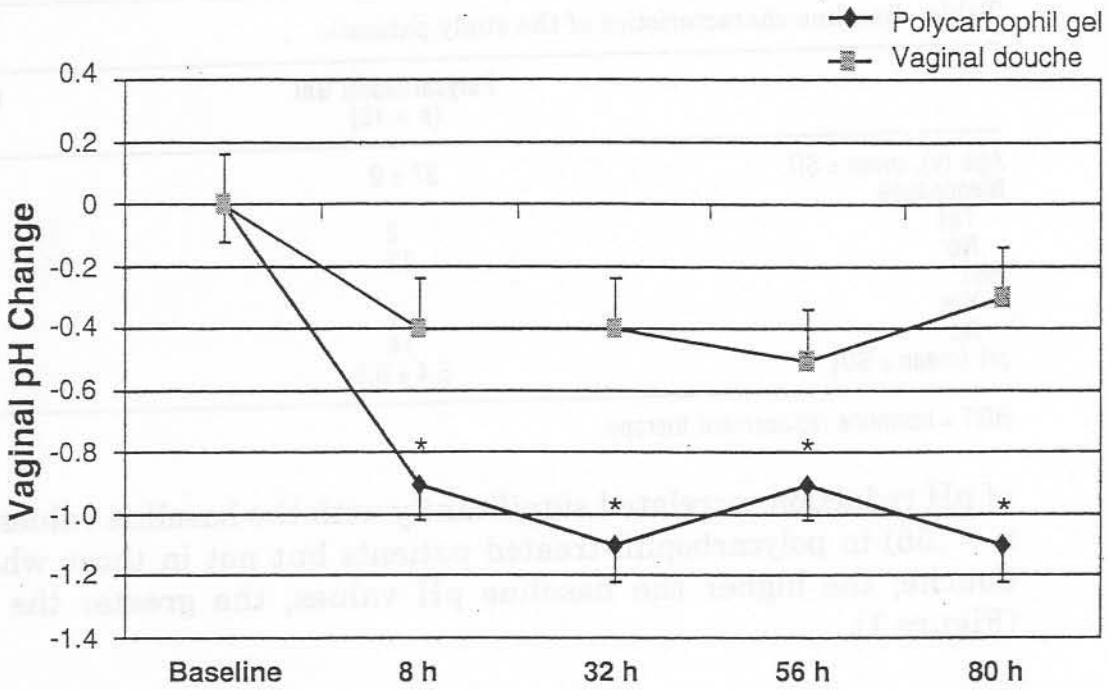

Figure 2. Vaginal pH reductions during time after single applications of polycarbophil gel or vaginal douche. *$P < 0.01$ versus vaginal douche, by analysis of variance.

At baseline, 7 of 15 women in the polycarbophil group and 4 of 15 in the vaginal douche group showed the classic signs of bacterial vaginosis: pH >4.5, presence of clue cells, a positive KOH test, and a Gram's stain score >7 according to Nugent et al.[14] At weeks 3 and 6 the results of the KOH test were negative in all 7 patients in the polycarbophil group and in 1 patient in the vaginal douche group. Of the 11 patients with clue cells at baseline, 6 of 7 patients in the polycarbophil group and none of 4 in the vaginal douche group had no clue cells at week 6.

DISCUSSION

Alterations of vaginal microflora observed during bacterial vaginosis are usually linked to changes in pH. Alkalinization of vaginal pH could promote the overgrowth of anaerobic bacteria.[16] A vaginal pH >5.0 reduces the ability of lactobacilli to bind to vaginal epithelium.[3] Moreover, the activity of sialidase, a *Gardnerella*-produced enzyme, is pH dependent, reaching a peak at a vaginal pH of 5.0 to 5.5.[17] In pregnant women with bacterial vaginosis,[18] sialidase vaginal activity correlated with the risk of obstetric complications (ie, low birth weight).

Our findings suggest that twice weekly use of polycarbophil gel in women with elevated vaginal pH can reduce and maintain vaginal pH in the physiologic range (ie, ≤4.5). In addition, the pH-lowering effect of polycarbophil vaginal gel after a single application is maintained up to

80 hours. In women with bacterial vaginosis, the normalization of pH not only eliminates the volatilization of amines, thus reducing the fishy odor, but also helps maintain a vaginal environment that is unfavorable to colonization by bacterial pathogens and restore lactobacilli as the dominant member of a healthy flora.

The clinical consequences of elevated vaginal pH have recently been amplified.[19] Polycarbophil may thus represent not only a way to reduce vaginal acidity and help maintain physiologic levels but may play an important role in preventing complications known to derive from an altered vaginal pH.

CONCLUSION

Our findings show that polycarbophil vaginal gel appears to reduce elevated vaginal pH to physiologic levels for 80 hours and reduce vaginal pH in women with suspected bacterial vaginosis. Such reduction may help prevent the clinical complications associated with an altered vaginal pH. Randomized, controlled, clinical trials are needed to assess the role of this compound in the long-term treatment of acute and recurrent episodes of bacterial vaginosis.

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