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Contents

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Aesthetic Medicine is a multidisciplinary Journal with the aim of informing readers about the most important developments in the field of Aesthetic Medicine.

Submission of manuscripts

All articles in their final version - completed with name, surname, affiliation, address, phone number and e- mail address of the author (s) - must be sent in word format to the Editorial Committee at the following e-mail address: aemj@aestheticmedicinejournal.org. Manuscripts must be written in English, and authors are urged to aim for clarity, brevity, and accuracy of information and language. All manuscripts must include a structured abstract. Authors whose first language is not English should have their manuscripts checked for grammar and stylistic accuracy by a native English speaker.

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The title page should include:
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· Conflict of interest
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· Use tab stops or other commands for indents, not the space bar
· Use the table function, not spreadsheets, to make tables

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The authors declare that they have no conflict of interest.
If potential conflicts of interest do exist, the authors should provide details (see below) for each affected author in a note in a separate DISCLOSURE section of the manuscript document text, before the list of references.

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References

References must be cited consecutively in the text as superscript numerals and listed on a separate sheet in numerical order at the end of the text. The references must be cited according to the AMERICAN MEDICAL AS- SOCIATION (AMA) CITATION STYLE.
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Journal article - online* *if there is no DOI, provide the URL for the specific article	Coppinger T, Jeanes YM, Hardwick J, Reeves S. Body mass, frequency of eating and breakfast consumption in 9-13- year-olds. *J Hum Nutr Diet.* 2012; 25(1): 43-49. **doi: 10.1111/j.1365-277X.2011.01184.x**
Journal article - online from a library database* *there is no specific way to cite articles found in library databases according to the AMA so double check with your professor	Calhoun D, Trimarco T, Meek R, Locasto D. Distinguishing diabetes: Differentiate between type 1 & type 2 DM. *JEMS* **[serial online].** November 2011; 36(11):32-48. **Available from: CINAHL Plus with Full Text, Ipswich, MA. Accessed February 2, 2012.**
Newspaper article - in print* *if the city name is not part of the newspaper name, it may be added to the official name for clarity * if an article jumps from one page to a later page write the page numbers like D1, D5	Wolf W. State's mail-order drug plan launched. *Minneapolis Star Tribune.* May 14, 2004:1B.
Newspaper article - online	Pollack A. FDA approves new cystic fibrosis drug. *New York Times.* January 31, 2012. http://www.nytimes.com/2012/02/01/business/fda-approves-cystic-fibrosis-drug.html?ref=health Accessed February 1, 2012.
Websites	Outbreak notice: Cholera in Haiti. Centers for Disease Control and Prevention Web site. https://www.cdc.gov Published October 22, 2010. Updated January 9, 2012. Accessed February 1, 2012.
Entire book - in print	Modlin J, Jenkins P. *Decision Analysis in Planning for a Polio Outbreak in the United States.* San Francisco, CA: Pediatric Academic Societies; 2004.
Book chapter - in print	Solensky R. Drug allergy: desensitization and treatment of reactions to antibiotics and aspirin. In: Lockey P, ed. *Allergens and Allergen Immunotherapy.* 3rd ed. New York, NY: Marcel Dekker; 2004:585-606.

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AMA Manual of Style: A Guide for Authors and Editors. 10th ed. Oxford: Oxford UP.

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Example Article

1. Zoellner J, Krzeski E, Harden S, Cook E, Allen K, Estabrooks PA. Qualitative application of the theory of planned behavior to understand beverage consumption behaviors among adults. J Acad Nutr Diet. 2012;112(11):1774-1784. doi: 10.1016/j.jand.2012.06.368.

In-Text Citation Example

LARGE INCREASES IN AMERICANS' CONSUMPTION OF sugar-sweetened beverages (SSB) have been a topic of concern. Between 1977 and 2002, the intake of "caloric" beverages doubled in the United States, with most recent data showing that children and adults in the United States consume about 172 and 175 kcal daily, respectively, from SSB,[1] it is estimated that SSB account for about 10% of total energy intake in adults[2,3]. High intake of SSB has....

References Section Example

References

1. Duffey KJ. Popkin BM. Shifts in patterns and consumptions of beverages between 1965 and 2002. *Obesity.* 2007:15(11):2739-2747.
2. Nielsen SJ. Popkin BM. Changes in beverage intake between 1977 and 2001. *Am J Prev Med.* 2004;27(3):205-210.
3. Drewnowski A. Bellisle F. Liquid calories, sugar, and body weight. *Am J Clin Nutr.* 2007;85(3):651-661.

Use commas to separate multiple citation numbers in text, like you see between references 2 and 3. Unpublished works and personal communications should be cited in the text (and not on the reference list).1 Superscript numbers are placed outside periods and commas, and inside colons and semicolons. When citing the same source more than once, give the number of the original reference, then include the page number (in parentheses) where the information was found. See pages 41-44 of the AMA Manual of Style for more information.

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Citing AMA guide website http://libguides.stkate.edu/c.php?g=101857&p. Updated April 2011. Accessed October 24, 2012.

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Editorial

In modern years, aesthetics has become quite important in every aspect of everyday life: following the hundreds of journals, magazines, blogs and websites pointing their attention towards this interesting and fascinating topic, the request for aesthetic medicine has increased manifolds.

Aesthetic Medicine is a new field of medicine, in which different specialists share the aim of constructing and reconstructing the physical equilibrium of the individual. Treatment of physical aesthetic alterations and unaesthetic sequel of illnesses or injuries, together with the prevention of aging, are perhaps two of the most iconic areas of intervention for Aesthetic Medicine.

However, in order to prevent frailty in the elderly, a program of education is similarly important.

Furthermore, the line between health and beauty is extremely thin: psychosomatic disorders resulting from low self-esteem due to aesthetic reasons are frequent and can- not be ignored by a clinician.

It is therefore clear that there is no figure in the field of medicine which is not involved in Aesthetic Medicine: endocrinologists, gynecologists, angiologists, psychologists and psychiatrists, plastic surgeons, dermatologists, dieticians, physiotherapists, orthopedists, physical education instructors, massophysiotherapists, podologists, and rehabilitation therapists are just some of the specialists who are sooner or later going to have to answer their patients' needs for aesthetic interventions.

The involvement of all these specialists fits the description of health as defined by the WHO: "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" for which, undeniably, a team of different physicians is required.

The number of patients requiring medical consultation for esthetic reasons is rapidly increasing: in order to be able to provide adequate feedback, medical and paramedical specialists should be trained and, more importantly, should be taught how to work together. Existing Societies of Aesthetic Medicine from different countries share the aim of creating such teams and provide constant updates to the literature: the creation of an international network of specialists from all around the world under the flag of Aesthetic Medicine represents a challenge, but at the same time it is the proof of the widespread interest in this topic.

The first issue of this Journal represents the results of the efforts of the many national Societies and of the Union Internationale de Medecine Esthetique, now together as one; it is our hope that in years to come this Journal might improve our knowledge in this field, and provide adequate scientific advancement in the field of Aesthetic Medicine.

Francesco Romanelli
MD Editor-in-chief
Associate Professor at "Sapienza" University of Rome

Editors' notes

Aesthetic Medicine, the booming medical activity

Aesthetic Medicine was born in France 40 years ago.
The French Society of Aesthetic Medicine was the first of its kind in the world, followed by Italy, Belgium and Spain. Starts were rather difficult as aesthetic procedures in those early years were only surgical.
At that time aesthetic doctors and cosmetic dermatologists had very few real medical procedures to offer to their patients for treating aesthetic problems on face and body.
At the beginning of the '80s, viable medical procedures started to emerge in Europe for aesthetic and cosmetic purposes. Mostly, at that time, they were imported from the United States: those included collagen injections for wrinkles (Zyderm by Dr. Stegman), and chemical peels (phenol by Dr. Baker, TCA by Dr. Oba- gi). But, subsequently, European research on Aesthetic Medicine gained momentum. Hyaluronic acid appeared on the market, as it was discovered that it could be used as a dermal filler for wrinkles. During the '90s, the use of lasers offered aesthetic doctors and cosmetic dermatologists new possibilities.
The "beam revolution" started with CO2 laser for facial resurfacing.
Today, CO2 resurfacing is not used as much anymore, because of the long and difficult postop. CO2 laser was replaced with the gentler Nd-YAG and Erbium lasers and more recently with non invasive photonic devices for facial rejuvenation, including IPL, US and radiofrequency. These new technologies allow today's aesthetic doctors and cosmetic dermatologists to offer their patients procedures with low risk of post- op complications. Then, Botulinum Toxin has "invaded" both sides of the Atlantic Ocean.
Today, Botox injections are the most popular treatment for facial expressive wrinkles.
Botox injections are now so common everywhere that many cosmetic surgeons have given up their bistouries for syringes. Last but not least, development in Aesthetic Medicine is shown by mesotherapy and adipolipolysis.
About lipolysis, new data and recent publications have explained that radiofrequency, ultrasounds and cryolyse could have positive action to dissolve fat and to improve some unaesthetic disorders like cellulite.
These non invasive procedures intend to replace the surgical liposculpture with success.
Nowadays, Aesthetic Medicine has the necessary tools to address all major disorders within the aesthetic field. After 40 years, Aesthetic Medicine is now active in 27 countries in the world (France, Italy, Spain, Belgium, Morocco, Poland, Russia, Switzerland, Romania, Kazakhstan, Algeria, Brazil, Argentina, Uruguay, Venezuela, Colombia, Chile, Mexico, U.S.A, Canada, South Korea, and recently Ecuador, China, South Africa, Turkey, Ukraine and Georgia).
All 27 national Societies are members of the Union Internationale de M decine Esth tique (U.I.M.E.). Aesthetic Medicine is taught in 8 countries (France, Italy, Spain, Brazil, Argentina, Mexico, Venezuela, Kazakhstan) in universities that deliver UIME's diplomas after 3 to 4 years of studies.

What is the future of Aesthetic Medicine?

In the last few decades, patients' desires to look and feel younge, have fueled Aesthetic Medicine and Cosmetic Dermatology: many different procedures have been developed to satisfy the demands.
As life-span have increased, patients today are not only asking about aesthetic procedures, they are also asking for a way to stay in good physical conditions in the last decades of their lives. As a direct result, Anti-Aging Medicine, which covers skin aging and general aging, has recently emerged and expanded very quickly. Anti-Aging Medicine can offer senior patients better nutrition, dietary supplementation with vitamins, minerals, antioxidants, and eventually hormone replacement therapy, but only when needed.
Today, and in the near future, both Aesthetic Medicine and Anti-Aging Medicine will offer to our patients, who now live longer, better wellness with aesthetic treatments for skin aging and anti-aging treatments for general aging. Aesthetic Medicine is booming, but all medical practitioners should be correctly trained, so its future will be bright.

Jean-Jacques Legrand
Former General Secretary and Honorary President of UIME

Aesthetic Medicine: a bioethic act

When in 1977 the Italian Society of Aesthetic Medicine published the first issue of the magazine “La Medicina Estetica” Carlo Alberto Bartoletti, the Founder, wrote an editorial in which traced the pathway of the discipline and of the Scientific Society, still valid and projected into the future.
Today from that Editorial Board arise an International Journal, which wants to be indexed, in order to give to the doctors practicing Aestehetic Medicine all around the world a solid basis of shared knowledge.
In the late ‘60s, what was called in Italy Aesthetic Medicine, moved its first steps thanks to “remise en forme and anti aging projects” imported from the experience the “Institutul de geriatrie Bucuresti”, directed by Dr. Ana Aslan.
For this reason,there is the bioethical imperative that the Discipline should be first prevention, then return to physiology and finally correction.
The worldwide diffusion and the efforts of Industries born on the wave of the phenomenon have often led to choose the fastest route to achieve and maintain the physical aspect in the myth of beauty at all costs, without considering that aesthetic is not synonymous of beauty, but it is a balance between body and mind, and the role of the doctor is to take care of the Person globally and not only focusing on the correction of “a badly accepted blemish”.
Faithful to the teaching of my Master had almost 50 years ago, this new journal will have the task of elevating the human resources, aligning and validating methodologies, but above all affirming the humanitas of the medical art in its purest sense to pursue the good and the graceful for the person who relies on it.

Fulvio Tomaselli, MD
Honorary President of the Italian Society of Aesthetic Medicine

Aesthetic Medicine needs science. All over the world

All Aesthetic Doctors know that science is the basis for safety. Safety is the most important issue in our discipline.
Unfortunately, Aesthetic Medicine is more often surrounded by marketing than by science, despite the hard work done by Scientific Societies all over the World. And, too often doctors working in this field are dealing with sellers that promote products with insufficient scientific studies.
However, they sell it anyway. I think that doctors must learn that the first thing to ask about a medical device is the scientific background regarding that product: patients treated, follow up period, adverse events and, most of all, publications.
With this new International Journal completely dedicated to Aesthetic Medicine, proposed by the Italian Society of Aesthetic Medicine, endorsed by UIME and shared by all the National Societies of Aesthetic Medicine belonging to UIME, World Aesthetic Medicine wants to stimulate scientific production in this discipline to increase safety and quality in aesthetic medical procedures.
Another important goal of the Journal is to catalyze the proposal of new protocols and guidelines in Aesthetic Medicine, with the consensus of the entire Aesthetic Medicine Scientific Community.
What this Journal should achieve in the near future is to improve the number and quality of scientific production in Aesthetic Medicine, in order to allow this discipline to grow in the field of evidence based medicine, not only in the rationale field.
I hope this can be the start of a new era for Aesthetic Medicine, with the commitment of all Scientific Societies all over the world.

Emanuele Bartoletti, MD
Managing Editor
President of the Italian Society of Aesthetic Medicine

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aesthetic medicine

Orginal article

Aptos thread lifting methods of the nasal tip lifting a minimally invasive approach for nose reshaping

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Abstract
Cosmetic surgery of the nose frequently produces unsatisfactory results that require modifications. The nose determines an individual's appearance and may affect interpersonal relationships. Patients are presently more interested in short procedures, under local anesthesia and in an ambulatory setting, with low cost, low risk, and a fast recovery time. As a minimally invasive nasal reshaping procedure, Aptos thread lifting methods are a good choice to achieve long-lasting, satisfactory results in selected patients with minimal hump deformity and an underrotated tip. The significance of this technique lies in the fact that it is one of very few office-based minimally invasive alternatives for aesthetic nasal surgery, with a recovery period of two to three days.

Keywords
aptos thread lift, nose tip lift, nonsurgical nose shaping, minimally invasive, rhinoplasty

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Introduction

Plastic surgeons are facing increasing pressure from patients to simplify their procedures, such as minimizing the scar or reducing the operation time and recovery period. In some areas of aesthetic surgery, we have noninvasive alternatives such as botulinum toxin injections, commercially available soft tissue fillers, or thread lifting to lift the ptotic tissue. Interestingly, aesthetic nasal surgery is one of the fields in which the minimally invasive options are few. However, some patients asking for nasal surgery do not necessarily need a standard aesthetic rhinoplasty procedure. In some cases, only nasal tip lift is enough to achieve satisfactory nasal harmony and aesthetics. Herein, we describe a simple, office-based procedure that can be performed under local anesthesia in a matter of minutes with virtually no downtime and also can be combined with any other minimally invasive procedure. Our technique allows the surgeon to rotate the nasal tip over the hump, only through a small access puncture made on the central nasal tip[1].

Patients and Methods

The author successfully performed a minimally invasive rhinoplasty with the Aptos thread lifting technique in 28 carefully selected patients. 4 of these patients had already been undergone primary rhinoplasty.
Between October 2016 and March 2018, with an eight - to twelve - months follow-up. Patient ages ranged from 21 to 50 years. All of the patients elected not to undergo any aesthetic nasal surgery but were requesting a slight improvement of their nasal shape.

Aptos Excellence Visage

Aptos Excellence Method - Absorbable threads P(LA/CL) (poly-L-lacticacid %75 + caprolactone %25) with multidirectional barbs for lifting and armouring. The threads have special barb arrangement. Each subsequent barb is located on the opposite direction from the previous one, that allows stronger hypodermic fixation and supports grouping the tissues on every micro-section of the thread. Round tip hollow blunt cannula is very safe and does not damage soft tissues. It has been more than 21 years since the first APTOS thread and method has been introduced to the aesthetic world. It was first developed in 1996 by plastic surgeon Dr. Marlen Sulamanidze. In Pack: P(LA/CL) threads with barbs USP 2/0, EP3, 190mm–10pcs. Round tip hollow blunt cannula 20Gx150mm. Straight - 10pcs. (*Figures 1 and 2*)[2-5].

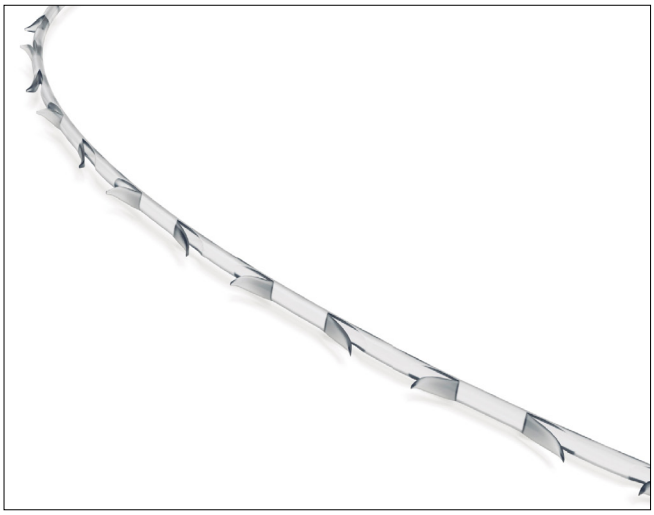

Figure 1 *- Absorbable threads P (LA/CL) (poly-L-lactic acid %75 + caprolactone %25) Multidirectional Barbs.*

Figure 2 *- Round tip blunt cannula 20Gx150mm - Round tip blunt cannula 23Gx80mm - Lancet point needle 18Gx40mm.*

Anatomy

Surface Appearance: the external nose has a pyramidal shape. The nasal root is located superiorly, and is continuous with the forehead. The apex of the nose ends inferiorly in a rounded 'tip'. Spanning between the root and apex is the dorsum of the nose. Located immediately inferiorly to the apex are the nares; piriform openings into the vestibule of the nasal cavity. The nares are bounded medially by the nasal septum, and laterally by the ala nasi (the lateral cartilaginous wings of the nose). Skeletal Structure: the skeleton of the external nose is made of both bony and cartilaginous components: bony component – located superiorly, and is comprised of contributions from the nasal bones, maxillae and frontal bone. Cartilaginous component – located inferiorly, and is comprised of the two lateral cartilages, two alar cartilages and one septal cartilage. There are also some smaller alar cartilages present.
Whilst the skin over the bony part of the nose is thin, that overlying the cartilaginous part is thicker with many sebaceous glands. This skin extends into the vestibule of the nose via the nares. Here there are hairs which function to filter air as it enters the respiratory system (*Figures 3, 4, 5 and 6*)[6].

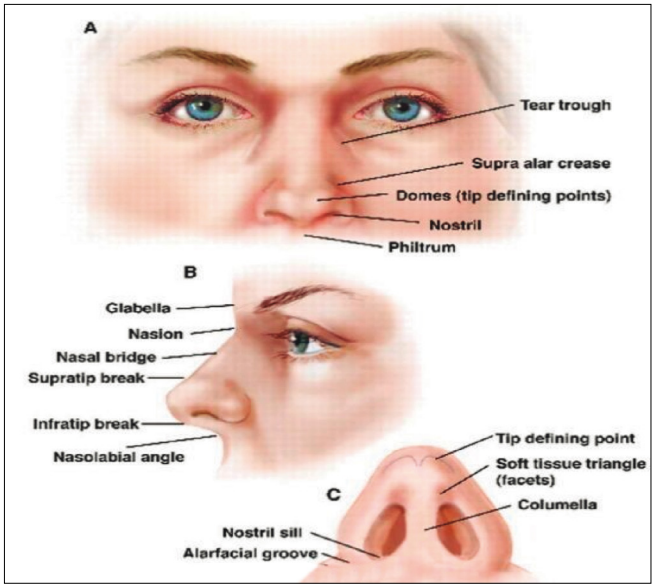

Figure 3 *- External Nose Anatomy [6].*

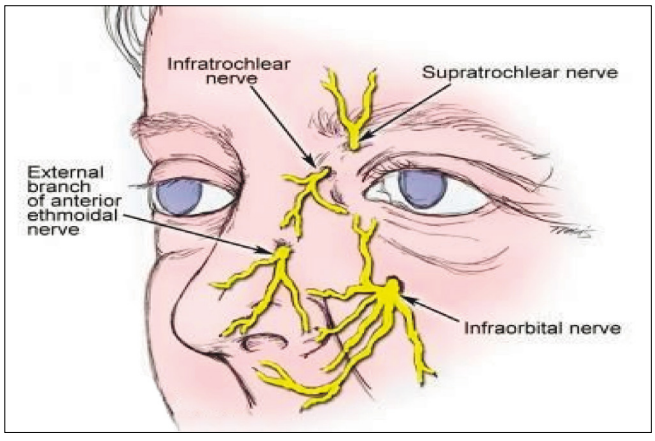

Figure 4 *- Nerve of Nose [6].*

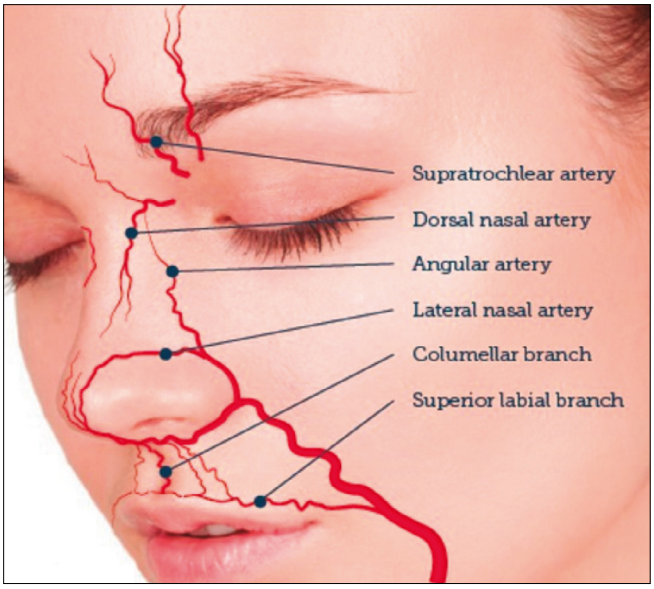

Figure5 *- Nose Artery [6].*

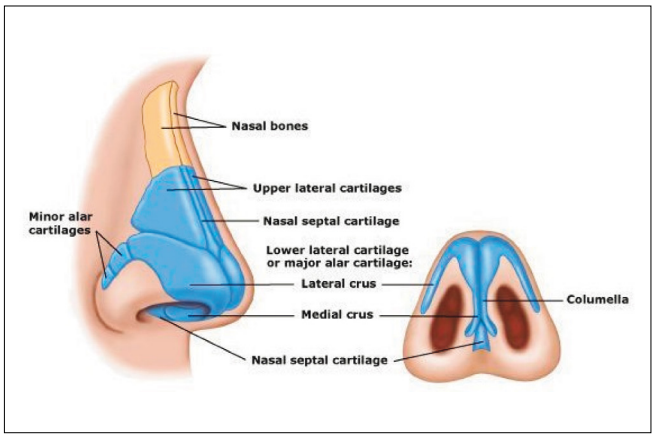

Figure 6 *- Nose Anatomy [6].*

Surgical Technique

Before the procedure, the midline and the most prominent spot of the nasal domes were marked, and the nasal dorsum and caudal septum and columella were infiltrated with local anesthetic - adrenalin solution. An 18 gauge needle was used through the nose tip to create the entry point (center of domes tip defining point) (*Figure 7*).

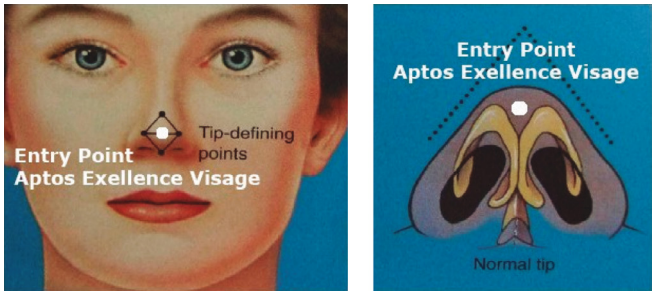

Figure 7 *- Entry Point. Center of Domes Tip defining point.*

First Step: with the Aptos excellence visage, the columella angle needs to be enlarged by moving the columella through the entry point and placing the thread into the nasal septal cartilage. The cannula is not removed at all during the procedure. Forward and backward maneuvering places the entire 190 mm multidirectional thread all into the columella. (*Figure 8*). Second Step: with the Aptos excellence visage, it is necessary to move along the nasal dorsum from the entrance point and to put the thread over the nasal periosteum and proceed to the glabella to lift the nasal bridge. The cannula is not be removed at all during the procedure. Forward and backward maneuvering places the entire 190 mm multidirectional thread all into the nasal dorsum (*Figure 9*).
Intraoperatively, the magnitude of change and the exact effect can be determined by observing the rotation of the tip as the thread is tightened. This is a crucial point at which the amount of tip rotation and projection should be evaluated. A slight overcorrection is suggested in all cases. The nose was taped for three to four days postoperatively at night, and each patient was instructed to apply the same tape for three weeks[7].

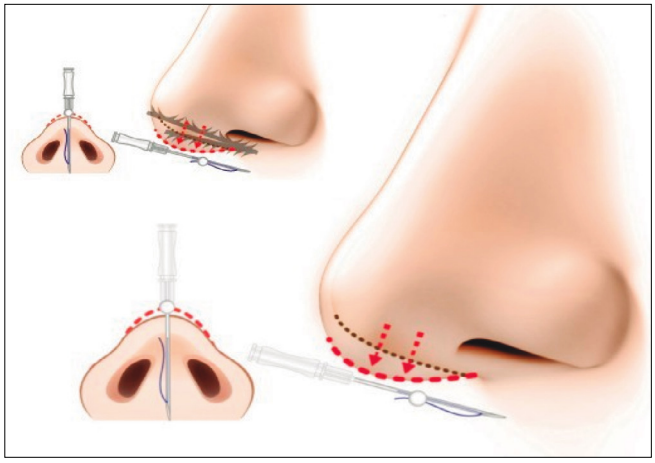

Figure 8 *- First Step: Nasal Tip Lifting. Enlarged the Angle of Columella.*

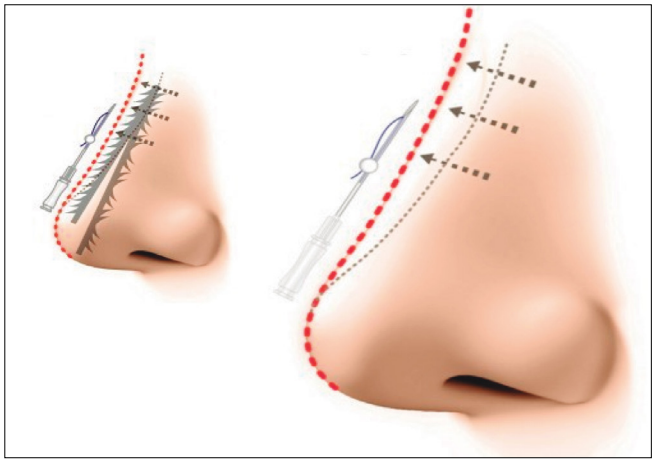

Figure 9 *- Second Step: Nasal Bridge Lifting. Reshaping the Ridge of Nose.*

Results

The results were satisfactory in all but 20 of the 28 cases based on patient feedback (*Table 1*).
Three patients did not find the result satisfactory and the procedure was repeated after 6 months.
Five patients found the results inadequate and those patients underwent normal rhinoplasty afterward. Four patients were not satisfied with the primary rhinoplasty operation and preferred the nose tip lift of Aptos thread lifting methods. The nose tip lift of Aptos thread lifting methods was also extraordinarily effective in secondary rhinoplasty patients. After an initial loss of the overcorrected projection and rotation, the results were durable throughout follow-up for both primary and secondary rhinoplasty patients.
The operation duration was under 30 minutes in all of the cases. Our longest follow-up was 12 months, during which we observed that the final outcome appeared after the third month and did not undergo any change afterward. No complication related to the absorbable thread, such as palpability or visibility through the skin (*Figures 10, 11 and 12*) have been observed.

Satisfied Patients	Repeated Procedure	Inadequate (Rhinoplasty Afterwards)	Total Patients
20	3	5	28

Table 1 *- Results.*

Clinical cases

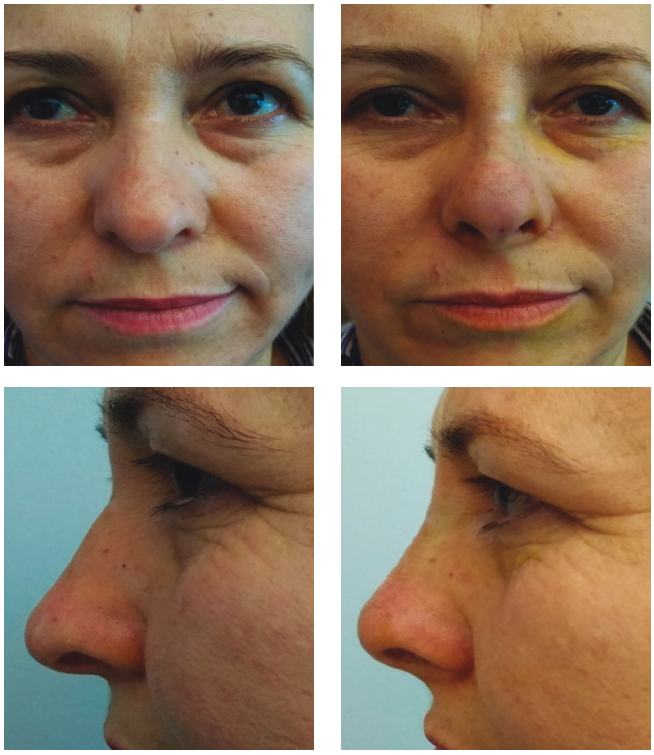

Figure 10 *- Female patient before and after nasal tip lifting with optimization of nasofrontal and nasolabial columella angles.*

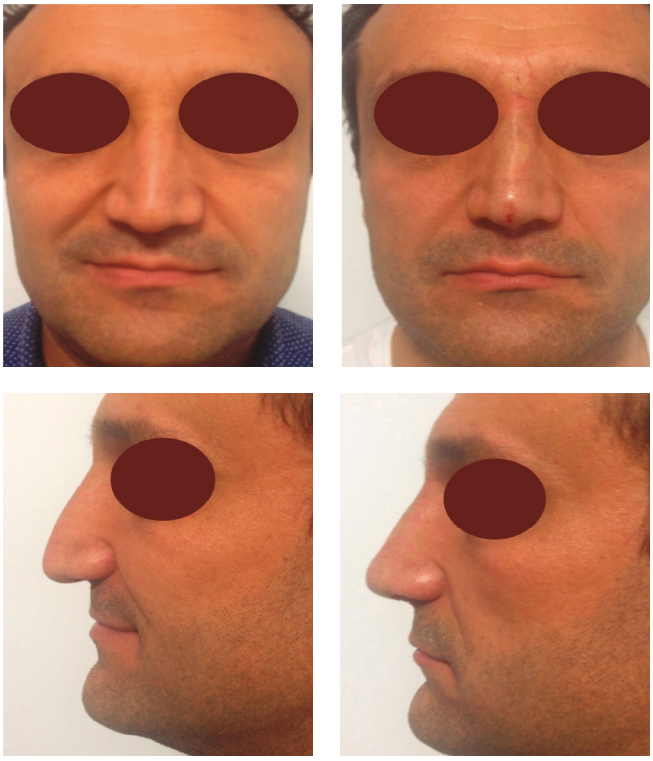

Figure 11 *- Male patient before and after nasal tip lifting with optimization of nasofrontal and nasolabial columella angles.*

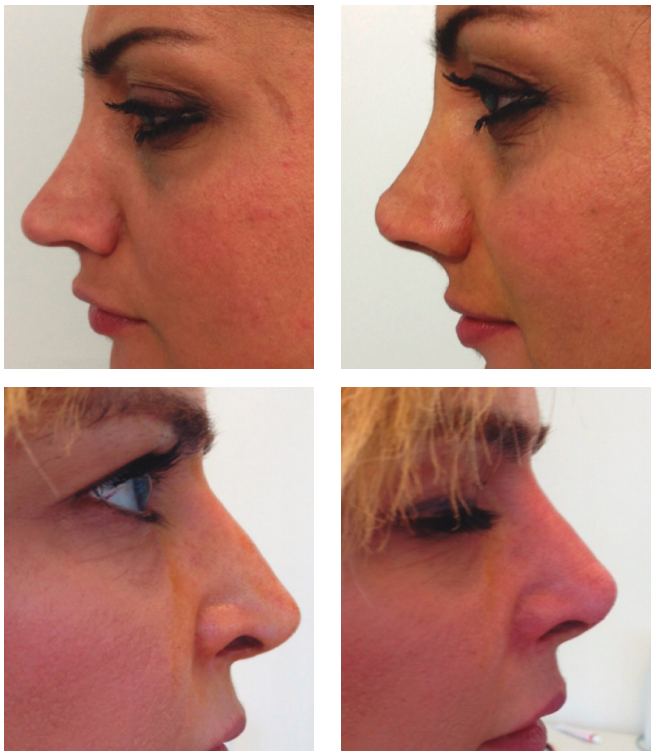

Figure 12 *- Female patients befor and after nasal tip lifting with optimization of nasolabial - columella angles.*

Discussion

Nasal aesthetic problems are one of the few fields in which we are not able to offer our patients an acceptable, minimally invasive alternative. Furthermore, we have patients who are incapable of arranging their daily programs to accommodate the required recovery period or who do not wish to undergo such a significant operation because of their associated health problems or anxiety over an irreversible change in their facial characteristics.

The main objective of the technique we describe is to provide patients with a simple method for nose reshaping, which can be performed in the office under local anesthesia in less than 30 minutes and is therefore comparable with Botolinum toxin or Fillers in the patient's mind.

For selected patients, however, our method can be proposed as a simple, office-based procedure that can be performed under local anesthesia in a matter of minutes with virtually no downtime.

In patients with very deep nasofrontal junctions, the Aptos Exellence Visage Absorbable thread can be used as filler in the glabellar area to mask the dorsal prominence. The rapid production of scar tissue in the interface of the skin acts as a biological glue that maintains the new tip position over time.

According to our experience, it takes a minimum of three to four weeks to achieve a strong subcutaneous fibrosis. The Aptos Exellence Visage Absorbable thread, if detached earlier than this period, might be reversible, which may be seen as an advantage of this procedure by the patients.

As a continuation of this study, it might be beneficial to measure the nasal length and the nasolabial angle pre- and postoperatively at different times, so that we can have data by which to precisely judge the necessary overcorrection[8].

Conclusion

The nose tip lift described herein is one of very few minimally invasive alternatives for aesthetic nasal tip surgery.

For selected patients, our method can be used as a simple, office-based procedure that can be performed under local anesthesia without any significant morbidity, a very high patient satisfaction, and a recovery period of only two to three days.

The absorbable thread serves as an internal splint, and the permanent result is attributable to tissue fibrosis. The reversibility of the result, at least for a short period of time, is also appealing to patients who are uncertain about the outcome of nasal surgery.

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The author thanks Dr. Marlen Sulamanidze for his inspiration regarding the development of this technique and Dr. George Sulamanidze for his useful comments and help in refinement of this technique.

Disclosures

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REFERENCES

1. Tiryaki KT. Shuttle Lifting of the Nose: A Minimally Invasive Approach for Nose Reshaping. *Aesthet Surg J.* 2009; 30(2):176-185.
2. Sulamanidze M. Patent publication number: WO2006011824.
3. Histocompatibility Study of APTOS threads, (2008) https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2840891/
4. Tonks S., Understanding thread lifting, Aesthetics journal (2015) https://aestheticsjournal.com/feature/understanding-thread-lifting
5. Sulamanidze G. Aptos Excellence, New possibilities in aesthetic medicine, Tecrussia (2013) http://www.tecrussia.ru
6. http://teachmeanatomy.info/head/organs/the-nose/external-nose/
7. http://www.mariefranceasia.com/beauty/beauty-sos/the-killer-question/nose-thread-lift-vs-nose-fillers-266294.html

   https://tiffinyyang.com/2016/03/01/nose-threadlift-tiffiny-yang-aesthetics/
8. Tiryaki KT. Shuttle lifting of the nose: a minimally invasive approach for nose reshaping. *Aesthet Surg J.* 2010; 30(2):176-185.

aesthetic medicine

Original article

Dermoelectroporation: a new painless and needleless way to treat Hyperhidrosis via Onabotulinum toxin A. A preliminary report

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Abstract

Background: hyperhidrosis is an idiopathic, chronic and usually lifelong condition that impacts negatively on an individual's quality of life. To date heterogeneous tools are available to treat such a condition. Those approaches are often invasive or complex to perform. Notably, BTX is effective and minimally invasive but has the disadvantage of being painful.
Aim: herein, we propose and test the use of dermo-electroporation as a new way to obtain a trans-cutaneous and painless passage of Onabotulinum toxin A.
Methods: ten hyperhidrotic areas have been treated. All patients had an idiophatic hyperhidriosis of Holze first or second degree. The Minor-Test was performed and the amount of sweating and its precise extension was evaluated. A microdermoabrasion was performed. Subsequentely, Onabotulinum toxin A was administered via a machinery for Dermo-electroporation to obtain the trans-skin passage of the drug. After 15 days post-treatment, the Minor test was performed again.
Results: from a clinical standpoint post-procedure Minor test showed a sensible and homogeneous decrease of sweating. No side effect have been noticed, and none of the patients had pain during and after the procedure. A good clinical satisfaction was shown by the evaluation test.
Conclusions: dermoelectroporation, according to our preliminary report, is a valid way to treat excessive sweating because it is minimally invasive, not painful, rapid and without documented side effects. At this stage there is a need for more trials assessing the role of dermoelectroporation in hyperhidrosis.

Keywords

Dermoelectroporation, onabotulinum Toxin A, hyperhidrosis, needless botulinum treatment

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Introduction

Hyperhidrosis is an idiopathic, chronic and usually lifelong condition characterized by excessive sweating. De facto, it has a very negative impact on the standard quality of life affecting emotional status, productivity at work and comfort in social situations.

In particular, the most common sites of hyperhidrosis are the axilla and the palmar surfaces of hands, face and feet. Notably, women present such a condition three times more often than men and around 1% of the population may suffer from this problem[1-4].

To date a wide variety of heterogeneous tools are available for the therapeutic management of such a condition: antimuscarinic drugs, topical aluminium chloride hexahydrate, ETS (Endoscopic Thoracic Sympathectomy), laser therapy and botulinum toxin injection (BTX)[1-4].

Antimuscarinic drugs in effective doses are poorly tolerated because of their side effects (blurred vision, dry mouth and others...) whilst topical aluminium chloride hexanhydrate may cause severe cutaneous irritations[1-4]. Furthermore, ETS interrupts, using an endoscopic approach, the transmission of sympathetic nerve impulses from the ganglia to the nerve endings. Despite this surgical technique providing good results, it can cause severe complications such as: arterial bleeding and subsequent conversion to open thoracotomy, intercostal vein bleeding, haemothorax, pneumothorax, pleural adhesion or effusion, peripheral nerve injury, Horner's syndrome, postoperative scars and above all compensatory sweating[4].

De facto, BTX has already been validated as an effective and safe option for the treatment of several cosmetic conditions such as chemical browlift, glabellar, forehead, periorbital, perioral wrinkles[5] and notably in the minimally invasive treatment of gummy smile[6].

In the same way, BTX can be considered the gold standard therapy for the treatment of hyperhidrosis because it is minimally invasive, effective - showing responders rate superior to 90 %[1-3] - and has only little, rare and temporary side effects[1-3]. BTX is injected intradermally into the hyperidrotic areas causing a temporary blockage of the release of acetylcoline from cholinergic submotor fibers. However, an important negative aspect of BTX is its temporary effect but even if there is a sweating recurrence, it is rarely as massive as before the treatment[1-3].

The development of neutralizing antibodies against BTX-A creating non-responders has been described in up to 10% of patients treated for dystonia and blepharospasm[7], but, to our knowledge, this resistance has not yet been described in hyperhidrosis. Notably, beside its efficacy, the injection of BTX in the palmar regions of hands and feet and in the axillary pit it is very painful for the patient.

Herein, we propose the use of dermo-electroporation as a new way to obtain a trans-cutaneous and painless passage of Onabotulinum toxin A.

Device Used

Ultrapeel® Transderm® Digital (MATTIOLI ENGINEERING ITALIA S.P.A. - Via Petrarca 80-82, 50041 Calenzano, Firenze - Italy), (*Figure 1*) is a device for transdermal administration of drugs. It has been approved by the FDA for "local administration of ionic drug solutions into the body for medical purposes and can be used as an alternative to injections". Ultrapeel® Transderm® combines the Dermoelectroporation technology, used to allow the transdermal passage of molecules, with the microdermoabrasion Ultrapeel® to decrease the cutaneous impedance facilitating the transdermal passage. Ultrapeel® Transderm® Digital has the following components:

- Ultrapeel®: a plus micro-dermoabrasive device with a digital control. This is endowed with Corundum crystals to guarantee the reproducibility of the treatment and it offers a constant control over the depth of action of the procedure.
- Transderm® delivery display with applicator devices. To get a homogenous molecule passage and to monitor the skin impedance.
- Digital Precision Dispenser - Super PLD. To guarantee a gradual molecule release without wasting any unnecessary amount.

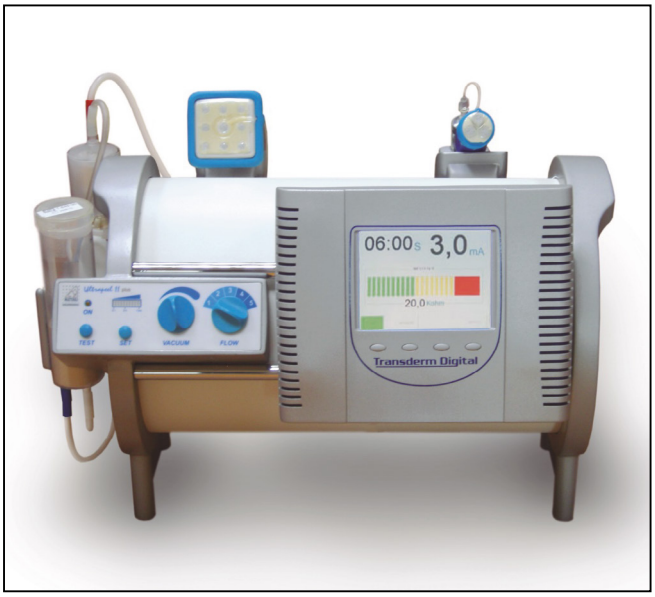

***Figure 1** - Ultrapeel® Transderm® Digital device (MATTIOLI ENGINEERING ITALIA S.P.A.Via Petrarca 80-82, 50041 Calenzano, Firenze- Italy).*

Materials and Methods

Ten hyperhidrotic areas (six axillary regions and four hand palmar regions) were treated, all the patients were women except for one male. The age range was between 19 and 52 years old, the mean age was 38 years old. A clinical evaluation was performed on every patient and all of them signed a consent form. Every patient in this study had an idiophatic hyperhidriosis of first or second degree (mild or moderate form) according to Holze. After that, the Minor-Test[8] was performed: an iodine solution (Betadine®) was applied to the skin before using a rice powder: in this way the areas with active sweating showed a purple-brown color and the precise extension of the sweating surface was evaluated. Subsequently, Onabotulinum toxin A was prepared (Vistabex Allergan®) using 50 units for each axillary region and 100 units for palmar regions creating a dilution with 2,5 ml of soldium chloride solution[9-14].

Afterwards, the prepared syringes with the drug were introduced into a particular dispenser in order to obtain a progressive trans-skin release with a 0.2 ml/minute rate. This dispenser was linked to a machinery for Dermo-electroporation (Transderm Mattioli®) equipped with dedicated devices to obtain the trans-skin passage of the drug. In the palmar regions 1,5 cm devices were used, whereas 5 cm devices were applied for the axillary regions.
Immediately before the dermo-electroporation a microdermoabrasion, using Corundum crystals, was performed in order to reduce the epidermal layer of the skin and to facilitate the use of the controlled electrical current. The drug diffusion lasted approximately 5 minutes for each area. After 15 days post-treatment, the Minor test was performed again. Furthermore, the patients completed an evaluation test in order to assess their satisfaction regarding the results of the procedure.

Results

From a clinical point of view, the results have been satisfactory for all patients. Minor test showed a sensible and homogeneous decrease of sweating linked to the width of the dedicated device that allowed a homogeneous distribution and penetration of the drug. After the treatment no side effects were noticed, and none of the patients reported pain during and after the procedure. A good clinical satisfaction was recorded by the evaluation test (*Table 1*).

	Region	Minor Pre-BTX	Minor Post BTX	Patient Satisfaction
Patient 1	Axilla	Positive	Negative	Good
Patient 2	Axilla	Positive	Negative	Good
Patient 3	Axilla	Positive	Negative	Good
Patient 4	Palm (hand)	Positive	Negative	Good
Patient 5	Palm (hand)	Positive	Negative	Good

Table 1 *- Regions treated, Minor test results and Patient Satisfaction.*

Conclusions

According to our results Dermoelectroporation is a valid way to treat palmar and/or axillary excessive sweating because it is minimally invasive and not painful, furthermore, it is rapid and without documented side effects.
This preliminary study represents a new international development, due to no previous experience in the past scientific literature, and it is a confirmation of the capability of Dermo-electropopration to allow the trans-cutaneous passage of macromolecules with high molecular weight. However, our study has some limitations mainly related to the sample size of this case-series preliminary report.
De facto, when a new surgical technology or technical approach is introduced it must be standardized in order to obtain inter-trials comparable data, for educational aims, for safety reasons, to keep and implement the obtained standards, and finally for repeatability and ratification aims. Furthermore, the new technique must be validated via well-powered and accurately designed prospective randomized studies in order to obtain statistically supported data and to detect potential differences among the heterogeneous surgical approaches under investigation [15-18]. Hence, despite our encouraging preliminary results, at this stage there is a further need for more trials assessing the role of dermoelectroporation in hyperhidrosis.

Acknowledgements

The *Figure 1* representing the device (Ultrapeel® Transderm® Digital) used in this article has been authorized with a written permission and consent given to Dr Maurizio Cavallini by the company MATTIOLI ENGINEERING ITALIA S.P.A. - Via Petrarca 80-82, 50041 Calenzano, Firenze- Italy.

Disclosure of commercial interest

All of the Authors do not have any kind of commercial interest relative to this article.

Conflict of interest

None

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REFERENCES

1. Walling HW, Swick BL. Treatment options for hyperhidrosis. *Am J Clin Dermatol.* 2011; 12(5):285-95.

2. Hamm H. Impact of hyperhidrosis on quality of life and its assessment. *Dermatol Clin.* 2014; 32(4):467-476.

3. Lakraj AA, Moghimi N, Jabbari B. Hyperhidrosis: anatomy, pathophysiology and treatment with emphasis on the role of botulinum toxins. *Toxins (Basel).* 2013; 5(4):821-40.

4. Moraites E, Vaughn OA, Hill S. Endoscopic Thoracic Sympathectomy. *Dermatol Clin.* 2014; 32(4):541-548.

5. Cavallini M, Cirillo P, Fundarò SP, et al. Safety of botulinum toxin A in aesthetic treatments: a systematic review of clinical studies. *Dermatol Surg.* 2014; 40(5):525-36.

6. Mangano A, Mangano A. Current strategies in the treatment of gummy smile using botulinum toxin type A. *Plast Reconstr Surg.* 2012; 129(6):1015e.

7. Benecke R. Clinical relevance of botulinum toxin immunogenicity. *BioDrugs.* 2012; 26(2):e1-9.

8. Minor V. Ein neues Verfahren zu der klinischen Untersuchung der Schweissabsonderung. *Dtsch Z Nervenheilkd.* 1928; 101302-7.

9. de Almeida AR, Montagner S. Botulinum toxin for axillary hyperhidrosis. *Dermatol Clin.* 2014; 32(4):495-504.

10. Allergan global medical scientific information product: Botox® (onabotulinumtoxina) topic: primary axillary hyperhidrosis - efficacy and safety.

11. Cavallini M. "Dimostrazione del passaggio transcutaneo di tossina botulina tipo a attraverso dermoelettroporazione" - VIII Congresso Nazionale di Medicina Estetica - *Abstract Book pag. 82*; 2006.

12. Nasr MW, Jabbour SF, Haber RN, Kechichian EG, El Hachem L. Comparison of microwave ablation, botulinum toxin injection and liposuction-curettage in the treatment of axillary hyperhidrosis: A systematic review. *J Cosmet Laser Ther.* 2017; 19(1):36-42.

13. Hornberger J, Grimes K, Naumann M, et al. Recognition, diagnosis, and treatment of primary focal hyperhidrosis. *J Am Acad Derm.* 2004; 51(2):274-286.

14. Solish N, Bertucci V, Dansereau A, et al. A comprehensive approach to the recognition, diagnosis, and severity-based treatment of focal hyperhidrosis: Recommendations of the Canadian Hyperhidrosis Advisory Committee. *Dermatol Surg.* 2007; 33(8):908-923.

15. Mangano A. No differences in aesthetic outcome or patient satisfaction between anatomically shaped and round expandable implants in bilateral breast reconstructions: a randomized study--the role of the sample size calculation. *Plast Reconstr Surg.* 2011; 128(2):593.

16. Mangano A, Albertin A, LaColla L. Use of 2-octyl-cyanoacrylate skin adhesive (Dermabond) for wound closure following reduction mammaplasty: a prospective, randomized intervention study. "tips and tricks" to improve statistical analysis and significance of results. *Plast Reconstr Surg.* 2009; 124(2):669.

17. Mangano A, Albertin A, La Colla L. A double-blind, randomized, placebo-controlled, two-dose comparative study of botulinum toxintype A for treating glabellar lines in Japanese subjects: what ifsample size and statistical tests mattered? *Aesthetic Plast Surg.* 2009; 33(5):788.

18. Mangano A, Marciano L. A double blind randomized prospective study comparing prilocaine versus ropivacaine in upper eyelid blepharoplasty. *J Plast Reconstr Aesthet Surg.* 2017; 70(8):1140-1141.

aesthetic medicine

Orginal article

Comparative efficiency of intralipotherapy with sodium deoxycholate alone and alternated with carboxytherapy in body non-surgical contouring treatments of the trochanteric region

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Abstract

Background: Localized fat deposits in the trochanteric region pose an aesthetic problem that is difficult to resolve. For this reason, many non-surgical techniques have been developed. One such technique is intralipotherapy combined with sodium deoxycholate. The anatomy of this region is largely controlled by female hormones which means that results are less predictable and less apparent than in other regions of the body contour. The need to establish guidelines, mechanisms of action, safety and clinical results has led to the use of intralipotherapy in combination with sodium deoxycholate. As demonstrated in publications by Motolese[1] and Rotunda[2], this treatment causes adipocytolysis, induced by sodium deoxycholate, which acts as a detergent and leads to notable results. These publications have also shown this to be a safe treatment.

Furthermore, numerous publications have demonstrated that the use of carboxytherapy, consisting of the localized subcutaneous infiltration of CO2, has two fundamental mechanisms of action (pharmacological and mechanical) which have multiple effects on lipolysis[3].

Aim: To determine the tolerance, effectiveness, safety and satisfaction of intralipotherapy with sodium deoxycholate alternated with carboxytherapy, and to compare this treatment with the use of sodium deoxycholate alone.

Method: This study was performed in nine women presenting localized fat deposits and skin changes in the trochanteric region.

Conclusions: We may conclude that intralipotherapy can significantly reduce volume and when alternated with carboxytherapy, the effects of intralipotherapy are enhanced. We may also conclude that alternating intralipotherapy with carboxytherapy can substantially improve skin appearance. A good tolerance was observed without evidence of significant complications (inflammation and bruising).

Keywords

Intralipotherapy, sodium deoxycholate, carboxytherapy, edematous-fibrosclerotic panniculopathy

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Introduction

Localized fat deposits in the trochanteric region pose an aesthetic problem that is difficult to resolve. Many non-surgical techniques have been used, based on both mesotherapy (homoeopathic techniques) and other techniques, leading to the development of intralipotherapy with sodium deoxycholate. The difficulty of intervention in this area is that, from an anatomical and evolutionary standpoint, it is a female hormone dependent area. This means that results are difficult to predict and less evident compared to other body regions. The volume of skin is as important for patients as its appearance and both features are related to underlying estrogen activity. The accumulation of fatty tissue in this part of the body causes aesthetic alterations in body contour that may be accompanied by edematous-fibrosclerotic panniculopathy. This is sometimes considered normal as it is part of the typical female contour. However, in other cases this accentuation of adiposities in the gluteal-trochanteric area results in compression of microcirculation with the consequent results and skin disorders.

It is important to bear in mind that adipose tissue is composed of two different layers, separated by the superficial fascia. The areolar or external fascia represents the first layer. It is in contact with the dermis and formed by large globular adipocytes, arranged vertically. The lamellar, or deep layer, is thicker, where cells are fusiform, smaller and horizontally arranged. This final layer thickens when a person gains weight. However, in the female gluteal-femoral region, areolar fat is thicker and adipocytes at that level are metabolically more stable and resistant to lipolysis. This tissue forms and thickens during puberty and is influenced by estrogens, since 17 beta estradiol stimulates adipocyte replication[4].

Lipolysis is regulated by a balance between beta and alpha-2 adrenergic receptors, with lipolytic and anti-lipolytic activity, respectively. In turn, adipocytes have estrogen receptors, underscoring the importance of this hormone for their metabolism. This hormone, like insulin, stimulates lipogenesis, inducing the hypertrophy of the adipocytes. In addition, estradiol (E2) stimulates subcutaneous alpha-2 adrenergic receptors through the activation of the receptor, but without affecting visceral expression, thus favoring subcutaneous fat but not visceral accumulation[5].

Estrogenic action is enhanced by the contours of the female anatomy where, according to studies by Nürnberg and Müller[6], skin appearance and edematous-fibrosclerotic panniculopathy are caused by herniation of fat, which protrudes from the subcutis to the lower part of the dermis where the dermo-hypodermic interface is weakened. This results in the characteristic edematous, fibrous or micro/macronodular appearance. Herniations, which originate in the fibrous septa of female adipose tissue, are arranged perpendicular to the skin surface, thus separating bulky lobes that push into the dermis. However, there are a number of other factors which may lead to women with normal BMI presenting skin irregularities. These include alterations in subcutaneous tissue where fibrous septa are lax and thin, alterations in skin strength and elasticity, alterations of the lymphatic system and microcirculatory alterations (micro hemorrhages and dermal edema) where there is an alteration in the precapillary arteriolar sphincter. These factors can cause an increase in capillary pressure coupled with increases in pore pressure caused by hyperpolymerization of glycosaminoglycans and vascular compression. This, in turn, can cause increased capillary and venular permeability, resulting in ectasia, dermal edema and interlobular septa, which are relevant factors in its etiopathogenesis. Therefore, the increase in volume, microcirculatory alterations and estrogenic activity are essential factors to be considered in cosmetic female contouring treatments[7].

Studies have been conducted since the 1970s to establish reference techniques for the treatment of localized fat using Lipostabil-Natterman (phosphatidylcholine, sodium dehydrocholate and benzyl alcohol). This was later studied in the 1980s by Ceccarelli (1987)[8], who used hyperosmolar serum, Rittes in 1995 using phosphatidylcholine[9,10] and Salti in 2008 using phosphatidylcholine and sodium deoxycholate[11], both for treating localized fat and non-surgical treatment of lipomas. Some procedures were either not fully effective or did not guarantee patient safety, hence the need to establish guidelines, a mechanism of action and safety. Clinical outcomes led to the marketing and use of the intralipotherapy technique with Aqualyx® (Marllor Biomedical) in 2009. Aqualyx® was designed as a medical treatment to reduce localized adipose tissue[12]. Aqualyx, along with Belkyra® (Allergan), is a drug for reduction of localized fat which has a CE marking. Aqualyx is currently approved in approximately 50 countries[13] and is sold only to medical professionals who have received additional training in intralipotherapy[14].

This micro-aqueous-gelatinous solution contains a polymer of 3:6-anhydro-I-galactose and D-galactose, buffer systems; 3-alpha-12alpha-dihydroxy-5-beta-24-oico cholanic acid sodium salt; and saline solution, which gives it a short average life and prevents diffusion to tissues surrounding the site of infiltration. This prevents complications and is therefore an effective alternative for the treatment of localized non-surgical accumulation of fat[15,16]. The publications by Motolese1 and Rotunda[2] established that this treatment causes adipocyte cell lysis (adipocytolysis), due to the detergent action of sodium deoxycholate. Findings demonstrated definitive and certain effects.

Aqualyx® was designed to be used in combination with external ultrasonography. However, it has since been demonstrated by various practitioners that Aqualyx solution is both safe and effective as a treatment in isolation, without the application of external ultrasonography[13,17,18]. A four-year study was conducted by Rauso and Salti[15] using Aqualyx injection as a treatment alone. This involved treatment of 186 patients and resulted in no cases of skin necrosis. All patients experienced mild to moderate swelling which resolved 3 to 5 days after injection. Aesthetic outcomes were considered 'very good, (score of 8/10) for 60.2% of patients.

However, a publication by Di Toro and Rauso[19] reports a case of skin necrosis following the injection of Aqualyx. The patient in this case was a 46-year-old Caucasian woman who underwent treatment of the anterior

thighs in Sicily, Italy. Prolonged, localized inflammation occurred and palpation of the treated areas caused pain to the patient and revealed hardened tissues. 3 weeks after the Aqualyx injections, an area of skin necrosis developed on each thigh. Following treatment with surgical curettage and antibiotics ointment, the skin healed in 3 months, leaving depressed scar tissue. Di Toro and Rauso concluded that, although this is the only documented case of post-Aqualyx skin necrosis, more investigations of the product are warranted.

Since 1930, many studies have been published on the use of carboxytherapy, which consists of the local and controlled subcutaneous infiltration of CO2. These studies have shown that this treatment has two fundamental mechanisms of action (pharmacological and mechanical), which have multiple effects. On one hand, CO2 has a vasodilator effect on microcirculation by decreasing the pH of smooth muscle fiber and stimulating beta-adrenergic receptors with the consequent phosphorylation of myosin, leading to an increase in blood flow and a greater contribution of hemoglobin[5].

Furthermore, local inflammatory reaction mechanically stimulates parasympathetic receptors, releasing acetylcholine, which contributes to vascular relaxation[5]. Also, the Bohr effect is enhanced because hemoglobin has a greater affinity for CO2 than for O2 so more O2 is released into the treated tissues. The formation of angiogenic factors and endothelial growth is stimulated as a result of tissue hypercapnia, and lymphatic stasis is reduced[3]. Moreover, mechanical action fosters the breakdown of the adipocyte cell membrane and since gas produces relaxation of subcutaneous tissue, bradykinin, serotonin, histamine and catecholamine are released, stimulating b-adrenergic receptors. This in turn increases lipolysis, which is favored by the increase in oxidative processes of fatty acids. This controlled damage results in an increase in collagen synthesis and retraction in the treated area, which affects skin appearance and the volume of the treated area[7].

Objectives

To determine and compare the tolerance, clinical efficacy, safety and satisfaction of intralipotherapy combined with sodium deoxycholate alone and alternated with carboxytherapy in the treatment of localized fat deposits and edematous-fibrosclerotic panniculopathy in the trochanteric region in the same patient.

Materials and method

Characteristics of the study: open, prospective non-randomized study.

Study population

Nine female volunteers were selected non-randomly with localized fat in the trochanteric region and saddlebags with a mean age of 29.7 ± 6.94 years, normal-weight with a BMI of 23.6 ± 3.01. According to Curri's classification20, seven patients presented grade II edematous-fibrosclerotic panniculopathy and two presented grade III. The location of gluteal-trochanteric fat according to the Gasparotti classification[21], was as follows: one Type 1 person; four Type 2; two Type 3 and two Type 4. The contour of the right thigh was 62.7 ± 4.60 cm, the contour of the left thigh 62.9 ± 3.45 cm and the bitrochanteric contour 103.1 ± 3.92 cm. Five of the patients had used hormonal contraceptives and all presented lower limb edema.

Inclusion criteria

Healthy patients with a presence of localized fat deposits in the trochanteric region and saddlebags, no history of previous surgical treatment (liposuction) or cosmetic medicine treatments six months prior to the start of the study. All patients read, understand and accepted the conditions of the study.

Exclusion criteria

Patients who were overweight/obese or had undergone previous liposuction of the trochanteric region, as well as patients with any inflammatory or infectious skin disorder in the treatment area. Pregnant or breastfeeding women.

Method of treatment

Infiltration of 12 ml of sodium deoxycholate Aqualyx® (microgelatinous aqueous polymer solution of 3:6-anhydro-I-galactose and D-galactose, buffered system, 3 alpha, 12 alpha-dihydroxy-5beta-24-oico cholanic acid sodium salt, saline solution and sodium chloride) diluted in 0.3 ml of lidocaine per treatment area. Infiltration was performed using intralipotherapy with fan-shaped infiltration and retrograde release with a 25G 0.50 x 70 mm Lipoinject needle. Subcutaneous infiltration of 150 – 200 ml CO2 (carboxytherapy), with a flow rate of 50ml per minute, in the area to be treated. A complete clinical record was kept and contour measurements taken of the right and left thighs and bitrochanteric diameter, together with a series of photographs (profile, front and side) of the gluteal-femoral region at baseline, after each session and at the end of treatment, in order to compare the results

of the intervention at different times of the study for each individual protocol and between both protocols. A 4-point Likert scale was used to assess the importance attributed by patients to lipodystrophy and skin disorders and to assess effectiveness and satisfaction. Ranging from Not important to slightly important, moderately important and very important. A 4-point Likert scale was also used to assess the tolerance to pain from each session of treatment. This ranged from No discomfort, little discomfort, fair discomfort to extreme discomfort.
The 4-point scale used to assess changes in volume ranged from no decrease to substantial decrease and the scale to assess changes in skin appearance ranged from no change to substantial change. Satisfaction was assessed on a 5-point scale ranging from poor to excellent.
In order not to modify body weight, the patients were on a balanced diet and were asked not to use creams with anti-cellulite effects after infiltration, not to use compression garments for 3 days after treatment and not to take analgesics and anti-inflammatory drugs after infiltration.

Protocol used

Trochanteric region and saddlebags. Right pelvic limb.
Three sessions were performed, each consisting of the administration of 12 ml sodium deoxycholate (diluted in 0.3 ml of lidocaine, according to Motolese) with intralipotherapy using retro-tracing and the fan-shape technique with a 25G 0.50 x 70 mm Lipoinject needle in the trochanteric and saddlebag region at intervals of 21 to 25 days.
Trochanteric and saddlebag region. Left pelvic limb.
In the same patient, three sessions were performed consisting of 12 ml sodium deoxycholate (diluted in 0.3 ml of lidocaine, according to Motolese) with intralipotherapy using retro-tracing and the fan-shape technique with a 25G 0.50 x 70 mm Lipoinject needle in the trochanteric and left saddlebag region at intervals of 21 to 25 days between sessions. Alternating with three carboxytherapy sessions, infiltration being 150-200 ml of CO2, with a flow rate of 50ml per minute, using a 30G x 1/2" needle at intervals of 6-8 days before each infiltration of intralipotherapy with sodium deoxycholate. The third was 24-48 hours before infiltration. A total of three sessions of 12 ml of sodium deoxycholate and nine sessions of carboxytherapy were performed (*Table 1*).

Session	0	1	2	3	4
Treatment	Measurements and questionnaire	Carboxytherapy Left pelvic limb	Carboxytherapy Left pelvic limb	Carboxytherapy Left pelvic limb	Aqualyx Left and right pelvic limb
Date	10.08.12	18.08.12	25.08.12	31.08.12	07.09.12

Session	5	6	7	8	9
Treatment	Carboxytherapy Left pelvic limb	Carboxytherapy Left pelvic limb	Carboxytherapy Left pelvic limb	Aqualyx Left and right pelvic limb	Carboxytherapy Left pelvic limb
Date	15.09.12	22.09.12	28.09.12	04.10.12	13.10.12

Session	10	11	12	13
Treatment	Carboxytherapy Left pelvic limb	Carboxytherapy Left pelvic limb	Aqualyx Left and right pelvic limb	End of study assessment and questionnaire
Date	19.10.12	27.10.12	29.10.12	29.11.12

Table 1 *- Table of treatment schedule.*

Results

All patients were given a questionnaire before starting the study to record the importance that they gave to skin appearance and volume. After each treatment, patients were asked to record the levels of discomfort they experienced and to record their opinion about how effective the treatment was. The final questionnaire was completed by patients one month after the treatment was completed. This allowed time for recovery from treatment. Results from questionnaires were collated and used to produce the following results.

89% of the patients described skin appearance as very important, 11% moderately important, while 44% described volume as very important and 56% moderately important (*Figure 2*).

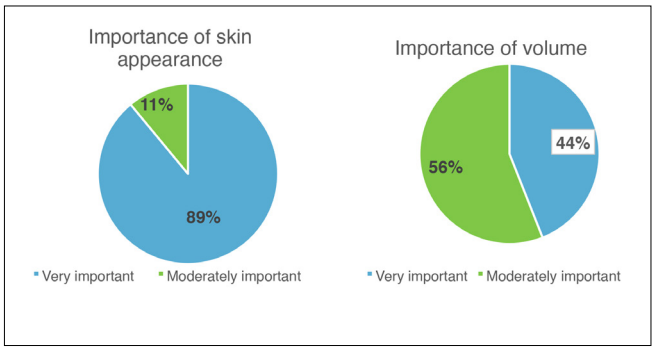

***Figure 2** - Importance given to skin volume and appearance.*

Tolerance

When assessing tolerance to sodium deoxycholate, during the first session we found that 11% of patients reported no discomfort, 33% little discomfort and 56% a fair amount of discomfort. Compared with sodium deoxycholate alternated with carboxytherapy where 11% of patients reported no discomfort, 22% little discomfort, 22% a fair amount of discomfort and 45% much discomfort (*Figure 3*).

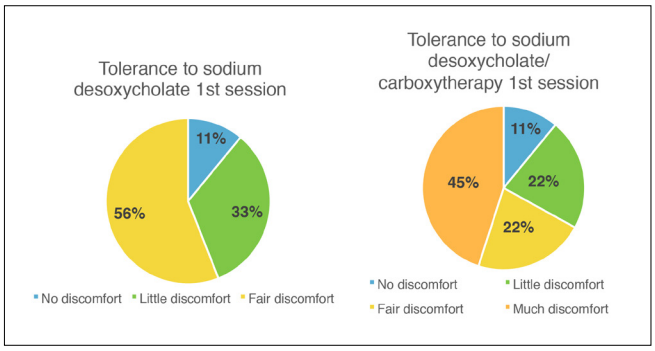

***Figure 3** - Tolerance to pain after the first infiltration of sodium deoxycholate alone and alternated with carboxytherapy.*

During the second and third sessions, the results in terms of patient discomfort after sodium deoxycholate infiltration were as follows: 11% no discomfort, 56% little discomfort and 33% a fair amount of discomfort. In the case of sodium deoxycholate alternated with carboxytherapy, 11% of patients reported having had no discomfort, 44% little discomfort and 45% a fair amount of discomfort. In terms of adverse effects, post-infiltration inflammation was only observed with hyperthermia, localized edema and in some cases hematoma, which in all cases remitted after approximately 15-20 days (*Figure 4*).

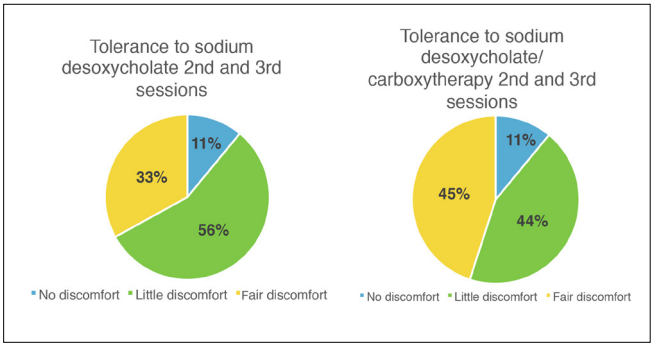

***Figure 4** - Tolerance to pain after the 2nd and 3rd infiltration of sodium deoxycholate alone and alternated with carboxytherapy.*

Sodium deoxycholate protocol

Changes observed after infiltration with sodium deoxycholate:

In the protocol of sodium deoxycholate alone there was an average loss of 1.3 ± 0.4 cm. In the assessment with respect to volume, the majority of patients - 89% - reported a moderate decrease and 11% a substantial decrease (*Figure 5*).

Regarding the improvement of skin appearance (edematous-fibrosclerotic panniculopathy) with sodium deoxycholate only, 33% of patients reported slight changes, 45% moderate changes and 22% substantial changes.

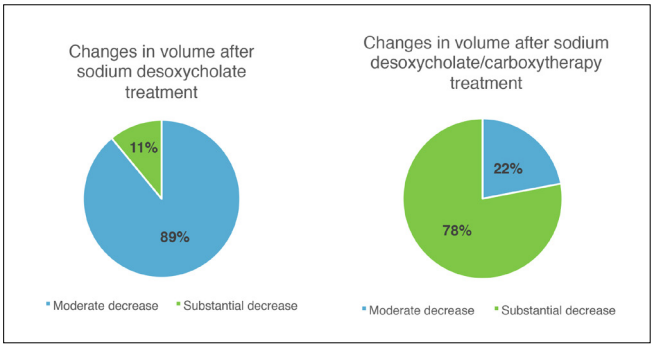

***Figure 5** - Comparison of changes in volume relative to the use of sodium deoxycholate alone or alternated with carboxytherapy.*

Protocol of sodium deoxycholate alternated with carboxytherapy

The authors of the study took measurements of areas to be treated and assessed skin appearance, prior to the beginning of the study. Photographs were taken after each treatment to support this assessment and to provide a visual record for each patient. The same assessments were made following treatment and at the end of the study.

Changes observed after infiltration with sodium deoxycholate/carboxytherapy:

In the protocol consisting of sodium deoxycholate alternated with carboxytherapy, there was an average loss of 2.7 ± 0.5 cm. In the assessment with respect to the decrease in volume, 22% of the patients reported

a moderate decrease and 78% a substantial decrease (*Figure 5*).
With regards to the improvement in skin appearance (edematous-fibrosclerotic panniculopathy) in the protocol alternating with carboxytherapy, 22% of patients observed slight changes, 22% moderate changes and 56% substantial changes (*Figure 6*).

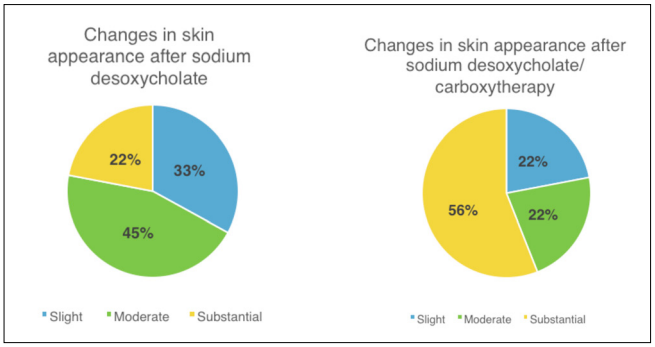

***Figure 6** - Comparison of changes in skin appearance in relation to the use of sodium deoxycholate alone or alternated with carboxytherapy.*

Satisfaction

When assessing the patients' opinion of the treatment and the results obtained in the protocol of Sodium deoxycholate alone, 32% of the patients said results were excellent, 25% very good, 22% good and 21% average.
When assessing the patient's opinion of the treatment and the results obtained in the protocol of Sodium deoxycholate alternated with carboxytherapy, 56% of the patients said results were excellent, 33% very good and 11% good (*Figure 7*).

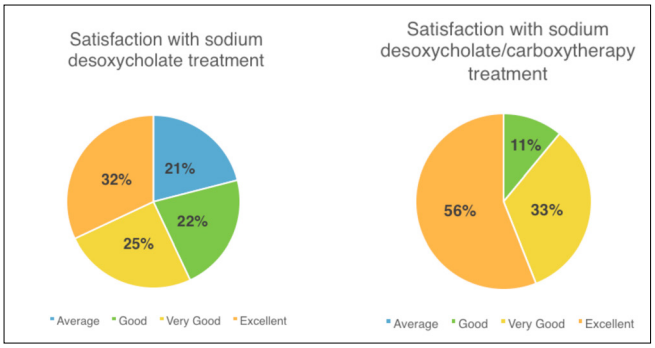

***Figure 7** - Comparison of general satisfaction with sodium deoxycholate treatment alone versus sodium deoxycholate alternated with carboxytherapy.*

In terms of satisfaction, all patients said they would repeat and recommend the sodium deoxycholate alternated with carboxytherapy protocol, while, with respect to the treatment consisting solely of sodium deoxycholate, only 66% said they would repeat the treatment and 34% said they may consider repeating it.

Clinical cases

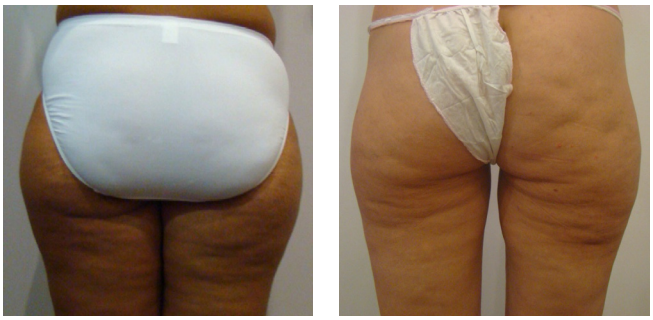

***Figure 8** - Comparison of protocols, right pelvic limb after 3rd session with sodium deoxycholate and left pelvic limb after the 3rd session of sodium deoxycholate alternated with carboxytherapy.*

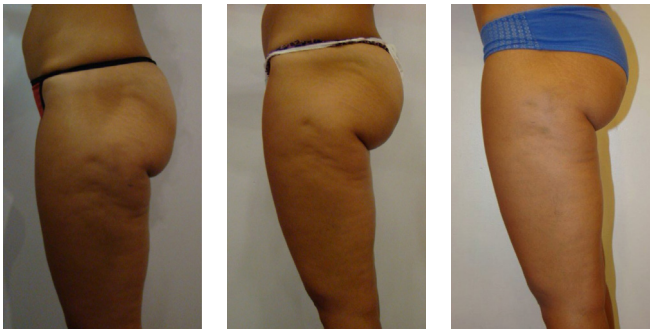

***Figure 9** - After two sessions of sodium deoxycholate alternated with carboxytherapy in the left pelvic limb.*

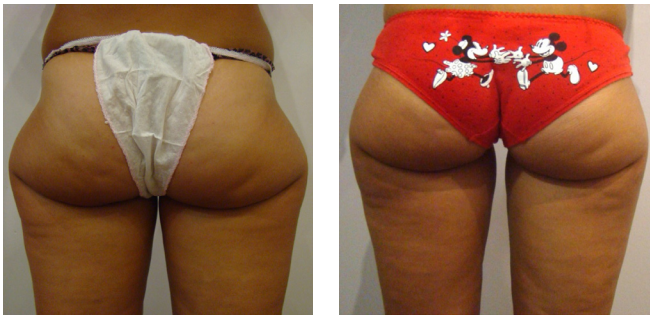

***Figure 10** - Evolution with the protocol of sodium deoxycholate alternated with carboxytherapy.*

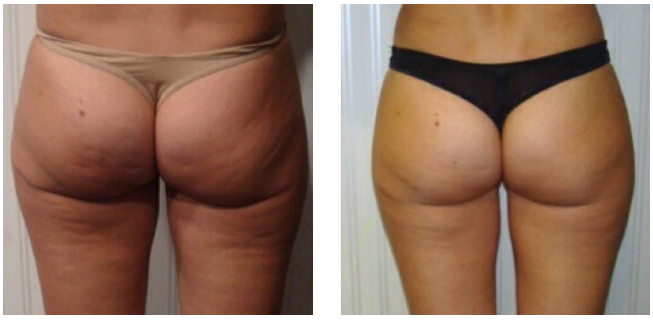

***Figure 11** - After three sessions of sodium deoxycholate alternated with carboxytherapy in the left pelvic limb, significant improvements were observed in volume, skin quality and contouring of the trochanteric region.*

Discussion and conclusions

Alterations in fatty tissue in female body contours are common for both anatomical reasons and due to estrogen activity, and their management has so far proved difficult.

Therefore, it is important to mention that in this study no significant complications were observed beyond inflammation, hyperthermia, edema, erythema post infiltration and in some cases hematomas. All side effects were resolved within a maximum of 10 to 15 days after procedure, without disrupting the daily activities of the patients. Likewise, despite the pain and inflammation after infiltration, patient satisfaction with such protocols was very high. In fact, all the patients who underwent treatment of sodium deoxycholate alternated with carboxytherapy said they would repeat and recommend the protocol. This was not only due to the few complications but also due to the loss of volume and the improvement of skin appearance.

Ultimately, with the technique of intralipotherapy with sodium deoxycholate, it was possible to reduce body volume. However, consideration must be given in this respect to the anatomy and the morphology of the type of fat in the region to be treated as treatment of areolar fat is essential, and will affect the depth at which infiltration must be performed. Furthermore, the effect of tissue shrinkage produced by treatment with sodium deoxycholate did not induce tissue sagging in the treated area. No significant changes were observed in the improvement of edematous-fibrosclerotic panniculopathy when only sodium deoxycholate was used, although no increase in skin disorders was observed either (*Figure 8*). In contrast, contouring was more evident and skin quality improved significantly with the protocol of sodium deoxycholate alternated with carboxytherapy, significantly enhancing patient satisfaction (*Figure 9*).

Contrary to initial expectations, inflammation and the resolution thereof did not decrease with the application of carboxytherapy, so the interval between each session was the same for both treatment protocols (21-25 days).

Tolerance and post-inflammatory pain were greater in the region treated with sodium deoxycholate alternated with carboxytherapy during the first session, but after the second session they evened out and the symptoms in both protocols were reported to be less pronounced.

Therefore, we can conclude that the effectiveness of the intralipotherapy technique with sodium deoxycholate can be enhanced by treatments such as carboxytherapy to improve tissue quality prior to infiltration.

Such treatments improve circulation and either mechanically or metabolically favor adipocyte lipolysis while improving the factors that favor edematous-fibrosclerotic panniculopathy.

The foregoing is coupled with the retraction effect induced by intralipotherapy, resulting not only in an improvement of body volume but also in the contouring of tissues in the treated area, thus allowing positive aesthetic and definitive overall results that enhance patient satisfaction (*Figures 10 and 11*).

REFERENCES

1. Motolese P. Phospholipids do not have lipolytic activity. A critical review. *J Cosmet Laser Ther.* 2008; 10(2):114-8.

2. Rotunda AM, Weiss SR, Rivkin LS. Randomized double blind clinical trial of subcutaneously injected deoxycholate versus phosphatidylcholine-deoxycholate combination for the reduction of sub mental fat. *Dermatol Surg.* 2009; 35(5):792-803.

3. Ito T, Moore JI, Koss MC. Topical application of CO2 increases skin blood flow. *J Invest Dermatol.* 1989; 93(2):259-62.

4. Geneser F. Tratado de histología. 3ra Ed. Editorial Panamericana.

5. Guyton AC, Hall JE. Tratado de fisiología medica. 2005 10ª.Ed. McGraw Hill.

6. Nürnberger F, Müler G. So called cellulite: an invented disease.*J Dermatol Surg Oncol.* 1978; 4(3):221-229.

7. Rossi AB, Vergagnini AL. Cellulite: a review. *J Eur Acad Dermatol Venereol.* 2000; 14(4):251-262.

8. Ceccarelli M, Pignatelli V, Bartoletti CA. Treatment of localised fat excess: A modification of the protocol and further evaluation. *La Med Estet.* 1995; 19:2.

9. Rittes PG. The use of phosphatidylcholine for correction of lower lid bulging due to prominent fat pads. *Dermatol Surg.* 2001; 27(4):392-6.

10. Rittes PG. The use of phosphatidilcholine for correction of localised fat deposits. *Aesthetic Plast Surg.* 2003; 27(4):315-18.

11. Salti G, Ghersetich I, Tantussi F, Bovani B, Lotti T. Phosphatidylcholine and sodium deoxycholate in the treatment of localised fat: a double blind, randomised study. *Dermatol Surg.* 2008; 34(1):60-6.

12. Aqualyx package leaflet. Motolese's solution. CE 0373. LELX0010 Rev 00.

13. Duncan DI. Response to "Injection lipolysis with phosphatidylcohline and deoxycholate". *Aesthet Surg J.* 2013; 33(7):1073-1075.

14. Salti G, Rauso R. Comments on "Injection lipolysis with phosphatidylcholine and deoxycholate". *Aesthet Surg J.* 2014; 34(4):639-640.

15. Rauso R, Salti G. A CE-Marked Drug Used for Localized Adiposity Reduction: A 4-Year Experience. *Aesthet Surg J.* 2015; 35(7):850-7.

16. Pinto H, Hernandez C, Turra C, Manzano M, Salvador L, Tejero P. Evaluation of a new adipocitolitic solution: adverse effects and their relationship with the number of vails injected. *J Drugs Dermatol.* 2014; 13(12):1451-1455.

17. Rauso R. Non surgical reduction of buffalo hump deformity. Case report and literature review. *Eur J Aesthet Med Dermatol.* 2011; 1(1):29-34.

18. Rauso R, Rusciani A, Curinga G. An adipocitolitic aqueous micro-gelatinous solution for buffalo hump deformity reduction. *J Drugs Dermatol.* 2014; 13(10):1282-1284.

19. Di Toro G, Rauso R. Skin Necrosis Following Adipocitolitic Solution Injections. *Aesthet Surg J.* 2016; 36(2):NP74-6.

20. Curri SB. Liposclerosi e microcircolo. *La dermoestetica.* 1990; 1: 6-7.

21. Gasparotti M. Superficial liposuction: a new application of the technique for aged and flaccid skin. *Aesthetic Plast Surg.* 1992; 16(2):141-53.

aesthetic medicine

Review

Choosing a hyaluronic acid for use in Aesthetic Medicine

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Abstract
The material most commonly used in Aesthetic Medicine is hyaluronic acid, both as a dermal filling material and to hydrate and stimulate the skin and mucosa.
This product plays several roles in normal tissues, but it is also involved in inflammatory processes, multiple drug resistance, angiogenesis, tumorigenesis, water homeostasis and altered viscoelasticity of the extracellular matrix[1].
The structure of native hyaluronic acid goes through many changes, leading to the belief that, from beginning to end, the molecule undergoes substantial modifications that should be known in order to choose the most appropriate one for its intended function.
The purpose of this paper is to reveal the parameters of injectable hyaluronic acid that should be known before its use for maximum efficacy and safety, based on the area to be treated and the desired effect, keeping in mind that the final result will depend not only on the product used, but also on the physician's knowledge and skills, and the response of the receptor.

Abbreviations
Hyaluronic acid (HA)

Keywords
Soft tissue fillers, hyaluronic acid, dermal filler rheology, filler manufacturer

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Introduction

According to the statistics of the American Society for Aesthetic Plastic Surgery[2], 3,372,445 Hyaluronic acid (HA) filler procedures were performed worldwide in 2016, making it the second most commonly used non-surgical aesthetic procedure after botulinum toxin.

Hyaluronic acid used as a cosmetic has a long history; in 1989, Balasz and Denlinger[3] described the first HA developed as a dermal filler, being used since 1995 in Aesthetic Medicine in Europe as a skin implant, although it had been used before in other areas of Medicine, basically in ophthalmology and traumatology.

The ability to correct defects in facial volume with an HA gel is basically related with its viscoelasticity and cohesivity. Both these properties establish the level of resistance to deformities and help integrate the filling material in the tissue by controlling the dispersal of the gel; therefore, choosing a dermal filler with the best rheological properties is key to obtaining desired, long-lasting aesthetic results.

Characteristics of hyaluronic acid

In vertebrates, HA is an essential component of the extracellular matrix. It is found around proliferating or migrating cells, and during inflammatory processes. It is a linear polysaccharide consisting of repeating disaccharide units of D-glucuronic acid and N-acetyl-D-glucosamine, with an approximate molecular weight (MW) of 2-6x106 Da. This same simple structure can be seen in all tissues and all species, that is, it is chemically homogeneous across all species and tissues, making it a perfect polysaccharide for use in Medicine. It is also biosynthesized by some bacteria[4].

It was first isolated in the vitreous humor of bovines in 1934 by Karl Meyer and John Palmer. Physiologically, it is not an acid, but a salt called hyaluronate.

It is synthesized in the cell membrane of many human cells like fibroblasts, endothelial cells, synovial cells, muscle fibers and oocytes, by synthases Has1, Has2 and Has3, and then extruded to the outside of the cell.

It is metabolized by receptor-mediated endocytosis and by specific enzymes, the hyaluronidases, which degrade it. Catabolism is very fast, with a mean duration in human tissues of between 12 hours and a few days. During an inflammatory process, its catabolism increases. HA concentration in tissues usually remains constant, which is slightly dependent on its molecular weight. HA cellular interaction is mediated by the CD44 receptor, which has wide tissue distribution and is responsible for modulating cellular metabolism, especially in synoviocytes and hematopoietic cells. This connection between HA and the CD44 receptor can explain HA's apparent ability to modulate inflammatory response, pain, GAG (glycosaminoglycans) normalization and PG (prostaglandins) production, cellular metabolism and stimulation of cellular cleansing of oxygen free radicals[5,6]. Currently, the HA used is of non-animal origin, synthesized in a lab setting through fermentation bacteria, which reduces its antigenic risk and its ability to create hypersensitivity reactions.

Synthetic hyaluronic acids can last from months to years and have a highly variable molecular weight. The human body can absorb a subcutaneous injection of HA in a variable time through enzyme digestion or disintegration through facial mimics. The time it takes to be eliminated has a direct impact on the duration of the treatment, it varies between individuals and is also affected by lifestyle (smoking habits, alcohol intake, sun exposure…)[7]. The majority of the products currently used lasts between 2-18 months based on complexity, molecular weight, etc., of the implanted molecule, although it has been described, and its presence has been confirmed, to last over 10 years after being implanted[8].

Since the introduction of ultrasounds, it was necessary to modify the concept of HA duration and distinguish between the HA that remains in the tissue and the duration of the effectiveness of the treatment, which is usually much shorter.

HA physical-chemical properties, like solubility and the availability of reactive functional groups, allow to perform chemical changes to it to obtain biocompatible materials that can be used to regenerate tissues. Bioscaffolds and dermal injections are manufactured in different ways, including hydrogels, tubes, meshes, etc[9]. One of these modifications is known as *crosslinking or intertwining*, and it consists of several acid molecule bindings, generating bonds that are hard to separate by hyaluronidases, thus increasing the time it remains in the tissue. Every brand uses a crosslinking method, but they all agree on the use of crosslinking agents like the 1,4-butanediol diglycidyl ether (BBDE) or the divinyl sulfone (DVD). Despite being toxic products, the dose used is very low, thus guaranteeing its safety[10].

Furthermore, the competition to get the perfect filler has caused the addition of other substances like mannitol, dextranomers, lidocaine, etc., to provide the implant with better properties.

HA has a natural antidote: hyaluronidase, an enzyme that in time only absorbs the injected hyaluronic acid, restoring the pre-treatment condition in a brief interval of time without affecting the hyaluronic acid present in the body[6]. The injection of hyaluronidase has been approved by the FDA as a temporary drug dispersal agent, because it binds to HA between the C1 of a molecule of N-acetylglucosamine and the C4 of glucuronic. However, its action as HA-degrading agent is currently off-label, despite the evidence of its efficacy to reverse HA fillers. As Rao points out[11], it is important to know that, because of the different biochemical composition of the varied HA products, each can have a different response to hyaluronidase.

Synthesis and Biotechnology

The high intertwining of hyaluronic acid with other components in the tissues makes its isolation and purification from animal sources difficult. In practice, it is inevitable that tissue-isolated hyaluronic acid products contain impurities.

As for the type and amount of these impurities, there are large, significant differences between the different preparations of hyaluronic acid. Purity depends on the choice of the source material, the manufacturing method and the molecular size of the isolated hyaluronic acid. The presence of impurities may affect biocompatibility, since they can cause severe adverse reactions in the human body, especially hypersensitivity reactions.

Tissues containing large amounts of hyaluronic acid have been used as source materials. Currently, cockscombs are the main tissue source. However, not only animal tissues contain cells able to produce hyaluronic acid. Some bacteria, like Streptococcus Equis and, more recently, Escherichia coli, have copied the specific enzymes that synthesize it[12].
These bacteria can be used to produce hyaluronic acid through the application of modern biotechnological methods. They are cultured in a setting containing water and nutrients. Synthesized HA within the cell membrane is excreted in the middle for easier access and purification. As long as the bacteria remain whole during the production, the resulting HA will contain insignificant amounts of other biomolecules. In recent years, the adverse effects of these implants, particularly hypersensitivity, have decreased, which has been associated with an improvement of HA's purity[13].
Long-term efficacy of fillers with hyaluronic acid gels comes from polymers intertwining, as well as water collecting, not only as fillers, but also to hydrate the area treated. According to some studies, stabilized hyaluronic acid can stimulate the synthesis of collagen by the body itself, as well as delay its disintegration, contributing to the efficacy and more durability of the product (Narins)[14].
HA used in Aesthetic Medicine as an injectable filling material or filler is a Class III Medical Device (FDA), so it must meet a series of requirements before being marketed.

Hyaluronic acid in aesthetic medicine

Different Hyaluronic Acid Products

The crosslinking technology, the uniformity and size of the particles, and HA concentration of the product determine its viscoelastic properties and, therefore, its clinical effect (Tran)[15].
The main characteristics that distinguish the different HA products are:
- the size of the particle,
- the type of crosslinking agent used,
- the level of crosslinking, the percentage of crosslinked HA and the amount of free (unchanged) HA and
- G' (elasticity modulus for rheological behavior).

All these physical and chemical attributes will affect each filler's characteristics, like clinical indications, easiness of injection, filling degree of tissues, longevity, clinical appearance and side effects[16].
Next, the different characteristics that determine a HA product will be analyzed (*Figure 1*).

Size of particles

The size of the particle and the distribution range of the particle size are additional significant components of HA gels that, among other things, affect the extrusion force needed for injection. A larger gel particle will be harder to inject through a small-bore needle, and a uniform distribution of particle size can decrease interruptions in the flow of particle extrusion. Uniformity is ideal for a better control of gel application[17].AH (Restylane®) was the first FDA-approved filling material.

Factor
HA Concentration
Cost
Characteristics, design and size of syringe
Level of crosslinking
Relationship between crosslinked and non-crosslinked HA
Type of intertwining used
HA Concentration
Duration of the correction
G'
Level of hydration of the product inside the syringe
Presence or absence of lidocaine
Necessary injection (extrusion) force
Technology of the needle

Figure 1 *- Factors to consider when choosing a hyaluronic acid as a filling material. Modified from Bogdan Allemann I, Baumann L. Preparaciones de gel de ácido hialurónico (Juvederm) en el tratamiento de arrugas y pliegues faciales. Clin Interv Envejecimiento 2008;3(4):629-34.*

All the products of the range of Restylane®, Perlane®, etc., use technology based on the size of the particles. The "size" or caliber is the process by which crosslinked HA is pushed through a special-size sieve, breaking into pieces. Restylane uses medium pieces of HA, while Perlane uses the largest ones, thus obtaining different products[18].

Concentration of Hyaluronic Acid

HA concentration in the filler differs based on the manufacturer and is usually shown as the total amount of HA (soluble and insoluble HA, mg/ml) in the filler. It is important to understand that only crosslinked HA, or the more insoluble HA, works as a dermal filler, resisting disintegration and giving more longevity to the dermis. The amount of free soluble HA, or native HA, is usually a byproduct of its chemical modifications and, given its solubility, it metabolizes fast[19].
The amount of HA in a product can contribute to its rigidity and longevity. In theory, the more the amount of HA in the product, the more rigid and long-lasting it will be. However, not all the HA in the product is crosslinked, so global crosslinking (amount of crosslinked HA) and the level of crosslinking (the HA molecule that is completely or partially crosslinked) must be considered. Since it works as a lubricant, non-crosslinked HA is often added to filler products to make its injection easier, resulting in two types of preparations with HA (monophasic and biphasic), like it will be described below.

Crosslinking

The most common crosslinking agent is 1,4-butanediol diglycidyl ether (BDDE). Some products are crosslinked with different crosslinking agents, like divinyl sulfone (DVS) in Prevelle®, Captique® and Hylaform®. Puragen® is crosslinked with 2,7,8-diepoxyoctane (DEO), forming

crosslinked ether and ester. The amount of crosslinking must be properly balanced in order to maintain both the duration and the biocompatibility of the HA filler.
The crosslinking technology, the uniformity and size of the particles, and HA concentration of the filler determine its viscoelastic properties and, therefore, its clinical effect. Crosslinked HA can be processed in different ways to create homogeneous (monophasic) gels or particles suspended in gel carriers (biphasic). Each type of HA filler has a different amount of HA, developed using different crosslinking processes, which significantly affect the gel properties and contribute to the aesthetic result and duration[19].

G' Modulus (G)

The G' or elasticity modulus of a product measures gel hardness.
The measurement of resistance to deformation is known as the G' or elastic modulus. Together with the product's cohesivity, G' values might be used to determine the proper placement of HA. Thus, products with a higher G' value and more cohesivity, like Juvéderm™ Ultra Plus and Perlane®, must be used on deeper lines, like nasolabial folds and puppet lines. More fluid products, like Juvéderm™ Ultra or Restylane®, are more appropriate for use in large areas, like cheekbones and cheeks. Products with low G', like Belotero Soft™ and Balance™, must be used in areas requiring a soft agent, like the wrinkles around the mouth and the area around the eyes. Knowing the G' value of a product is useful to place it in the right depth and location (*Table 1*)[20].
Any facial filling, to be effective, must be viscoelastic, changing its form enough to be injected under pressure and be initially shaped, but elastic enough to provide a lasting correction that resists the forces of deformation by shearing, once implanted, in the soft tissue.

Brand Name(s)	G'
Belotero Balance	128
Juvederm Ultra XC	207
Restylane Lift-L	977
Juvederm Ultra Plus XC	398
Voluma	263
Restylane-L	864

***Table 1** - G' values of different fillers of Hyaluronic acid taken by Gutowski [20].*

Cohesivity and Compression / Stretching / Viscosity

Cohesivity characterizes how the filler behaves as a gel deposit once it is implanted. It is described as the internal adhesion forces holding together the individual crosslinked HA particles comprising the filler material. The filler implanted in the face is constantly subjected to compression forces that affect its performance. For example, it is subjected to force from contact with external surfaces, such as lying on a pillow, etc., or to the force applied by skin tension over a filling material placed subcutaneously. When subjected to these forces, the less cohesive HA filler tends to lose projection more easily than the filler with higher cohesivity and an equivalent G'. Highly cohesive fillings can resist vertical compression and maintain the initial shape of the gel deposit[21].
Cohesivity measures the ability of the gel to resist compression/stretching. This is an important concept, because fillers are made of multiple units of crosslinked HA in the form of visible particles or discrete units adhered through non-covalent bonds. Cohesivity affects the initial dispersal of the implant in a variable manner that is related to its depth and underlying muscle and skin compression. Highly cohesive fillers are better suited for deep facial volumization, while fillers with low cohesivity are easy to mold and tend to form thin even layers in the skin. This type of filler creates natural-looking correction of small wrinkles, and the high cohesivity of the product maintains its structure and integrity. According to authors like Tran[15]: Cohesion is key for integration of the skin. Cohesivity is not the same as Viscosity (measurement of a material's resistance to flow). Viscosity measures the ability to spread. The higher the viscosity (high resistance), the less ability to spread. Elasticity measures the ability of the gel to return to its initial shape after applying a mechanical force, and Plasticity is the ability of a gel to be shaped or molded.

There are currently two big groups of HA fillers:

1. Biphasic HA

The first HA dermal injections on the market were non-cohesive biphasic gels, characterized as crosslinked particles suspended in a non-crosslinked HA matrix acting as a lubricant[22]. These products (e.g. Restylane®; HA concentration 20 mg/ml) are manufactured with NASHA®, a stabilized hyaluronic acid of non-animal origin). The difference between the products of the range (Restylane®, Perlane®, Restylane Lips®) lies in the size of the particle. Since then, a large variety of HA dermal fillers has been created. In 2012, Edsman et al.[23] analyzed 13 HA filler products available in the market, assessing gel resistance and level of crosslinking. They concluded that: both measures of gel strength, G´ and c(min), can be used because the results from the two methods are well correlated. No differentiation in filler properties could be seen as a result of manufacturing process used, except that the nonanimal stabilized HA stabilization process resulted in products with high gel strength and a low degree of modification.

2. Monophasic HA

Monodensified monophasic products, compared with biphasic gels, do not undergo a process that breaks down the gel[24]. In consequence, they have just one phase of HA with one single density. There are different groups of monodensified monophasic fillers based on the manufacturing technology, such as the HYLACROSS® technology (e.g. Juvéderm® Allergan; HA concentration 24 mg/ml) or the Vycross® technology. In 2015, Goodman presented a study[25], "evaluating the available literature to research the relatively new Vycross® technology that combines HAs of low and high

molecular weight, but varying the HA concentration with higher crosslinking to create a series of products with different clinical indications." Thus, for example, Voluma® has the larger concentration of HA (20 mg/mL), a high G', while Volbella® has a much lower concentration (15 mg), which allows a more superficial infiltration in lips, lines and more subtle depressions. Polydensified cohesive monophasic gels (Belotero®, formerly Anteis SA, owned by Merz Pharmaceuticals) have been recently introduced. Compared with monodensified gels, which are crosslinked once, polydensified fillers contain a single phase of HA that is crosslinked continuously. They are manufactured with the cohesive polydensified matrix (CPM ®) technology, resulting in a gel with non-uniform crosslinking and high molecular weight, and a viscosity that is lower than that of other gels (comparing gels targeting the same indication)[26]. These properties allow for a more homogeneous intradermal distribution of the material.

How can i choose the filling material with the best suited hyaluronic acid?

Many factors must be understood in order to know what HA filler material is to be used, like it is described in *Table 1*. Since there seems to be no scientific publications reviewing and comparing all the aforementioned properties, it is currently impossible to fully know the significance of these varied characteristics when choosing a filler. It is necessary to gather more data to properly understand if, for example, the dimension technology makes a difference, or if the ester bonds last longer than the ether bonds... These distinctions will become clearer and more significant as more information is gathered and more studies are conducted[27].

Objectively, it is a fact that rheological properties response to deformation and flow of matter are different in each product on the market, and that choosing a filler with the right rheological properties is key to achieving desired outcomes of natural appearance and aesthetic long duration[28]. In this respect, Salwowska et al's review[29], "*Physicochemical Properties and Application of Hialuronic Acid: a systematic review*", of 2016 is of note, where they assessed not only its application in Aesthetic Medicine, but also in other disciplines, like traumatology and ophthalmology.

Rheological differences of fillers do not always mean clinical differences, since more variables would have to be analyzed; but, generally speaking, it can be said that the G' measurement can be used to describe a product's firmness and projection ability. A product with a high G' will hardly be deformed, while a low G' means that it will deform with little tension applied.

The edema that can occur in tissues due to its capacity to retain water depends on the modifications performed in the HA molecule and in the level of crosslinking[30].

What should be assessed about a filling material?

The first thing to know is that the product was manufactured under quality conditions, of which there is enough information (*Figure 2*), being conveniently studied and providing its own bibliographic references availing its properties and safety. In Europe, the product used needs to have a CE brand and, in Spain, it must also be registered with the AGEMED.

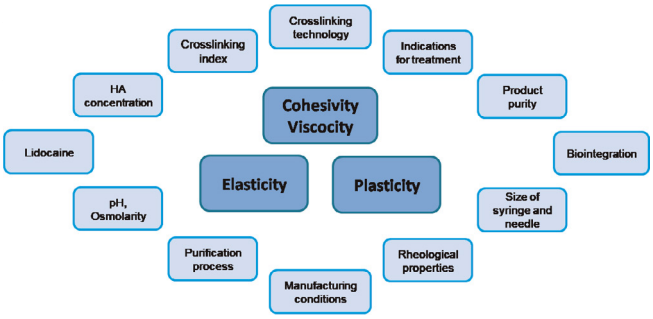

***Figure 2** - What does a good filler contain? (extracted from Belotero® commercial material)*

offer the same description of the characteristics of their products. For instance, the study by Dr. Alcolea et al.[32] (*Table 2*) shows the lack of information to compare all gels. Second, the best suited filler must be chosen based on the area to treat and the defect to correct.

	PM	DENSITY	NUMBER OF PARTICLES	SIZE	NUMBER AND INTENSITY OF CROSS-LINK PHASE	BIPHASIC/ MONOPHASIC	OSMOLARITY	PH	PROTEIN, BACTERIAL OR TOXIC RESIDUES
ESTHELIS BASIC		22,5 mg/ml			Dinamic cross-linked (puttensted)	Monophasic polidensified	305	7	Endotoxines <0.103
ESTHELIS soft		20 mg/ml			Dinamic cross-linked (puttensted)	Monophasic polidensified	305	7	Endotoxines <0.103
FORTELIS extra		25,5 mg/ml			Dinamic cross-linked (puttensted)	Monophasic	305	7	Endotoxines <0.103
MHA 18 (Filorga)	3,5 millons dalton	18 mg/dl	150000		Monophasic reticualtion. Cuaternary matrix	Monophasic	280-330	6,8-7,6	Prot 14 ppm Endotoxines <0.05
Xha3	2,5 millons dalton	23 mg/dl	500000		Monophasic reticualtion. Cuaternary matrix	Monophasic	280-330	6,8-7,4	Prot 11 ppm Endotoxines <0.05
Xha vol	2,5 millons dalton	23 mg/dl	1000000		Monophasic reticualtion. Cuaternary matrix	Monophasic	280-330	6,8-7,4	Prot 8,7 ppm Endotoxines <0.05
PRINCESS filler	2,7 millons dalton	23 mg/ml	500000 mPas		+++	Monophasic	300	7	Prot 11 ppm Endotoxines <0.05 EU/g
PRINCESS volume	2,7 millons dalton	23 mg/ml	1000000 mPas		++++	Monophasic	291	7,1	Prot 8,7 ppm Endotoxines <0.05 EU/g
JUVEDERM Ultra 2,3,4 y smile		24 mg/ml			++/+++	Monophasic monodensified		7,2	Residues prot <2 ppm
JUVEDERM Voluma		20 mg/ml			++++	Monophasic monodensified		7,2	
Restylane		20 mg/ml	100000	250 microns		Biphasic		7	
Restylane finas lineas		20 mg/ml	200000			Biphasic		7	
Pedane		20 ml	10000	550 microns		Biphasic		7	
Teosyal global action, Touch up, Deep Lines, Kiss Ultra Deep		25 ml			Global action +++ Touch up +++ Deep Lines +++ Kiss ++++ Ultra Deep ++++	Monophasic			Prot <5 ppm Micrograms/gr
Teosyal first lines		20 mg/g			First lines+	Monophasic			
Emervel Touch		20 mg/g				Monophasic		7	
Emervel classic		20 mg/g				Monophasic		7	
Emervel Deep	Emervel Deep	20 mg/g			Emervel Deep	Monophasic		7	
Emervel Volume		20 mg/g				Monophasic		7	
Emervel Lips		20 mg/g				Monophasic		7	
Glyton 2	AH cross-linked 1-1.4 MDa+2.5-3MDa AH free 1-1.4 MDa	20 mg/g			+	Monophasic	300	7,1	proteins residues (<0.002%) and endotoxines (10 EU/G)
Glyton 3	AH cross-linked 1-1.4 MDa+2.5-3MDa AH free 1-1.4 MDa	20 mg/g			++	Monophasic	300	7,1	proteins residues (<0.002%) and endotoxines (10 EU/G)
Glyton 4	AH cross-linked 1-1.4 MDa+2.5-3MDa AH free 1-1.4 MDa	24 mg/g			+++	Monophasic	300	7,1	proteins residues (<0.002%) and endotoxines (10 EU/G)

***Table 2** - Most representative HA gels registered in Spain. Cornejo P., Alcolea J.M., Trelles M.A. Perspectivas en el uso de materiales de relleno inyectables para tejidos blandos, desde nuestra experiencia: 1ª Parte. Cir plást iberolatinoam 2011 Dic [quoted 2017 Aug 19]; 37(4): 393-402.*

The dossier of the product to be used shows the indications and conditions of use that must be followed. Prior to treatment, the doctor must have a plan, knowing that, as a rule, it is impossible to treat the whole face with one single product.

The face is a complex, dynamic structure. Any filling implanted in the face will be subjected to several combinations of lateral and pressure forces. Within each anatomical plane, the filler is subjected to a complicated series of forces varying in intensity and frequency. Furthermore, normal daily activities, like resting the face on a pillow, eating and kissing, cause different

pressures. Therefore, new filling materials must be able to adapt to different mechanical properties for each specific indication and facial area[33].

Facial aging can manifest as changes in skin texture and color (dyschromia, lentigos, etc.), and in the formation of fine lines and wrinkles that become deeper and deeper, and they are at first dynamic and then static. Changes occur in the skin, but also in muscles, fat and bone tissues, which contribute to the loss of facial fullness. Each one of these components of facial aging must be treated with specific treatments, sometimes combined, considering that surgery may be necessary as a gold standard, although many patients reject it.

Treatments with filler materials, especially with hyaluronic acid, have become the main tool both to look young and to improve facial characteristics in younger patients.

In high-risk areas, like the glabella and the area around the eyes, and when attempting to reduce fine wrinkles, dermal fillers with low G' must be used, as they integrate better with tissues.

To increase volume in the lip area, it is recommended to use products with a medium G'.

A high G' means a hard gel that can be palpated if it is not injected in a deep, subcutaneous or supraperiosteal plane.

Ultrasounds have also revealed differences in the varied hyaluronic acid products. From an imaging perspective, high G's are similar to cysts, while low G's spread more like oil stains, although a standard pattern cannot be established. This also leads to the belief that it may have a different behavior with hyaluronidases, if its use were necessary[34].

When volumizing the middle or lower third of the face (jaw remodeling or chin projection), the selected filler must be able to maintain its form and projection, resisting the shearing and compression forces of weight and the tension of the overlying soft tissues, the dynamic forces of contraction of the elevator muscle of the lips and cheeks, and the aforementioned external compression forces (support, kissing, etc.). Rheologically speaking, this means a filler with an elasticity (G') modulus high enough, with medium-to-high cohesivity to resist compression forces. Besides, it is necessary to be cohesive enough to ensure minimum separation and displacement of the product due to the repeated contraction of the overlying muscles.

It is essential to have a good knowledge of facial anatomy and the risk areas to adjust the materials and injection techniques and maximize safety. However, in the words of Scheuer[35], "Despite the detailed descriptions available about facial vasculature, anatomy can be highly variable, and vascular lesions can occur even after taking all precautions. Furthermore, the real depth of the needle can be hard to follow and, sometimes, unpredictable."

Conclusions

Given the short time of recovery and the immediate results obtained, the use of HA injectable filling materials keeps growing in popularity, although it still shows complications, which should be minimized by having a good knowledge of facial anatomy, the different products to use, injection techniques and handling of hyaluronidase.

Patients must have all the information and sign an informed consent, showing the product that will be implanted.

Viscoelasticity and cohesivity play an important role in the design of HA fillers and must be known before choosing one to obtain the best clinical outcomes, since these rheological properties can make facial correction more predictable when the right product is used in the proper place. These properties refer to the ability of fillers to withstand different kinds of deformation and forces when implanted in several facial planes and areas. Viscoelasticity measures the elastic and viscous behaviors of a filler. Fillers with moderate to high elastic modulus (G') can withstand shear stress.

Fillers with low G' are better suited for superficial areas, they better integrate with the tissue and cannot be seen after implantation.

Products with high G' are better suited for volumization, but for a best implantation, they must have medium to high cohesivity to withstand a vertical projection.

Furthermore, it should not be forgotten that the final outcome will not only depend on the selected product, but and this is essential on the physician's skills and expertise to implant it and the patient's response.

Conflict of interests

The authors declare no conflict of interests or funding.

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REFERENCES

1. Jiang, D, Liang J, Noble PW. Hyaluronan as an immune regulator in human diseases. *Physiol Rev.* 2011; 91(1):221–64.
2. http://www.isaps.org
3. Balazs EA, Denlinger JL. Clinical uses of hyaluronan. *Ciba Found Symp.* 1989; 143:265-75; discussion 275-80, 281-5.
4. Milas M, Rinaudo M, Roure I, Al-Assaf S, Phillips GO, Williams PA. Comparative rheological behavior of hyaluronan from bacterial and animal sources with cross-linked hyaluronan (hylan) in aqueous solution. *Biopolymers.* 2001; 59(4):191-204.
5. Day AJ, de la Motte CA. Hyaluronan cross-linking: a protective mechanism in inflammation? *Trends Immunol.* 2005; 26(12):637-43.
6. Tian X, Azpurua J, Hine C, et al. High-molecular-mass hyaluronan mediates the cancer resistance of the naked mole rat. *Nature.* 2013; 499(7458):346-9.
7. Marinelli E, Montanari Vergallo G, Reale G, et al. The role of fillers in aesthetic medicine: medico-legal aspects. *Eur Rev Med Pharmacol Sci.* 2016; 20(22):4628-34.
8. Tejero P. Efectos secundarios de los implantes tisulares. *Tesis doctoral.* UCM 2013.
9. Hemshekhar M, Thushara RM, Chandranayaka S, Sherman LS, Kemparaju K, Girish KS. Emerging roles of hyaluronic acid bioscaffolds in tissue engineering and regenerative medicine. *Int J Biol Macromol.* 2016; 86:917-928.
10. De Boulle K, Glogau R, Kono T, et al. A review of the metabolism of 1,4-butanediol diglycidyl ether-crosslinkedhyaluronic acid dermal fillers. *Dermatol Surg.* 2013; 39(12):1758-66.
11. Rao V, Chi S, Woodward J. Reversing facial fillers: interactions between hyaluronidase and commercially available hyaluronicacid based fillers. *J Drugs Dermatol.* 2014; 13(9):1053-6.
12. Hoshi H, Nakagawa H, Nishiguchi S, Iwata K, Monde K, Nishimura S. An engineered hyaluronan synthase: characterization for recombinant human hyaluronan synthase 2 Escherichia coli. *J Biol Chem.* 2004; 23:279(4):2341-9.
13. Tezel A, Fredrickson GH. The science of hyaluronic acid dermal fillers. *Cosmet Laser Ther.* 2008; 10(1):35-42.
14. Narins RS, Brandt F, Leyden J, Lorenc ZP, Rubin M, Smith S. A randomized, double-blind, multicenter comparison of the efficacy and tolerability of Restylane versus Zyplast for the correction of nasolabial folds. *Dermatol Surg.* 2003; 29(6):588-95.
15. Tran C, Carraux P, Micheels P, Kaya G, Salomon D. In vivo bio-integration ofthree hyaluronic acid fillers in human skin: a histological study. *Dermatology.* 2014; 228(1):47-54.
16. Bogdan Allemann I, Baumann L. Hyaluronic acid gel (Juvéderm) preparations in the treatment of facial wrinkles and folds. *Clin Interv Aging.* 2008; 3(4):629-34.
17. Attenello NH, Maas C. Injectable fillers: review of material and properties. *Facial Plast Surg.* 2015; 31(1):29-34.
18. Brandt F, Cazzaniga A. Hyaluronic acid gel fillers in the management of facial aging. *Clin Interv Aging.* 2008; 3(1):153-159.
19. Tezel, A; Fredrickson, GH. La ciencia de los rellenos de ácido hialurónico. *J Cosmet Laser Ther.* 2008; 10:35-42.
20. Gutowski KA. Hyaluronic Acid Fillers Science and Clinical Uses. Downloaded from ClinicalKey.com at Hospital Ramon y Cajal JC November 11. 2016.
21. Pierre S, Liew S, Bernardin A. Basics of dermal filler rheology. *Dermatol Surg.* 2015; 41 Suppl 1:S120–S126.
22. Flynn TC, Sarazin D, Bezzola A, Terrani C, Micheels P. Histología comparativa de la implantación intradérmica de rellenos de ácido hialurónico mono y bifásico. *Dermatol Surg.* 2011; 37(5):637-43.
23. Edsman K, Nord LI, Ohrund A, Lärkner H, Kenne AH. Gel properties of hyaluronic acid dermal fillers. *Dermatol Surg.* 2012; 38(7 Pt 2):1170-9.
24. Kerscher M, Agsten K, Kravtsov M, Prager W. Effectiveness evaluation of two volumizing hyaluronic acid dermal fillers in a controlled, randomized, double-blind, split-face clinical study. *Clin Cosmet Investig Dermatol.* 2017; 10:239-247.
25. Goodman GJ, Swift A, Remington BK. Current Concepts in the Use of Voluma, Volift, and Volbella. *Plast Reconstr Surg.* 2015; 136(5 Suppl):139S–148S.
26. Santoro S, Russo L, Argenzio V, Borzacchiello A. Rheological properties of cross-linked hyaluronic acid dermal fillers. *J Appl Biomater Biomech.* 2011; 9(2):127-36.
27. Pierre S, Liew S, Bernardin A. Basics of dermal filler rheology. *Dermatol Surg.* 2015; 41(1):S120-6.
28. Sundaram H, Cassuto D. Biophysical characteristics of hyaluronic acid soft-tissue fillers and their relevance to aesthetic applications. *Plast Reconstr Surg.* 2013; 132(4 Suppl 2):5S-21S.
29. Salwowska NM, Bebenek KA, Żadło DA, Wcisło-Dziadecka DL. Physiochemical properties and application of hyaluronic acid: a systematic review. *J Cosmet Dermatol.* 2016; 15(4):520-6.
30. Scheuer J3rd, Sieber DA, Pezeshk RA, Campbell CF, Gassman AA, Rohrich, RJ. Maximizing Safety During Soft-tissue Filler Injections. *Plast Reconstr Surg.* 2017; 139(1):50e-58e.
31. Monheit G, Rzany B. Soft Tissue Augmentation E-Book: Procedures in Cosmetic Dermatology Series. Capitulo 9. Páginas 57-61. *Fourth edition.* 2018. https://books.google.es/books?isbn=032348008X.
32. Cornejo P, Alcolea JM, Trelles MA. Perspectivas en el uso de materiales de relleno inyectables para tejidos blandos, desde nuestra experiencia: 1ª Parte. *Cir Plást Iberolatinoam.* 2011; 37(4):393-402.
33. Pierre S, Liew S, Bernardin A. Basics of dermal filler rheology. *Dermatol Surg.* 2015; 41 Suppl 1:S120-6.
34. Micheels P, Besse S, Sarazin D, et al. Ultrasound and Histologic Examination after Subcutaneous Injection of Two Volumizing Hyaluronic Acid Fillers: A Preliminary Study. *Plast Reconstr Surg Glob Open.* 2017; 5(2):e1222.
35. Monheit G . Rzany B. Soft Tissue Augmentation E-Book: Procedures in Cosmetic Dermatology Series. Capitulo 9. Paginas 57-61 Fourth edition. 2018. https://books.google.es/books?isbn=032348008X.

aesthetic medicine

Mini-review

The therapeutic role of s. thermophilus-containing cream in CO2 laser surgery

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Short title: Probiotics and CO2 laser surgery

Abstract
The concept of probiotic is evolving. Most often in foods and oral formulations, the probiotics are mainly used as a means to restore microbiota balance, mainly in the gastrointestinal tract. Even if this approach appears particularly significant since the gut microbiota is involved in homeostasis, intestinal development, and immune system modulation, an emerging approach to help preventing and treating skin inflammatory conditions is represented by topical probiotics. In the last years, an increasing interest has been focused on the possible topical use of probiotics for treating inflammatory and allergic conditions suggesting that they can exert profound beneficial effects on skin homeostasis. In our clinical practice fractional CO2 laser skin resurfacing is more effective than non-ablative ones against aging signs, but post-operative redness and swelling prolong the overall downtime of patients. In this article, our experience in general in this field has been summarized, highlighting in particular the effects of an experimental cream containing S. thermophilus able to modulate the inflammatory reaction associated to fractional CO2 laser surgery. The topical treatment with the experimental cream induces a quicker reduction of postoperative erythema and swelling.

Keywords
S. thermophilus, skin inflammation, fractional CO2 laser surgery

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Probiotics are defined by the World Health Organization as "live microorganisms which, when administered in adequate amounts, confer a health benefit on the host"[1]. Clinical and experimental articles document that beyond capacity to positively influence the gut functions, probiotics can exert their benefits also at the skin level[2-7].

The evidence available from literature as well as registered patients have been summarized by our group in relation to actual or potential topical application of probiotics in the field of cutaneous patologies[8,9].

Indeed, probiotics represent an emerging approach to help preventing and treating skin conditions, including the external signs of aging, acne, rosacea, yeast and bacterial infections, psoriasis, and dermatitis, as also shown by the growing marketplace for topical formulations available for skin care and antiaging benefits.

The rapid increase in the use of probiotics in recent years has confirmed their excellent safety profile[1].

As immunomodulators, they have been used also in atopic dermatitis (AD)[10]. The results of a recent study indicate a strong positive effect in reducing the SCORAD index and use of topical corticosteroids in the AD group treated with a probiotic mixture thus supporting a more extensive use of probiotics in clinical practice[11].

In the last twenty years, our attention has been focused on probiotics' beneficial effects, reporting, in particular, in vivo and in vitro findings regarding their antiaging, anti-inflammatory, and anti-cancer properties[12].

Overall, the obtained results led us to suggest that selected probiotic strains possess peculiar biochemical characteristics underlying, at least partially, that the observed effects are mainly related to the enzymatic activities of sphingomyelinase and/or arginine deiminase[13-21]. In particular, the involvement of probiotic sphingomyelinase was studied in skin aging and inflammation. Sphingomyelinases hydrolyse the most abundant membrane lipid sphingomyelin into phosphorylcholine and ceramide and possess acid, alkaline or neutral pH optima. Ceramide is a bioactive sphingolipid involved in many biological functions such as proliferation, apoptosis, differentiation and inflammation[22]. Recently, the advancements in the maintenance of skin barrier/skin lipid composition and the involvement of metabolic enzymes i.e. sphingomyelinase have been reviewed[23,24].

The presence of high levels of sphingomyelinase activity in S. thermophilus could be responsible for the observed increase of stratum corneum ceramide levels, thus leading to an improvement in barrier function and stratum corneum flexibility[13].

A 2-week topical administration of a S. thermophilus-containing cream was able to positively and significantly influence stratum corneum ceramide levels in AD patients resulting also in the improvement of associated signs and symptoms i.e. erythema, scaling, pruritus[15].

The same experimental cream was able to improve the lipid barrier and increase the resistance against aging-associated xerosis in healthy elderly women by increasing skin ceramide levels as well hydration values[20].

In a recent article, we have reported the results of a study aimed at verifying the ability of a probiotic topical treatment to reduce the erythema and swelling associated to fractional CO2 laser surgery[25].

It is well known that these side effects, related to the machine's setting and the modalities of treatment, can prolong the overall downtime of the patients also requiring up to anti-inflammatory administration[26-31].

In our published study, the experimental cream containing S. thermophilus was administered postoperatively to 42 patients with aged skin features treated with fractional CO2 laser[25]. All patients adopted the cream twice a day for 2 weeks and had follow-up checks at 7, 15, and 30 days after the end of treatment. The effects of the experimental cream were compared with a control group (20 patients, with a superimposable age and similar clinical features), treated after laser surgery with topical antibiotic cream administered three times a day for 3 consecutive days, and a hyaluronic acid-based cream applied twice a day for 15 days.

The results showed that the average time for the erythema resolution in patients treated with the experimental cream was of 14.31 days vs 24.4 days in the control patients. The average time for swelling reabsorption was 9.3 days in the experimental group vs 16.35 days for the control group. The experimental treatment was thus able to significantly reduce the average time of erythema and oedema resolution when compared to control therapy ($P<0.0001$ for both erythema and swelling vanishing as expressed in days).

Finally, the rationale of our study was intimately connected to the necessity of overall downtime reduction by improving the patient's outcome.

Our experimental and clinical observations are really encouraging and confirm that the anti-inflammatory effects exerted by the experimental cream containing S. thermophilus make it an excellent tool for reducing the predictable side effects related with CO2 laser surgery.

Moreover, according to our previous studies, we believe that daily use by the patient of the experimental probiotic-based cream, for its proven anti-aging properties, is able not only to improve but also to maintain much longer the CO2 laser clinical results.

In conclusion, topical probiotic formulations are becoming increasingly available for healthy skin care, anti-aging approaches, and prevention and treatment of skin diseases. However, but it should be stressed that changes in the bacterial culture conditions, manufacturing processes, equipment, or facilities can influence the probiotic itself as well as its properties, therefore, a great attention today is focused on the need to verify safety and efficacy for each probiotic product[32-37].

Conflicts of interest

None declared

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REFERENCES

1. Hill C, Guarner F, Reid G, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol.* 2014; 11(8):506-514.
2. Baquerizo Nole KL, Yim E, Keri JE. Probiotics and prebiotics in dermatology. *J Am Acad Dermatol.* 2014; 71(4):814-821.
3. Fuchs-Tarlovsky V, Marquez-Barba MF, Sriram K. Probiotic in dermatologic practice. *Nutrition.* 2016; 32(3):289-295.
4. Notay M, Foolad N, Vaughin, AR, Sivamani RK. Probiotics, Prebiotics and Synbiotics for the treatment and prevention of adult dermatological diseases. *Am J Clin Dermatol.* 2017; 18(6):721-732.
5. Arck P, Handjiski B, Hagen E, et al. Is there a 'gut-brain-skin' axis? *Exp Dermatol.* 2010; 19(5):401-405.
6. Bowe W, Patel NB, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. *Benef Microbes* 2014; 5(2):185-199.
7. Lukic J, Chen V, Strahinic I, et al. Probiotics or pro-healers: the role of beneficial bacteria in tissue repair. *Wound Repair Regen.* 2017; 25(6):912-922.
8. Cinque B, Palumbo P, La Torre C, et al. Probiotics in aging skin. In: Springer ed. *Textbook of aging skin.* Berlin Heidelberg. 2010:811-820.
9. Cinque B, La Torre C, Melchiorre E, et al. Use of probiotics for dermal applications. In: M-T Liong ed. Probiotics, *Microbiology Monographs 21*, Springer-Verlag Berlin Heidelberg. 2011:221-241.
10. Kober MM, Bowe WP. The effect of probiotics on immune regulation, acne, and photoaging. *Int J Womens Dermatol.* 2015; 1(2):85-89.
11. Navarro-López V, Ramírez-Boscá A, Ramón-Vidal D, et al. Effect of Oral Administration of a Mixture of Probiotic Strains on SCORAD Index and Use of Topical Steroids in Young Patients With Moderate Atopic Dermatitis: A Randomized Clinical Trial. *JAMA Dermatol.* 2018; 154(1):37-43.
12. Palumbo P, Lombardi F, Evtoski Z, et al. Potential molecular and cellular mechanisms underlying the anti-inflammatory and anti-tumor properties of probiotics: our experience. *Cancer Studies Therapeutics*, 2017.
13. Di Marzio L, Cinque B, De Simone C, Cifone MG. Effect of the lactic acid bacterium Streptococcus thermophilus on ceramide levels in human keratinocytes in vitro and stratum corneum in vivo. *J Invest Dermatol.* 1999; 113(1):98-106.
14. Di Marzio L, Russo FP, D'Alò S, et al. Apoptotic effects of selected strains of lactic acid bacteria on a human T leukemia cell line are associated with bacterial arginine deiminase and/or sphingomyelinase activities. *Nutr Cancer.* 2001; 40(2):185-196.
15. Di Marzio L, Centi C, Cinque B, et al. Effect of the lactic acid bacterium Streptococcus thermophilus on stratum corneum ceramide levels and signs and symptoms of atopic dermatitis patients. *Exp Dermatol.* 2003; 12(5):615-620.
16. Linsalata M, Russo F, Berloco P, et al. The influence of Lactobacillus brevis on ornithine decarboxylase activity and polyamine profiles in Helicobacter pylori-infected gastric mucosa. *Helicobacter* 2004; 9(2):165-172.
17. Di Marzio L, Di Leo A, Cinque B, et al. Detection of alkaline sphingomyelinase activity in human stool: proposed role as a new diagnostic and prognostic marker of colorectal cancer. *Cancer Epidemiol Biomarkers Prev.* 2005; 14(4):856-862.
18. Cinque B, Di Marzio L, Della Riccia DN, et al. Effect of Bifidobacterium infantis on Interferon-gamma-induced keratinocyte apoptosis: a potential therapeutic approach to skin immune abnormalities. *Int J Immunopathol Pharmacol.* 2006; 19(4):775-786.
19. Riccia DN, Bizzini F, Perilli MG, et al. Anti-inflammatory effects of Lactobacillus brevis on periodontal disease. *Oral Dis.* 2007; 13(4):376-385.
20. Di Marzio L, Cinque B, Cupelli F, De Simone C, Cifone MG, Giuliani M. Increase of skin-ceramide levels in aged subjects following a short-term topical application of bacterial sphingomyelinase from Streptococcus thermophilus. *Int J Immunopathol Pharmacol.* 2008; 21(1):137-143.
21. Angulo S, Morales A, Danese S, et al. Probiotic sonicates selectively induce mucosal immune cells apoptosis through ceramide generation via neutral sphingomyelinase. *PLoS One.* 2011; 6(3):e16953.
22. Canals D, Perry DM, Jenkins RW, Hannu YA. Drug targeting of sphingolipid metabolism: sphingomyelinases and ceramidases. *Br J Pharmacol.* 2011; 163(4):694-712.
23. Cui L, Jia Y, Cheng ZW, et al. Advancements in the maintenance of skin barrier/skin lipid composition and the involvement of metabolic enzymes. *J Cosmet Dermatol.* 2016; 15(4):549-558.
24. Danso M, Boiten W, van Drongelen V, et al. Altered expression of epidermal lipid bio-synthesis enzymes in atopic dermatitis skin is accompanied by changes in stratum corneum lipid composition. *J Dermatol Sci.* 2017; 88(1):57-66.
25. Zoccali G, Cinque B, La Torre C, et al. Improving the outcome of fractional CO2 laser resusrfacing using a probiotic skin cream: Preliminary clinical evaluation. *Lasers Med Sci.* 2016; 31(8):1607-1611.
26. Hunzeker CM, Weiss ET, Geronemus RG. Fractionated CO2 laser resusrfacing: our experience with more than 2000 treatments. *Aesthetic Surg J.* 2009; 29(4):317-322.
27. Prignano F, Campolmi P, Bonan P et al. Fractional CO2 laser: a novel therapeutic device upon photobiomodulation of tissue remodeling and cytokinic pathway of tissue repair. *Dermatol Ther.* 2009; 22 Suppl 1:S8-S15.
28. Geronemus RG. Fractional photothermolysis: current and future applications. *Laser Surg Med.* 2006; 38(3):169-176.
29. Kohl E, Meierhöfer J, Koller M, et al. Fractional carbon dioxide laser resurfacing of rhytides and photoaged skin-a prospective clinical study on patient expectation and satisfaction. *Lasers Surg Med.* 2015; 47(2):111-119.
30. Miller L, Mishra V, Alsaad S, et al. Clinical evaluation of a non-ablative 1940 nm fractional laser. *J Drugs Dermatol.* 2014; 13(11):1324-1329.
31. Brauer JA, McDaniel DH, Bloom BS, Reddy KK, Bernstein LJ, Geronemus RG. Nonablative 1927 nm fractional resurfacing for the treatment of facial photopigmentation. *J Drugs Dermatol.* 2014; 13(11):1317-1322.
32. Sanders ME, Klaenhammer TR, Ouwehand AC, et al. Effects of genetic, processing, or product formulation changes on efficacy and safety of probiotics. *Ann NY Acad Sci.* 2014; 1309:1-18.
33. Cinque B, La Torre C, Lombardi F, Palumbo P, Van der Rest M, Cifone MG. Production conditions affect the in vitro anti-tumoral effects of a high concentration multi-strain probiotic preparation. *PLoS One.* 2016; 11(9):e0163216.
34. Cinque B, La Torre C, Lombardi F, et al. VSL#3 probiotic differently influences IEC-6 intestinal epithelial cell status and function. *J Cell Physiol.* 2017; 232(12):3530-3539.
35. Biagioli M, Laghi L, Carino A, et al. Metabolic variability of a multispecies probiotic preparation impacts on the anti-inflammatory activity. *Front Pharmacol.* 2017; 8:505.
36. Trinchieri V, Laghi L, Vitali B, et al. Efficacy and Safety of a Multistrain probiotic formulation depends from manufacturing. *Front Immunol.* 2017; 8:1474.
37. Zacarìas MF, Costa Souza T, Zaburlìn N, et al. Influence of Technological Treatments on the Functionality of Bifidobacterium lactis INL1, a Breast Milk-Derived Probiotic. *J Food Sci.* 2017; 82(10):2462-2470.

Courses and Congresses

2018

7 - 8 September - Paris (France)
39th National Congress SFME
French Society of Aesthetic Medicine
Palais des Congrès de Paris
President: J.J. Legrand
Email: congres@sfme.info
Website: www.sfme.info

27 - 30 September - Warsaw (Poland)
XVIII International Congress of Aesthetic and Anti-Aging Medicine
Poland Society of Aesthetic and Anti-Aging Medicine - PTMEiAA
Hilton Warsaw Hotel and Convention Center - Warsaw
President: A. Ignaciuk
Web: www.icaam.pl

26 - 27 October - Toronto (Canada)
CAAM 15th Annual Conference
Canadian Association of Aesthetic Medicine
Hilton Toronto / Markham Suites Conference Centre
President: R. Van Aardt
Web: www.caam.ca/annual-conference

9 - 11 November - Miami (Florida - USA)
15th Annual AAAM Congress
American Academy of Aesthetic Medecine
JW Marriott, Miami
President: M. Delune
Email: delegate@aaamed.org
Web: www.aaamed.org

2019

9 - 10 March - Seoul (Korea)
22th World Congress of Aesthetic Medicine - UIME
Organised by: Korean Academy of Aesthetic Medicine
Coex, Seoul
President: Wooha Han
E-mail: with@thewithin.co.kr

26 - 27 April - Brussels (Belgium)
Congress SBME - BVEG 2019
Belgian Society of Aesthetic Medicine
Radisson Blu Royal Hotel
President: J. Hebrant
Web: www.radissonblu.com

2020

15 - 17 October - Quito (Ecuador)
XIII Pan American Congress of Aesthetic Medicine - UIME
Organised by: Ecuatorian Society of Aesthetic Medicine
President: V. Tinoco Kirby
Email: medesteticapanam2020@gmail.com
Web: www.seem.com.ec

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