

Vaginal Dryness in Menopausal Women:

Clinical Characteristics and Nonhormonal Treatment

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Nonhormonal vaginal therapy appears to be an effective addition or alternative to estrogen therapy in relieving vaginal symptoms associated with insufficient vaginal secretion.

A decrease in vaginal moisture, a frequent accompaniment of menopause, is often ignored or treated with estrogen. While estrogen replacement is generally the preferred treatment, it is not suitable for all women or the effects may not be sufficiently rapid. Therefore, it is important to study other options. We investigated 89 perimenopausal and postmenopausal women complaining of the symptoms of vaginal dryness, including itching, burning, irritation, pressure, and dyspareunia, and the effects of two nonhormonal vaginal preparations (a water-based lubricant and a new polycarbophil-based vaginal moisturizer).

The women for this two-center, randomized, double-blind crossover study were recruited from two gynecologic clinical practices. Both nonhormonal preparations improved vaginal moisture; the polycarbophil-based moisturizer also lowered pH, increased the quantity of vaginal fluid volume, and decreased the friability of the vaginal surface with speculum insertion. Over 80% of the women noted improvement of their vaginal

symptoms with nonhormonal therapy, with 61.5% preferring the polycarbophil-based moisturizer, 26.5% preferring the water-based lubricant and 12.9% having no preference.

Background

Progressive loss of vaginal secretions, marked vaginal ischemia, thinning of the epithelial surface, and decreased subcutaneous fat occur in the majority of older women due to loss of estrogen stimulation to the genitalia.¹⁻⁷ Prevention of vaginal dryness symptoms traditionally has focused on hormonal therapy and maintenance of sexual activity.^{1,8-12} Nonhormonal vaginal therapies have not been thoroughly evaluated as a method of maintaining vaginal health and reversing symptoms associated with the loss of vaginal secretions.^{1,13}

Inadequate vaginal moisture often leads to difficulties with sexual arousal, pruritus, dysuria, burning, purulent and malodorous discharge, and other sexual and non-sexual complaints.^{1,2,14-16} When its cause is not recognized,

Vaginal Dryness

TABLE I					
Vaginal Health Index					
	1	2	3	4	5
Elasticity	none	poor	fair	good	excellent
Fluid Volume (Pooling of Secretions)	none	scant amount, vault not entirely covered	superficial amount, vault entirely covered	moderate amount	normal amount
pH	6.1 or above	5.6 - 6.0	5.1-5.5	4.7- 5.0	4.6 or below
Epithelial Integrity	petechiae noted before contact	bleeds with light contact	bleeds with scraping	not friable-thin epithelium	normal
Moisture (Coating)	none, surface inflamed	none, surface not inflamed	minimal	moderate	normal

inadequate vaginal moisture may be attributed to loss of sexual desire, or emotional and interpersonal difficulties.^{2,17,18} The latter may lead to a vicious cycle of increasing hostility and dissatisfaction, decreasing frequency of sexual encounters, pain with coitus, and increased symptoms of poor vaginal health.^{2,9,19,20}

Although a decline in vaginal fluid volume has often been described as a symptom occurring many years after menopause, recent data show that it can be a problem early in the climacteric despite the presence of superficial cells on vaginal cytologic examination.^{1,10,11,13,20-23} Transient menopausal states (e.g., lactation, anxiety, and medications such as GNRH agonists and danazol) can also cause inadequate moisture levels.^{1,20,24} While symptoms of poor vaginal health are often mentioned only briefly in medical descriptions of the menopausal symptoms complex, inadequate moisture has been reported to occur in 25% of perimenopausal women and over 50% of postmenopausal women in their fifth decade and may be as troublesome as the other more highlighted menopausal complaints, such as hot flushes and night sweats.^{6,16,20,25-27} Unlike many other menopausal symptoms, vaginal dryness increases in prevalence with age rather than abat-

ing over time. Over 72% of women in their seventh decade may report inadequate vaginal moisture,²⁸ with up to two-thirds of postmenopausal women associating their complaint of dyspareunia with vaginal dryness.¹⁴

With aging, vaginal secretions, composed mainly of vaginal transudate with some contribution from desquamated cells from the upper genital tract (vagina, oviduct, endometrium), endocervical glands and Bartholin's glands, not only decrease in quantity (from a production rate of 3-4 g/4h to 1.7g/4h), but also composition is markedly altered such that the pH increases from premenopausal levels below 4.5 to levels above 5.0 with menopause.^{10,21,29-31} Elevation of pH is detrimental to the maintenance of normal vaginal flora creating an environment more vulnerable to infection and trauma.^{1,32,33}

Although therapies for vaginal dryness have included the vaginal insertions of egg whites, yogurt, oil- and water-based lubricants, saliva, and warm water douches, estrogen is considered the treatment of choice as it reverses the atrophic changes which are responsible for the decline in secretions.^{2,7,8,10,20,34-36} In addition, estrogens can give continuous relief of vaginal dryness symptoms, whereas traditional nonhormonal treat-

TABLE II

Characteristics of Study Sample with Vaginal Dryness

Age (years)	55.7 ± 7.7
Partners' Age (years)	58.4 ± 9.0
Years with Partner	22.2 ± 15.1
Height (cm)	162 ± 7
Weight (kg)	66.5 ± 12.3
Years Postmenopausal (n=69)	10.1 ± 7.8
Estrogen users (%)	44.0
Years Estrogen Use (n=40)	2.7 ± 3.5
Years Vaginal Dryness (n=89)	3.9 ± 4.3
Religiosity* (mean rank) (n=86)	2.9 ± 0.8
Educational level** (mean rank) (n=88)	3.4 ± 1.2
No. vaginal deliveries (n=88)	2.4 ± 1.6

* Scale - 1-not religious, 2-slightly religious, 3-moderately religious, 4-very religious

**Scale - 1-some high school, 2-H.S. graduate, 3-some college, 4- college graduate, 5-postgraduate education

ments are often transient in effect and are mainly of use in relieving inadequate lubrication with coitus. However, nonhormonal therapy, by itself or in conjunction with estrogen therapy, is often desired as estrogens may take up to two years to restore adequate vaginal lubrication, are dependent on chronic, uninterrupted use, are medically contraindicated in some women, and rejected by some women who choose not to use hormone therapy.^{10,21,37}

The need for long-lasting and well-tolerated nonhormonal therapy prompted this study in which we sought to describe the clinical characteristics of climacteric women who report inadequate vaginal lubrication, and to evaluate and compare the acceptability and efficacy of two nonhormonal vaginal preparations; a water-based lubricant and a new nonhormonal polycarbophil-based vaginal preparation which uses bioadhesive technology.

Materials and Methods

Ninety-three perimenopausal and postmenopausal women, in good health, complaining of vaginal dryness were recruited at two study centers via announcements in local newspapers and from a letter sent to private patients aged 40 years and above. Women with known or suspected malignancy or other serious diseases, those with undiagnosed genital bleeding, those

who used any investigational drug in the previous three months, women who were regarded as unreliable for the study, and women in whom estrogen therapy was to be initiated or where the dose would possibly be changed during the study were excluded. Systemic estrogen therapy was permitted only if initiated at least three months prior to the study. Vaginal estrogen use was not permitted.

For study purposes, vaginal dryness was defined by subjects' report of inadequate lubrication at the time of sexual arousal or vaginal intercourse, or a history of perimenopausal and/or postmenopausal vaginal discomfort (e.g., irritation, burning, soreness) attributed to inadequate secretions of at least one year in duration. Subjects were initially screened by phone to insure study eligibility. Those who met enrollment criteria were given a clinic appointment at which time an informed consent was obtained. At the initial study visit each study participant was interviewed by a nurse regarding demographics, medical, psychological and sexual health, as well as numerous details regarding her history of vaginal dryness. A physician then performed a physical and pelvic examination which included a pap smear. Assessment of vaginal health was based on an adaptation of the vaginal atrophy index,⁹ by physician grading of five vaginal parameters: the quantity of secretions pooled in the

TABLE III

Sexual Profile of Menopausal Women with Vaginal Dryness

Sexual Satisfaction+ (n=81)	2.5 ± 1.1*
Importance of Sex+ (n=84)	2.8 ± 0.9*
Sexual Activities (per month)	
Physical Affection (n=66)	21.7 ± 8.6
Sexual Caressing (n=63)	15.9 ± 10.7
Intercourse (n=63)	6.1 ± 6.6
Sexual Fantasies (n=55)	5.8 ± 8.6
Oral Sex (n=56)	2.6 ± 4.0
Masturbation (n=54)	1.9 ± 4.7
Dyspareunia: # reporting complaint	71
Mean duration of complaints (yrs)	3.8 ± 6.1

* Mean Rank

+ Scale - 1) none, 2) somewhat, 3) moderate, 4) high

posterior vaginal vault (vaginal fluid volume), the appearance and spread of the secretions coating the vaginal vault (moisture), epithelial integrity as determined by color, rugation and friability of the vaginal surface with speculum insertion (vaginal epithelial integrity), elasticity of the tissue as determined by the resistance of stretch noted with digital palpation (elasticity), and pH measured from the lateral vaginal side wall (Table 1).

Study products consisted of two nonhormonal vaginal preparations: a bioadhesive polycarbophil-based vaginal moisturizer* (moisturizer) and a water-soluble lubricating jelly** (jelly).

The moisturizer is unique in that it uses bioadhesion to hold water in place on the vaginal epithelial surface. The primary ingredient, polycarbophil, carries up to 60 times its weight in water and is not absorbed. Polycarbophil is also bioadhesive, which allows it to attach to mucin or epithelial cell surfaces through anionic bonding. As this polymer is insoluble, it remains attached until the mucin or cells slough, typically 24 hours or more, and allows the water delivered with the polycarbophil to continuously hydrate the underlying cells. Polycarbophil is a weak acid with a pH of 2.8 and a high buffering capacity, allowing it to

lower pH in the vagina.

Patient acceptance and efficacy of the study products were investigated in a double-blind randomized cross-over study design. Both preparations were packaged in identical single-use, pre-filled applicators marked only as "study product." Subjects were instructed to insert daily for five consecutive days one applicatorful of study product into their vagina and were asked to fill out a study diary on a daily basis. The diary asked questions about lubrication, sexual activity, study product side effects, length of study product effect, and rating of overall study product performance.

Subjects first used either the moisturizer or jelly for five consecutive days; on the last day of application of the study product and the next three days, the women returned to the clinic for a pelvic examination and for a personal interview. The washout period, during which there was no use of study product or any other vaginal preparation, was seven days for half the sample and fourteen days for the other half. For the second study phase, the women were crossed over to the opposite study product which they used daily for five consecutive days. Subjects were again examined and interviewed on the last day of study product use and for the next three days. On the last day of the second study phase, questions regarding comparison of the two study products by the subject and her perception of her partner's

* REPLENS, Columbia Laboratories, Inc, Miami, Florida

** K-Y Brand Lubricating Jelly, Johnson & Johnson, New Brunswick, N.J.

TABLE IV

Effect of Vaginal Dryness on Menopausal Sexuality (%)

	Increased	Decreased	Unchanged	N/A
Sexual Frequency (n=62)	0	72.6	25.8	1.6
Sexual Desire (n=60)	1.6	71.7	26.7	0
Sexual Satisfaction (n=61)	0	78.7	21.3	0
Sexual Arousal (n=58)	0	77.6	22.4	0
Effect on Partner (n=57)	0	35.1	61.4	3.5

view were asked. Efficacy, acceptance and comparisons of the study products were determined by daily diaries completed by the subjects, on days 5, 6, 7, and 8 of each study product sequence, by a pelvic examination with vaginal health assessment, and patient interview.

Eighty-nine women completed the study protocol. Two subjects were dropped from the study for noncompliance with protocol, and two subjects while on moisturizer voluntarily discontinued participation because of urethral irritation. Urine culture on both subjects was negative.

Pooled data from the two centers were analyzed. Responses to diary questions were studied by cross tabulation and chi square. Answers to all inquiries on the questionnaire were not completely obtained from all subjects, therefore percentages stated are of those who responded. For the vaginal health assessment (moisture, vaginal epithelial integrity, elasticity, vaginal fluid volume and pH), analysis variance from baseline prerandomization was performed. In addition to the overall statistical significance of the effects, between-group comparison was done using the Duncan's post hoc test. Descriptive statistics of dependent variables by visit and product, as well as of the large number of baseline variables obtained, were also done.³⁸

Results

Clinical Characteristics. Characteristics of the study subjects are shown in Table II. The average age of married subjects was 56 ± 8 and of single subjects was 64 ± 10. Sixty-nine (77.5%) of the women were menopausal (absence of menses for more than six months) and 20 (22.5%) were perimenopausal. Of those menopausal subjects, 33 (48%) had little or no difficulty with menopause, 27 (35%) experienced some difficulty and 9 (17%)

experienced great difficulty. Sixty-one (69.3%) of the women had not had a hysterectomy, 16 (18.2%) had a simple hysterectomy and 11 (12.5%) had a hysterectomy with bilateral oophorectomy. All subjects reported vaginal dryness, with a mean duration of 3.9 years.

Sexuality of women with vaginal dryness. Overall, the majority of the group reported moderate sexual satisfaction, and regarded sex as important (Table III). The reported monthly frequency of various sexual activities is also reported in Table III.

Multivariate analysis showed that the most important association of dyspareunia was with vaginal dryness (f=55.7). In addition, absence of estrogen therapy (f=12.3), poorer vaginal health assessment ranking (f=10.7), and increasing age (f=4.0) were other important determinants of painful intercourse.

Sixty-one (79.2%) of the cohort reported that vaginal dryness had adversely affected them sexually. Other effects of vaginal dryness on sexuality are shown in Table IV.

Vaginal Dryness: Associated symptoms. Women with vaginal dryness reported one or more associated symptoms (Table V). Fifty of the subjects had prior vaginal lubricant use. When asked why they started to use lubricants, pain with intercourse was considered the most important factor by 35 subjects. With aging, women had a lower grading on vaginal health assessment (p<0.05); had a higher vaginal pH (p<0.01) and were more likely to report sexual improvement after the use of study products (p<0.05).

Estrogen Use. Estrogen users were more likely to have had a hysterectomy, were less likely to have used vaginal lubricants, and had more complaints of vaginal itching, irritation, pressure and dyspareunia (p<0.05), as compared to non-users.

TABLE V

Vaginal Dryness Symptoms in Menopausal Women

	# Experiencing	Duration (years)
Vaginal itching	44	2.4 ± 2.9
Vaginal irritation	55	2.8 ± 3.2
Vaginal pressure	17	3.1 ± 2.4
Vaginal dyspareunia	71	3.8 ± 6.1

Estrogen users were more educated, tended to be younger, married and have older partners; they assigned more importance to sex but reported lower levels of sexual satisfaction, and had a lower frequency of intercourse, oral sex and self stimulation ($p < 0.05$). On pelvic examination, estrogen users tended to have a lower pH and better vaginal health ($p < 0.05$).

Results of Nonhormonal Therapy. On physical examination performed on the fifth day of study product in both study phases, pH was significantly lower with the moisturizer as compared to the control and jelly ($p < 0.01$), while there was no significant difference between control and jelly. The pH with moisturizer remained below 5 up to 72 hours after product discontinuation. By vaginal health assessment, pH, vaginal epithelial integrity and secretions were ranked better, while on moisturizer than control, while pH and secretions ranked better on moisturizer than jelly (Table VI).

The lubricating effect tended to last longer while on moisturizer than while on jelly ($p < 0.001$). A greater number of subjects reported more than 12-hour duration of moisturizer effect while less than six hours of effect was more frequently reported on jelly. In eliminating vaginal dryness and associated vaginal and sexual problems, the women were more likely to relate moisturizer efficacy as excellent, very good, or good ($p < 0.04$), although the most frequent response for both study products was "good" (30.4% for moisturizer and 28.3% for jelly). The women tended to describe the vaginal lubrication as more natural with moisturizer than jelly ($p = 0.069$).

Residue was reported in 7.8% of women on moisturizer and by none on jelly ($p < 0.01$). Although side effects such as urethral irritation, vaginal burning and product residue were reported more frequently on moisturizer (13.8%)

than jelly (10.8%), this difference was not statistically significant ($p = 0.112$). Except for two women on moisturizer and one woman on jelly, those reporting these problems had the symptoms present at baseline, and complaints of the side effects continued during both phases of the trial using either moisturizer or jelly. Ten of the women reported that vaginal symptoms were worse while using jelly compared to one on moisturizer. Five women reported worsening of vaginal symptoms while on each study product.

When asked which study product they preferred, (61.5%) of women reported the moisturizer, (25.6%) the jelly and (12.9%) had no preference.

Pap smear results from all subjects were normal.

Discussion

Previous descriptions of vaginal dryness often focused on this problem as an occurrence in the postmenopausal years without emphasis on its impact in the early menopausal years.^{1,10,11,13,20,21,23} From this small sample, in which 22.5% of the study women were perimenopausal, it appears that vaginal dryness is an early sign of declining estrogen levels.

Estrogen deficiency is the major cause of vaginal function decline with age. This is supported by the fact that estrogen levels decline while estrogen receptors in the vagina are unregulated after menopause.^{22,39-41} As expected, the older women in this study were found to have a more atrophic vaginal vault and higher vaginal pH than the younger subjects.⁴² Subjects on estrogen tended to be younger than non-users but had older partners, tended to be married and to report more dissatisfaction with the sexual life. Possible explanations of this dissatisfaction are self selection, in that women with sexual problems seek

TABLE VI

Vaginal Health Assessment Scores at baseline and after nonhormonal vaginal treatment

	Moisturizer	Jelly	Baseline
Elasticity	2.9 ± 0.8	3.0 ± 0.8	2.9 ± 0.8
Secretions	2.8 ± 1.1 [∂]	2.4 ± 1.1	2.4 ± 1.0
pH	4.9 ± 1.1 [∂]	5.7 ± 1.0	5.6 ± 1.1
Epithelial Integrity	3.9 ± 0.9 [∞]	3.7 ± 1.1	3.4 ± 1.3
Moisture	3.3 ± 0.8 [∞]	3.0 ± 0.9 [∞]	2.8 ± 0.9

[∞] p < 0.05 versus baseline
[∂] p < 0.05 versus jelly

solutions or that these women have older partners with presumably more sexual dysfunctions. Although this study was not designed to evaluate the effect of systemic estrogens on vaginal dryness (local estrogens were an exclusion criteria), as expected, estrogen users had a significantly lower pH and tended to have better vaginal health assessment than women who were not using estrogen.

Estrogen replacement, either systemic or local, is the traditional approach to the treatment of vaginal dryness. This approach is associated with additional benefits—resolution of hot flushes, beneficial effects on bone density and cardiovascular status, and improvement of vaginal atrophy.^{37,39} However, 44% of the study subjects were using systemic estrogens. This again confirms other studies reporting that although estrogen therapy reverses the vaginal cytologic picture to one of cellular maturity with a predominance of superficial cells, this does not always equate with complete elimination of lubrication difficulties.^{2,6,10,21} Also one to two years may be necessary before vascular changes are significantly improved to eliminate vaginal dryness.^{10,21} Lastly, hormone replacement may be medically contraindicated for some women and may be avoided by another subset of women who do not choose to take estrogen. Nonhormonal therapy is beneficial in those women on estrogen replacement therapy who continue to have vaginal dryness symptoms or in those women with severe vaginal atrophy who cannot or will not use estrogen.

In this double-blind, randomized study the

bioadhesive vaginal moisturizer which lowered vaginal pH as well as having several positive effects on vaginal secretions, moisture and vaginal epithelial integrity, was preferred to the jelly by the majority of women. Women may have preferred the moisturizer because of the longer duration of action and because it tended to feel more like natural secretions.

Our study confirms the negative effect of aging on the sexual function of women and the significant role of vaginal dryness in such dysfunctions. Our findings of increased sexual dysfunctions and decreased sexual frequency and desire with aging are in agreement with numerous published reports.^{6,14,16,18} The majority of the cohort (79.2%) ascribed an adverse effect on their sexual function (i.e., sexual frequency, desire, satisfaction, and arousal) from the symptoms associated with inadequate vaginal lubrication. Almost 80% of this cohort with complaints of vaginal dryness report dyspareunia, which is consistent with other published data.^{13,14} The complaint of painful coitus was associated with vaginal dryness more than with other important determinants of dyspareunia including absence of estrogen therapy, greater vaginal atrophy and increasing age. Vaginal dryness also was reported to have adversely affected partner function in some instances.

It appears that early recognition and treatment of vaginal dryness will not only improve sexual function in those women who remain sexually active, but will eliminate associated vaginal symptoms (i.e., irritation, itching, burning, and pressure). From this study use of nonhormonal

vaginal therapies, especially a bioadhesive technique, appears to be beneficial both for sexual function as well as for overall vaginal comfort. Nonhormonal vaginal therapy appears to be well

accepted by women with vaginal dryness and associated symptoms, as noted by the positive responses of the majority of women in this study.

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