

**Interest of a new anti-ageing treatment combining the
transdermal application with Roller of the Products
Mesoline[®] Refresh and Mesoline[®] Tight, and the injections of
Pluryal[®]**

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I INTRODUCTION

The aging of the face is actually the most common reason for consulting a physician in aesthetic medicine. Wrinkles of the face are the result of the reduction of the mechanical properties of the skin in relation to the alteration of the elastic tissue and the collagen of the dermis. They must be differentiated from the dynamic folds that are generated by the repetitive tractions on the skin caused by the facial expression muscles. Also, the gravity effect is responsible for the ptosis in the lower third of the face. A new anti-ageing concept is developing and it combines aesthetic mesotherapy by transdermal means and the injection of dermal fillers. The mesotherapy using a “roller” improves the glow, hydration and tone of the skin and attenuates the superficial wrinkles. A “roller” is a medical device consisting of a cylindrical head with very fine needles (from 0.5mm to 1mm in length). According to previous studies, this device has a triple effect: it stimulates the cells of the skin in response to the needles’ aggression, it creates micro-channels to optimise the penetration of the active principles applied and last, it improves blood circulation in the treated area. The subcutaneous injections of dermal fillers are used to correct the wrinkles and facial depressions.

It is this combination of aesthetic mesotherapy and injection of hyaluronic acid fillers that was used in this study in the aim of assessing its anti-ageing efficacy in 15 subjects.

II STUDY OBJECTIVE

The clinical study involved 15 female subjects of skin phototype II to IV, aged at least 45 years old and presenting signs of facial aging. The objective of this trial was to put in evidence the efficacy and tolerance of the mesotherapy associated to the injection of hyaluronic acid dermal fillers.

III CLINICAL EVALUATION

The clinical assessments were obtained using semi quantitative dermatological scores to evaluate the cutaneous signs of the facial ageing: the skin tone and the depth of the nasolabial folds, glabellar line and bitterness lines as well as the importance of the crow’s feet fine lines. Macropictures, chromametric measurements as well as wrinkles’ depth measurements (Skin Station) have been also performed. Face pictures, a tolerance assessment and a self-evaluation completed these analyses.

1-INCLUSION CRITERIA

- Women aged 45 years and more and presenting signs of cutaneous ageing.

2-EXCLUSION CRITERIA

The following subjects were excluded from the study:

- history of allergy to metals,
- autoimmune diseases,
- skin diseases of the face,
- healing problems and keloid formation,
- patients previously treated with permanent injectable implants or unidentified dermal fillers.

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3- TREATMENT PROTOCOL

The subjects received 3 sessions of transdermal mesotherapy using the Mesoline® Roller, a sterile medical device consisting of a cylindrical head with 540 very fine needles measuring 0.5mm or 1mm in length, selected according to the thickness of the skin. 2 products manufactured by MD Skin Solutions have been used during the mesotherapy sessions. Mesoline® Refresh, supplied in a sterile vial of 5ml, contains hyaluronic acid (25mg per vial), growth factors of synthetic origin, DNA and vitamins (A, B3, B5 and B6). Mesoline® Tight, supplied in a sterile vial of 5ml, composed of dimethylaminoethanol, siliconium, antioxidants (coenzyme Q10 and ferulic acid) as well as panthenol.

Before each session of mesotherapy, the subjects' make-up was removed and a gentle scrubbing was performed, after which the skin was disinfected with chlorhexidine. Mesotherapy sessions were performed at D0, D30 and D60.

The injections of dermal fillers were performed at D0 for all the subjects, using Pluryal® or Pluryal® Volume (MD Skin Solutions, Luxembourg) in the nasolabial folds and bitterness lines. Pluryal® is a dermal filler that has obtained EC certification (CE 1015) and is composed of monophasic reticulated (BDDE) hyaluronic acid at a concentration of 23mg/ml. The basic form (Pluryal®) has an ideal viscosity and reticulation for correcting superficial to medium wrinkles whereas Pluryal® Volume, thanks to its higher viscosity and reticulation, is suitable for the correction of deeper deficits and volume creation. In some subjects, Pluryal® Volume was also injected to restore the volume of the lower third of the face (facial contours and cheeks). Local anesthesia was performed using an injection of lidocaine. The injection technique used was the retro-tracing technique, in a linear and slow manner, using microcannulas (MN Needle P250®, Needle Concept) to limit the occurrence of hematomas. A gentle cutaneous massage after the injection improved the diffusion of the product and homogenised its distribution.

4- DERMATOLOGICAL ASSESSMENTS

The following facial assessments were made on D0 before the first session of mesotherapy and have been repeated after 1 month, 2 months, 3 months and 6 months. 4 semi-quantitative scores have been considered for the dermatological evaluation of the cutaneous ageing of the face:

- Aspect of the depth of the wrinkles of the nasolabial fold, glabella and bitterness lines as well as the size of the fine lines, according to their importance, depth and surface (visual scale

from 1 to 4, where the score 4 represents a significantly depressed aspect of the epidermic surface and score 1 represents a skin which surface is smooth)

- Tone (tonic aspect on touch) using scores from 1 to 4, where 4 represents a very important tone of the skin.

5- ANALYSES REALIZED USING MEASUREMENT EQUIPMENTS

Chromametric and SkinStation® assessments have been performed on D0 before the first session of mesotherapy and after the last session, as well as on assessments at 3 months and 6 months.

The chromametric analysis of the skin's clarity was obtained using a Konica Minolta CR/DP-400® Chroma Meter. An increase in the value of parameter L* indicates an increase in the skin's lightness.

The measurement equipment called Skin Station® allowed the in vivo assessment of the volume of the facial wrinkles through a measurement of the volume that these wrinkles occupy, thanks to a probe containing a camera (magnification x50) and connected to a computer. An assessment of the volume the crow's feet lines, marionette lines and nasolabial folds (V/mm²) was obtained.

6- FACE PICTURES AND MACROPICTURES

Face pictures using a Canon EOS 50D camera with Macro MR-14 EX (ring flash) were performed, always in the same conditions as far as the light, the distance, the lighting, the zoom and the shooting location are concerned.

Macropictures using the US Microscope Proscope (SCALAR®) were performed and allowed a visualisation of the skin at high magnification (x50) and an analysis of the microdepressionary network.

7- TOLERANCE ASSESSMENT AND SELF ASSESSMENT

In order to determine the tolerance of these products on the facial skin and to calibrate the level of satisfaction of the subjects, an assessment of the tolerance and a self-assessment were also performed.

The subjects have assessed the immediate tolerance using a scoring from 0 to 5 allowing the quantification of the "itching" and "burning" sensations felt after the transdermal application by roller of the products Mesoline®. A score of 5 represents the most important sensation.

A scoring from 0 to 4 has been used to analyze the self-assessment of the subjects as far as the efficacy of the treatment is concerned where value 0 represents a worsening, 1 represents the absence of change, 2 represents a slight improvement, 3 represents a clear improvement and 4 represents a substantial improvement.

IV RESULTS

1- POPULATION DATA

In total, 15 subjects were included in the trial whose average age was 55.27 ± 6.75 years, of phototype II to IV.

2- MESOTHERAPY EFFICACY

The tone of the skin, the depth of the wrinkles and lines, as well as the brightness of the complexion have been significantly improved after 3 sessions of mesotherapy. The dermatological score assessing the skin's tone increases of $1,7 \pm 0,60$ (D0) to $2,97 \pm 0,5$ ($p=8,10-7$) 3 months after the first session of treatment (an average improvement of 74,7%). At 6 months, the skin's tone has increased substantially from the level observed after 3 months ($p=0,01$).

The depth of the wrinkles is significantly reduced as it was observed at 3 months: in the crow's feet, the dermatological score decreases from $1,97 \pm 1,18$ to $1,68 \pm 1,01$ ($p=0,01$) (meaning a decrease of 14,58%). At 6 months, a more important decrease of the depth of these lines is noted (dermatological score of 1.44 versus 1,68 at 3 months), but a non-significant one. Also, a statistically significant reduction of the glabellar wrinkles depth is observed at 3 months with a mean score decreasing from $2,4 \pm 1,07$ to $1,91 \pm 1,15$, meaning a decrease of 20,28%. At 6 months, a more important decrease in the depth of the glabellar wrinkles is noted with a dermatological score dropping from $1,91 \pm 1,15$ to $1,81 \pm 1,07$, corresponding to a significant change ($p=0,04$).

The radiance of the complexion has been assessed by chromatic analysis according to the L^* parameter which measures the brightness of the skin. A statistically important increase of L^* parameter was observed at 3 months with an average increase from 61,32 to 66,72 in the sub-ocular region, that to say 8,8% of improvement. At 6 months, the level of increase of L^* parameter remains identical to the one observed after 3 months.

The depth of the crow's feet lines measured using the SkinStation® is significantly diminished after the treatment with an average decrease of volume from $31,53 \pm 13,39$ to $22,8 \text{ mm}^2 \pm 9,5 \text{ mm}^2$, that to say a decrease of 27,7%. At 6 months, the level of decrease of the depth of the crow's feet lines remains identical to the one observed after 3 months.

Face pictures 1 and 2 (subject no. 3) and 3 and 4 (subject no. 6) demonstrated the effect of the mesotherapy treatment. Macropictures has allowed observing, for all the subjects, a significant improvement of the microdepressionary network. This effect is particularly visible in pictures 5 and 6 (subject no. 11) by comparing the results before the treatment and at D84, after 3 sessions of mesotherapy.

3- EFFICACY OF THE INJECTIONS

The depth of the wrinkles is substantially reduced 3 months after the treatment, because of the dermal fillers injections. At the level of the bitterness lines, the dermatological score drops from $2,78 \pm 0,88$ (D0) to $1,3 \pm 0,91$ ($p=0,000047$), that to say a diminution of 53,25% and at the level of the nasolabial folds the score drops from $2,64 \pm 0,96$ to $0,8 \pm 0,877$ ($p=0,0000024$), that to say 69,96% of improvement. At 6 months,

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the level of the decrease in the depth of the bitterness lines and nasolabial folds remains identical to the one observed after 3 months.

The depth of the bitterness lines measured with the SkinStation® is significantly diminished after the treatment with dermal fillers: it drops from $40,34 \pm 16,86$ to $28,19 \pm 7,66$ per mm^2 ($p=0,000054$) 3 months after the injection, that to say 30,12% of decrease.

Pictures 7 and 8 (subject no.10) allow us visualizing the effect of the injections.

4- TOLERANCE ASSESSMENT AND SELF-ASSESSMENT

The average score obtained for the 15 subjects is $2,2 \pm 0,5$ over 5 for the "itching" sensation and $2,2 \pm 0,8$ over 5 for the "burning" sensation. These effects disappeared for all the subjects within one hour following the mesotherapy session. The Dermatologist observed mild to medium erythema in all subjects after the sessions of mesotherapy. This effect lasted no longer than 24 hours. Two subjects noted the appearance of hematomas after the injection of dermal fillers. These secondary effects were always temporary and disappeared within less than a week. A week after the treatment, one subject (no. 13) reported the appearance of a swelling of the right cheek, without fever, but accompanied by insomniatic pain over 3-4 days. This swelling has disappeared after 10 days without sequela. The rapid disappearance of this nodule makes it possible, a priori, to eliminate the diagnosis of giant-cell granuloma.

The self-assessment highlighted the satisfaction of all subjects when it comes to the improvement of the tone and brightness of the skin. Amelioration in the tone was significant 2 months after the first treatment ($p=0,04$). The subjects have noted a clear improvement of the tone of the skin, in average, after 3 months compared to their assessment at 1 month ($p=0,002$). Moreover, the improvement at 6 months was also significant compared to the assessment at 1 month ($p=0,003$).

The subjects have valued that the brightness of their skin was improved after 3 months of the treatment ($p=0,001$). A clear improvement was noted in average starting the second month.

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Picture 1. Subject no. 3 at D0 before treatment



Picture 2. Subject no. 3 at D180 (3 months after the last treatment): important improvement of the complexion tone and brightness.



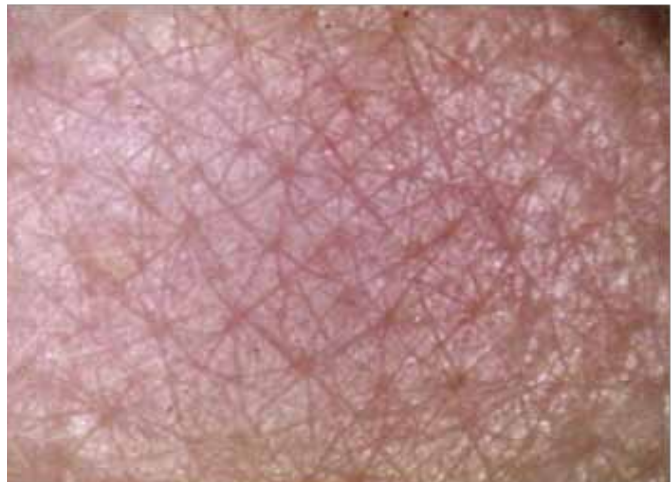
Picture 3. Subject no. 6 at D0 before the treatment



Picture 4. Subject no. 6 at D84 : increase of the skin tone and brightness associated with a decrease in forehead wrinkles after 3 sessions of mesotherapy.



Picture 5. Microdepressionary analysis at high magnification (x 50) of subject no.1 at Day 0 before treatment.



Picture 6. Improvement of the microdepressionary network with decrease of the depth of wrinkles in subject no.1 at D84 after 3 sessions of mesotherapy.

V CONCLUSION AND DISCUSSION

This trial confirmed the value of combined therapies in aesthetics for the treatment of cutaneous aging, combining mesotherapy and the injection of dermal fillers. This technique makes it possible to avoid cosmetic surgery for the correction of facial imperfections that appear with age. Unlike surgery, the reversibility of the obtained results reassures the subjects worried about eventual excessive modifications of their face. The challenge of facial rejuvenation is to obtain the best results using simple and repeatable techniques with the least possible trauma.

In this study, monophasic dermal fillers based on pure and reticulated hyaluronic acid, whose tolerance and efficacy are well known, made it possible to correct the deep wrinkles of the face, thus giving it a younger appearance. The assessment of results at 6 months showed the durability of the products Pluryal® and Pluryal® Volume as well as their tolerance in all treated subjects.

The transdermal mesotherapy using 2 products (Mesoline® Refresh and Mesoline® Tight) produced a hydrating and re-densifying effect of the skin, while attenuating the cutaneous flaccidity and the superficial wrinkles (crow's feet). These results were confirmed by the different assessments performed in this trial and were maintained after 6 months, three months after the last treatment was carried out. The satisfaction of all subjects when it comes to the treatment combining the transdermal application by roller of the products Mesoline® Refresh and Mesoline® Tight and the injections of Pluryal® dermal fillers, was very high.



Picture 7. Subject no. 1a at D0 before treatment



Picture 8. Subject no. 10 at the end of the treatment (D84) : important attenuation of the nasolabial folds and bitter lines after injection of dermal fillers.

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