Effects and side-effects of 2% progesterone cream on the skin of peri- and postmenopausal women: results from a double-blind, vehicle-controlled, randomized study

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Summary

Background For many years topical progesterone has been prescribed by gynaecologists as an anti-ageing and skin-firming treatment, without any clinical scientific evidence of its effects, tolerability and safety when applied to skin.

Objectives To evaluate the influence of 2% progesterone cream on function and texture of the skin in peri- and postmenopausal women.

Methods A double-blind, randomized, vehicle-controlled study was conducted in 40 subjects. Objective methods for measuring skin elasticity, epidermal hydration and skin surface lipids, clinical monitoring and self-assessment, and determination of blood hormone levels (luteinizing hormone, follicle-stimulating hormone, oestrogen and progesterone) were used to determine effects and side-effects of this treatment at four visits over a 16-week period.

Results The study demonstrated a significant \( P \leq 0.05 \) increase of the elastic skin properties in the treatment group, as demonstrated by objective measurements of three skin elasticity parameters, whereas in the control group no such effect was observed. This effect in the treatment group was further paralleled by the results of the clinical monitoring, where the 2% progesterone cream yielded consistent superiority over vehicle in counteracting different signs of ageing in the skin of peri- and postmenopausal women. Clinical monitoring showed a greater reduction in wrinkle counts (29\%-10\% vs. 16\%-50\%) and wrinkle depth (9\%-72\% vs. 7\%-35\%) around the right eye, a greater decrease in nasolabial wrinkle depth (9\%-72\% vs. 6\%-62\%) and a significantly higher \( P < 0.05 \) increase in skin firmness (23\%-61\% vs. 13\%-24\%) in the treatment group. Epidermal hydration and skin surface lipids did not change significantly in either group during the study. Progesterone was well absorbed in the systemic circulation: mean blood levels rose minimally, but statistically significantly \( P = 0.001 \), by 0.53 ng mL\(^{-1}\). No serious side-effects of the treatment were observed.

Conclusions The results of this study demonstrate that topical 2% progesterone acts primarily in increasing elasticity and firmness in the skin of peri- and postmenopausal women. These effects in combination with good tolerability make progesterone a possible treatment agent for slowing down the ageing process of female skin after onset of the menopause.

The ageing process of human skin is attributed to two superimposed processes, intrinsic and extrinsic ageing.1 While the major cause for extrinsic ageing is sun exposure (photaging), several factors account for intrinsic ageing; changes in hormonal balance during the lifetime is one major causative factor.2,3 The beginning of the menopause is the cardinal point in time for the ageing process of the female body, as the continuous decline in sex steroid synthesis accelerates age-dependent changes in several tissues.

In female skin menopausal hormonal changes lead to thinning1 and wrinkling of the skin and to loss of skin elasticity and firmness.3 These signs of ageing skin are caused by decreased collagen synthesis and increased collagen degradation,1 irregularities in size and shape of
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evidential cells and a decrease in interfibrillar ground substance and blood vessels.⁴

In peri- and postmenopausal women, hormone replacement therapy (HRT) has been greatly beneficial in the treatment of climacteric problems and has led to new perspectives in the management of ageing women. The beneficial influence of systemic oestrogen and its derivatives alone or in combination with progesterone on the skin of postmenopausal women is well documented and includes an increase in skin thickness,⁵,⁶ collagen content,⁷,⁸ skin elasticity,⁵,⁹ epidermal hydration,⁵,¹⁰ and skin surface lipids.⁵

Nevertheless, the findings of recent clinical and epidemiological studies have raised critical discussion about the health benefits of long-term replacement of these two hormones for the ageing woman. Their short-time use might be beneficial in counteracting signs and symptoms of the menopause such as hot flushes and urogenital atrophy.¹¹ However, as revealed by large epidemiological studies,¹²-¹⁵ the side-effects of long-term HRT might outweigh other potential measurable benefits. Thus, the use of long-term HRT as a lifelong preventive strategy against chronic menopausal complaints has to be reconsidered. Consequently, tissue-adjusted treatment options can represent effective and valuable alternatives to systemic HRT to avoid side-effects. Topical application of sex hormones on selected sites of postmenopausal skin might be such an alternative for replacing hormones in postmenopausal skin, thereby slowing down the ageing process that rapidly progresses with the onset of menopause. The steroid structure of the sex hormones and their high lipid solubility makes them suitable for a percutaneous route of administration.

Only a few studies¹⁴-¹⁶ have documented the beneficial effect of topical oestrogen and its derivatives on mature female skin and their effect in the treatment of the signs of ageing. It is already known that oestrogen and its derivatives increase collagen production¹⁵,¹⁶ and epidermal hydration in the skin and reduce the typical signs of ageing such as wrinkling and elastosis.¹⁴,¹⁵ Studies on the topical effects of progesterone in the skin of menopausal women have so far been sparse.

Progesterone acts on several extragenital tissues of the body via its two receptors, which belong to the superfamily of nuclear steroid hormone receptors:¹⁷ PR-A and PR-B. PR-A, weighing 94 kDa, is a transcriptional activator, whereas PR-B, weighing 114 kDa, functions as a repressor. Progesterone receptors have been detected in whole skin,¹⁸ keratinocytes¹⁹ and fibroblasts.²⁰,²¹ For years unpublished oral communications have attributed skin firming and antiageing properties to progesterone, but they did not reveal any scientific evidence for its potential effects and side-effects. The aim of the present study was to investigate the influence of topical progesterone on different skin parameters and to evaluate whether this hormone, which has fewer systemic side-effects than oestrogen, could represent a topical alternative to systemic HRT in reversing skin ageing in postmenopausal women.

Patients and methods

Study design and population

Forty consenting peri- or postmenopausal women between the age of 45 and 60 years were enrolled into the study; of these, seven had had a hysterectomy and two more had previously undergone ovariectomy, i.e. before the study (Table 1). Recruitment criteria for the study were as follows: (i) no menstruation or irregular menstruation cycles for at least 6 months; (ii) hormone levels [luteinizing hormone (LH), follicle-stimulating hormone (FSH), oestrogen, progesterone] in the range for perimenopausal or postmenopausal women (postmenopausal hormone levels were designated as: LH, 15–64 mU mL⁻¹; FSH, 20–138 mU mL⁻¹; estradiol, < 25 pg mL⁻¹; progesterone, < 1·5 ng mL⁻¹); (iii) no kind of hormonal treatment and no medical or cosmetic treatment interfering with the general ageing process (dermabrasion, chemical peeling, topical treatment with retinoid acid, tretinoin, glycolic acid or vitamin C on face or neck, high-dose vitamin C nutrition supplementation > 1 g daily) for at least 6 months before the study; (iv) no history of lifelong extensive, regular exposure to sun or artificial ultraviolet radiation; (v) no history of previous severe or chronic skin diseases. The study was approved by the ethical committee of the Medical University of Vienna.

All 40 participants were randomly assigned to the treatment group or to the placebo group. Participants of the first

Table 1 Participants’ baseline characteristics (intent-to-treat population); data are expressed as mean ± SD

<table>
<thead>
<tr>
<th></th>
<th>Treatment group (n = 20)</th>
<th>Control group (n = 20)</th>
<th>NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years) (range)</td>
<td>55·5 (46–61)</td>
<td>55·8 (50–59)</td>
<td></td>
</tr>
<tr>
<td>Sex (female)</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Hormone status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luteinizing hormone (mU mL⁻¹)</td>
<td>30·7 ± 12·70</td>
<td>33·7 ± 11·79</td>
<td>NS</td>
</tr>
<tr>
<td>Follicle-stimulating hormone (mU mL⁻¹)</td>
<td>78·23 ± 41·37</td>
<td>74·39 ± 22·48</td>
<td>NS</td>
</tr>
<tr>
<td>Estradiol (pg mL⁻¹)</td>
<td>23·79 ± 19·42</td>
<td>21·63 ± 21·14</td>
<td>NS</td>
</tr>
<tr>
<td>Progesterone (ng mL⁻¹)</td>
<td>0·36 ± 0·25</td>
<td>0·27 ± 0·13</td>
<td>NS</td>
</tr>
<tr>
<td>Hysterectomy (n)</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Ovariectomy (n)</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

NS, not statistically significant (p > 0·05).
group received a night cream containing 2% progesterone in a neutral standard cream vehicle (Ultrasicc®, an oil-in-water cream base, or Ultrasba®, a water-in-oil cream base; Schering AG, Vienna, Austria), while participants of the control group were given the equivalent placebo cream containing just the vehicle. All participants had to apply exactly measured amounts of 1 g of the ointment every evening upon the face and neck. In addition, all study participants used the same mild cleanser for skin cleaning and received a moisturizing day cream (Ultrasicc®). All creams, including the day creams, were prepared, quality controlled and supplied by a pharmacist at the Pharmacy Department, General Hospital of Vienna.

At week 0 (before treatment), 4, 12 and 16 measurements were made of the skin parameters skin surface lipids, epidermal hydration and elasticity, clinical monitoring was performed and determinations were made of progesterone, oestrogen, prolactin, FSH and LH from blood samples. All blood tests were performed by electrochemoluminescent immunoassay (ECLIA; Roche Diagnostics, Mannheim, Germany). In addition, photographs were taken in a standardized manner. They were assessed by the two independent investigators.

The primary endpoint was the change of the viscoelastic properties of the skin from baseline to the end of the treatment after 16 weeks within the two groups, as measured objectively using a cutometer. Additional analyses were done on the parameters of the clinical monitoring and on the measurements of skin hydration, skin surface lipids and hormone levels.

**General conditions of measurement**

In order to minimize the variability during skin measurements caused by exogenous factors which might affect the participants’ general skin condition and lead to avoidable bias, several measures were introduced. Participants were asked not to smoke or to drink alcohol for 24 h before the measurements. In the morning before the visits they were not allowed to clean their face and neck with anything but pure water or to use any cosmetic products in these areas.

The measurements took place in a humidity- and temperature-controlled room of the hospital; the temperature of this room is constantly 21°C and ambient humidity ranges between 40 and 45%. Study subjects’ skin was given 2 h to adjust to the room conditions. All measurements were performed by the same two investigators.

**Measurement of elasticity**

The cutometer SEM575 (Courage and Khazaka, Cologne, Germany)22,23 was used to determine the elastic and viscoelastic properties of epidermis and papillary dermis, as described before.22,23 In short, the viscoelastic properties of the skin are measured as variations in skin elevation in response to traction through negative pressure (450 mbar) and plotted as a function of time (3 s traction time, followed by 3 s relaxation time). Measurements were conducted on the right temple, horizontally 1 cm distant from the right lateral canthus of the eye. The following parameters were analysed:

(i) the absolute parameters Ue, immediate distension; Uv, delayed distension; Uf, final distension (skin distensibility); Ur, immediate retraction; and Ua, final retraction; and
(ii) the relative parameters R2 (Ua/Uf), gross elasticity of the skin, including viscous deformation; R5 (Ur/Ue), net elasticity of the skin without viscous deformation; and R7 (Ur/Uf), biological elasticity, i.e. the ratio of immediate retraction to total distension. Absolute parameters are influenced by skin thickness, whereas relative parameters are not and thus can be compared without preliminary standardization to skin thickness.

**Measurement of skin surface lipids**

Skin surface lipids were measured with the sebumeter SM 810PC (Courage and Khazaka).5 This device works on the principle of photometry of a special plastic strip that becomes transparent with fat absorption. Lipids from the skin are collected on the strip with a constant pressure of 6 N for 30 s. The sebumeter measures the variation of light transmission through the strip. This variation is proportional to the quantity of lipids absorbed. Skin surface lipids were measured on the right forehead and at the right parathyroidal region of the neck, 7 cm beneath the chin (with the head held straight).

**Measurement of epidermal hydration**

Hydration of the epidermis (stratum corneum) was measured with the noninvasive corneometer CM 820PC (Courage and Khazaka).5 This device determines the water content of the superficial epidermal layers down to a depth of about 0.1 mm and expresses the values in arbitrary units. We used mean values of three measurements for our statistical calculations. Similar to measurements of skin surface lipids, we measured epidermal hydration on the corresponding areas of the face and neck on the left side.

**Clinical assessment**

Clinical assessment was always performed by the same two investigators. We investigated the number and depth of wrinkles around the right eye, skin firmness, the depth of nasolabial wrinkles and skin dryness and oiliness. Skin firmness was determined clinically as a combination of optical impression and mechanical resistance against traction. The participants’ skin was also assessed with regard to side-effects such as burning, itching, seborrhoea, development of comedones, inflammatory lesions, hypertrichosis and hyperpigmentation.

Of the above-mentioned clinical assessment parameters and side-effects, wrinkles around the right eye and inflammatory lesions were counted, while all of the rest was graded using the following clinical score: 0, absent (0%); +, minimal
(25%); ++, moderate (50%); ++++, marked (75%); ++++, very marked (100%).

Self-assessment

Subjects were asked to give their own subjective assessment of firmness, depth of nasolabial wrinkles, dryness and oiliness of the treated skin by the above-mentioned score at every visit.

Calculations and statistics

The decrease in wrinkles was counted as follows. Fine lines and deep wrinkles were counted separately and then their change was calculated in the all wrinkle count, where deep wrinkles were counted twice and fine lines just once. This calculation allowed us to get a better evaluation of the decrease of wrinkling around the eye, as during the treatment period fine lines were diminished, while some of the deep wrinkles became more superficial and thus were graded as fine lines.

Reduction of wrinkles in the all wrinkle count was also calculated as percentage reduction in order to obtain more comparable and objective results. Calculations were made according to the following formula: \( wr = \frac{(w1 - w0) \times 100}{w0} \), where \( w0 \) is overall wrinkle count prior to treatment, \( w1 \) is overall wrinkle count post-treatment and \( wr \) is percentage overall wrinkle reduction.

The Wilcoxon rank test was used for calculating statistically significant differences. A statistically significant difference was achieved if the difference from the null hypothesis reached \( P \leq 0.05 \). All statistical calculations were made with SPSS 10.0 for Windows (SPSS, Chicago, IL, U.S.A.).

Results

Forty female volunteers entered the study, of whom 35, 18 in the treatment group and 17 in the control group, completed the 16-week study period. The remaining five patients were withdrawn because of failure to keep to the protocol (Fig. 1). None of these subjects withdrew because of adverse reactions to the treatment.

Skin elasticity

Participants in the treatment group showed a general improvement of the viscoelastic properties of the skin, as measured by various relative parameters on the subjects’ temples (Table 2). All parameters of viscoelasticity improved markedly, i.e. their mean values increased (Fig. 2a). Gross elasticity (R2) and net elasticity (R5) of the skin improved significantly (\( P = 0.04 \) and \( P = 0.05 \)); biological elasticity (R7) also improved, but this improvement did not quite attain significance (\( P = 0.06 \)). There were no such changes in the same parameters in the control group.

Clinical assessment

Participants in the treatment group showed a continuous tendency towards improvement in all clinically monitored parameters of ageing (skin firmness, wrinkle count and wrinkle depth around the right eye and nasolabial wrinkles) at all four visits (Tables 3 and 4). The increase in skin firmness was significantly greater (\( P = 0.031 \)) in the treatment group than in the control group (23.61% vs. 13.24%; Fig. 2b). At the end of treatment a greater reduction in wrinkle depth (9.72% vs. 7.34%)

Fig 1. Patient flow through the double-blind, vehicle-controlled, randomized study.
7.35%) around the right eye was seen in the treatment group (P > 0.05; Figs 2b and 3). Similarly, there was a trend towards a higher reduction (29.10% vs. 16.50%) in wrinkle count around the right eye in the treatment group (P > 0.05; Figs 2b and 3). In the treatment group there was also a slightly greater mean decrease in nasolabial wrinkles (9.72% vs. 6.62%; P > 0.05; Fig. 2b). Skin oiliness and skin dryness according to clinical assessment decreased by 9.72% and 15.28% in the treatment group, and by 8.82% and 25.74% in the placebo group. Again, these differences did not reach statistical significance (P > 0.05).

The reduction in wrinkle depth around the right eye correlated well with the changes in parameters measured with the cutometer on the temple in the treatment group. The correlations with net elasticity and biological elasticity of the skin were highly significant (both P = 0.01), and the correlation was very close to significance with gross elasticity of the skin (P = 0.06).

Self-assessment

Several parameters of subject self-assessment showed a general improvement (skin firmness improved by 14.58%, nasolabial wrinkles decreased by 9.03% and wellbeing of the skin increased by 27.78%) (Table 3). Corresponding values in the placebo group were 12.50%, 7.03% and 25.00%, respectively.

**Table 2** Viscoelastic skin parameters measured by cutometer at baseline (before treatment) and after 16 weeks (after treatment)

<table>
<thead>
<tr>
<th>Elasticity</th>
<th>Treatment group</th>
<th>Control group</th>
<th>P-value</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
<th>Mean</th>
<th>SD</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
<td></td>
<td></td>
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<tr>
<td>Gross elasticity</td>
<td>18</td>
<td>0.516</td>
<td>0.082</td>
<td>0.615</td>
<td>0.160</td>
<td>0.03</td>
<td>17</td>
<td>0.533</td>
<td>0.154</td>
<td>0.058</td>
<td>0.162</td>
<td>0.05</td>
<td>17</td>
<td>NS</td>
</tr>
<tr>
<td>Net elasticity</td>
<td>18</td>
<td>0.420</td>
<td>0.096</td>
<td>0.508</td>
<td>0.162</td>
<td>0.05</td>
<td>17</td>
<td>0.492</td>
<td>0.207</td>
<td>0.500</td>
<td>0.142</td>
<td>0.05</td>
<td>17</td>
<td>NS</td>
</tr>
<tr>
<td>Biological elasticity</td>
<td>18</td>
<td>0.290</td>
<td>0.057</td>
<td>0.343</td>
<td>0.096</td>
<td>NS</td>
<td>17</td>
<td>0.323</td>
<td>0.120</td>
<td>0.316</td>
<td>0.093</td>
<td>NS</td>
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</table>

NS, not statistically significant (P > 0.05).
Table 3 Parameters of the clinical monitoring and subject self-assessment: mean at baseline (before treatment) and after 4, 12 and 16 weeks (during and after treatment)

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Treatment group</th>
<th></th>
<th></th>
<th></th>
<th>Placebo group</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<td>SD</td>
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<tr>
<td>0</td>
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<td>12</td>
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<td>16</td>
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</table>

These improvements were slightly greater in the treatment group, but differences between the groups were not statistically significant (P > 0.05).

Sebumetry and corneometry

In the treatment group a decrease in skin surface lipids was observed on the forehead and to a smaller extent on the neck (Table 5). Nevertheless, none of these changes reached significance (P > 0.05). In the placebo group no change of skin surface lipids was observed.

Skin hydration, as measured by corneometry, stayed more or less the same, and changes in values before and after treatment did not change significantly (P > 0.05) in either the placebo or the treatment group (Table 5).

Table 4 Mean percentage changes in clinically monitored skin ageing parameters from baseline (before treatment) to last visit (after 16 weeks of treatment)

Hormones

Of the hormones measured FSH, LH and oestrone did not show any significant changes in levels during the treatment period. Progesterone levels, however, increased significantly (P = 0.001) in the treatment group during the study (by 0.53 ng mL⁻¹), but values still stayed in the physiological range of perimenopausal women, i.e. < 1.35 ng mL⁻¹.

Adverse effects

In the treatment group one participant complained about a minimal increase in facial hair and facial pigmentation, two noted a minimal increase in facial hair and one observed a minimal increase in facial pigmentation. None of these observations could be verified objectively, either by the clinical examiners or by photodocumentation. In addition, two participants in the control group observed a minimal increase in facial hair. Again, these observations could not be substantiated by objective methods.

The most common side-effect consisted of inflammatory lesions (papules, pustules) occurring in nine participants of the treatment group and in seven of the control group. The mean count of inflammatory lesions was highest at the second visit in both groups and then gradually decreased. The mean increase in inflammatory lesions in the affected subjects was small (the inflammatory lesion count increased by a mean of 0.44), while in the placebo group it decreased by 0.29. This difference was not significant (P > 0.05). Increased comedo formation was also observed in two
Discussion

For many years topical progesterone has been prescribed for its potential firming and antiaging effects on skin. However, no scientific studies have been performed to verify its effects or side-effects on skin in vivo. To our knowledge, this is the first report on the effects of this steroid hormone on mature skin investigated in a clinical, double-blind, randomized and placebo-controlled trial.

A decrease in firmness and elasticity is one of the major signs of aging skin and can be easily measured by a computerized suction device. In the present study, all three skin elasticity parameters measured by this device showed a continuous and mostly significant improvement in the treatment group while there were no such changes in the control group. The results of the objective cutometer measurements were paralleled and confirmed by the subjective results of the clinical examination, where members of the treatment group in general showed a greater improvement in the skin aging parameters monitored than those of the control group. The difference in improvement was significant for skin firmness, but not for the other parameters monitored, which might be due to the small sample size.

Progesterone has a definite influence on the remodelling of several nongenital tissues of the female body. The primary target of this steroid in the extracellular matrix remodelling process seems to be a group of tissue-degrading enzymes, the matrix metalloproteinases (MMPs). Several in vitro studies have demonstrated inhibitory effects of

<table>
<thead>
<tr>
<th></th>
<th>Treatment group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td><strong>Skin surface lipids</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forehead</td>
<td>18</td>
<td>158±50</td>
</tr>
<tr>
<td>Neck</td>
<td>18</td>
<td>49±78</td>
</tr>
<tr>
<td><strong>Epidermal hydration</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forehead</td>
<td>18</td>
<td>73±00</td>
</tr>
<tr>
<td>Neck</td>
<td>18</td>
<td>84±28</td>
</tr>
</tbody>
</table>

NS, not statistically significant (P > 0.05).
progesterone on the expression and activity of these enzymes. The following MMPs can be detected in the dermis: MMP-1 (collagenase), MMP-3 (stromelysin 1) and MMP-9 (gelatinase). Recent data demonstrate that chronological ageing and photoageing are associated with increased expression of MMP-1 and MMP-9. The combined actions of these enzymes can fully degrade skin collagen and components of the elastic network, leading to the typical signs of ageing skin such as decreased firmness and elasticity and increased wrinkling. Topical progesterone could exert a suppressive effect on this age-dependent increased extracellular matrix degradation, thereby improving skin firmness and viscoelastic properties of the skin, as demonstrated in this study.

Our clinical results and measurements with the cutometer are further confirmed by the significant correlations between the elastic parameters on the temple and the clinically observed decrease in wrinkle depth in the same area. Clearly, as a result of the local effect of progesterone on the extracellular matrix of the dermis wrinkles became more shallow as the skin tissue texture and elasticity improved.

Epidermal hydration did not improve during the study period in the treatment group. To our knowledge there exist no data on topical progesterone and epidermal hydration. While the increase of epidermal hydration during systemic HRT is observed as a combined effect due to the influence of oestrogen, experimental data indicate that progesterone does not exert any effect on the epidermal lipid barrier which is responsible for epidermal hydration. In view of our results, we conclude that topical progesterone has no effect on epidermal hydration.

There were no significant changes in skin surface lipids during the study. In the treatment group the measurements with the sebimeter documented a moderate decrease in skin surface lipids on the forehead and clinical examination revealed a general decrease in skin oiliness in the same group, while the mean amount of skin surface lipids on the neck did not change. There are studies documenting a sebum-producing effect of systemic progesterone, but there is also evidence of a sebum-suppressing effect of topical progesterone in women and of systemic progesterone in animals. Synthetic progesterone also showed an in vitro inhibitory effect on 5α-reductase, a key enzyme in the metabolism of androgens, which have been shown to increase sebum synthesis. The observed (statistically nonsignificant) decrease of skin surface lipids on the forehead might be attributed to a moderate suppression of the sebaceous gland function by topical progesterone.

Topical progesterone is well absorbed and transported into the circulation. We observed a significant increase in the subjects’ progesterone levels in the treatment group, but the mean progesterone levels stayed within the normal range of perimenopausal women. Side-effects were minimal: the increase in inflammatory skin lesions was moderate and also occurred to the same extent in the placebo group. Thus, the vehicle cream, rather than the hormone, appears to be responsible for this effect.

We demonstrate in this study that topical progesterone can diminish some of the ageing phenomena in the skin of peri- and postmenopausal women by improving the viscoelastic properties and firmness of the skin. As skin ageing is not an indication for long-term HRT, topical progesterone could be a topical, alternative replacement therapy for the hormone-depleted skin of postmenopausal women. The results of this study also indicate that topical progesterone could represent a new therapeutic approach for other dermatological conditions involving pathological tissue degradation by MMPs. Even though the cutaneous side-effects were minimal, the resorption of the hormone, leading to increased blood levels, should be well considered before prescribing this treatment. Future investigations will try to elucidate whether higher local concentrations of this hormone could lead to better effects without the risk of more side-effects.

References
Effects of progesterone cream on the skin, G. Holzer et al.


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