# Hybrid Skin Booster Injectables Hyaluronic Acid with Growth Factors and/or Hyper Diluted Calcium Hydroxyapatite "For Treating Facial Skin Pigmentations"

#### NOURY ADEL, M.Sc

The Department of Oral and Maxillofacial Surgery Specialist, Private Practice, Cairo, Egypt

#### Abstract

*Background:* Hyaluronic acid has an important role in skin viscoelasticity.

*Objective:* The present study was performed to evaluate the effect of injecting the non-cross linked hyaluronic acid with growth factors and/or hyper diluted calcium hydroxyapatite for treating facial skin pigmentations and face rejuvenation including texture, elasticity and firmness through collagen induction.

*Methods:* 30 female patients who suffered from dry skin with pigmentations, were included in the study. All patients were randomly divided into three groups, the first group was injected with non-cross linked hyaluronic acid with growth factors, and the second group was injected with hyper diluted calcium hydroxyapatite filler, while the third group was injected with a hybrid mixture of non-cross linked hyaluronic acid with growth factors and hyper diluted calcium hydroxyapatite filler. Digital pictures were taken before the injection and immediately after the injection for assessment of the clinical results as well as during the follow up periods (2 weeks, 1 month & 3 months).

*Results:* The third group showed a marked reduction in the amount of skin pigmentations at 2 weeks after injection along with improvement in the skin texture and elasticity, those changes remained stable up to three months after treatment.

*Conclusion:* The use of a hybrid mixture of non-cross linked hyaluronic acid with growth factors & calcium hydroxyapatite filler provides a marked reduction in the amount of facial pigmentations and provides a better skin texture than the use of each product alone.

Key Words: Skin boosters – Facial rejuvenation – Pigmentations – Skin care – Hyaluronic acid – Calcium hydroxyapatite fillers.

Disclosure: No conflict of interest.

#### Introduction

Hyaluronic acid (HA) plays an important role in skin viscoelasticity, therefore HA based fillers & skin boosters are widely used for purpose of volumization & maintaining skin elasticity through stimulation of collagen synthesis [1]. Moreover calcium hydroxyapatite fillers are used for both volumization and biostimulation depending on whether it is hyper diluted or not [2].

The depigmenting effect of hyaluronic acid in human skin explants was observed in a research [3], on the other hand the hyper diluted calcium hydroxyapatite was suggested as an alternative treatment for periorbital hyperpigmentation [4]. Most of the researches in the literature focuses on observing the skin quality after the use of non-cross linked hyaluronic acid or hyper diluted calcium hydroxyapatite fillers [5-8]. As far as we know there is no single research that discusses the combined use of both products as a hybrid mixture for reducing skin pigmentation and/or rejuvenation, and that is why the necessity for our study.

#### **Material and Methods**

Thirty Middle Eastern female patients (28-47 years old range) came to our clinic suffering from dehydrated facial skin associated with pigmentations. These patients desired to achieve a healthy looking hydrated skin and elimination of those pigmentations. Written informed consent were obtained from all patients. All patients were randomly divided into three groups, each group contains 10 patients. The products used were a non-cross linked hyaluronic acid vial & calcium hydroxyapatite vial. All products were injected with a Softfil micro cannula.

Patient satisfaction were recorded based on a score from 1 to 5, where 1 means not satisfied,

Correspondence to: Dr. Noury Adel,

E-Mail: dr.noury100@gmail.com

2 means less satisfied, 3 means quite satisfied, 3 means satisfied and 5 means very satisfied. The satisfaction score were recorded preoperative and during each follow-up interval.

## Vials preparation:

The first group of vials included non-cross linked hyaluronic acid, which comes as a vial of 40mg/3ml to be mixed with a 8ml liquid ampoule that's comes with the same kit which contains DMAE (dimethylaminoethanol) 3%, GAG (Glycosaminoglycan) 1%, Procaine 2% & nanofactors such as; Transforming growth factor Beta 3 "TGFB3" 1%, Insulin growth factor "IGF" 1%, Immune defense proteins "IDP2" 1%.

The second group of vials included calcium hydroxyapatite vial 15% per 6ml which was mixed with two ampoules; 2ml of lidocaine & 2ml of liquid nanofactors similar to those factors mentioned above. We also added a 1ml of saline free of preservative to the calcium vial.

#### Patients grouping & Injection technique:

The first group of patients were injected with the non-cross linked hyaluronic acid skin booster only, each patient received a total of 3ml. As for the second group of patients were injected with the hyperdiluted calcium hydroxyapatite only, each patient received a total of 3ml. While the third group of patients received a hybrid 3ml mixture of both the non-cross linked hyaluronic acid and the hyperdiluted calcium hydroxyapatite mixed in a single syringe of 1:1 ratio. All patients were injected in a superficial plane by placing a series of retrograde linear threading using a 22 G Softfil cannula.

All patients were instructed not to use any cosmetic products, chemical peeling or to do any facial aesthetic treatment that may affect the results of the injection.

## Statistical analysis:

Microstat 7 for Windows statistical package (Microstat Inc) was used for statistical analysis in this study. One-Way ANOVA was used to evaluate the effect of time on the selected parameters followed by calculating Least Significant Difference (LSD) for paired comparisons. Differences were considered statistically significant when  $p \le 0.05$ .

## Results

None of the patients reported any complications, there was no observations of any nodules nor any signs of vascular occlusion. Clinical observations were taken at four follow-up sessions (immediately after the injection, 2 weeks, 1 month and 3 months). The first group only showed a decrease in the redness of the acne and skin, the second group showed a minor improvement of the pigmentation, while the third group of patients showed more superior results at 2 weeks interval than the patients of other groups, as there was a marked reduction in the facial pigmentations along with marked improvement in the skin elasticity. All patients of group 3 reported a high degree of satisfaction which lasted up to 3 months after the treatment. (Table 1) (Figs. 1-5).

Table (1): One-Way ANOVA evaluating effect of time on patient satisfaction in all groups.

	First group		Second group		Third group			
	Mean	St Dev	Mean	St Dev	Mean	St Dev	Probability	LSD
14 Days	1.00	0.75	1.17	0.00	5.00	0.00	0.050 *	0.756
1 Month	0.00	0.00	1.00	0.00	5.00	0.00	0.0000*	0.745
12 Months	0.00	0.00	0.00	0.00	4.75	0.27	0.0000*	0.195
F ratio	44.697		106.176					
Probability	0.0000		0.0000					
LSD	0.815		0.453					



Fig. (1): Pre & post-operative picture for a patient from group "1" after receiving a non-cross linked hyaluronic acid skin booster with growth factors "pictures shows only a minor decrease in the redness of the acne".



Fig. (2): Pre & post operative picture for a patient from group "2" after receiving a hyper diluted calcium hydroxyapatite. (minor improvement of the pigmentation).



Fig. (3): Pre & post operative picture for a patient from group "3" after receiving a hybrid mixture of non-cross linked hyaluronic acid skin booster & hyper diluted calcium hydroxyapatite. (marked improvement in the pigmentation).



Fig. (4): Pre & post-operative picture for a patient from group "3" after receiving a hybrid mixture of non-cross linked hyaluronic acid skin booster & hyper diluted calcium hydroxyapatite. (Improvement in the pigmentation).





Fig. (5): Mean values of patient satisfaction in all groups throughout the follow-up period.

#### Discussion

Hyaluronic acid plays a great role in determination of the skin viscoelasticity, hydration and firmness. The HA improves skin turgor and increases collagen type I production [9]. A study showed that Restylane vital light® (HA concentration 12mg/ml) provides an increased hydration in addition to improvement in skin elasticity with increased collagen production [10].

We could not find any study to evaluate the effect of hyperdiluted calcium hydroxyapatite on the facial pigmentations, neither did we find a significant improvement in the pigmentations in the second group of patients who received hyperdiluted calcium injections only. It seems that the combination of hyaluronic acid and calcium hydroxyapatite may boost the results of depigmentation due to a certain unknown intracellular action. This point was not addressed properly in our study due to the fact that there was no histological samples taken for microscopic analysis. We do not also believe that the presence of nanofactors in the skin boosters vial contributed to the superior results in group 3 patients as it was a very minimal amount of nanofactors so we think that the effect was due to the combined effect of non-cross linked hyaluronic acid and calcium hydroxyapatite only.

All injections in this study were performed in a superficial plane in order to provide the maximal effect of the skin booster which targets the dermal layer of the skin, the use of large borne softfil cannula® (22G) provides a safe injection thus decreasing the risk of vascular occlusion. Despite that many clinicians advocates the use of needles for intradermal injections of skin boosters, we did not find in our practice that the use of needles provides superior results to cannulas in terms of the aesthetic outcomes. According to the results of this study, the combined use of both products may offer a promising results for facial hyperpigmentation and skin quality than the use of each product alone.

#### Conclusion:

The combined use of non-cross linked hyaluronic acid skin booster mixed with hyperdiluted calcium hydroxyapatite may offer a promising result for treating skin pigmentations in addition to its ability in improving the skin quality. This approach needs to be studied on a larger sample of patients to test the efficacy of such a procedure along with a more systematic evaluation using a digital software skin analysis.

## References

- Bertucci, Vince and Carrie B. Lynde: "Current Concepts in the Use of Small-Particle Hyaluronic Acid." Plastic and reconstructive surgery Vol. 136 (5 Suppl): 132S-138S, 2015.
- 2- De Almeida A.T., Figueredo V., da Cunha A.L.G., Casabona G., Costa de Faria J.R., Alves E.V., Sato M., Branco A., Guarnieri C. and Palermo E.: Consensus Recommendations for the Use of Hyperdiluted Calcium Hydroxyapatite (Radiesse) as a Face and Body Biostimulatory Agent. Plast Reconstr. Surg. Glob Open, 7 (3): e2160, 2019.
- 3- Siquier-Dameto G., Boisnic S., Boadas-Vaello P. and Verdú E.: Anti-Aging and Depigmentation Effect of a Hyaluronic Acid Mechanically Stabilized Complex on Human Skin Explants. Polymers (Basel), 15 (11): 2438, 2023.
- 4- Corduff N.: An Alternative Periorbital Treatment Option Using Calcium Hydroxyapatite for Hyperpigmentation Associated with the Tear Trough Deformity. Plast Reconstr Surg. Glob Open, 8 (2): e2633, 2020.
- 5- Wohlrab J., Wohlrab D. and Neubert R.H.: Comparison of noncross-linked and cross-linked hyaluronic acid with regard to efficacy of the proliferative activity of cutaneous fibroblasts and keratinocytes in vitro. J. Cosmet Dermatol., 12 (1): 36-40, 2013.
- 6- Huang Y. and Yang P.: Application of Cross-Linked and Non-Cross-Linked Hyaluronic Acid Nano-Needles in Cosmetic Surgery. Int J Anal Chem., 2022: 4565260, 2022.
- 7- Guida S., Longhitano S., Spadafora M., Lazzarotto A., Farnetani F., Zerbinati N., Pellacani G. and Galadari H.: Hyperdiluted calcium hydroxylapatite for the treatment of skin laxity of the neck. Dermatol. Ther., 34 (5): e15090, 2021.
- 8- de Almeida A.T., Figueredo V., da Cunha A.L.G., Casabona G., Costa de Faria J.R., Alves E.V., Sato M., Branco A., Guarnieri C. and Palermo E.: Consensus Recommendations for the Use of Hyperdiluted Calcium Hydroxyapatite (Radiesse) as a Face and Body Biostimulatory Agent. Plast Reconstr Surg. Glob Open, 7 (3): e2160, 2019.
- 9- Distante F., Pagani V. and Bonfigli A.: Stabilized hyaluronic acid of non-animal origin for rejuvenating the skin of the upper arm. Dermatol Surg., 35 (Suppl 1): 389-394; discussion 394, 2009.
- 10- Kerscher M., Bayrhammer J. and Reuther T.: Rejuvenating influence of a stabilized HA–based gel of Nonanimal origin on facial skin aging. Dermatol. Surg., 34: 720-726, 2008.