

Pilot study evaluating the therapeutic effects of a new pre-mixed injectable product of low molecular weight (LMW) hyaluronic acid added to six amino acids (HY6AA +Formula) in facial skin aging

Abstract

Introduction: Skin aging is a complex biological phenomenon, it is the result of an intrinsic decline in cellular functions due to age and genetically programmed, added to a continuous exposure of various harmful external factors that influence its trend. Both mechanisms modify the structure of the extracellular matrix (ECM) by acting on the quantity and composition of its proteins: type III collagen constitutes 50% of the collagen in the dermis of the neonatal skin but only 5% of the collagen in the aging adult skin, type IV collagen, an important component of the basement membrane, forms anchor plates between types of structural collagen, it decreases with age after 35 years affecting the thickness of the epithelial basement membrane significantly.

Aims of the study: The Aim of the study was to evaluate the therapeutic effects of a new pre-mixed injectable product of not cross-linked LMW Hyaluronic Acid (50-250 KDaltons) added to a specific mixture of six amino acids (HY6AA + Formula) to improve the signs of chrono and photo-aging of the skin of the facial area, through a simple and minimally invasive injectable procedure with fast obtaining results.

Materials and methods: The open clinical pilot trial was conducted by two centres under medical control. 3,5 ml HY6AA+Formula was performed by injecting 3 times at intervals of 2 weeks each. The Visia device as well as the GAIS (Global Aesthetic Improvement Scale) and VAS scale, the skin elasticity scale and the wrinkle correction scale were used for the assessment. Efficacy evaluations were performed previously to each injection treatment, performed every two week for three times, and 4 weeks after the third injection. Skin elasticity was evaluated by Pinching Test immediately after each treatment and at 4 weeks after the third injection.

Conclusions: The photo analysis by Visia device proves the significant effectiveness of HY6AA + Formula. The data recorded on the skin texture improvement, dyschromia and skin elasticity are very encouraging, especially considering the minimal invasiveness of the procedure and the limited number of sessions required. The improvement of skin quality in most cases occur after the first treatment, and as the treatment protocol progresses, patients' feelings and their individual assessment of skin quality also gradually improve.

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Elena Fasola,¹ Edyta Adamczyk Kutera²

¹General Secretary of the Italian Association of Aesthetic and Functional Gynecology (AIGEF), Italy

²Faculty of Medicine and Dentistry of the Medical Academy in Łódź, Poland

Correspondence: Elena Fasola, General Secretary of the Italian Association of Aesthetic and Functional Gynecology (AIGEF), Italy, Tel +393476441423, Email fasolaelena@yahoo.it

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Introduction

Skin ageing is a complex and inevitable biological phenomenon of human life, it is the result of an intrinsic decline of cell functions, due to age, added to a to the cumulative exposure of various and influencing harmful external factors (extrinsic aging).

At the level of the External Cellular Matrix (ECM), both mechanisms determine not only a noticeable reduction in total skin collagen, but also a change of the composition: type III collagen makes up 50% of the collagen in the dermis of neonatal skin but only 5% of the collagen in adult aging skin, Type IV collagen, an important basement membrane component, forms the anchor plaques among structural collagen types (Figure 1), it decreases with age after 35 years and the epithelial basement membrane thickness increases significantly.¹

The reduction of the basement membrane thickness suggests a total change in the cell turnover of the whole tissue, so we witness:

- An increase in the degradation of Elastin and the reduction of its production as well as an increase in Matrix Metalloproteinases (MMP);

- A reduction in hyaluronic acid due to a decrease in fibroblastic activity and down-regulation of CD44 and RHAMM membrane receptors with a consequent reduction in gene transcription for hyaluronic acid.³
- An increase in the quantities and activity of Hyaluronidase.

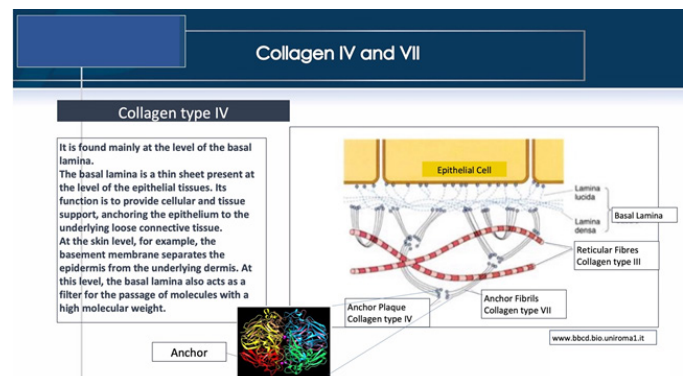


Figure 1 Collagen type IV.²

Background

The increase in time spent on video calls due to teleworking and forced distancing, which began with the COVID-19 pandemic in 2020, now known as the “Zoom boom”, has led people around the world to further shift attention to their physical appearance, in many cases even compulsively.

Beyond the specific treatment on the collective psychological impact of the pandemic and on which it would obviously deserve a separate discussion, also because triggering a profound change in the perception of the state of subjective wellbeing, already evidently in precarious balance before it, the objective data subsequently recorded as resulting in the aesthetic medical field, have undoubtedly been an increase in the demand for minimally invasive and surgical cosmetic treatments.

On the other hand, in the first phase of the pandemic, the increased time available to the medical device manufacturing industries has further pushed the already flourishing research in this area. For example, according to the American Society of Plastic Surgeons (ASPS), nearly 18 million minimally invasive and surgical cosmetic products were performed in 2020, including nearly 16 million minimally invasive products.

Therefore, the increasing adoption of minimally invasive surgeries, along with the availability of a wide range of such treatment options, is driving market growth with a Compound Annual Growth Rate (CAGR) estimated at around 9.3%, from 2020 to 2030.⁴

Aims of the study

We are evaluating the therapeutic effects of a new pre-mixed injectable product of free LMW Hyaluronic Acid (50-250 KDaltons) added to a specific mixture of six amino acids (HY6AA + Formula, *SuneKos Performa- ®Professional Dietetics*) on the Dermis of the face area affected by chrono aging and photoaging. The aim of this pilot study is not aesthetic as an end in itself but is Aesthetic through the achievement of the state of health of the skin, the improvement of its trophism and the restructuring of the Extra Cellular Matrix.

The evaluation of the skin quality and health improvement was conducted on a group of 10 female patients. Inclusion Criteria provided 10 healthy adult volunteers women with age range between 40-67 years old, all with willingness to improve the condition and quality of the skin and all claiming that they have not undergone any medical aesthetic treatments in the last 1 year.

Patients aged under 18yr, patients with Auto-immune soft tissues diseases and neoplastic diseases, with ongoing anti-inflammatory therapy, inflammatory or infection diseases affecting treatment area or with presumed or confirmed sensitivity towards one of the contents or ingredients of the product were excluded from the study. A detailed medical history and physical examination were performed on all subjects on the first day. An interview was conducted to collect subjective anamnesis on general health, past illnesses, drugs, nutraceuticals, cosmetics, and family one.

Rational use of HY6AA formula (Glycine, L-Proline, L-Lysine MHC, L-Leucine, L-Valine, L-Alanine) in skin ageing

The mixture of LMWHA added to this specific 6 amino acids (HY6AA+ Formula), in particular L-Valine and L-Alanine, is able to over express collagen IV and elastin,⁵ the promoting the assembly of matrix components and to give a good neo-angiogenesis, hydration,

anti-oxidant and anti-inflammatory tissue response.⁵ This particular pre-mixed mixture also provides to decrease (by 40%) the degradation process of HA by the enzyme hyaluronidase (Figure 2).⁶

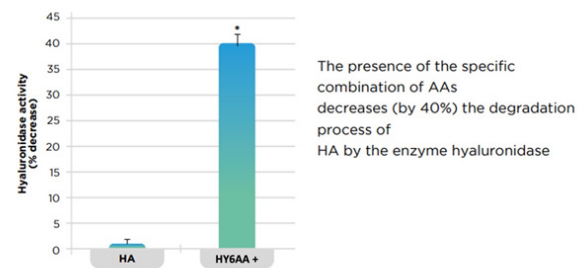


Figure 2 Injection of HY6AA + Formula provides to reduce action of Hyaluronidase.⁶

Material and methods

The open clinical pilot trial was conducted by two centres under dermatological control. The study was conducted 10 healthy female adult volunteers, age range 40–67 years, whose informed consent had been obtained. 3,5 ml HY6AA+Formula was performed by injecting 3 times at intervals of 2 weeks each. Efficacy evaluations were performed previously to injection treatment at T0, at T1, and T2 (after 4 weeks from T0) and at T3, 14 weeks after T0. The Visia device as well as the GAIS (Global Aesthetic Improvement Scale) and VAS scale, the skin elasticity scale and the wrinkle correction scale were used for the assessment.

Technique

The procedure was performed with the use of 1 ml syringes and 30G x 4 mm needles.

Each patient was administered a total of 3.5 ml of the premixed HY6AA+ Formula, using the deposit technique in the deep dermis, at the border of the subcutaneous tissue, by inserting the needle at an angle of 45 degrees, which allowed to reach a depth of about 2 mm, in the volume of 0.1 ml of the preparation per injection point.

The premixed mixture of HY6AA+ Formula was administered using the High Performance Technique (HPT) technique (Figure 3), following the ideal lines in orthogonal direction to the natural tension line of the skin (Langer Lines)⁷ over the entire face, with a number of injection points of 3 or multiples of 3, called by Autor: “ The rule of 3” Technique). The peri-ocular and peri-labial areas were treated with 3 points of injections per half face side with amount of 0,3 ml per point or, thanks to the “rule of 3” technique and in case of particular skin thinness, with 9 points with 0.1 ml per point, for side. After the treatment, a massage was performed.

Results

The evaluations were performed both using different scales for the wrinkles and elasticity and tension and with the use of VISIA.

The VISIA results showed the following:

There was a 71% decrease of the wrinkles on the forehead (Figure 4)

In the following case the improvement is of 44% of the wrinkles in the periorcular area (Figure 5).

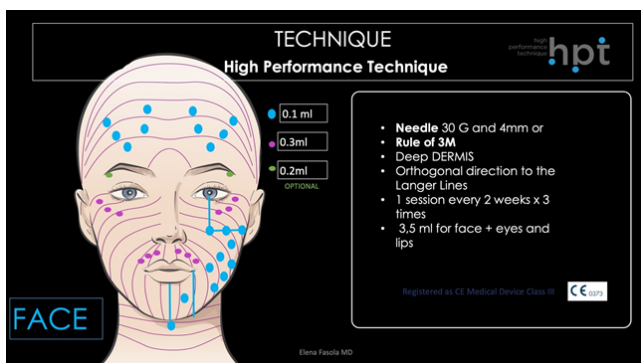


Figure 3 High performance technique.



Figure 4 Before and after.



Figure 5 Before and after.

The texture of the skin showed an improvement as shown in the following Before & After pictures (Figure 6-8).

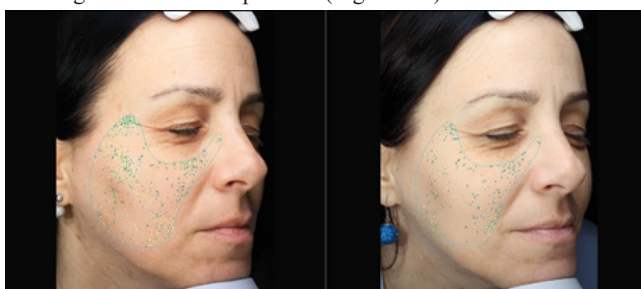


Figure 6 Before and after.



Figure 7 Before and after.

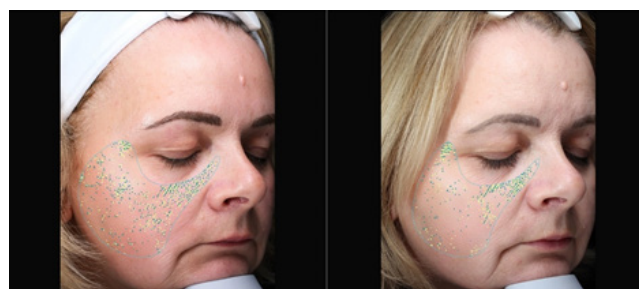


Figure 8 Before and after.

Improvement of 16% on skin dyschromia due to photo-ageing as per following Before & After pictures (Figure 9-10).

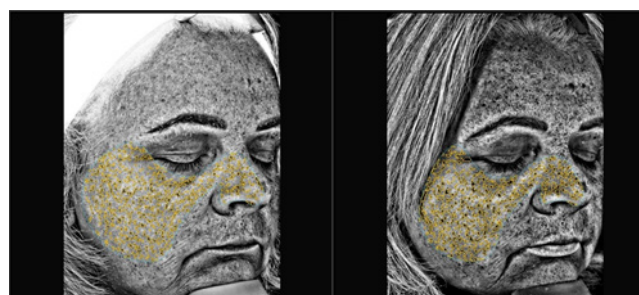


Figure 9 Before and after.

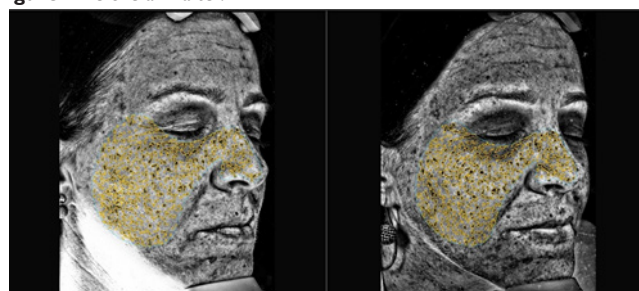


Figure 10 Before and after.

The elasticity was evaluated with the use of Pinching Test by the following 3-point scale:

1. very good elasticity - immediate skin relaxation
2. medium flexibility - relaxation less than 10 seconds (approximate number of seconds)
3. lack of flexibility - relaxation time over 10 seconds.

This evaluation was performed at T0, T1, T2, T3 (after 4 weeks from T0) and T4 (after 6 weeks from T0). The results were the following (Figure 11).

The assessment of the wrinkles grade was obtained on a 4-point evaluation scale where:

1. no improvement
2. slight improvement in 1 -33% correction
3. moderate correction 34-66%
4. significant improvement of 67-100% of corrections.

The results show that the majority of patients showed a moderate improvement (scale 3), 30% of patients saw a significant improvement (scale 4), and there was no patient who showed no improvement (Figure 12).

The VAS scale was used to assess changes in the improvement of skin tension and elasticity (Figure 13).

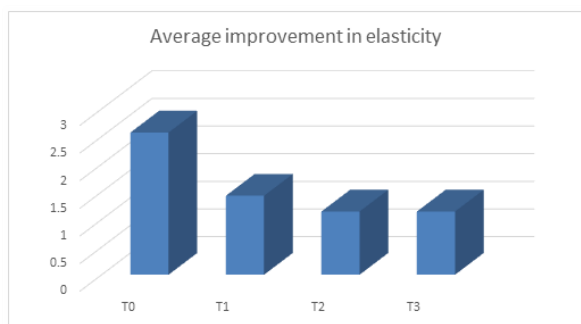


Figure 11 The greatest improvement was noticed already after the first treatment, it progressed after the next treatment and during the observation it remained at the level of 1 on a 3-point scale.

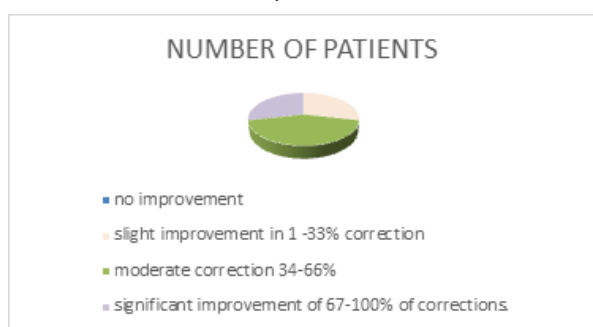


Figure 12 Wrinkles assessment.

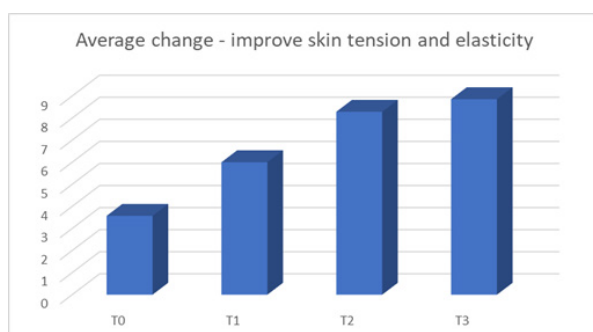


Figure 13 The graph shows the mean improvement in skin tone and elasticity among all patients.

All subjects noticed a significant improvement in skin tension and elasticity. None of the subjects noticed any deterioration. The changes were observed after the first treatment, the greatest improvement was achieved after treatment 2. The beneficial effects were still observed after the end of the study and declared at the visit 14 days from the last - 3rd administration.

According to GAIS - the Global Aesthetic Improvement Scale, all subjects noticed an improvement in appearance. The vast majority noticed a significant improvement in appearance right after the first injection, only 28% of patients experienced a moderate improvement in appearance, and there was no patient without improvement or worsening (Figure 14).

All patients completed the observational study. Therapy with the use of an injectable, patented formula of hyaluronic acid and amino acids (HY6AA+ Formula) has shown a beneficial and satisfactory effect both on the level of patient satisfaction and the parameters assessed using photo analysers. Despite the use of non-cross-linked

hyaluronic acid, the tissue volume improved. There has been a noticeable improvement in the texture, colour and firmness of the skin. The treatments were well tolerated by the patients and the number of side effects was minimal: a case of superficial ecchymosis was recorded which resolved spontaneously.⁸

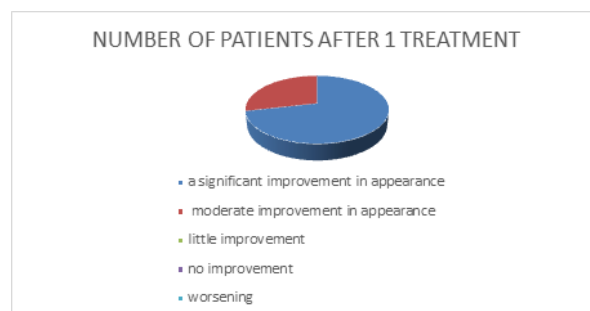


Figure 14 GAIS after one treatment.

Conclusion

The photo analysis by Visia device proves the significant effectiveness of HY6AA + Formula. The data recorded on the skin texture improvement, dyschromia and skin elasticity are very encouraging, especially considering the minimal impassivity of the procedure and the limited number of sessions required. The improvement of skin quality in the vast majority of cases occur after the first treatment, and as the treatment protocol progresses, patients' feelings and their individual assessment of skin quality also gradually improve.

Acknowledgments

None.

Conflicts of interest

Authors declare there is no conflict of interest.

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