

ABSTRAK

Issue No.5 in a series of informative newsletters from Anglian Pharma Sales & Marketing

REPLENS GAINS NEW 'INDICATION' AND STATUS

ReplensMD is the new title for Replens the hormone free vaginal moisturiser. The new name results from a change in status from a registered PL (MCA) to a registered Medical Device (MDA).

A new product presentation is added to the 3 and 6 single use applicator packs, an 'economy system', comprising a 35g tube with re-usable applicator that, for the same cost as a 6 pack, doubles the number of applications delivered.

ReplensMD has a new, additional, indication for the 'symptomatic relief of vaginal atrophy',

ATROPHY - NEW EVIDENCE

Since Abstrax - Issue No 2, more clinical information about Replens has been published. In this newsletter Abstrax No. 5, the latest clinical abstract - The Effect of Replens on Vaginal Cytology in the Treatment of Postmenopausal Atrophy. Cytomorphology Versus Computerised Cytometry - is to be found in section 9, on the back page.

THE IMPORTANCE OF VAGINAL MOISTURE

Vaginal moisture is essential for vaginal health and comfort in women of all ages, whether or not they are sexually active.

Vaginal moisture cleanses the vaginal passage, serves as a lubricant during sexual intercourse, and allows ease of movement and personal comfort. Additionally, because natural vaginal moisture is acidic (pH < 5), it serves to discourage the proliferation of potentially pathogenic microorganisms.

THE COMPOSITION OF VAGINAL MOISTURE

Vaginal moisture is derived mainly from blood. It consists of a clear fluid which flows through the vaginal walls from local capillaries - a process referred to as transudation. Additional moisture in the form of mucus is contributed around mid-cycle by glands within the cervix and, during sexual arousal, by Bartholin's glands situated at the introitus. Discarded epithelial cells within the vaginal passage may also add moisture and lubricity.

THE ROLE OF OESTROGEN

The production and acidity of vaginal moisture is directly controlled by oestrogen:

- * Oestrogen augments blood flow to sub-epithelial tissues (thereby facilitating transudation)
- * In pre-menopausal women the rise in oestrogen levels around mid-cycle has a direct effect on cervical mucus, causing it to become translucent and fluid.
- * Oestrogen causes the basal cells of the vaginal epithelium to mature to superficial cells. These produce glycogen which in turn is used by commensal lactobacilli to produce weak acids - and hence a low (acidic) vaginal pH.

VAGINAL DISCOMFORT

Any medical condition, treatment or surgical procedure that directly affects ovarian function (e.g. the menopause, chemotherapy, radiotherapy or hysterectomy) may give rise to vaginal dryness, a corresponding predisposition to vaginal infection, and ultimately, vaginal atrophy. Typical symptoms include itching, irritation, burning and (where applicable) painful intercourse (dyspareunia).

REPLENISHING VAGINAL MOISTURE

As oestrogen replacement therapy is not always indicated and may sometimes be contraindicated, effective nonhormonal treatments have long been sought. Now, thanks to recent advances in bioadhesive technology, an effective alternative to local oestrogen therapy is available.

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BIOADHESION is a new form of drug delivery based on polycarbophil - an inert, acidic, negatively charged, hydrophilic polymer which acts as a carrier for therapeutic agents. Polycarbophil is mucomimetic and adheres to epithelial cells and to mucin (where present) until the cells to which it clings are naturally shed. Meanwhile, the therapeutic agent is driven into the underlying cells and vasculature.

The following abstracts from published papers confirm the efficacy of Replens (a nonhormonal, bioadhesive, aqueous vaginal gel) in relieving all the symptoms of vaginal dryness whilst simultaneously restoring vaginal pH to normal physiological levels.

1. MANAGEMENT OF MENOPAUSE WHEN ESTROGEN CANNOT BE USED

Ronald L Young, Nirmala S Kumar and Joseph W Goldzieher

Drugs 40 (2) 220-230, 1990

Abstract

Estrogen deficiency, whether surgically induced or as a consequence of natural ovarian failure, has destructive effects on many organ systems. With current levels of life expectancy, untreated women may expect to spend a third of their lifetime in this state. Appropriate estrogen replacement therapy (ERT) can avert (if started promptly) or ameliorate these devastating consequences, some of which (osteoporotic fractures, increased cardiovascular morbidity) can be lethal. Nevertheless, from 10 to 20% of postmenopausal women may have significant contraindications to ERT. Treatment of symptoms and improving the quality of life is imperative, yet many physicians abjure intervention, for reasons which are not entirely clear. Recent studies of conventional intervention with sedatives or tranquilisers show results equivalent to placebo therapy. On the other hand, specific agents with demonstrated effectiveness are available for management of the major estrogen-deficiency effects, although none of them are truly adequate replacement for the effect of estrogen itself.

2. REPLENS VERSUS DIENOESTROL CREAM IN THE SYMPTOMATIC TREATMENT OF VAGINAL ATROPHY IN POSTMENOPAUSAL WOMEN

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Maturitas (1996) 23: 259-263

Abstract

Objectives: This study was designed to evaluate the efficacy of Replens, a non-hormonal moisturizing gel, on symptoms of vaginal atrophy in postmenopausal women, in comparison with Dienoestrol (Cilag), an oestrogenic vaginal cream.

Methods: Thirty-nine patients were randomly allocated to either of the two treatments. Replens was given three times a week during the 12 weeks of the study, while Dienoestrol was administered daily during the first two weeks and thereafter three times a week. Vaginal dryness index, itching, irritation, dyspareunia, pH and safety were evaluated every week in the first month and every month thereafter.

Results: Both treatments had a significant increase on vaginal dryness index as soon as the first week of treatment, and the hormonal compound was significantly better than the non-hormonal one. All symptoms such as itching, irritation and dyspareunia significantly decreased or disappeared without any difference between the two treatments. For pH, no significant difference was seen either in each group or between the two groups. No adverse events related to the two drugs were found.

Conclusion: This study shows that Replens applied vaginally three times a week, is a full therapy for all symptoms of vaginal atrophy as well as local estrogen. No serious adverse event was related. Replens is an alternative treatment to local estrogen and perhaps a good complement of systemic HRT in patients suffering from vaginal dryness.

3. COMPARATIVE STUDY: REPLENS VERSUS LOCAL ESTROGEN IN MENOPAUSAL WOMEN

Lila E. Nachtigall, MD New York University School of Medicine, New York, New York.

Fertility and Sterility (1994) 61 (1): 178-180

Summary

This was an open-label study comparing effects of a nonhormonal drug-free bioadhesive vaginal moisturiser to a local estrogen therapy in the treatment of vaginal dryness symptoms. There were 15 women evaluated in each treatment group during a 12-week period. Results indicated that the bioadhesive moisturizer was a safe and effective alternative to estrogen vaginal cream, with both therapies exhibiting statistically significant increases in vagina moisture, vaginal fluid volume, and vaginal elasticity with a return of the premenopausal pH state. A vaginal pH of 4 to 5 with the return of vaginal fluid volume, moisture and elasticity is probably satisfactory for prevention of vaginal infections and comfortable return of sexual function even without complete vaginal atrophy reversal and recornification. An acid vagina not only protects against secondary invaders but supports the beneficial vaginal flora as well.

4. TREATING VAGINAL DRYNESS IN BREAST CANCER PATIENTS: RESULTS OF APPLYING A POLYCARBOPHIL MOISTURIZING GEL

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Journal of Women's Health (1994) 3 (6): 427-434

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-centre, 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 (2.5g) of Replens (Columbia Laboratories, Miami, FL), a polycarboxophil vaginal moisturizing gel, into the vagina three times a week at night for 3 months. Patients were given the option of using an additional application of polycarboxophil 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 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 per cent of the patients rated the gel as good to excellent as a vaginal moisturizer. This study demonstrates that a polycarboxophil moisturizing gel can significantly relieve vaginal dryness in women with a history of breast cancer.

5. VAGINAL DRYNESS IN MENOPAUSAL WOMEN: CLINICAL CHARACTERISTICS AND NONHORMONAL TREATMENT.

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2. Director, Women's Medical and Diagnostic Center and Climacteric Clinic, Gainesville, Florida.

Clinical Practice in Sexuality (1991); 7: 25-32.

Abstract

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 [K-Y Jelly] and a new polycarboxophil based vaginal moisturizer [Replens]).

The women for this two-center, randomised, double-blind crossover study were recruited from two gynecologic clinical practices. Both nonhormonal preparations improved vaginal moisture; the polycarboxophil-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 polycarboxophil-based moisturizer, 26.5% preferring the water-based lubricant and 12.9% having no preference.

6. LONG TERM NONHORMONAL TREATMENT OF VAGINAL DRYNESS

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Clinical Practice in Sexuality (1993); 8: (8/9): 12-17

Abstract

Eighty-three women completed stage one of the protocol [see above] and of these fifty-four women chose to continue in the stage 2 protocol which was an extension of the stage one protocol. In the stage 2 protocol, the study was open label and there was no cross-over. Subjects used the bioadhesive vaginal moisturizer three times a week and were evaluated at 3,6,9 and 12 months. At three month intervals patients were asked questions regarding product satisfaction and at the same time the study physicians completed a vaginal health index which evaluated vaginal elasticity, vaginal fluid volume, pH, vaginal epithelial integrity and

vaginal moisture.

Over the course of the study the vaginal health index continued to show that not only had vaginal health improved but this improvement was maintained as long as subjects were using the product. In fact all parameters of the vaginal health index showed improvement including vaginal moisture, vaginal fluid volume, vaginal pH, vaginal epithelial integrity and vaginal elasticity. None of the women reported serious side effects and all women reported continued improvement in their original symptoms, i.e. vaginal dryness, irritation, burning, itching, and painful intercourse. Overall the product studied [Replens] was found to be well tolerated and effective in improving overall vaginal health for one year of continuous use.

7. DOUBLE-BLIND STUDY OF THE COMPARATIVE EFFECTS OF TWO GELS ON VAGINAL pH IN POSTMENOPAUSAL WOMEN

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Today's Therapeutic Trends (1991) 8 (4): 65-72

Abstracts

Excessive dryness is often a cause of vaginal itching and painful coitus (dyspareunia) among menopausal women. Another change secondary to diminished estrogen production is an increase in vaginal pH leading to increased susceptibility to vaginal infections.

A single-center, randomized, double-blind trial compared two vaginal gel products, Replens and KY Jelly, in a total of 50 non-hysterectomized, postmenopausal women complaining of vaginal dryness. The parallel-group study design involved the administration of either Replens or KY Jelly to the study patients over a period of four weeks.

Patients were examined every week during the trial, and maintained diaries documenting the time of application of the treatment and any side effects or discomfort experienced. Efficacy was evaluated by comparing the changes in vaginal pH within and between the two treatment groups.

Analysis of the study data showed that

Replens lowered pH to a statistically greater extent than did KY Jelly. This pH-lowering effect with Replens was statistically significant ($p < 0.01$) at every visit compared to baseline, while pH reduction with KY Jelly was significant only at Week 3, and to a lesser extent. Statistically significant differences in the relative levels of efficacy of the two treatments were noted at Weeks 1, 3, and 4, with the Replens group demonstrating a greater mean decrease in pH.

No serious adverse effects were reported in either treatment group.

8. A NONHORMONAL BIOADHESIVE VAGINAL MOISTURIZER. I. EFFECT ON SPERM MOTILITY AND OVA PENETRATION II. EFFECTS ON CONDOM STRENGTH

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Clinical Practice in Sexuality Vol 8 No.5

Abstracts

I. It is estimated that 25 million peri- and postmenopausal women suffer from vaginal dryness. The condition in this population of women is most commonly caused by a decline in estrogen. An additional group of younger reproductive aged women, however, may suffer from vaginal dryness as well. For these women in their child-bearing years, certain drug therapies may result in vaginal dryness as a secondary condition ...

Therefore, the following studies were conducted to provide useful information to physicians treating vaginal dryness symptoms. The results indicated that the nonhormonal bioadhesive vaginal moisturizer did not adversely affect sperm motility and ova penetration.

II. When recommending the use of the vaginal nonhormonal bioadhesive moisturizer, Replens, physicians have been concerned about the effects of

these on latex products, especially condoms and diaphragms.

The results of this second report showed the volume and burst pressures for condoms treated with the moisturizer to be well above the ISO recommended minimum.

In similar studies conducted in the U.K., the effects of Replens on the tensile strength and elongation at break of condoms were examined.

Based on these findings, condom strength and integrity are not at risk when using the nonhormonal bioadhesive vaginal moisturizer; the moisturizer is therefore compatible for use with the lubricated and non-lubricated condoms included in these studies.

9. THE EFFECT OF REPLENS® ON VAGINAL CYTOLOGY IN THE TREATMENT OF POSTMENOPAUSAL ATROPHY; CYTOMORPHOLGY VERSUS COMPUTERISED CYTOMETRY

J A W M van der Laak, L M T de Bie, H de Leeuw, P C M de Wilde, A G J M Hanselaar.

J Clin Pathol 2002;55:446-451

Background: After the menopause decreased concentrations of oestrogen may result in insufficient maturation of the vaginal epithelium, which can lead to a range of vaginal discomforts. This state of vaginal atrophy may be treated with oestrogen replacement treatment, Replens®, a non-hormonal alternative to oestrogen replacement treatment has been shown to be effective in relieving symptoms related to vaginal atrophy in previous studies.

Aims: To study the effect of Replens on the maturation of the vaginal epithelium and morphology of the vaginal cells and compare the results of a recently developed cytomorphometric method with manual assessment of the degree of maturation in vaginal smears.

Methods: Vaginal smears from 38 postmenopausal women suffering from symptoms related to vaginal atrophy were analysed manually and by cytomorphometry. The maturation value

(MV) and the percentages of (para)basal, intermediate, and superficial cells (maturation index; MI) were measured by both methods before and after treatment with Replens. Cytomorphometry also measured mean cellular area, mean nuclear area, and mean area ratio.

Results: A correlation was shown between the two methods in assessment of percentages of (para)basal and intermediate cells and MV. Cytomorphometric data showed a significant increase in mean cellular area, indicating a positive effect of Replens on the maturation of the vaginal epithelium. Changes in the nuclear area and the ratio between nuclear and cellular areas were not significant. Treatment with Replens did not influence MI of MV, as assessed by the two methods.

Conclusion: Replens did have an effect on vaginal morphology. The automated procedure may be useful for assessment of maturation in vaginal smears and is more sensitive to small (subvisual) changes.



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