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Treating Vaginal Dryness in Breast Cancer Patients: Results of Applying a Polycarbophil Moisturizing Gel

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ABSTRACT

This study was undertaken to determine whether patients who have a history of breast cancer and who may experience vaginal dryness, vaginal irritation, or dyspareunia will benefit from application of a nonhormonal polycarbophil moisturizing gel. The study design was a single-center, open label, prospective study in women with a history of breast cancer. Twenty-five women who were being treated or who had been treated for breast cancer at the clinic were enrolled from November 1990 through March 1992. Patients were instructed to insert the contents of a prefilled applicator (2.5 g) of Replens (Columbia Laboratories, Miami, FL), a polycarbophil vaginal moisturizing gel, into the vagina three times per week at night for 3 months. Patients were given the option of using an additional application of polycarbophil gel before intercourse, if desired. The main outcome measures were vaginal health assessment index, including the dryness index and measures of vaginal pH, patient acceptance, and the incidence of dyspareunia. There was a statistically significant reduction in mean vaginal pH and an improvement in vaginal moisture, mucosa secretions, and elasticity scores, as well as significant improvement in vaginal health measures, at monthly evaluations during the treatment period. No patients withdrew from the study because of adverse events. Eighty percent of the patients rated the gel as good to excellent as a vaginal moisturizer. This study demonstrates that a polycarbophil moisturizing gel can significantly relieve vaginal dryness in women with a history of breast cancer.

INTRODUCTION

VAGINAL DRYNESS IS A WELL-ESTABLISHED SYMPTOM of menopause.[1] Between 30% and 60% of women seeking treatment for menopausal symptoms report vaginal dryness, and the incidence increases with the duration of menopause.[1-3] The seriousness of this menopausal symptom should not be minimized, as vaginal dryness represents an uncomfortable problem, with physical and psychologic consequences that can have a deleterious impact on the patient's quality of life.[4-6]

Estrogen deficiency has been clearly shown to contribute to vaginal dryness,[2,5,7,8] and hormone replacement therapy can relieve it in many cases.[2,7-10] However, women with a history of breast cancer and who are menopausal are often discouraged by their physicians from taking hormone replacement therapy, or they simply refuse to do so. This practice persists even though a recent review of the literature found no evidence that estrogen replacement

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therapy increases the risk of recurrent breast cancer.[11] In any case, supplemental estrogen may fail to resolve the problem of vaginal dryness in some women.[12,13]

Consequently, patients who have a history of breast cancer often are candidates for nonestrogen-containing therapies for relief of menopausal symptoms, including vaginal dryness. A polycarbophil-based vaginal gel (Replens, Columbia Laboratories, Miami, FL) has been found effective for this purpose.[4,5,13] Being bioadhesive, polycarbophil has been shown in laboratory and clinical studies to adhere to tissue for 24–72 h, resulting in diffusion of water from the gel to the underlying vaginal mucosa. Hydration of the vaginal mucosa stimulates normal lubrication and decreases the incidence of vaginal irritation and dyspareunia. The pH of the polycarbophil gel is 3.0, and it buffers to a normal vaginal pH of 3.5 to 5.0.

The objective of this study was to observe, both subjectively and objectively, the efficacy, duration of action, effect on vaginal pH, and acceptance of this polycarbophil gel in patients who have been diagnosed with breast cancer.

SUBJECTS AND METHODS

Study Population

We recruited 25 patients at our hospital who had been treated or who were being treated for breast cancer. Nineteen patients were found to have abnormalities at the initial pelvic examination, including 17 patients with vaginal atrophy and 3 patients with abnormal Pap smears. Twenty-one of the patients received concomitant medication during the study period, the most common being tamoxifen (10 patients) and antibiotics (6 patients). None of these findings were expected to affect the study outcome, however.

All subjects were menopausal owing to surgical intervention, chemotherapy, or naturally occurring menopause (Table 1). The mean age of the patients enrolled was 60.1 years, with the youngest being 43 and the oldest being 78.

TABLE 1. MENOPAUSAL STATUS AND CAUSE FOR ALL PATIENTS AT STUDY ENROLLMENT

Patient No.	*Age*	*Months since last menstrual period*	*Cause*		
			Natural	*Surgical*	*Chemical*
1	43	11			X
2	73	180	X		
3	65	240		X	
4	57	180	X		
5	53	96			X
6	53	12			X
7	59	84	X		
8	56	5			X
9	64	21		X	
10	60	60	X		
11	59	96	X		
12	45	4			X
13	68	156	X		
14	64	228	X		
15	64	348		X	
16	59	72	X		
17	70	204	X		
18	65	204	X		
19	78	396	X		
20	51	12		X	
21	59	132	X		
22	55	180		X	
23	61	30		X	
24	63	192	X		
25	58	60	X		

Design

Before admission to the study, a complete medical history was obtained and a complete physical examination was performed. At this time, a vaginal examination was conducted using the vaginal health assessment index, which includes measures of vaginal dryness and vaginal pH (Table 2).[13] A Pap smear was obtained for vaginal cytology, and a lateral wall smear was taken for maturation index.

To assess the patients' perspective of the gel, patients were given a clinical diary and asked to record their experience of vaginal dryness throughout the study. As a measure of compliance, all unused applicators were returned, and patients received new supplies during each assessment appointment.

Patients returned to the clinic on a monthly basis for 4 months. Assessment appointments were scheduled so that the gel would have been applied during the 24 h before the appointment. During each evaluation, the patient's diary was reviewed, a vaginal examination was performed, and the vaginal health index was completed. A lateral vaginal wall smear was obtained for the maturation index. Our primary outcome measures were changes in the overall vaginal health index and, as a separate measure, vaginal pH. Secondary outcome measures were the patients' evaluation of the study gel and the incidence of dyspareunia. Adverse events were recorded in the patients' diaries.

The approval of the Institutional Board of Research Associates was obtained before commencement of the study. The details of the study design and expected outcomes were fully explained to all patients, and written, witnessed, informed consent was obtained before their enrollment in the study. Patients were further advised that they were free to refuse to participate or to withdraw from the study at any time, without prejudicing the patient–doctor relationship.

Instrumentation

Vaginal pH was measured using pH indicator strips (ColorpHast, E. Merck, Germany). Overall vaginal elasticity, vaginal secretions, mucosa, and moisture were assessed by clinical observation. The vaginal dryness index score was determined. Patient acceptance was assessed by the investigator's review of the patients' diaries.

Intervention

Patients were instructed to insert the contents of one applicator (2.5 g of polycarbophil gel) into the vagina three times per week at night for 3 months. Patients were given the option to use an additional application before intercourse.

Hypotheses

Our scientific hypothesis was that measures of vaginal health, especially pH and assessments of vaginal dryness, would show im-

TABLE 2. SCORING OF VAGINAL HEALTH INDEX[a]

	Score				
	1	2	3	4	5
Vaginal moisture coating	None, surface inflamed	None, surface not inflamed	Minimal	Moderate	Normal
Vaginal fluid volume (pooling of) secretions	None	Scant; vault not entirely covered	Superficial; vault entirely covered	Moderate	Normal
Elasticity	None	Poor	Fair	Good	Excellent
Epithelial integrity (mucosa)	Petechiae visible	Poor; bleeds with light contact	Fair; bleeds with scraping	Not friable; thin epithelium	Normal
Vaginal pH	≥6.1	5.6–6.0	5.1–5.5	4.7–5.0	≤4.6

[a]From ref. 13.

provement with treatment. Based on previous experience with this gel, we expected to observe few if any side effects attributable to it. We further hypothesized that patients would report that the gel improved their condition.

Analytic methods

Descriptive statistics were determined for the observed values for the vaginal dryness index score and each of its components. The vaginal dryness index score was calculated by summing all the individual scores obtained regarding elasticity, secretion type and consistency, vaginal pH, vaginal mucosa, and vaginal moisture.

Descriptive statistics were also generated for pain with intercourse and the use of other vaginal products as recorded in the patients' diaries. The effect of the study medication on sexual comfort, sexual satisfaction, sexual frequency, and its duration of effect and the patients' rating of the gel were assessed as descriptive statistics.

We used the PC SAS statistical package (SAS Institute Inc., Cary, NC), version 6.04, to generate descriptive and inferential statistics. To test our statistical hypotheses for significance, we used the Wilcoxon matched-pairs, signed-rank test for change at alpha = 0.05.

RESULTS

All 25 patients originally enrolled completed the study. The data from 2 patients were excluded from the efficacy analysis, however, because their diaries showed they used other vaginal products in addition to the study gel. Also, the study period was extended by 1 month for patient 23, who was unable to see the investigators for her fifth scheduled appointment, although she adhered to protocol during this time.

Study findings

We observed a statistically significant reduction in mean vaginal pH and improvement in overall vaginal elasticity scores, as well as significant improvement in vaginal health measures, at each monthly evaluation during the treatment period compared with the assessment at month 1.

The observations made at baseline and at month 1 were not statistically significant from each other. At month 1, the mean vaginal pH was 6.8, with a range of 5.8–8.1, whereas by month 4, the mean had decreased to 4.1, with a range of 3.0–4.7 (Table 3). Similarly, the mean vaginal dryness index score was 10.8 at month 1, with a range of 6–13, whereas by month 4, the mean score had improved to 23.9, with a range of 19–25 (Table 4). The patients' assessments, as recorded in their diaries, also showed improvements in vaginal dryness and irritation. Vaginal dryness index scores and pH are shown by patient in Table 5.

Some patients also reported improved sexual satisfaction (Table 6). By month 4, 10 (77%)

TABLE 3. VAGINAL PH

Statistic	*Baseline*	*Month 1*	*Month 2*	*Month 3*	*Month 4*
n	25	25	24	21	23
Mean	6.9	6.8	5.5	4.9	4.1
SD	0.15	0.12	0.21	0.19	0.07
Median	6.5	6.5	5.4	5.0	4.0
Minimum	5.0	5.8	4.0	4.0	3.0
Maximum	8.1	8.1	8.1	7.0	4.7
Missing	0	0	1	4	2
p value[a]			<0.001	<0.001	<0.001

[a]*p* value resulting from the Wilcoxon matched-pairs signed-rank test for change since month 1. Changes from baseline to month 1 were not statistically significant.

TABLE 4. VAGINAL DRYNESS INDEX SCORES[a]

Score	Baseline	Month 1	Month 2	Month 3	Month 4
n	23	25	25	21	23
Mean	10.1	10.8	16.6	19.7	23.9
SD	0.45	0.38	0.52	0.74	0.35
Median	11	11	17	20	25
Minimum	5	6	12	12	19
Maximum	12	13	23	25	25
Missing	2	0	0	4	2
p value[b]			<0.001	<0.001	<0.001

[a]A higher vaginal index score indicates approaching normal vaginal status.
[b]*p* value resulting from the Wilcoxon matched-pairs signed-rank test for change since month 1. Changes from baseline to month 1 were not statistically significant.

of the 13 patients who said they were sexually active reported that sex was more comfortable with the medication than without, and a similar number reported improvement in sexual satisfaction. Also at this time (month 4), we found that 9 (69%) of the 13 patients reported pain-free intercourse compared with only 4 (36%) at month 1.

Eleven of the 21 patients who responded reported at month 4 that the moisturizing effect of the gel lasted more than 18 h, the longest duration reportable. Seventeen of these patients also said that the medication made them feel, overall, better or much better compared with pretreatment.

Adverse events

No patients withdrew from the study because of adverse events. One patient reported continuing minor vaginal irritation at two points in the study, month 2 and month 4. This reaction was attributed by the investigators to the study gel. Another patient reported vaginal staining after gel administration, an event the investigators considered possibly related to the study medication. A fourth patient noted continuous external labial irritation that was possibly related to the study medication. The patient was given Lidex cream for this reaction.

DISCUSSION

The purpose of this study was to determine whether patients with a history of breast cancer could benefit from regular application of a moisturizing gel. Such patients may be discouraged from taking hormone replacement therapy to relieve their symptoms, or in some cases, they may refuse to do so.

We conducted this trial as a prospective, open-label trial without benefit of placebo control. As such, it is subject to the normal limitations of such studies, including the placebo effect and the biased investigator effect. Especially in light of the minimal side effects induced by the study medication, which make the maintenance of a placebo-controlled trial highly feasible, we believe that any future trials of this medication should be double-blinded, randomized trials. We note, however, that the present study is strengthened by its being a prospective, rather than a retrospective, trial and by the participation of the patients in the data acquisition process.

Despite its limitations, our study suggests that a polycarbophil vaginal moisturizing gel effectively relieves vaginal dryness in most patients without causing significant side effects. Because the gel is nonsystemic, it has the added advantage of avoiding interaction with any systemic medication that may be concomitantly administered to the patient with a history of breast cancer.

TABLE 5. pH AND VAGINAL DRYNESS INDEX SCORES AT MONTHLY EVALUATION FOR EACH PATIENT

Patient No.	Evaluation month[a]	Vaginal pH	Vaginal dryness index score
1	0	6.5	11
	1	6.5	11
	2	5.8	17
	3	4.0	23
	4	4.0	25
2	0	8.1	9
	1	7.8	9
	2	8.1	12
	3	8.1	17
	4	4.0	19
3	0	8.1	6
	1	7.2	6
	2	5.8	14
	3	5.0	17
	4	4.0	19
4	0	6.5	b
	1	6.5	10
	2	5.0	17
	3	4.0	b
	4	4.4	23
5	0	7.6	10
	1	8.1	9
	2	5.5	14
	3	5.3	15
	4	4.4	22
6	0	6.5	10
	1	6.5	10
	2	4.4	23
	3	4.0	b
	4	4.4	22
7	0	6.5	11
	1	6.5	11
	2	5.3	19
	3	5.3	19
	4	4.3	25
8	0	6.5	12
	1	6.5	13
	2	4.4	20
	3	4.4	25
	4	4.0	25
9	0	6.5	12
	1	6.5	12
	2	5.0	18
	3	b	20
	4	4.5	23
10	0	6.8	12
	1	5.8	13
	2	5.0	18
	3	5.0	20
	4	4.0	25
11	0	6.5	11
	1	6.5	11
	2	5.5	16
	3	5.6	18
	4	4.0	24
12	0	6.5	12
	1	6.5	13
	2	4.7	19
	3	4.0	25
	4	4.5	25
13	0	6.5	12
	1	6.5	13
	2	5.3	17
	3	5.0	20
	4	4.5	25
14	0	7.8	5
	1	7.6	7
	2	7.0	12
	3	4.3	20
	4	4.0	22
15	0	6.5	12
	1	6.5	13
	2	b	17
	3	4.4	22
	4	4.0	24
16	0	7.6	8
	1	7.6	9
	2	7.0	14
	3	4.0	21
	4	4.7	21
17	0	7.8	7
	1	7.6	9
	2	7.0	14
	3	7.0	12
	4	4.0	23
18	0	6.5	10
	1	6.5	10
	2	6.8	17
	3	5.3	17
	4	4.0	25
19	0	5.0	12
	1	6.5	11
	2	5.5	16
	3	5.0	20
	4	4.0	24
20	0	6.8	b
	1	6.5	11
	2	4.0	16
	3	4.7	20
	4	4.0	25
21	0	6.8	12
	1	6.5	13
	2	5.3	17
	3	4.4	25
	4	4.0	25
22	0	6.5	11
	1	6.5	11
	2	4.0	18
	3	4.0	21
	4	4.0	25
23	0	6.5	11
	1	6.8	11
	2	4.7	20
	3	b	b
	4	3.0	25
24	0	6.5	7
	1	6.5	12
	2	5.8	17
	3	5.8	18
	4	4.0	25
25	0	8.1	9
	1	8.1	11
	2	5.8	14
	3	7.0	15
	4	4.5	25

[a]Month 0 denotes baseline values.

TABLE 6. PATIENTS' ASSESSMENT OF SEXUAL EFFECTS WHEN USING MEDICATION

Question	*Response*	*Month 1*	*Month 2*	*Month 3*[a]	*Month 4*[a]
Was sex more comfortable with medication than previous sex without this product?	Yes	0	9 (38%)	6 (27%)	10 (48%)
	No	3 (13%)	5 (21%)	3 (14%)	3 (14%)
	N/A[b]	21 (88%)	10 (42%)	13 (59%)	8 (38%)
	Data missing	1	1	3	4
What effect did the gel have on your sexual satisfaction?	Worse with gel	0	1 (7%)	0	0
	No change	1 (100%)	8 (53%)	3 (23%)	3 (23%)
	Better with gel	0	6 (40%)	10 (77%)	10 (77%)
	N/A	0	0	0	0
	Data missing	24	10	12	12
What were your partner's comments regarding sexual activities when using the gel?	Worse with gel	0	1 (8%)	0	0
	No change	0	3 (23%)	2 (15%)	1 (8%)
	Better with gel	0	8 (62%)	9 (69%)	10 (77%)
	Superior with gel	0	0	1 (8%)	0
	N/A	0	1 (8%)	1 (8%)	2 (15%)
	Data missing	25	12	12	12
What effect did the gel have on your sexual frequency?	Decreased	0	0	0	0
	No change	1	13 (87%)	7 (58%)	6 (50%)
	Increased	0	2 (13%)	5 (42%)	6 (50%)
	N/A	0	0	0	0
	Data missing	24	10	13	13
Pain with intercourse	None	4 (17%)	8 (33%)	7 (32%)	9 (43%)
	Minimal	4 (17%)	4 (17%)	2 (9%)	0
	Moderate	2 (8%)	2 (8%)	0	4 (19%)
	Severe	1 (4%)	0	0	0
	N/A	13 (54%)	10 (42%)	13 (59%)	8 (38%)
	Data missing	1	1	3	4
Did you use any other products for vaginal dryness?	Yes	0	0	2 (9%)	2 (9%)
	No	19 (100%)	24 (100%)	21 (91%)	21 (91%)
	Data missing	6	1	2	2

[a]Patients 2 and 4 used other vaginal products in months 3 and 4 and have been excluded from the analyses of those months.

[b]N/A, not applicable.

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