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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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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 consumption 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.

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References

Citing AMA guide website. http://libguides.stkate.edu/content.php?pid=99799&sid=749106. 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 cannot 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 Médecine Esthétique,* 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. Obagi). 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 post-op. 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 Médecine Esthétique* (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, MD
General Secretary 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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Atenea®, a new technique for the correction of tear trough deformity

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ABSTRACT

Tear trough deformity is one of the most frequent complaints from for patients who want an aesthetic procedure and one of the most challenging non-invasive treatments for physicians. Recently, there has been consensus in accepting restoration of volume as part of an overall rejuvenation strategy. Hyaluronic Acid (HA) filler injection is the procedure most frequently performed for the correction of this area and although the standard technique is safe when carried out by experienced doctors, adverse effects are still quite common. In order to overcome such adverse events, I recently developed the Atenea® tear trough correction technique, which delivers spectacular results while minimizing side effects. Its pillars are: top product selection and highly skilled application.

In this non-interventional, non-randomized, retrospective and descriptive work, 101 tear trough deformity correction procedures were evaluated.

Aesthetic results were immediately visible, a long-lasting effect was observed and unlike conventional techniques, Atenea® was characterized by almost no edema or downtime: patients were able to resume their daily activities immediately after injection.

Keywords
tear trough, nasojugal line, filler, rejuvenation

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Introduction

Tear trough deformity is one of the most frequent complaints form patients who want an aesthetic procedure and one of the most challenging non-invasive treatments for physicians[1,2,3,4]. Ten years ago it was even declared to be the most challenging procedure[3]. Since then, tear trough deformity treatment has been significantly developed and now many techniques are available. Physicians and surgeons who want to treat tear trough deformity can now choose the most suitable solution among different options from the well-known Hyaluronic Acid filler injection to fat grafting or even a skeletal implant[5]. Non-surgical techniques have gained wider acceptance by both patients and doctors[6,7], and the global trend is to choose non-invasive, natural, short-downtime, long-lasting and non-permanent procedures when possible.

Despite this more recently there has been consensus in accepting restoration of volume as part of an overall rejuvenation strategy. In youth, malar fat extends below the orbicularis oculi muscle (its ocular portion) to the orbitalrim. This occurs because of the fastening of the orbitomalar ligament fastening but, as time goes by, the strength of this ligament diminishes, fat tissue is lost and the skin gets thinner, revealing the nasojugal line. Because of tissue absorption, the globe will have a sunken appearance that will result in the casting of a shadow over the lower eyelid which ultimately characterizes the tear trough deformity[5] (commonly perceived as dark circles)[8]. The cause of this shadow maybe due to several factors, such as skin thickness, pigmentation or superficial blood vessels[9]. Though all these may play a role in tear trough deformity, it is not clear to what extent each factor is more or less individually relevant. From a clinical point of view, patients always look tired even if they are well rested. Thus, this look will not change unless treated properly. Unfortunately, most of aesthetic protocols overlook tear trough area treatment.

Hyaluronic Acid injection is the procedure performed the most frequently performed for the correction of the tear trough deformity. At the same time, too many commercial brands are available and provide physicians with an enormous choice of products (some of them are not even suitable for an effective and safe treatment of this area). Moreover, although the standard technique is safe for experienced doctors, adverse effects remain quite common[10]. Indeed, typical adverse effects with dermal filler injection in the tear trough area most often include bruising, erythema, and local swelling. In addition, there is always a risk of: asymmetry, pain, Tyndall effect, edema, post-inflammatory hyperpigmentation, infection or product protrusion. Because of all these associated risks, a proper product selection and a physician's expertise are the two determining factors towards a good treatment outcome and true patient satisfaction.

A new technique was also urgently needed to avoid these complications. This was the main reason for me to create the Atenea® technique. I named it after the Greek goddess, because she was admired and venerated for her sharp looks and the beauty radiating from her eyes. Atenea® tear trough area correction technique is based on the two pillars mentioned above: a) a proper product selection and b) a highly skilled application.

Materials and Methods

In this non-interventional, non-randomized, retrospective and descriptive work, 101 procedures performed during 2014 were evaluated (74.1% women and 25.9% men). Age ranged from 25 to 65 years old. Inclusion criteria: tear trough deformity correction treatment due to weight-loss, age and/or phenotype related causes.

Analyzing the tear trough symptomatology was also crucial. Negative results in all semiological tests were required for patient inclusion: semi-recumbent position, pressure, and Snap Test. All procedures were performed by the same physician at "*Dra. Natalia Ribé Institut*", Barcelona, Spain. Exclusion criteria included: pigmented under-eye circles, large palpebral and malar bags and history of:

a) hypersensitivity to any of the components of the products used;

b) autoimmune diseases such as: type 1 diabetes, rheumatoid arthritis, ankylosing spondylitis, psoriasis, thyroid pathologies, inflammatory bowel diseases, all types of lupus, multiple sclerosis or hemorrhagic rectocolitis;

c) skin conditions such as herpes, acne or rosacea;

d) unhealed skin alterations;

e) prior injection of permanent products such as silicones, polymers or acrylics.

Product used

Teosyal® Redensity [II]® from Teoxane Laboratories (Geneva, Switzerland), was used for the treatment of all cases in the study because this product has technical and mechanical specificities that are highly suitable for the treatment of the tear trough[11,12]. Composition: Semi cross-linked Hyaluronic acid 15mg/g, Lidocaine hydrochloride 3mg (0.3% final), nutrients' enriched buffer (patented) consisting of: 8 amino-acids (L-glycine, L-valine, L-threonine, L-proline, L-arginine, L-isoleucine, L-leucine, L-lysine), 3 antioxidants (α-lipoic acid, glutathione, N-acetyl-L-cysteine), 2 minerals (zinc acetate dihydrate and copper sulfate pentahydrate) and vitamin B6.

Protocol

First, the needle (ideally 28 G x 19mm) is gently inserted into the skin perpendicular to the skin

surface, until it touches the periosteum. The needle is then reoriented horizontally so that it is parallel to the underlying bone plane and further inserted (without injecting) until it reaches the injection area. The product is applied deeply between the orbicular muscle and the orbital contour.

With the Atenea® technique, multiple entries are not required: it was actually designed to allow a comfortable treatment of the entire area with only 2 entry points. The injection itself is then applied using a classic, linear, retrograde, fan technique. Topographically, the procedure sweeps from the anterior lacrimal crest (nasojugal line) to the lateral rim.

Overcorrection was also avoided using a specific amount of product. The maximal quantity applied per session was 1 ml in total (0.5 ml for each tear trough area). Only 10.31% of procedures required more product injection during a touch-up session. Patients were followed-up for 12 months: 4 post-treatment control visits were done at 1 week, 6 months, 9 months, and 12 months.

Results

Of the 101 patients included in the study, 4 were lost for reasons unrelated to treatment: 2 patients moved to another country, one patient refused to take control pictures and a fourth patient was travelling. Therefore, the results shown here are for a final sample of 97 patients. As with any other filler, aesthetic results were immediately visible.

However, unlike with conventional techniques and unspecific products, injection of Teosyal® Redensity [II] with the Atenea® technique was characterized by no edema or downtime. Patients were able to resume their daily activities immediately after injection. Adverse effects were rare, mild, and reversible. The most common adverse effects were edema (3.88%) and hematoma (4.85%). Edema occurred in patients with sunken under-eye circles together with edema due to fluid retention. All cases were resolved with local manual lymphatic drainage. In one case the patient massaged the treated area too forcefully and required corticoids (Zamene® 6 mg, two tablets every 12-24 hours for 3 days).

Hematomas were resolved with oral homeopathic therapy, topical cream with vitamin K oxide, and application of galvanic current (Mei Light Technology®). No significant adverse effects were observed (Tyndall effect 0%). Regarding the follow-up, almost all patients (96.91%) still enjoy the benefits of treatment at the 12-month control visit (89.69% of these patients received only 1 ml). The observed long-lasting effect of the product is likely due to its composition, which is especially designed for the tear trough area, and to the fact that this area is not rich in hyaluronidase. Future studies should be able to estimate the maximum duration of this product, which is clearly over one year.

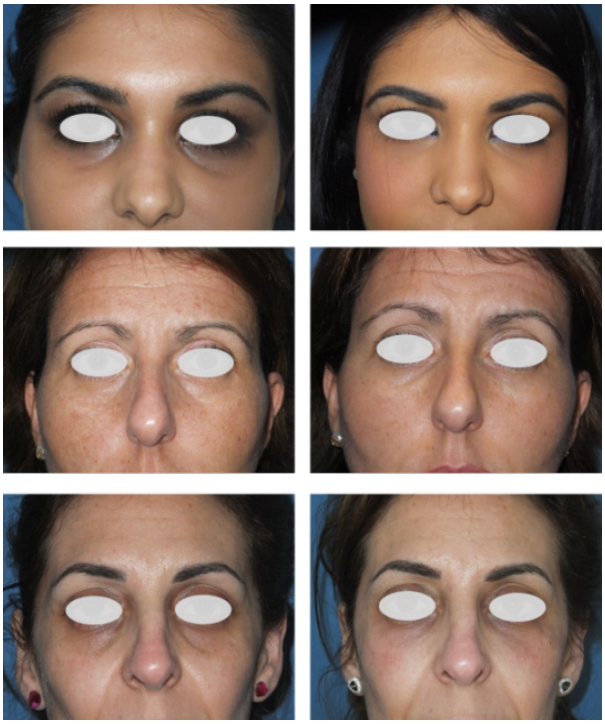

Figure 1 - Before and after pictures

Discussion

The product used is not a standard and traditional hyaluronic acid filler, but a gel containing a combination of hyaluronic acid and a nutrients' enriched buffer.

The formula, specially designed for the treatment of the under-eye circles, consists of a semi cross-linked HA with a concentration of 15 mg/g. This mix between the free and the cross-linked HA generates a moderately hygroscopic gel that absorbs a minimum amount of water. Its low hygroscopic power, combined with the improved skin elasticity and quality it appears to produce, are most likely caused by a very low incidence of post-injection edema with this product.

This is a significant advantage that translates to virtually no downtime, compared to the high frequency of edema reported with other products and techniques[10].

In addition, another huge benefit associated with the combined use of the Atenea® technique and Redensity [II] is the greater comfort it generates during and after the whole process. Indeed, Atenea® is a painless technique and Redensity [II]® includes lidocaine.

The formula of the product includes 8 amino acids, 3 antioxidants, 2 minerals and vitamin B6. The improvement promoted by these nutrients in terms of tear trough skin quality, increased skin thickness, synthesis of collagen and skin's mechanical properties, may also be responsible for the absence of adverse

effects observed with the combination of Atenea® and this product. It is important to note that, as with any other filler injection technique, patient selection is mandatory. Atenea® also needs two additional and important considerations:

a) it requires a broad anatomic knowledge of this specific area, and b) expert needling technique and injected volume must be extremely precise as the tear trough area has low levels of hyaluronidase.

It is also worth noting that with this product and technique no patients required another injection for at least 12 months, which is apparently a longer lasting effect of the treatment compared to the use of other techniques and products. Indeed, other authors have reported that certain techniques require repetition of treatment in up to 90% of cases[13], and results usually last from 8 or 10 to 12 months[10,14], depending on the author. A point of controversy remains the use of either a needle or a cannula. I personally prefer to use a needle because it allows me to control the depth of injection and the amount of injected product with a lesser degree of post-treatment inflammation. The 101 procedures described in this work were carried out with a needle technique.

To conclude, Atenea® is a safe, outcome- and comfort-improving technique that can be applied to any skin type and for patients suffering any kind of compromise of the tear trough or periorbital area: under-eye circles, lacrimal line, palpebromalar line, malar under-eye circles or minimal palpebral fissure.

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7-point lift effect technique with hybrid cooperative complexes for the treatment of laxity associated with the inner arm

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ABSTRACT

In female patients, the medial region of the arms is often affected by skin laxity and reduction of elastin and collagen fibres. The author proposes a treatment with a 7-point technique using an innovative non cross-linked hyaluronic acid, based on hybrid cooperative complexes of high and low molecular weight hyaluronic acid. The treatment showed a visible improvement of tone and texture in the treated tissue and may be employed in combination with other treatments for this area for a synergic effect.

Keywords
Natural hyaluronic acid, hybrid cooperative complexes, skin laxity, inner arm, bioremodeling

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Introduction

In recent years concern with body appearance has gained great importance in society because beauty affects self-esteem and quality of life[1]. This fact contributes to the increased demand for beauty treatments. Among unaesthetic disorders, roughness and loss of elasticity (laxity), especially of the skin have a great impact on the quality of life in psychological and sociocultural terms[2].

Skin laxity is an aesthetic problem that first appears between the ages of 35 and 40, although it generally becomes evident from age 40 onwards. Problems with skin laxity sometimes appear in younger people as a consequence of pregnancy or sudden weight loss[3].

Laxity is a skin disorder that occurs with natural or accelerated ageing and is structurally linked to diminished collagen production. The number and vitality of fibroblasts decrease and both dermis and fibrous septa undergo partial loss of their natural ability to replace themselves. The morphological changes that appear are the result of diminished biosynthesis of collagen and elastin and abnormalities of the extracellular environment with a decrease in the concentration of hyaluronic acid[4]. These changes occur early in the inner arms, legs and abdomen. Skin laxity is associated with lack of physical exercise, rigorous dieting and other causes and it often appears in combination with cellulite. Cellulite is an inflammation of the subcutaneous adipose tissue and has several causes. It occurs mainly in the legs, buttocks, hips, breasts, arms, and neck[5].

In female patients, the medial region of the arms is often affected by skin laxity due to the reduction of elastin and collagen fibres caused by weight loss and menopause.

The human dermis consists mostly of type I collagen, composed of 3 polypeptide chains stabilised by a triple-helical conformation[6]. Using the microscope, it is observed that with age there is an increase of collagen network density and reduced stability of cross-links[6,7]. Elastin, the main component of dermis elastic fibres, shows signs of decreased function and therefore provides less resistance and traction capacity. Atrophy of subcutaneous fat is also noted[7]. Despite the relatively better results of invasive treatments on skin laxity, sequelae and complications caused by treatment lead to increased demand for non-invasive or minimally invasive procedures[8,9].

To meet the ever-growing public demand for significant, non-invasive skin lifting and tightening procedures, numerous solutions have been developed. Some devices based on a range of energy technologies have recently been developed including High Frequency Ultrasound (HFU) and monopolar radiofrequency (RF)[10,11,12].

Both RF and HFU act through selective and controlled temperature increase in the tissue. The goal is to induce thermal damage to stimulate neocollagenesis in the skin's deep layers and subcutaneous tissue[13]. Literature is however not unanimous in relation to the occurrence of these benefits[14]. Other solutions are based on mechanical actions resulting from the use of other medical devices such as non cross-linked or cross-linked hyaluronic acid implants or polylactic acid implants or PDO threads. The goal is not only immediate mechanical support but also long term stimulation of the neocollagenesis process.

The aim of this article is to share my personal clinical experience on treatment of skin laxity, associated with the inner arm, using an innovative 7-point technique by means of a medical device for intradermal use based on stabilised hybrid cooperative complexes of non cross-linked hyaluronic acid (HA) obtained by a new technology (NAHYCO technology).

Materials and methods

The subject of this clinical experience is the 7 point technique: a technique that I have personally developed thanks to the characteristics of low viscosity and high spreadability of hybrid cooperative complexes that, once injected in seven boluses following the scheme in Figure 1, achieve a homogeneous result with a high lifting effect.

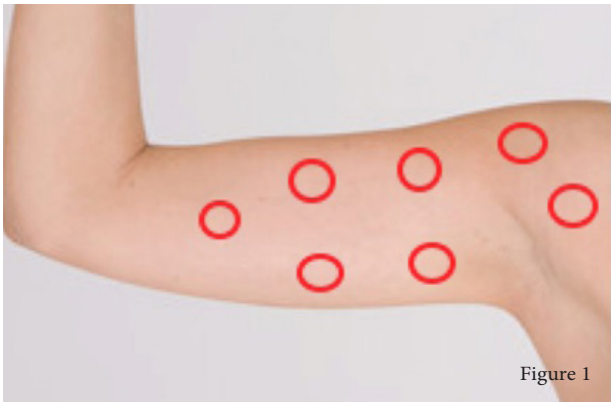


Figure 1 - Scheme of the injection points of the 7-point technique

A new medical device for intradermal use containing 64 mg of hyaluronic acid sodium salt in 2 ml of buffered saline (HA concentration 32mg/ml) was employed in this evaluation. The device is produced and distributed by IBSA Farmaceutici Italia Srl with the name PROFHILO® and is available in a blister containing a 2.25 ml syringe with two 29G TW 13 mm needles. This product is based on hybrid HA cooperative complexes. NAHYCO technology is a patented thermal process which allows the combination of 32mg low molecular weight (LMW, MW: 80–100 KDa) and 32mg high molecular weight (HMW, 1100–1400 KDa) ultrapure hyaluronic acid sodium salt to create a stabilised hybrid cooperative complex with a total HA concentration of 32 mg/ml.

The stabilised hybrid HA cooperative complexes are formed without the addition of any chemical cross-linking compound.

The hybrid cooperative complexes have several advantages compared to HMW-HA and LMW-HA alone[15]:

a) Greater half-life - hybrid cooperative complexes have a greater resistance to hyaluronidase (BTH) compared to H-HA.

b) Low inflammatory response - TGF-β1 are less up-regulated in hybrid cooperative complexes treated samples compared to cells treated with L- HA.

c) Low viscosity - hybrid cooperative complexes have a lower viscosity than L-HA and H-HA alone.

In order to maximize the benefits of hybrid cooperative complexes (high concentration, spreadability, long tissutal duration and high biological activity), following the rationale of the BAP (BioAsthetic Points) technique[16-19], a safe, effective and minimally invasive technique has been developed and employed for the treatment of skin laxity associated with the inner arm.

Four female patients aged between 35 and 65 years were treated using the 7-point technique.

Before treatment the patients were informed about the risks and benefits of this treatment and an informed consent form was signed.

The ideal patient for the 7-point technique doesn't present an excessive subcutaneous fat layer and/or skin laxity. To establish these exclusion criteria the Pinch-Test and the Stretch-test were performed, using a plicometer and caliper respectively. Patients undergoing the Pinch-Test with an upper fold thickness higher than 2 cm were excluded (Figure 2a). Patients undergoing the Stretch-Test with stretching greater than 50% of the initial length were excluded (Figure 2b).

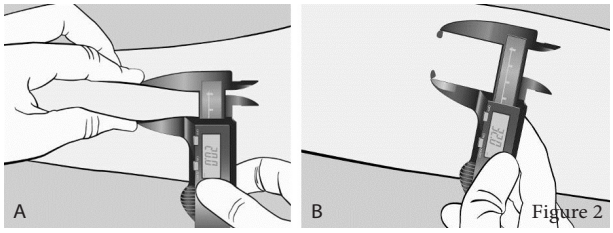


Figure 2 a-b - Evaluation of the exclusion criteria: a) Pinch-Test - b) Stretch-Test

Both the Pinch-Test and Stretch-test measurements were taken with the patient standing and the arms relaxed along the body.

Moreover, patients presenting the following exclusion criteria were excluded:

- Patients with permanent fillers at the injection site
- Patients being treated for hemostasis disorders and/or with coagulants
- Patients with autoimmune collagenopathies
- Patients with an active skin infection or inflammation
- Patients with localized head infections or generalized inflammation
- Chronic inflammatory state
- Hypersensitivity to HA
- Pregnancy or breast-feeding

About 0.3 cc of the product was injected at each point using a 29G 13 mm needle: the injection depth was about half the needle length. 2 ml (one syringe) per arm was injected during each treatment and 2 treatments with a 3 week interval were performed.

Pictures of the treated area were collected at baseline before the first treatment and during the last follow-up visit one month after the second treatment.

Results

The treatment showed a visible improvement in tone and texture of the treated tissue as clearly illustrated in Figures 3-6.

Two patients were already satisfied after the first treatment and 2 were very satisfied. After the second treatment 3 were very satisfied and one was satisfied. The procedure was well tolerated by the patients and only light bruising was reported in 3 out of 8 cases

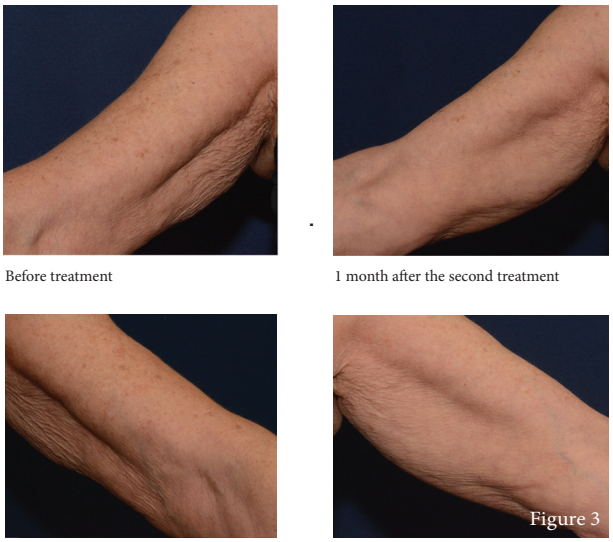
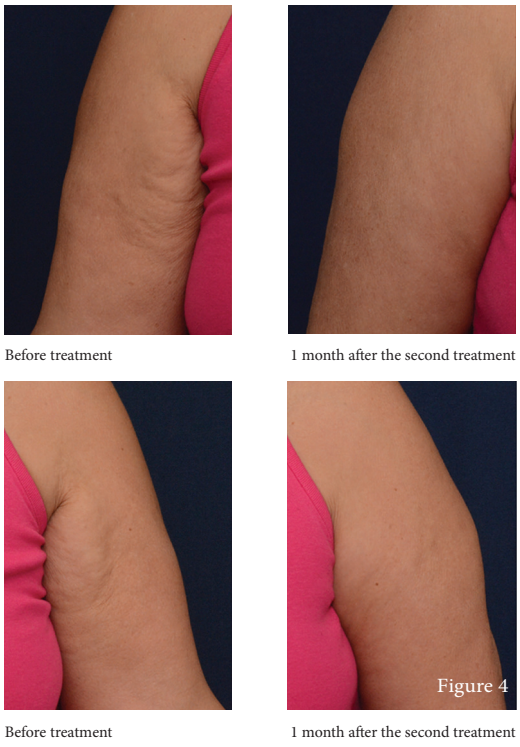


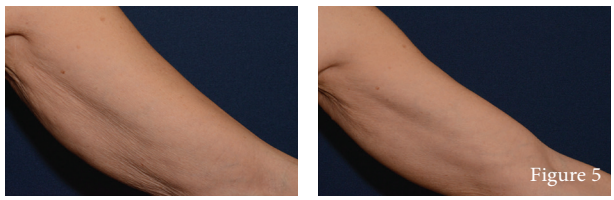
Figure 3 - Patient age 61. Left picture: before treatment; Right picture: 4 weeks after the second treatment



Before treatment | 1 month after the second treatment

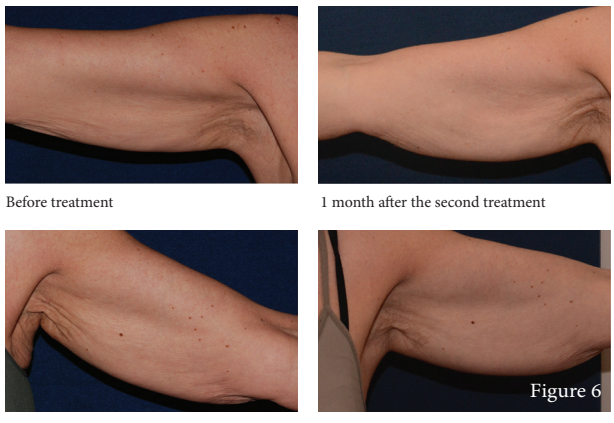
Before treatment | 1 month after the second treatment

Figure 4 - Patient age 57. Left picture: before treatment; Right picture: 4 weeks after the second treatment



Before treatment | 1 month after the second treatment

Figure 5 - Patient age 55. Left picture: before treatment; Right picture: 4 weeks after the second treatment



Before treatment | 1 month after the second treatment

Before treatment | 1 month after the second treatment

Figure 6 - Patient age 65. Left picture: before treatment; Right picture: 4 weeks after the second treatment

Discussion and conclusions

Skin ageing can be divided into two processes: intrinsic and extrinsic ageing or photoageing. The first is a natural, slow and gradual process due to internal factors. The second is exacerbated by environmental factors such as improper exposure to sunlight. Both are accompanied by changes in morphological and biomechanical properties of the skin[20-24]. The main clinical characteristics of aged skin are increased rugosity and loss of elasticity (laxity)[25].

In female patients, the medial region of the arms is often affected by skin laxity and reduction of elastin and collagen fibers caused by weight loss and menopause. Currently, there are several invasive and non-invasive strategies to treat unaesthetic disorders[11,12].

Despite relatively better results of invasive treatments, sequelae and complications caused by treatment lead to the increased demand for non-invasive or minimally invasive procedures[8,9].

HA hybrid cooperative complexes were developed to support tissue regeneration and activate remodeling of collagen and elastic fibers[14]. For this reason, hybrid complexes are indicated for remodeling skin laxity. Starting from the experience of Beatini A et al.[16], Moises RA et al.[17], Laurino C et al.[18] and Sparavigna A et al.[19] of skin laxity associated with the malar-submalar area treated using hybrid complexes with the BAP Technique, the 7-point technique was developed and employed for the treatment of skin laxity associated with the inner arm.

The considerations about my experience are that treatment was easy, minimally invasive and well tolerated by patients. At the same time the results were impressive both from a clinical point of view and from of the patients' point of view.

Although this was only the first, preliminary and limited experience regarding this indication, the 7-point technique has met all requirements to be considered a safe and effective new option for the treatment of skin laxity associated with the inner arm. The 7-point technique has been developed thanks to the characteristics of hybrid cooperative complexes.

In fact the most common non cross-linked HA injectable devices indicated for facial implants show a poor-to-no lasting result on the inner arms. At the same time cross-linked HAs have a poor spreadability with unnatural results.

The next step, aside from increasing the number of treated patients, will also be to evaluate the efficacy of this treatment in combination with other technologies in order to maximize the final results (RF, HIFU, threads).

A combined approach should be strongly recommended in those patients who do not meet the inclusion criteria of the Stretch-test and Pinch-test.

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Biostimulation threads: scientific evidence and systematic review of their efficacy and safety

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ABSTRACT

Introduction: Sustaining and/or biostimulation threads are procedures requested very frequently because they are less invasive treatments than classical lifting, carry a lower risk and allow for a quicker recovery.

Objective: To assess the efficacy, safety and scientific evidence of sustaining and/or biostimulation threads.

Materials and Methods: Various databases were consulted, using a systematised search from 1999 through June 2016 in the attempt to extract the greatest possible number of publications related to threads and placement techniques, adverse effects and complications.

Results: The publications studied were divided into 4 large groups: a) Antecedents and historical evolution, b) Clinical studies, c) Reviews on efficacy and effectiveness, and d) Studies on adverse effects and complications.

Conclusions: Clinical efficacy of thread treatments, whether absorbable or non-absorbable, is still unknown. Adverse effects and complications are well known and are, generally speaking, minor, transitory and easy to prevent and/or resolve. New studies are needed to obtain accurate assessment of treatments with biostimulation threads.

Keywords
Threads, biostimulation, effectiveness and safety, adverse effects, complications

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Introduction

Over the current century, treatments with various threads have been increasing more and more. Absorbable thread procedures, which are deemed to have biostimulating and bioregenerative properties, have undergone the greatest growth, in line with so-called minimally-invasive treatments. The threads are mainly used in facial and neck rejuvenation, to lift up flaccid tissue and place it in its original site. Thread treatment attempts to imitate what is still the gold standard, surgical lifting, when the aim is to correct flabbiness and eliminate excess skin.

Good results have been obtained with classical surgical lifting. However, physicians and patients look forward to the development of less invasive treatments with a lower incidence of undesirable effects such as those associated with classic rhytidectomy: infection, skin necrosis, haematoma, seroma, neuritis of the facial nerve, complications from general anaesthesia and/or sedation and the risk of visible scars. The new treatments, besides being associated with lower risks, have a shorter recovery time, although the results obtained do not always fulfil the expectations of patients and doctors involved.

Among the pioneers in using threads for aesthetic purposes was Buttkewitz[1], who used a nylon suture to correct the nasolabial fold in 1955. The concept of applying subcutaneous threads as currently used began however with Sulamanidze, who first introduced and reported on this procedure in 1999, although the first Medline indexed publication dates from 2002[2]. These initial polypropylene threads, marketed as Aptos™ (anti-ptosis), matched the concept of tensor threads while simultaneously inducing the formation of collagen, essential for the threads to maintain their traction on the tissue. From then on new materials and varying techniques were developed with the objective of acting against the gravitational fall of the face soft tissue, especially in the middle third.

There are currently numerous threads available to doctors, and of many different compositions, as can be seen in Table 1 (only a brief summary of the best known at present). These threads are constantly evolving and are manufactured in different types of materials, chiefly polypropylene (PP), polylactic acid (PLA) and polydioxanone (PDO). Their range varies considerably, depending on the type of thread and the areas of the face and/or neck where they are placed. The threads are also known according to their physical properties: mono- or polyfilament, with spicules, barbs or cones (uni- or bidirectional). The feature that all share is that they are placed using needles of various thickness or length, depending on the chosen technique or the problem to be treated (Table 2).

Even though the use of threads is increasingly common, the base mechanism of action in tissue is still unknown, although the tensor effect is usually obvious as soon as the threads are implanted. The threads produce traction, either by positioning them with spicules, teeth or cones, or by anchoring them to fixed structures such as the fascia or in the periosteum itself.

Type	Brand	Material	Technique
Non-absorbable	Aptos Contour Polycon	Polypropylene Polycaproamide	Sulamanidze Wu: MIZ-lift Serdev: Attatchment bone
	Premicron 3/0	Twisted Polyester	Flórez&Trelles: Face up
Mixed	Silhouette Suture	Polypropylene + Lacto-Glycolic	Fascial anchorage
	Happy Lift	Caprolactone	Savoia
Absorbable	Silhouette Soft	Polylactic acid + Lacto-Glycolic	Subcutaneous anchorage
	V Lift Pro JBP V Lift	Polydioxanone (PDO)	Skin tension lines

Table 1 - Summary of different biostimulation threads used in treating facial and neck ptosis

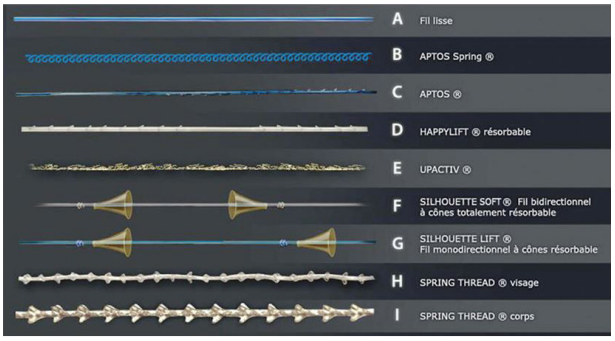

Table 2 - Selection of models and brands of threads commonly used in the treatment of facial ptosis

The biostimulating effect is more controversial because studies are still limited and it remains to be seen which part is due to trauma secondary to introducing the needles, to the role that vasodilatation and hyperaemia play or to the inflammatory effect triggered after inserting the thread in the skin. A true biostimulating effect should include increasing type III collagen and connective tissue, with improvement of skin elasticity, firmness and thickness whilst also increasing action against free radicals. Until now, based on what has been published, it seems clear that a fibrosis reaction is induced around the threads and their extensions, although this is mainly due to the appearance of type I collagen[3].

Placing PP and PLA threads normally requires a loco-regional anaesthesia injection, while PDO threads can be implanted with topical cream anaesthesia. There is general

consensus on adverse effects and complications associated with using threads. They are mild or moderate and easily resolved, although there have been more dramatic cases reported. In contrast, the efficacy of thread treatment and how long it lasts are what generates most questions as the published studies only cover follow-up periods of no longer than 2 years.

Another problem that this review study brings to light is the frequent combination of thread treatment with other aesthetic techniques: peelings, laser use and filling materials are common. This makes it difficult to attribute the benefit to only the threads. It is likewise appropriate to point out that the same surgeons who developed the various types of threads also patented them. This presents an undeniable conflict of interests in communicating patient satisfaction results, long-term efficacy and secondary effects from the use of these treatments.

Objective

The objective of this study was to assess the efficacy, safety and scientific evidence of suspension and/or biostimulation threads used in the treatment of face and neck ptosis. To do so, various scientific publications have been searched and analysed. The first publications considered were those indexed in the Medline database (PubMed), followed by those published by scientific societies of proven reliability and, lastly, publications found in Google Scholar that complied with the requirements of this bibliographical review. Our personal experience was also taken into account.

Materials and methods

To gather the information, various databases ranging from 1999 to June 2016 were consulted. These were systematically searched, beginning with the Medline database (PubMed). The initial search terms were: *threads, rejuvenation, facial, neck, facelift, threadlift*.

These were then added to and combined with the following terms: *sutures, barbed, cones, cogs*. Specific brands and types of threads were also searched for: *aptos, contour, silhouette, polydioxanone, polylactic acid and polypropylene*. Finally, the terms *adverse effects* and *complications* were added to the search.

The information on threads, gathered from the journals of the Aesthetic Medicine Societies in Spain, France and Italy were considered relevant, given that these societies are the oldest and most prestigious in Europe. The search for journals with scientific support was widened to include other Latin American medical societies. The same criteria were also used in the Google Scholar search. The purpose was to extract the maximum number of publications related to techniques and types of threads. In addition, information on adverse effects and complications (from both clinical and histological point of view) was sought.

Results

A total of 57 publications were chosen based on their content with regard to applying different tensor, suspension and/or biostimulation threads. The technique used, clinical assessment, histological evidence, patient satisfaction, achieved results and adverse effects or complications associated with their use were taken into consideration.

The publications studied covered a period of 15 years, from 2001 until June 2016, and were divided into 4 groups: a) Antecedents and historical evolution, b) Clinical studies, c) Reviews of efficacy and effectiveness and d) Studies on adverse effects and complications.

Group I: antecedents and historical evolution of treatment using threads

Sulamanidze is considered to be a pioneer in the development and application of threads to lift the face soft tissue for aesthetic purposes[4,5]. As the owner of the international patent for Aptos™ threads (or Russian threads), he was the first to report good results obtained with this type of PP thread[2]. Treatment with the original threads was relatively simple, requiring local injection of anaesthetic and it was not very invasive. The results however did not meet the expectations of the medical community. Consequently, new types of Aptos™ threads were designed along with different placement techniques for a better approach to facial ptosis, including recommendations aimed at avoiding possible secondary effects and complications that had been detected with this type of threads in previous years[7–13].

Many authors have reported their personal experience with the use of threads in the following years. Their publications cannot however be considered clinical studies since they only describe the authors' own procedures and lack the methodology required for a clinical study on a group of patients.

In 2004, Wu[14] reported the combination of 2 types of PP threads: one was the well-known Aptos™ thread, while the other was a type of longer threads, appropriate for heavier tissue, that had been developed and patented by the author, who called them Woffles™ threads. According to the author, better results could be obtained than using only Russian threads. Nonetheless, this was not a true clinical study, but rather a descriptive study on results achieved in patients that had undergone this treatment technique.

In 2006, it was the group of Horne et al.[15] that reported on some new PP threads, Contour™ threads.

Their study indicated very satisfactory results, although it lacked, in particular, an in-depth follow-up of the duration of these results and complications were not reported throughout the study period mentioned.

In 2008, Paul[16] published an article, based on his experiences, on indications and techniques for using threads with spicules to address drooping at the end of the eyebrow, of the middle and lower third of the face and for neck ptosis. He indicated that he obtained good results with permanent spiculated threads as long as the sutures were adjusted after the intervention. In that same year, Kalra[17] reported his personal clinical experience without providing reliable data on effectiveness or efficacy.

Also in 2008, Isse[18] reported his technique using mixed PP suture and resorbable PLA cones for the treatment of tissue repositioning in the cheek area. He indicated that the technique was appropriate if what was sought was a moderate lifting, with a short improvement period otherwise it should be combined with an open surgery technique.

In 2014, in a new article[19], Wu confirmed the same points he had made 10 years earlier, indicating that his long threads (Woffles™) for temporal fascial implantation offered better lifting results than other procedures and that it was possible to combine them with Aptos™ threads.

We again described his 2004 technique, which he named *Waptos*. Curiously, he made it clear that this technique produced better results if it was combined with other aesthetic procedures, such as implantation of autologous fat.

Group II: clinical studies

The second group is characterised by articles based on the study of specific patient groups. Many are retrospective studies but their methodology makes it difficult to evaluate the results mentioned by the authors.

Firstly there is a 2002 retrospective study by Adamyan and Sulamanidze[12] on 186 patients who received treatment between 1999 and 2001. The systematisation of the study is limited, given that 53 patients received a treatment combined with other techniques and that there is no objective or subjective assessment of the results achieved or of patient satisfaction. Follow-up varies from 2 months to 2 years. In 2004, Lycka et. al[20] carried out a retrospective study on 350 interventions with Aptos™ thread. The authors reported excellent results, comparable to those of a surgical lifting although the study design makes it impossible to reach such conclusions. The adverse effects and complications (which they classified as minor) are well documented.

In a 2005 article on PP sutures with spicules, Lee and Isse[21] concluded that good midface results could be achieved, as long as the patients were carefully selected. The treatment was designed to improve the infraorbital hollow, nasolabial and labiomental creases and cheek ptosis. Of the 44 patients included in the study, 34 received an open procedure and 10 patients a closed one, with regard to the manner in which the threads were placed to improve their lifting functions over the selected areas.

In 2008, Flórez and Trelles[22] published a retrospective study on their own technique, which they called *Face up*. The importance of the study lies on the size of the sample: they performed 600 interventions using conventional braided polyester suture on 1 or more areas of the face in the same surgical step. The study is important because the authors described this technique very well through appropriate images (Figures 1, 2 and 3).

Patients were followed up for an additional 2 years (although many patients were lost to follow-up).

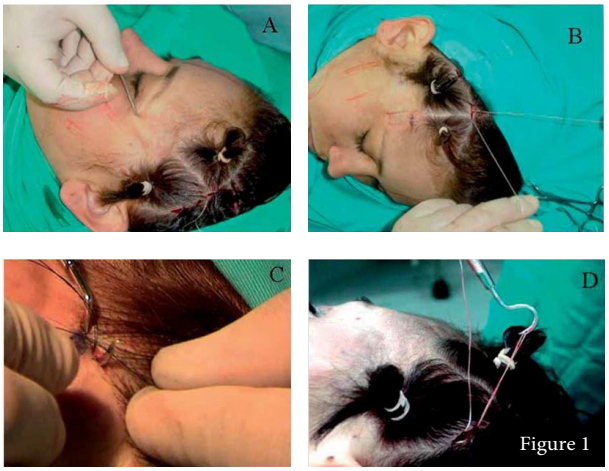

Figure 1 - Taken from the Flórez and Trelles article (Ref. 23). The technique is performed with special needles. (A) Twist of the Demax needle to perform the first anchoring; (B) upon return the needle provides the suture for the cephalic incision; (C) the hooked needle goes into the periosteum to pass the suture to the second anchoring; and (D) detailed view of the 2 ends of the sutures before making a knot to tighten the area of ptosis

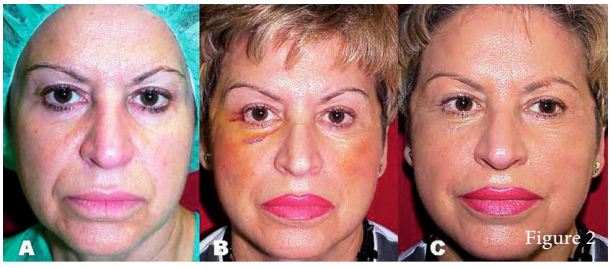

Figure 2 - 52-year-old patient, phototype III. (A) Before surgery with the "Face up" suture. (B) 24 hours postoperative. Note the excellent result. Good elevation of the treated areas has been achieved and ecchymosis that can appear as a secondary effect is clearly visible. (C) 24 hours postoperative. In the same control, once makeup cover has been applied, the secondary effects are hidden; this allows the patients to return to their jobs, which they appreciate, in contrast to the traditional facelift

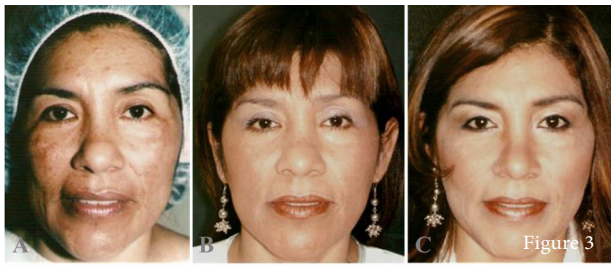

Figure 3 - 52-year-old patient, phototypes IV-V. (A) Before surgery, (B) 1 month after intervention, and (C) 1 year after surgery. Note the good results in elevation of the areas treated and their persistence

It should be mentioned that the study included both subjective and objective assessment of results.

In 2009, Gamboa and Vasconez[23] reported the results obtained with 17 patients to whom PP threads with PLA cones and surgical mesh were applied. In all, they performed 23 procedures aimed at improving midface and throat. Beyond the results obtained, it was the first time that a microscopic study was carried out on the fibrosis formed around sutures and cones.

Another 2009 publication was the retrospective study by Garvey et al.[24] on 72 patients, who were treated with spiculated PP threads. The study showed that the results using this technique alone were clearly insufficient. It should be emphasised that 76% of the patients were treated with only threads, while the remaining 24% received other treatments. The follow-up period was 2 years and included the assessment of the percentage of complications and new interventions, as well as how long the results lasted. 42% of patients required new treatment, with the new procedure being performed on average at 8.4 months after the initial thread placement. Some 31% of patients required a new surgical revision at an average of 8.7 months, while 11% of the patients treated had to have the threads extracted because they could be clearly palpated. In the same year, the study by Abraham el al[25] was published shortly afterwards. This study was well designed methodologically and it is the only one to date that includes a correct statistical analysis. The study covered 33 patients, with an average follow-up of 21 months (range between 12 and 31 months). Ten patients were treated with threads alone (Contour™ threads), while 23 patients received threads and other combined treatments. Another 10 patients were added as a control group, undergoing other procedures that were not threads. Results were assessed by 4 independent plastic surgeons unrelated to the procedure. In their conclusions they indicated that they thought the results were only short-term and were mostly due to oedema and surgical trauma. In the conclusions this type of threads was rejected for the treatment of aging and facial ptosis. A year later, in 2010, Rachel et al.[26] published a retrospective study carried out with 29 patients, treated with PP threads with spicules. Their objective was to determine the morbidity associated with this type of threads. Their analysis showed adverse effects in 69% of the patients treated, with an early recurrence rate of 45%. In the conclusions they clearly indicated that thread treatment is not a procedure with long-term results, that it is associated with a high morbidity rate and that it requires significant critical review.

In 2011, De Benito et al.[27] studied 316 patients with a follow-up period of 18 months. They recorded complications that they classified as minor, including pain over the temporal area in 7% of patients. This occurrence should be more common among the threads attached to the temporal fascia, but we have not found this in other studies. The authors of this study also concluded that result permanence beyond 18 months was still to be established.

In 2014, Park et al.[28] presented a retrospective study on 102 patients, of which 81 (79.4%) also received a fat implant. They nonetheless attributed the good results (98.1% satisfied patients) to the new spiculated PP threads, 15 cm long, placed in the submucosal plane of the superficial musculoaponeurotic system, between the superficial and deep fascia, through the premasseter space and then anchored to the temporal fascia. It is impossible to tell which patients obtained the best results in this study, whether it was those who received a fat implant plus threads or those who were treated with threads alone. In that same year, Savoia et al.[29] reported the results obtained with absorbable speculated PDO threads in 37 patients. The patients were selected because they needed only a moderate lifting. The study did not specify the number of patients who underwent complementary procedures, only that these were carried out on patients more than 45 years old. The treatments consisted of phenol or trichloroacetic (TCA) peelings, laser, radiofrequency or autologous fat implant. The methodological errors in the study are evident; it was however the first study on absorbable PDO threads indexed in Medline. Shortly afterward the article by De Carolis and Gonzalez[30] was published. In their study, inverted spicule nylon sutures were used to tighten the neck and define the mandibular line. The technique that they used is well described and they considered the selection of 67 patients (all aged under 50 years) to be important in obtaining good results.

Lastly, Consiglio et al.[31] published a histological and dynamometrical study on PP sutures with absorbable lacto-glycolic cones in 2016. They divided the 8 patients treated into 4 groups of 2 patients each, to obtain the threads implanted in the abdomen at 1, 3, 6 and 12 months, coinciding with the abdominoplasties programmed sequentially. Chronic inflammatory reaction lasted until the third month, drastically decreasing from the 6th month on, when collagen began to be deposited (although collagen type was not specified in the study). Degradation of cone material began at around 6 months and ended towards

12 months. According to the study, resistance to thread tension ebbed around the 12th month, coinciding with the weakening of the threads.

Group III: reviews on efficacy and effectiveness

The first review, in 2006, was carried out by Trevédic and Alkebaisi[32] based on their personal experience. They concluded that treatments with threads represented an aid in face lifts, especially when combined with other techniques. In their review on the duration of permanent thread treatment, they indicated that the results could vary quite a bit, from 2 to 4 years, although they did not quantify the rates. However, they also commented that the treatments could be short-lasting or have barely any effect after thread placement; they did not quantify these cases either. Villa et al.[33] carried out a systematic review in 2008 and found only 6 indexed articles that fulfilled the criteria of elevating midface tissue using threads with spicules.

The adverse effects that they found, common to all the studies, were mild or moderate, self-limiting and short-lasting. However, the data as to the degree of improvement reached and the duration of the lifting effect were not well gathered in the studies mentioned. Among the conclusions they emphasised that it was a technique in its early stages and that it needed improvements, both in laboratory and in clinical practice.

In 2010, Atiyeh et al.[34] selected articles related to using non-absorbable PP threads with spicules.

The articles focused on the results and how long they lasted, emphasising that it was impossible to compare thread treatment with the traditional facelift. The conclusions coincided with Villa's review: the lack of efficacy and duration of the results achieved were more relevant than the possible complications.

In 2012, Guillo et al.[35] reviewed complications associated with the use of threads, looking at the most common together with the appropriate treatment for resolving them. As with other authors, these investigators referenced and quantified complications according to whether the threads were smooth or spiculated and absorbable or permanent. In the article they did however point out an aspect that is seldom mentioned i.e. complications of a psychological nature, along with recommendations on how to approach them in difficult patients who are rarely satisfied with the results. Later on, in 2014, Guillo[36] carried out a comparative review between absorbable and non-absorbable threads, emphasising the differences found between advertising and the biochemical reality.

The article is well documented and gives an idea of efficacy comparing one type of material to another. It advocates that information should be handled with rigour and should be based on precise knowledge as to the mean duration of the threads in the tissue without giving the patient false expectations.

Group IV: studies on adverse effects and complications

This group includes the articles on adverse effects and complications in patients when submitted to treatments with threads. They are generally well documented although the patient groups are small. In 2005, Silwa-Sawady et al.[37] described the expulsion of a PP thread (Aptos™ thread) in a patient 28 days after placement. Resolution was good after removing the thread and providing antibiotic coverage.

More serious were the 2 cases that occurred in women and were presented by Winkler et al.[38] in 2006. One of the women presented a ranula secondary to puncture of Stensen's duct. The other patient suffered chronic parotitis because the gland was pierced with a PP thread; despite removing the thread, the difficult course of evolution made it necessary to remove the gland.

In 2007, Helling et al.[39] presented 4 cases of patients treated with Contour™ threads. Two of these patients complained of sensation of a foreign body; another presented paresis with one of the sutures partially in the parotid, crossing Stensen's duct in the anterior direction; the last complained of facial asymmetry and had hollows in one of the cheeks. In all these cases the sutures were removed and the problems were resolved.

The authors commented that the spicules underwent eversion, especially in the distal segment of the tissue, becoming oriented along with the tissue, which made them stop producing traction. In their study, they concluded that the rate of complications with threads is underestimated. Shortly afterwards, Cruz Höfling et al.[40] reported the first indexed case of infection by *Mycobacterium fortuitum* in a 48-year-old female patient who received a PP thread treatment.

The suspicion of infection made it necessary to set up appropriate cultures to identify the causal agent. This is especially important in mycobacterial infections. In 2008, Sulamanidze[9] himself also cited a case of perforation of Stensen's duct among the possible adverse effects and/or complications that might happen with Aptos™ threads. However, he provided no further data on the occurrence.

In 2012, Sapountzis et al.[41] communicated a late extrusion of Aptos™ threads in a 48-year-old woman. The threads had been placed some 13 months earlier. It was necessary to extract the thread and perform an autologous fat graft. In follow-up a year later the patient was satisfied and no new extrusions had occurred.

Once again, in 2015, Yau et al.[42] reported a case of infection (caused by *Mycobacterium abscessus*) linked to the use of PP threads for aesthetic purposes. They pointed out that infections from mycobacteria are increasing and that the doctor should suspect them when infections do not remit using the appropriate

prescribed antibiotics. Lastly, in that same year Amuso[3] carried out a histological study on PDO threads, to determine if treatment with this type of absorbable threads, so widely used, responded to the expectations of a biorevitalising treatment. Consequently, 5 patients were treated with 5 different brands of PDO threads. Histological studies were performed at 6, 12 and 18 months respectively. The authors concluded that PDO threads induced fibrosis up to 12 months after implantation with production of type I collagen but without evidence of type III collagen.

Discussion

Many published articles and papers have been presented at congresses since 2001. Despite this fact there is a lack of efficacy-based clinical studies on the threads chosen and on the technique used for treatment. Each author is more interested in reporting his or her own method, often carried out with threads patented by that same author[2,3,9,10,14]. Clinical studies have not been randomised nor submitted to the controls that should be normal in this type of clinical studies[6,8-19]. Well designed methodology and correct evaluation of results (both objective and subjective) are also missing. Reporting optimistic results leads to a very favourable impression of the use of this type of treatment[18,19,21]. Other previous bibliographic reviews, logically including fewer studies, coincide with our evaluation[24–26].

The majority of the studies refer to non-absorbable or permanent threads although the results shown vary considerably due to the irregularity of follow-ups. This leads to think that treatment with so-called permanent threads could lead to results that are far from being so permanent. The results achieved are not comparable to classic rhytidectomy either; many procedures with threads have however been concluded with surgical excision of extra skin or with autologous fat implants[19,26]. Additionally the information of the patients (through websites or informative pamphlets) indicates results that last for 5 years. We have not however found even a single published study whose follow-up is that long. Most studies have irregular follow-ups, reaching (in the best of cases) 2 years[2,7,9–15,18,19,22].

It should be remembered that 30% of the studies published mention adverse effects, lack of efficacy and/or complications[24–26]. In many studies, using threads as one of the rejuvenating techniques is even advised against, above all if the concept of biorevitalisation (so trendy nowadays) is considered. With regard to this last point a histological study on PDO threads concluded that although they did indeed induce the formation of new collagen, it was fibrous type I collagen, which does not encourage the tissue interchanges needed for the cells to properly develop their functions[3].

We also agree with one of the best conducted studies in stating that there is a lack of scientific rigour which, then and now, has characterised most publications on threads[25]. Many of the publications refer to the use of other different or concomitant procedures with thread treatment.

Giving chemical peelings (phenol or TCA) and using lasers or radiofrequency equipments is normal, in addition to combining threads with autologous or heterologous fat filling[14,21]. In line with what has been reported, well designed statistical analyses are also missing; this makes some publications reach excessively optimistic conclusions. This is especially true in the case of absorbable threads[36] where, although histological and sonography studies confirm the presence of reactive fibrosis, it is still not possible to infer how long the results will be maintained (Figures 4-5).

Likewise, it is possible to find publications in which the degree of satisfaction is abnormally high, such as the

Figure 4 - 57-year-old patient, phototype II. (A) Before treatment with polylactic suture and absorbable cones in the lower third face. (B) 1 year after treatment it is possible appreciate the improvement in jawline

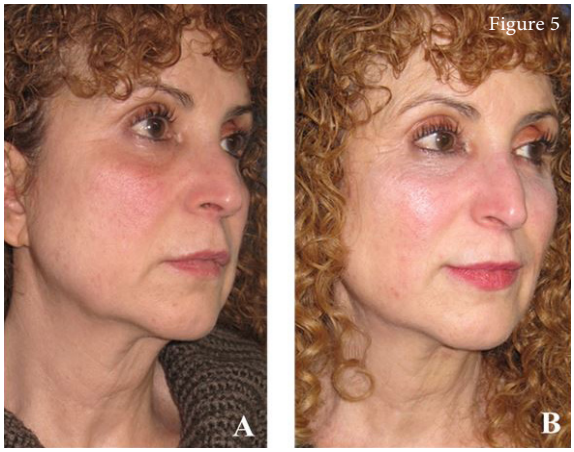

Figure 5 - The same patient in side view. (A) Before treatment with polylactic suture and absorbable cones in the lower third face. (B) 1 year after treatment she keeps the improvement in jawline

cases of Lycka[20] and Park[28]. In the first case, 348 patients out of 350 treated were satisfied or very satisfied, although the time periods for which the evaluations were performed were not indicated. In Park's case, the satisfaction index stood above 98%, although the majority of patients had received coadjuvant treatments (specifically, 79% received autologous fat implants). In many studies the level of patient satisfaction alone is taken into consideration without including any objective assessments by independent experts. In a clinical study worthy of its name, both satisfaction indexes should be present and the scores should be awarded based on the same values for patients and examiners. That is the only way in which it is possible to establish reliable comparisons.

Another important factor with respect to objective assessments is that the majority are handled through photographs and low photographic quality is a common characteristic of many publications.

The Before and After photographs should share common characteristics: they should be taken with the same camera and lens, have the same, non-zoom frame with the same background in all photographs, and the patient should be placed in the identical position and under the same lighting conditions[22].

Many publications have financial backing, which is always acknowledged and disclosed by the authors themselves. This obviously detracts from the credibility of scientific work which should be independent, well designed, have appropriate methodology and have treatment statistical data to allow informed conclusions. Beyond mere marking purposes, published material should make it possible for the medical profession to form an adequate idea of the materials to be implanted and to know the technique to be used so that the results that can be obtained with each treatment can be reported in detail.

Scientific societies must request caution from specialised journals when it comes to publishing results that are excessively optimistic. Reviewers and publishers should share the same vision. Likewise, they should have the same standards of rigour as to the data provided by various clinical studies with emphasis on efficacy and safety in procedures using threads.

Conclusions

Given the review of the data analysed it can be concluded that biostimulation threads have a good medium-term level of patient satisfaction. The clinical efficacy of treatments with threads, both absorbable and non-absorbable, is still unknown. In contrast, the adverse effects and complications are well known and are, generally speaking, minor, temporary and easy to avoid and/or to resolve. Patients ask for minimally-invasive treatments more and more often, but they should be informed about the results that can be reached with the various threads, so that they do not fall prey to false expectations.

In the experience of the authors of this review study (unpublished data), the results for the implantation of threads as an alternative to a facelift are not satisfactory in the long term (corresponding to more than 2 years). Implanting facial threads, if not combined with facial filling treatments or with the alternative of facial rejuvenation sessions with energy sources, is not satisfactory, as patients report.

In the analysis of the papers prepared by the authors, a potential financial interests bias appears. This reduces strength and seriousness of the evaluation of results classified as good and obtained with patients who had other treatments besides just threads. Consequently, new well designed studies, using threads only and inclusive of longterm control, will be needed in order to obtain an accurate assessment of this treatment's reach. Studies with these characteristics will make it possible to establish the validity of biostimulation thread implantation as a treatment and they will help us to understand the role that these threads play in bioregeneration and facial rejuvenation.

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Comparison between the therapeutic efficacy of a combined theraphy containing inositol isomers associated with different molecules and treatment with metformin in patients affected by polycystic ovary syndrome

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ABSTRACT

Introduction: Inositol isomers have recently shown to improve ovarian function.

Purpose: To compare the effectiveness of inositol isomers associated with different molecules and metformin in patients affected by polycystic ovary syndrome (PCOS).

Materials and methods: 80 patients with PCOS were randomized in two groups: A group, receiving D-kiro-acid (500 mg) + myoinositol (200 mg) + lipoic acid (150 mg) + folic acid (200 mcg) + manganese (5 mg) per day and B group, receving metformin (850 mg twice per day) for six months.

Results: In A and B group, after six months of treatment a significant reduction of Homeostasis model assessment index (HOMA – IR), and of Testosterone and FSH serum levels was detected, with no significant side effects only in patients receiving inositol isomers associated with different molecules (A group).

Conclusions: Our study shows that inositol isomers do improve clinical and metabolic values in patients with PCOS, as is the case with metformin but without the onset of side effects.

Keywords
Polycystic ovary syndrome, endocrine features

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Running title: PCOS and Endocrine features

Introduction

Polycystic ovary syndrome (PCOS), one of the most common endocrine metabolic disorders among pre-menopausal women, concerns about 5-10% of reproductive-age Mediterranean women[1]. PCOS is characterized by oligo-anovulatory menstrual cycles, larger and micropolycystic ovaries and a variable degree of hyperandrogenism. It is usually associated with metabolic disorders (insulin-resistance, hyperinsulinemia, obesity, diabetes mellitus type 2, dyslipidaemia) which can lead to a higher cardiovascular risk[2,3,4].

Insulin resistance (IR), with compensatory hyperinsulinemia, has been identified as a key component in the pathophysiology of PCOS in both lean and obese women[3]. The prevalence of insulin resistance in PCOS ranges from 50%-70% and occurs independently from obesity[3,4,5,6]. The pathogenic role of obesity is additional to that of PCOS and both can trigger different disorders, the most important of which is the hyperinsulinemic state. Insulin can stimulate ovary androgen secretion and plays a key role in the metabolism of androgens and in their transport to peripheral tissues[7,8].

Insulin directly stimulates the ovary theca cells to produce greater amount of androgens, and to inhibit hepatic synthesis of sex hormone-binding protein (SHBG), thus indirectly increasing the levels of circulating free androgens. Moreover, theca cells in PCOS patients present a greater sensitivity to insulin action on androgen secretion[9]. Evidence-based guidelines recommend lifestyle modifications as the first line treatment for PCOS, however engagement, compliance, and sustainability remain challenging. The importance of insulin resistance in PCOS is further underlined by the fact that insulin-sensitizing compounds such as metformin, pioglitazone and troglitazone have been proposed as treatment for PCOS-associated hyperinsulinemia[10]. It is worth noting that metformin may antagonize some hyperandrogenic signs by reducing total and free testosterone concentrations[11]. Metformin reduces IR and inhibits ovarian androgen production in PCOS patients by acting on steroidogenic acute regulatory protein and 17α-hydroxylase[12,13].

It has been suggested that metformin might play a key role in PCOS when combined with lifestyle changes and assist in weight management and cycle regulation[14].

Some studies have demonstrated that metformin improves glucose effectiveness, fertility, and live-birth rates and reduces clinical hyperandrogenism[11].

The discovery that impairment of insulin signalling could be due to a defect in the inositolphosphoglycans (IPGs) second messenger pathway opened a new horizon in the clinical management of PCOS. IPGs are known to have a role in activating enzymes that control glucose metabolism. In PCOS women, a defect in tissue availability or altered metabolism of inositol or IPGs mediators may contribute to insulin resistance[15].

Myo-inositol and D-chiro-inositol have been shown to improve insulin-resistance, hyperandrogenism and to induce ovulation in PCOS women[16].

Myo-inositol is one of nine stereoisomers of a C6-sugar alcohol of the vitamin B-Complex group. Inositol is a carbohydrate, assayed at half the sweetness of table sugar[17,18].

Myo-inositol is basically incorporated into cell membranes as phosphatidyl-myo-inositol, the precursor of inositol triphosphate that acts as second messenger regulating the activities of several hormones such as FSH, TSH and insulin. In addition, inositol is an important component of structural lipids, specifically phosphatidyl-inositol (PI) and its various phosphates, including phosphatidyl-inositol phosphate (PIP) lipids. Myo-inositol and D-chiro-inositol (DCI) are chemical mediators of insulin, acting through different mechanisms[20]. Myo-inositol produces second messengers for FSH and glucose uptake, while D-chiro-inositol provides for second messengers for promoting glucose uptake and glycogen synthesis. Myo-inositol is a precursor of D-chiro-inositol. D-chiro-inositol is synthetized by an insulin dependent epimerase that converts myo-inositol into D-chiro-inositol[19]. In this study we aimed to compare the effects of two different therapies (Inositols and Metformin) within clinical, endocrine and metabolic parameters in patients affected by PCOS.

Materials and methods

80 patients affected by PCOS were enrolled for the study and were treated with two different therapies for six months; they had all been diagnosed as having PCOS according to the 2003 Rotterdam ESHRE/ASRM PCOS Consensus Workshop Group criteria (presence of two out of the following three features: menstrual irregularity; clinical or biochemical hyperandrogenism; positive ultrasound presentation of polycystic ovaries by scan)[4]. Patients were age-matched, with a similar socio-economic background, were randomly divided in two groups, according to a cross–over design, on the basis of their treatment: D-chiro-inositol (500 mg) + myoinositol (200 mg) + lipoic acid (150 mg) + folic acid (200 mcg) + manganese (5 mg) per day (A group: age 25,9±4,2 y; BMI 24,9 ± 6,5 kg/m^2) and metformin (850 mg twice per day) (B group: age 26,5±5,4 y; BMI 32,8 ± 7,9 kg/m^2). At baseline and after 6 months of treatment all subjects underwent clinical examination and blood sampling to evaluate hormonal values: fasting FSH, LH, PRL, E2, 17OH progesterone, testosterone, androstenedione, DHEAS levels and metabolic parameters: total cholesterol, HDL cholesterol,

triglycerides, serum glucose, and insulin levels, Oral glucose tolerance test (OGTT), Homeostasis model assessment: insulin resistance index (HOMA-IR index). Blood samples were obtained in the morning between 8,00 and 9,00 a.m., during the early proliferative phase of the cycle. The degree of hirsutism and acne were evaluated, respectively, with Ferriman-Gallwey's and Cremoncini's score. Finally the regularity of menstrual cycles was evaluted based on a monthly diary and ovary morphology was assessed by ultrasound scan.

The Ferriman-Gallwey score assessment grades the severity of hirsutism. Each of the nine body areas most sensitive to androgen production is assigned a score from 0 (no hair) to 4 (heavy hair growth).

A score of more than 15 is considered to indicate moderate or severe hirsutism. BMI was calculated as the ratio between body weight (Kg) and squared height (m2). HOMA-IR was used to predict relationship between beta-cell deficiency and insulin resistance. HOMA-IR was calculated using the following formula: glucose x insulin/405; Normal HOMA-IR IS < 3; HOMA-IR ≥ 2,5 is considered a reasonable indicator of IR. Informed consent was obtained from all subjects. Exclusion criteria were: pregnancy, diabetes or other endocrine disorders, as well as the use of oral contraceptives or insulin-sensitizing agents.

Statistical analysis

Data are expressed as mean ± SD and were log transformed before analysis when skewed. Two-tailed analyses were performed using SPSS13 for Windows (SPSS, Inc., Chicago, IL, USA). Statistical significance was set at p< 0,05.

Baseline parametric data were assessed using a one-way ANOVA. For comparison between time points, a repeated measure of ANOVA was used for parametric data. Bonferroni adjustments were performed on multiple comparisons. Correlations were expressed by Pearson's values.

Results

The age was similar in both groups (A: 25,9 ±4,2 yrs B: 26,5 ±5,4 yrs; p = 0,585). Baseline and post-treatment characteristics of selected patients (A group and B group) are shown in table 1 and in table 2.

In A group after six months of treatment there was a reduction of acne in 2 patients while in B group there was a reduction of acne in 3 patients (5% versus 7.5%, respectively, p=1.000). After six months of treatment there was a mean improvement in hirsutism of 7.5 % in A group (3 patients) and about 10% in B group (4 patients) (p=1.000).

Mean improvement in menstrual cycle after both treatments was not statistically significant: 66,7% in A group (26 patients) vs 71,7% in B group (27 patients) (p=0,807). Nausea has been reported for 2.5% in A group (1 patient) and 12.5% in B group (5 patients); diarrhoea and flatulence only for 15% (6 patients) and 10% (4 patients) in B group (p=0.026 and p=0.116, respectively). Overall the appearance of side effects has been reported in 1 patient (2.5%) of A group and in 8 patients (20%) of B group (p=0.029).

Multivariate analysis, after correction for clinical and demographic variables, showed that an increasing BMI is associated with increased risk of oligo-anovulatory menstrual cycles (OR: 95% CI: 1.28, 1,584-1,033, p = 0.024). By evaluating the percentage changes of the main metabolic and hormonal parameters (figures 1 and 2) we found a similar improvement in the delta% HOMA-IR index (A:-30.9 + 95.4 vs B:-29.5 + 70.7, p = 0946) and delta values% of circulating testosterone (A:-3.25 + 41.3 vs b:-14.2 + 24.9, p = 0185) in both groups.

In A and B group six months after treatment there was a statistically significant reduction of circulating serum testosterone (A: 37,9 ± 15,1 vs B: 36,8 ± 12,3; p = 0,042 vs p = 0,001 respectively), HOMA-IR (A: 1,6 ± 1,4 vs B: 1,9 ± 1,5; p = 0,002 vs p = 0,002 respectively) and circulating serum FSH (A: 5,1 ± 1,6; vs B:5,5 ± 1,7; p = 0,066 vs p = 0,001 respectively).

As compared with B group, in A group six months after treatment, there was a statistically significant reduction of DHEAS (A: 219,5 ± 58,9 vs B: 176,7 ± 55,9; p = 0,117 vs p =0,010 respectively) and 17OH-progesterone (A: 0,9 ± 0,3 vs B: 1,3 ± 0,5; p = 0,004 vs p = 0,730 respectively). As compared with A group, in B group six months after treatment, there was a statistically significant reduction of prolactin (A: 18,4 ± 9,2 vs B: 12,9 ± 5,4; p= 0,878 vs p =0,023 respectively).

	Baseline	Post-Inositol Isomers treatment	P
Weight (kg)	64 ± 14,8	64,1 ± 7,8	0,979
BMI (Kg/m^2)	24,9 ± 6,5	24,9 ± 4,2	0,994
Total Cholesterol (mg/dl)	182,5 ± 25,4	190,1 ±22,8	0,424
Triglycerides (mg/dl)	85 ± 31,4	93,2 ± 40,9	0,687
LDL Cholesterol (mg/dl)	115 ± 26	109,2 ± 21,7	0,516
HDL Cholesterol (mg/dl)	55 ± 13,1	53,9 ± 17	0,725
Glucose time 0 (mg/dl)	82,3 ± 10,5	76,9 ± 4,6	0,029
Insulin time 0 (iU/ml)	16,8 ± 7,3	8,8 ± 8,5	0,007
Glucose time 120 (mg/dl)	105,5 ± 29,9	88,6 ± 20,9	0,007
Insulin time 120 (iU/ml)	53,3 ± 55,1	34,6 ± 38,6	0,153
HOMA – IR (%)	3,4 ± 1,5	1,6 ± 1,4	0,002
FSH (mU/ml)	7,2 ± 4,8	5,1 ± 1,6	0,066
LH (mU/ml)	18 ± 14,2	18,4 ± 9,2	0,307
Prolactin (ng/ml)	15,8 ±7,4	12,9 ± 5,4	0,878
E2 (pg/ml)	43,8 ± 11	54,6 ± 25,9	0,070
17-hydroxyprogesterone (ng/ml)	1,3 ± 0,5	0,9 ± 0,3	0,004
Testosterone (ng/dl)	43,4 ± 18,1	37,9 ± 15,1	0,042
Δ4-androstenedione (µg/dl)	3,1 ± 1,6	3,4 ± 1,6	0,476
DHEAS (µg/dl)	221,3 ± 86,9	176,7 ± 55,9	0,010

Table 1 - Change of metabolic and hormonal variables from baseline after 6 months of treatment in Inositol Isomers group

	Baseline	Post-Metformin treatment	P
Weight (kg)	87,9 ± 20,2	90,9 ± 20,8	0,344
BMI (Kg/m^2)	32,8 ± 7,9	33,5 ± 7,0	0,546
Total Cholesterol (mg/dl)	175,3 ± 22	176,8 ± 17,9	0,618
Triglycerides (mg/dl)	107,8 ± 88,3	108,5 ± 65,3	0,953
LDL Cholesterol (mg/dl)	99,6 ± 25,2	105,3 ± 29,6	0,398
HDL Cholesterol (mg/dl)	53,8 ± 18,2	52,8 ± 13,3	0,802
Glucose time 0 (mg/dl)	86,4 ± 8,3	81,9 ± 6,8	0,038
Insulin time 0 (IU/ml)	15,3 ± 6,2	10,2 ± 8,1	0,011
Glucose time 120 (mg/dl)	106,7 ± 37,6	93,1 ± 18,5	0,048
Insulin time 120 (IU/ml)	56,9 ± 43,1	31 ± 22,5	0,005
HOMA – IR (%)	3,2 ± 1,2	1,9 ± 1,5	0,002
FSH (mU/ml)	6,8 ± 1,7	5,5 ± 1,7	0,001
LH (mU/ml)	6,6 ± 4,9	6,2 ± 3,9	0,576
Prolactin (ng/ml)	15,8 ± 7,4	12,9 ± 5,4	0,023
E2 (pg/ml)	44 ± 14,1	42,4 ± 17,9	0,651
17-hydroxyprogesterone (ng/ml)	1,4 ± 0,7	1,3 ± 0,5	0,730
Testosterone (ng/dl)	43,3 ± 10,3	36,8 ± 12,3	0,001
Δ4-androstenedione (µg/dl)	3,1 ± 0,5	3,1 ± 0,7	0,898
DHEAS (µg/dl)	259,9 ± 104,3	219,5 ± 58,9	0,117

Table 2 - Change of metabolic and hormonal variables from baseline after 6 months of treatment in Metformin group

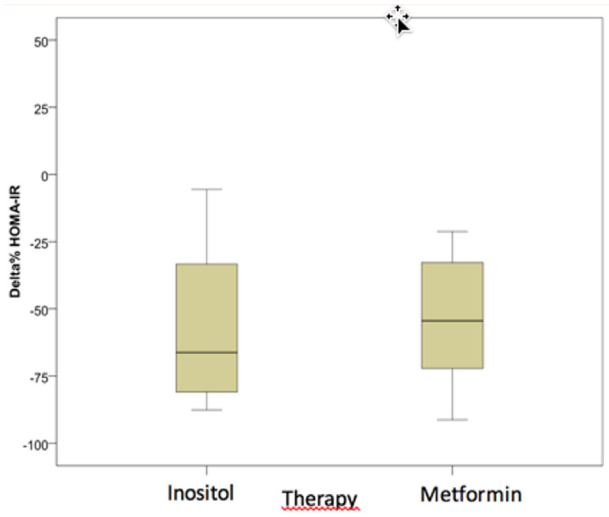

Figure 1 - Percentage changes of HOMA-IR levels stratified on the basis of treatment

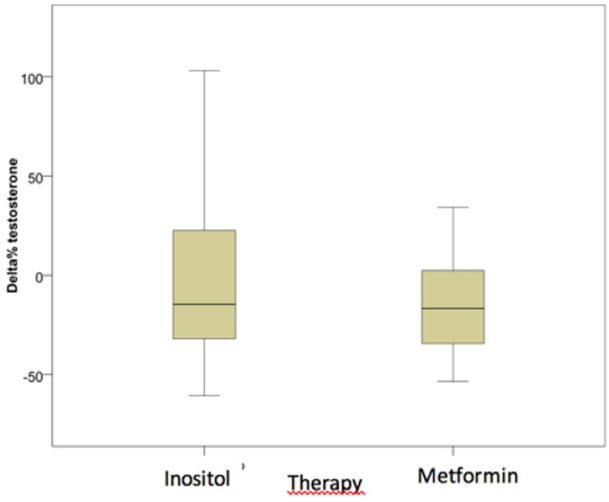

Figure 2 - Percentage changes of levels stratified on the basis of treatment

Discussion

PCOS therapy consists of various treatments depending on the clinical features a woman presents. Insulin sensitizers, including metformin, myo-inositol and D-chiro-inositol[20] have also been shown to increase ovulation and reduce hyperandrogenism in women with polycystic ovary syndrome but metformin remains the most commonly used agent. In women with polycystic ovary syndrome, insulin sensitizers (metformin or thiazolidinediones) promote ovulation and lower androgen levels by about 20%, but there is little evidence of a clinically significant improvement in hirsutism with the use of these agents[21].

In our study participants in the metformin group showed a significant reduction of prolactin, FSH, testosterone and HOMA-IR, while there was no significant improvement in menstrual cycle and no significant reduction of clinical hyperandrogenism (acne and hirsutism).

The patients experienced a significantly higher incidence of gastrointestinal side effects including nausea and vomiting compared with the group treated with inositol isomers associated with different molecules. D-chiro-inositol and Myo-inositol can be used to improve compliance to PCOS therapy.

D-chiro-inositol is an agent that can be found naturally in fruits and vegetables; it utilizes body's insulin and promote ovulation and overall health.

Deficiency of D-chiroinositol has been postulated in some studies to cause insulin resistance seen in women with PCOS[20].

In an interesting study on insulin resistant women with PCOS, it was shown that oral administration of D-chiro-inositol alone would improve insulin sensitivity[22].

An Italian research group[9,23] concluded a clinical study on the use of myo-inositol in PCOS patients. Twenty-five PCOS patients were enrolled in this study and continuously dosed with myo-inositol combined with folic acid twice a day.

During an observation period of 6 months, ovulatory activity was monitored with ultrasound scan and hormonal profile and the number of spontaneous menstrual cycles and pregnancies was assessed.

On the basis of the results, the authors[9,23] proposed that myo-inositol is effective in restoring spontaneous ovarian activity and consequently also fertility in PCOS patients.

A recent study highlighted that both inositol isoforms are effective in improving ovarian function and metabolism of patients with PCOS, although myo-inositol shows the most marked effect on the metabolic profile, whereas D-chiro-inositol reduces hyperandrogenism[24] to a higher degree.

These striking results obtained by combined treatment are likely linked to the fact that the administration of both stereoisomers is able to regulate glucose metabolism in a physiological way. While DCI is able to promote glycogen synthesis, MI is able to promote glucose cell intake.

The different inositol functions are directly transferred to body tissues; indeed, DCI is present at high concentrations (although always lower than MI) in glycogen storage tissues, such as muscles, liver and fat. On the other hand, DCI is present at low concentrations in those tissues that must have a high energy status such as brain, ovary and heart[16].

Our data showed that with the association myoinositol/D-chiro-inositol/lipoic acid/folic acid/manganese there was a significant reduction of testosterone, FSH, HOMA-IR, 17OH-progesterone and DHEAS, while there was a not significant improvement in menstrual cycle and no significant reduction of clinical hyperandrogenism.

In summary, both treatments (inositol isomers and metformin) improved ovarian function, metabolic profile and hormonal parameters in patients with PCOS by decreasing insulin levels. Additionally, our study shows the therapeutic efficacy of inositol in the PCOS, as for metformin, without the onset of side effects, which may cause suspension of treatment.

This study shows that the association myoinositol/D-chiro-inositol/lipoic acid/folic acid/manganese represents an excellent therapy choice to suggest to those PCOS-affected women who do not wish to take hormones nor experience severe side effects. Due to the chronic nature of PCOS and the young age at which both hormonal and metabolic symptoms begin to manifest, lifelong strategies that improve the care of women with PCOS are essential. Identifying effective new therapy can be advantageous in the treatment of any condition when it is considered safe and associated with few notable side effects.

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Courses and Congresses

2016

16-17 September – Paris (France)
37th National Congress of Aesthetic Medicine and Dermatologic Surgery
French Society of Aesthetic Medicine
French Association of Morpho-Aesthetic and Anti-Aging Medicine
National Institute of education in aging prevention
Venue: Palais de Congres
www.sfme.info
congress@sfme.info

9-10 December – Lisboa (Portugal)
1st National Meeting of Aesthetic Medicine
Portuguese Society of Aesthetic and Anti-Aging Medicine
President: Joao Pedro Vale
Venue: Sana Maloha Hotel
www.spme2016.com
secretariado@spme.pt

2017

12-14 May – Rome (Italy)
38th National Congress of the Italian Society of Aesthetic Medicine
12th National Congress of the Italian Academy of Aesthetic Medicine
Venue: Congress Centre Rome Cavalieri
President: Emanuele Bartoletti
sime@lamedicinaestetica.it
congresso@lamedicinaestetica.it
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French Society of Aesthetic Medicine
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