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# An alternative approach for the treatment of vaginal atrophy

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**Aim.** The aim of this study was to determine the efficacy of a new topic non-hormonal treatment for postmenopausal women complaining of symptoms of vaginal atrophy.

**Methods.** Patients included in the study were prescribed Sinacol gel (AM PHARMA Srl, Vimercate, Monza and Brianza, Italy) application once a day for 20 consecutive days. Sinacol gel is a topic compound for vaginal atrophy containing hyaluronic acid, that is known to improve vaginal elasticity, lactoperoxidase, Xantham gum and glucose oxidase, which have protective and antibacterial action. We evaluated each patient before and after treatment, both subjectively with the "Visual Analogical Scale" (VAS) and objectively with the "Vaginal Health Index" (VHI).

**Results.** We observed a significant clinical improvement of the subjective and objective assessment of symptoms severity with a p value <0.001 at the end of the treatment compared to baseline.

**Conclusion.** Sinacol gel appears to be an effective and valid non-hormonal alternative to the estrogen therapy for vaginal atrophy.

**KEY WORDS:** Hyaluronic acid - Estrogens - Menopause.

The lack of estrogen in postmenopausal women contributes to determine the common condition of vaginal atrophism that affects 10-40% of women, according to data of the North American Menopause So-

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ciety (NAMS) <sup>1</sup> (North American Menopause Society, 2007). Women with vaginal atrophy usually complain of typical symptoms such as vaginal itching, dryness, irritation associated with dyspareunia or mucosal bleeding during sexual intercourse.<sup>2</sup>

The treatment of vaginal atrophy aims to relieve symptoms as well as reverse atrophic histological changes. The Cochrane report recommends <sup>3</sup> the use of the smallest effective estrogen dose for chronic therapy of atrophic vaginitis. Once urogenital function has improved, the dose of local estrogen can be tapered for long-term maintenance therapy. However, safety data from studies on local estrogen do not go beyond one year. Moreover, the use of exogenous estrogen delivered to the chronically estrogen-deprived vaginal cell may only partially effect change in these atrophic cells, which are already deplete of intracellular estrogen, and the full effect of the intervention may not be realized.<sup>4</sup> Other limitations to the use of local estrogens are contraindications and poor tolerance.

This, together with a poor willingness to take estrogen, encouraged the increasing

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request of alternative therapies for atrophic vaginitis. Alternative non-hormonal treatment options include water-based lubricants, vaginal moisturizers, vitamin E oil and others.<sup>5</sup>

The aim of this study was to determine the efficacy of a new topic non-hormonal treatment for postmenopausal women complaining of symptoms of vaginal atrophy.

## Materials and methods

We recruited postmenopausal women who referred to the Gynecological Outpatient Clinic at the San Raffaele Hospital (Milan, Italy) from January 1<sup>st</sup> to December 31<sup>st</sup>, 2010. We defined menopause as the absence of menstrual bleeding for a minimum of 12 months in women aged more than 40 years. All women complained of at least one symptom of vaginal atrophy such as: vaginal dryness, vaginal and vulvar irritation, vaginal soreness, dyspareunia.

All women were thoroughly evaluated for medical history with a specific questionnaire, including the following variables: age, parity, drug history, medical conditions and previous surgery. Clinical assessment was also considered, taking note for each patient of her height, weight and pelvic examination in order to determine patient eligibility. This was confirmed when signs of vaginal atrophica were observed and scored accordingly to the Vaginal Health Index (VHI), proposed by Bachmann *et al.*<sup>2</sup> The VHI is determined by an evaluation at the inspection of the following parameters: vaginal secretions, elasticity of the epithelium, vaginal pH, mucosal atrophy and moisture. Each single parameter received a grade based on 5-point scale and the final sum of each single score for specific parameter represented the final VHI value. A subjective evaluation of severity for each symptom of vaginal atrophy was obtained using a 10-point "Visual Analogical Scale" (VAS).

Women were, therefore, finally included in this study if they were postmenopausal

for at least 3 years, if they had a VHI score <14 and vaginal atrophy symptoms reported as bothering defined as a VAS value  $\geq 5$ . As exclusion criteria we considered the use of local or systemic estrogens or the known intolerance to any component of the product used in this study.

Once recruited each patient was prescribed Sinecol gel (AM PHARMA Srl, Vimercate, Monza and Brianza, Italy) application once a day for 20 consecutive days. Sinecol gel (AM PHARMA Srl, Italy) is a topic non-hormonal treatment for vaginal atrophy containing hyaluronic acid (known to improve vaginal elasticity), lactoperoxidase, Xantham gum and glucose oxidase (which have protective and antibacterial action).

Treatment efficacy was evaluated by a dedicated and trained gynecologist after weeks using always the VAS and the VHI.

For this study we obtained the approval of our local Institutional Review Board. All patients gave their written consent to the anonymous use of their clinical data for statistical evaluations and/or research purposes.

## Statistical analysis

Primary efficacy endpoint was the change from baseline in the composite score of VAS for vaginal symptoms; additional efficacy assessments included the change in vaginal health (VHI) during the study period.

Descriptive statistics were used to characterize the patient population. For univariate analysis, continuous data were reported as median and mean  $\pm$  SD. Baseline characteristics and treatment outcome were compared using Student's *t*-test, non-parametric Wilcoxon test, as appropriate. Differences were considered statistically significant at  $P < 0.05$ .

The SPSS statistical software program (SPSS 15.0 for Windows, Chicago, IL, USA) was used.

## Results

A total of 31 postmenopausal women complaining of symptoms of vaginal atrophy were originally included for analysis;

one patient was excluded because not attending the follow-up evaluation. The mean age of the remaining 30 patients was  $61.5 \pm 5.19$  years (range: 52-70) with a mean time since the onset of menopause of  $12 \pm 5.31$  years (range: 3-26).

The frequencies of symptoms before and after treatment are described in Figure 1.

In general we observed a significant clinical improvement in the subjective assessment of symptoms severity with a mean VAS value of  $22.8 \pm 6.2$  (SD) at baseline and a mean VAS value of  $10.3 \pm 4.8$  (SD) at the end of the study. This change reached the statistical significance with a  $P < 0.001$ .

The objective evaluation of vaginal atrophy signs using the VHI also showed a significant improvement with a mean score of  $9 \pm 2.8$  at baseline and a mean score of  $14.5 \pm 4.2$  at the end of the treatment, with a statistically significant P value  $< 0.001$ .

More specifically the treatment with Sinecol determined a marked and significant improvement on vaginal secretions and moisture ( $P < 0.001$ ) and, consequently, a significant decrease in vaginal burning and dyspareunia ( $P < 0.001$ ). These findings are illustrated in Tables I and II.

No adverse events have been reported during treatment and at follow-up.

## Discussion

Vaginal atrophy is a common condition characterized by the following signs: presence of pale and dry vulvo-vaginal mucosa with the appearance, in the most severe cases, of spontaneous petechiae; disappearance of vaginal rugae, a thinning of the vaginal epithelium, loss of elasticity, decreased secretions and lubrication, and vaginal pH of 4.6 or more supports the diagnosis of vulvovaginal atrophy.<sup>6</sup> This change in vaginal acidity is determined by a reduction or absence of glycogen production with a decrease of lactobacilli and an increase in the likelihood of developing vaginal infection.<sup>7</sup>

The treatment of vulvovaginal atrophy focuses on relieving symptoms as well as reversing atrophic anatomical changes.

Water-based lubricants, vaginal moisturizers, vitamin E oil are non-hormonal treatment options commonly used. Lubricants reduce friction during sexual activity, decreasing dyspareunia, whereas moisturizers replace normal vaginal secretions and are used as a chronic therapy.<sup>5</sup>

The most common alternative treatment consists of creams containing hyaluronic acid.

In this study, we evaluated the efficacy of Sinecol gel on vaginal atrophy related symptoms. Sinecol gel is a topic non-hormonal treatment for vaginal atrophy; it contains hyaluronic acid, that is known to improve vaginal elasticity, and lactoperoxidase, Xanthan gum and glucose oxidase, which have protective and antibacterial action. Hyaluronic acid is a hydrophilic molecule and is known to modulate the hydration of tissues, restoring the water-retaining ability of the vagina that is lost at menopause.

Hyaluronic acid is an anionic, non-sulfated glycosaminoglycan distributed widely throughout connective tissues. It is one of the most hydrophilic molecules in nature: it maintains the elastoviscosity of liquid connective tissues. Lactoperoxidase is an enzymeperoxidase secreted from mammary, salivary, and other mucosal glands; the lactoperoxidase system plays an important role in the innate immune system by killing bacteria in milk and mucosal secretions.

Xanthan gum is a polysaccharide and functions as a natural antibacterial agent; it is commonly used as a food stabilizer.

The glucose oxidase enzyme is an oxidoreductase that acts as an antimicrobial barrier.

There is a poor literature concerning the efficacy and safety of hyaluronic acid vaginal preparations in post-menopausal women with urogenital atrophy; according to these studies, there is a significant improvement in vaginal atrophy related symptoms and signs with the use of non-hormonal therapy.<sup>8-10</sup>

Our data shows that Sinecol gel significantly improved vaginal atrophy both subjectively (VAS) and objectively (VHI). This improvement resulted statistically significant either when considered as an overall score

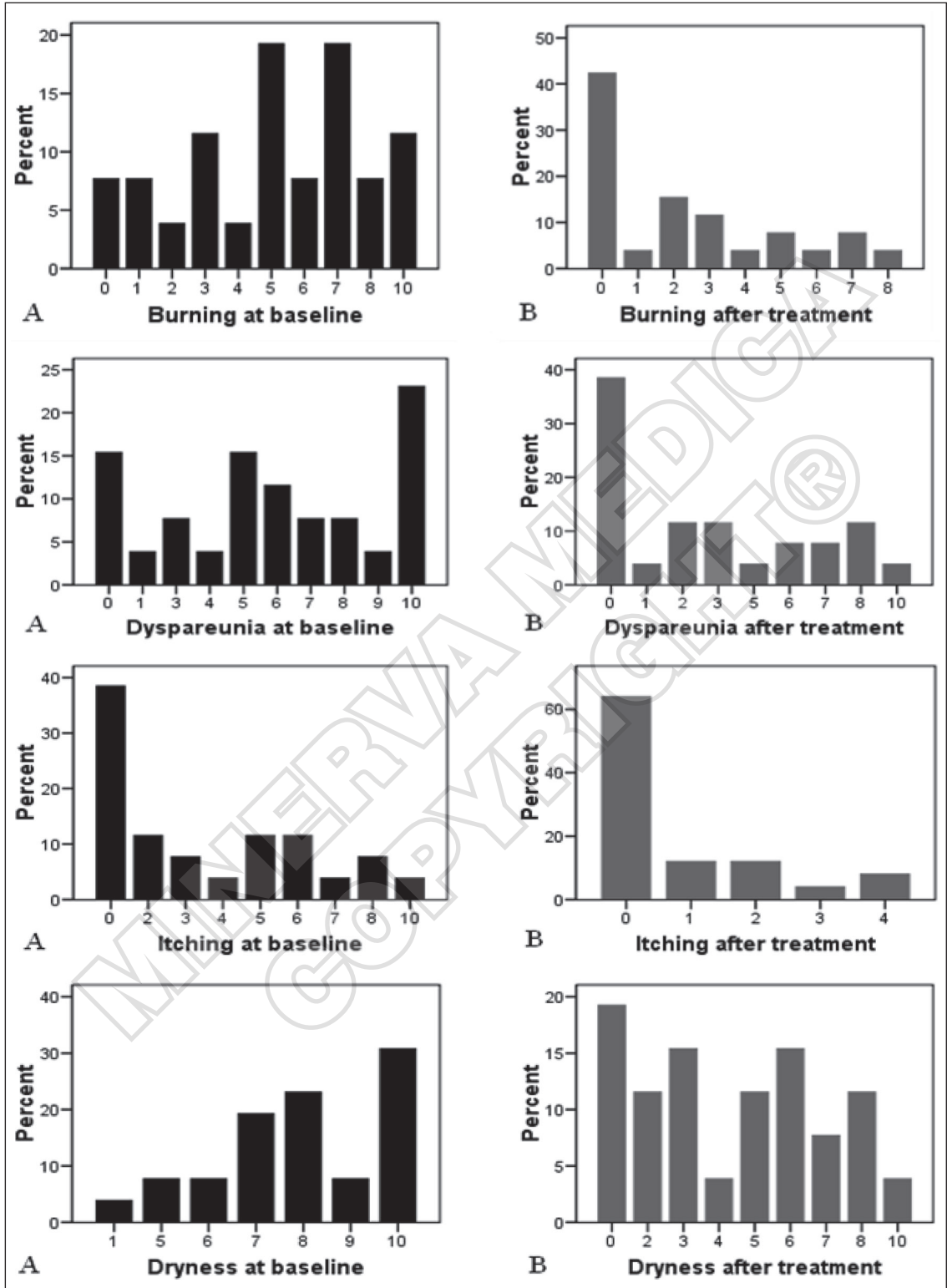


Figure 1.—The frequency (%) of vaginal complaints before (A) and after treatment (B).

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TABLE I.—*The comparison of composite score of vaginal symptoms (VAS) before and after treatment (value are expressed as mean±SD).*

Symptoms	Baseline	Follow-up	P
Burning	5.19±2.15	2.31±1.11	<0.001
Dyspareunia	5.69±2.47	3.12±1.32	<0.001
Itching	3.28±1.43	0.80±0.22	<0.001
Dryness	7.85±2.13	4.19±2.01	<0.001
Vas	22.80±6.20	10.30±4.80	<0.001

TABLE II.—*The comparison of composite score of vaginal signs (VHI) before and after treatment (value are expressed as mean±SD).*

Signs	Baseline	Follow-up	P
Elasticity	2.04±0.6	2.96±0.82	<0.001
Vaginal secretions	1.27±0.61	2.65±0.89	<0.001
Vaginal pH	2.52±0.91	3.61±0.98	<0.001
Mucosal atrophy	2.73±0.99	3.62±0.99	<0.001
Moisture	1.62±0.80	2.96±0.99	<0.001
VHI	9.80±2.81	14.50±4.21	<0.001

or in case of each single symptom, with the greatest efficacy observed for vaginal secretions and moisture. No unexpected or adverse effects have been reported by patients.

### Conclusions

Although estrogen therapy is considered the gold standard treatment for vaginal atrophy, the worldwide low rate of women taking estrogens encourages the increasing request of alternative therapies for atrophic vaginitis. Sinacol gel appears to be an effective and valid non-hormonal

alternative to the estrogen therapy for vaginal atrophy.

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*Conflicts of interest.*—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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