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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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Periorbital anatomy: avoiding complications with tear trough fillers

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ABSTRACT

Cosmetic treatments with fillers in the periorbital region are becoming more common. However, this is a complex anatomical region that must be known well to avoid complications such as chronic lymphedema, bruising, embolisms, infection, the periodontal pocket effect or nodules. The objectives when filling tear troughs are: determine the anatomical bases of the periorbital region, including fat compartments, the *septa* and lymphatic drainage; know the process of aging of the orbital region and midface (herniation of palpebral bags, loss of support, sequential atrophy of fat compartments, lower migration of these compartments and redistribution of intracompartmental volume); use the safest techniques for filling the lacrimal groove (anatomically safe, appropriate markings); determine the sequence that must be followed when applying a full facial treatment with fillers, including the lacrimal groove; and finally, determine which are the products of choice. A refined technique, a suitable product and knowledge of anatomy allow the periorbital region to be treated successfully with fillers, minimizing complications.

Keywords
tear trough, malar edema, facial lymphatic drainage, filler complication, periorbital anatomy

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Introduction

The periorbital region is one of the most affected areas by aging, with the appearance of periorbital wrinkles, deep lacrimal groove, palpebral bags, excess skin in the upper eyelid (blepharochalasis), malar bags, a loss of skin elasticity and a downwards tilt in the external canthus. In an attractive and youthful face, transitions between the pre-septal portion and the orbital portion of the orbicularis muscle, and between the eyelid fat and cheek compartments, should be smooth and not very pronounced. With the age process, these transitions become increasingly pronounced, with the appearance of grooves like the lacrimal groove (from the inner canthus to the mid-pupil line) and the palpebro-malar groove (lateral to the mid-pupil line).

Cosmetic treatments designed to improve this region combine different techniques such as botulinum toxin, fillers and surgery. However, the periorbital region presents anatomical characteristics that must be taken into account in order to achieve good results and avoid complications. This is a complex region with its own *septa* and ligaments, fat compartments, muscles, vascularization and lymphatic drainage.

Anatomy of the periorbital region

Orbicularis oculi (OO) muscle: this acts as a sphincter around the eye and allows the eyelids to close. It is responsible for periocular expression wrinkles that can be treated with botulinum toxin. The inferomedial edge of the OO muscle anatomically coincides with the lacrimal groove. The tear trough that crosses the cheek of some patients also anatomically coincides with the lower edge of the OO muscle (Figure 1).

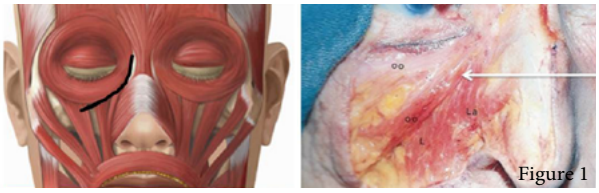

Figure 1

Figure 1 - The lacrimal groove anatomically coincides with the inferomedial edge of the *Orbicularis Oculi* muscle (OO: *orbicularis oculi muscle*; L: *levator labii superioris* muscle; La: *levator labii superioris alaeque nasi* muscle)

Deep fat compartments of the infraorbital region

-Intraorbital fat: the lower eyelid has three eye fat bags: inner, medial and outer. With age the orbital septum containing these bags weakens and the bags herniate leading to the appearance of eyelid bags. The treatment involves the excision of these bags by surgery (lower blepharoplasty). They can also be disguised by using fillers in the lacrimal groove (Figure 2). The upper eyelid has two eye fat bags (medial and inner; there is no external fat bag) that are surgically resectable together with the excess skin of the upper eyelid. This procedure is known as blepharochalasis (upper blepharoplasty).

-Suborbicularis oculi fat (SOOF): this is located behind the orbicularis oculi muscle and is divided into a medial portion and a lateral portion[1]. The medial SOOF extends from the medial limbus of the iris to the external canthus, while the lateral SOOF runs from the external canthus to the temporary fat compartment. The lower limit of the SOOF is the lacrimal groove (Figure 2 and Figure 3).

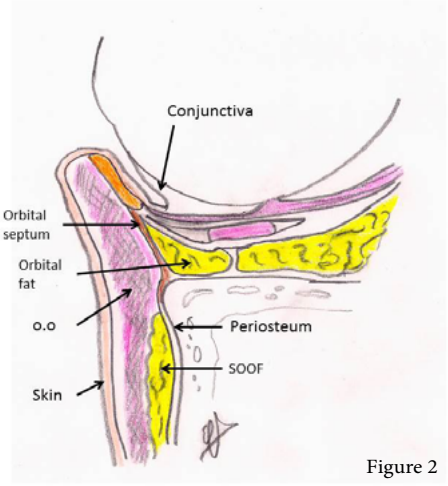

Figure 2

Figure 2 - Sagittal view of the orbit and anatomic relationships of its structures. (OO: *orbicularis oculi* muscle; SOOF: *suborbicularis oculi* fat compartment)

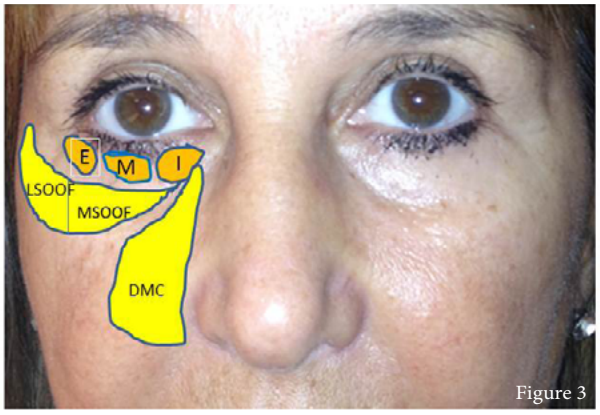

Figure 3

Figure 3 - Relationship between the internal (I), medial (M) and external (E) intraorbital eye bags with the medial (MSOOF) and lateral (LSOOF) portions of the *suborbicularis oculi* fat compartment and the deep medial fat compartment of the cheek (DMC)

-Deep medial cheek fat compartment (DMC): this corresponds to the medial edge of the SOOF. The DMC atrophies during aging[2], being more noticeable the transition between the orbital fat compartments

and the cheek fat compartments, making the lacrimal groove deeper. Restoring volume in the DMC with fillers rejuvenates the middle third of the face and reduces the transition between the lower eyelid and the cheek.

The deep infraorbital fat compartments - SOOF and DMC - can be filled to improve the lacrimal groove and rejuvenate this region.

The septum malaris: this anatomical structure was described by Pessa[3,4] and is of great relevance in lacrimal groove treatments with fillers. It is a thin facial structure that originates in the periosteum of the orbital rim and continues in the direction of the skin, dividing the SOOF into one upper portion and one lower portion. Before reaching the skin, it crosses the OO muscle and interdigitates with the fibrous septum of the surface fat in the cheek. It is inserted into the dermis at a point 3 cm below the external canthus (Figure 4). It is an impermeable membrane that prevents the diffusion of pigments and fluids from the periorbital region to the cheek. It is responsible for four different clinical conditions (malar edema, malar bag, periorbital ecchymosis and festoons), which share the same anatomical area since all of them have their lower limit approximately 2.5-3 cm below the external canthus. If the filler is placed in the area marked by the *septum malaris*, due to its impermeability, this may compress surface lymphatic vessels and cause chronic lymphedema (Figure 5). Therefore, fillers in the tear trough should preferably be introduced below the *septum malaris* to avoid chronic lymphedema, a characteristic complication of this region. If a supraperiosteal injection is performed, then the filler will be injected safely (Figure 6).

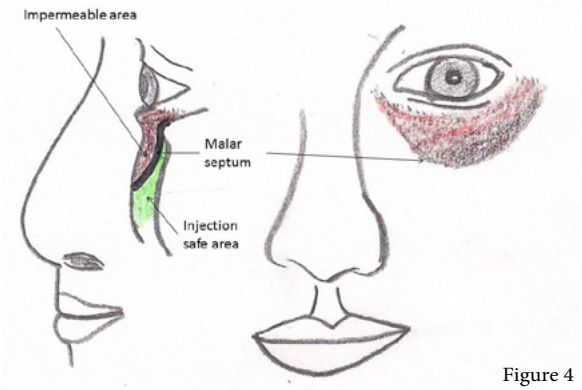

Figure 4

Figure 4 - Safe area for injecting fillers behind the *malar septum* (in green) in the supraperiosteal plane

Arterial vascularization: when filling a tear groove, consideration must be given to two main arteries: the infraorbital artery and the angular artery (Figure 7). The infraorbital foramen is easily located medial to the pupillary line and approximately 1 cm from the

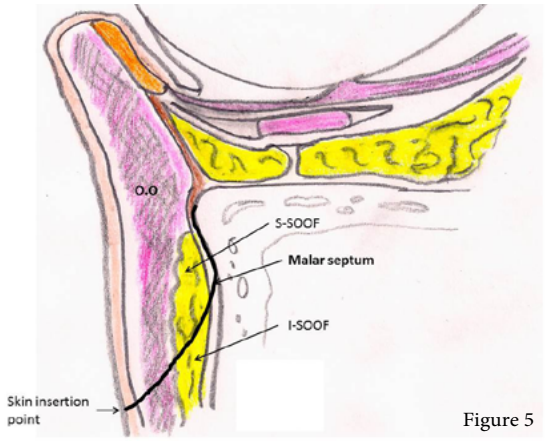

Figure 5

Figure 5 - The *malar septum* originates in the periosteum of the orbital rim and continues in the direction of the skin, through the *suborbicularis oculi* fat, and divides the latter into an upper portion (S-SOOF) and a lower portion (I-SOOF). On its way to the skin, it crosses the orbicularis oculi (OO) muscle and penetrates the dermis at a point 3 cm below the outer canthus

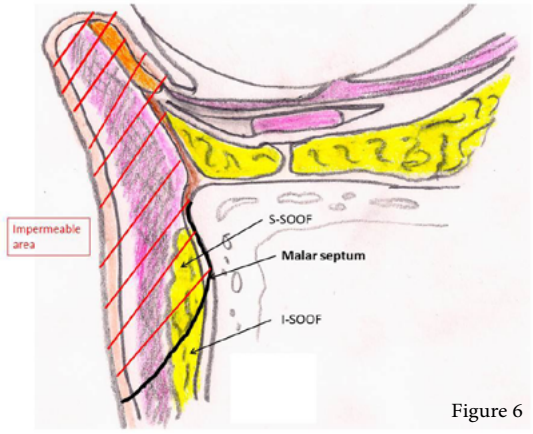

Figure 6

Figure 6 - The *malar septum* is an impermeable membrane that prevents the diffusion of pigments and fluids from the periorbital region to the cheek

infraorbital rim. The angular artery, a branch of the facial artery, runs along the inner canthus of the eye and anastomoses with the supratrochlear and supraorbital arteries; lesions to these arteries must be avoided. An infraorbital hematoma will increase pressure on soft tissue and may trigger a lymphatic insufficiency and malar lymphedema. An embolism in the angular artery could have catastrophic consequences if it causes an occlusion of the ophthalmic artery or central retinal artery, which could cause a rare but very serious complication, such as blindness.

Lymphatic system: Lymph is part of interstitial fluid. Interstitial fluid supplies nutrients to cells and eliminates waste. When this liquid passes into the lymphatic vessels, it is called lymph. The lymphatic system absorbs proteins that are too large to enter the venous capillaries and returns them together with excess interstitial fluid into the venous circulation.

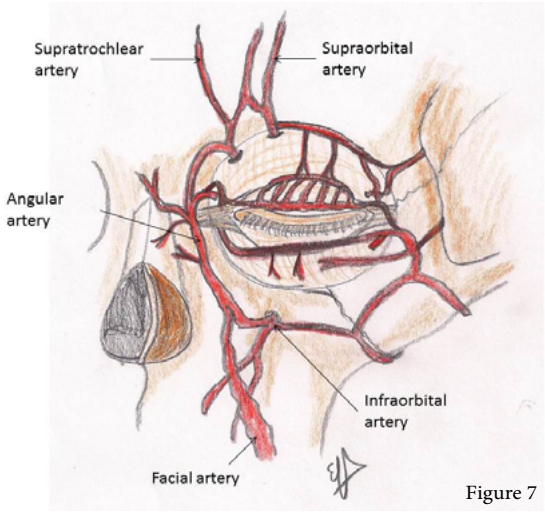

Figure 7

Figure 7 - Vascularization of the periorbital region.

Therefore, the main function of cutaneous lymphatic vessels is to maintain fluid balance and the load of lymph proteins draining interstitial fluid from the skin to the venous circulation. *Lymphatic transport capacity* is the maximum lymphatic flow per unit of time, corresponding to ten times the basal lymphatic flow. *Lymphatic insufficiency* occurs when lymphatic load exceeds transport capacity, inevitably leading to interstitial edema.

Facial lymphatic drainage occurs through different types of lymph vessels[5]:

-*Lymph vessels of the dermis:* these are approximately 0.014 to 0.15 mm and are valveless. They form a mesh-like network in the dermis and are the first to receive lymphatic drainage from the skin.

-*Pre-collector lymph vessels:* these are approximately 0.1-0.3 mm in diameter and already have valves, giving them a tubular shape resembling a *bamboo trunk*. They run from the dermis into the subcutaneous cellular tissue in search of collector vessels.

-*Collector lymph vessels:* these are approximately 0.1-2 mm in diameter, have valves and are located in the subcutaneous cellular tissue. They are tubular in shape and are classified as afferent (in the direction of the node), internodal (between nodes) and efferent (leaving the node).

So far we have described the facial lymphatic vessels. The next level of drainage is in the neck.

-*Lymphatic trunks:* these are between 1.5 and 3 mm in diameter, have valves giving them a rosary shape and are located in the deep tissues of the neck.

-*Thoracic duct:* this drains lymph into the venous system in the angle between the internal jugular vein and the left subclavian vein. It is also rosary shaped due to the presence of valves.

As can be seen, facial lymph vessels are superficially located in the dermis and in subcutaneous cellular tissue. Therefore, superficial injections of *fillers* can potentially compromise lymphatic drainage even more than deep injections. However, injections can be made superficially at other locations of the face where the risk of lymphedema is lower than in the periorbital region. This is explained by the presence of the *septum malaris*, which increases the risk of edema in the periorbital region, since it is an impermeable area at the surface, just where the lymphatic vessels that could be potentially compromised are located.

Regarding the lymphatic drainage of the upper eyelid, this generally runs to a parotid node or preauricular node and the lower eyelid and inner canthus of the eye are generally drained to a submandibular node[6] (Figure 8).

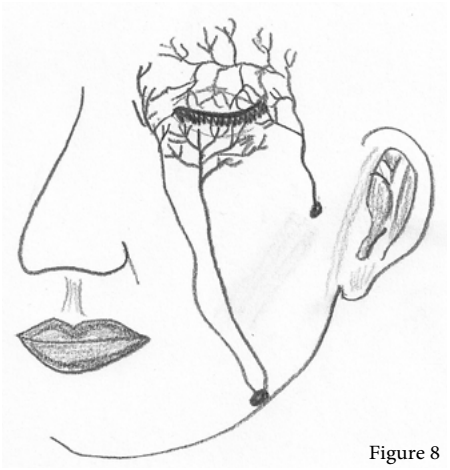

Figure 8

Figure 8 - Standard lymphatic drainage pattern of the periorbital region. The lymphatic drainage of the upper eyelid is generally performed to superficial parotid glands, and lymphatic drainage of the lower eyelid and the inner canthus of the eye to the submandibular glands. *(Based on the book illustration: The McGraw-Hill Companies from Lemke BN, Della Rocca RC. Upper facial anatomy. in: Lemke BN, ed. Surgery of the Eyelids and Orbit. An Anatomical Approach. Norwalk, Connecticut: Appleton and Lange; 1990).*

Factors leading to the appearance of malar lymphedema after filler injection

-*Location of injections:* a surface injection in the *septum malaris* increases its impermeability, and may compress the lymphatic vessels, obstruct lymphatic drainage and cause malar edema.

-*Volume of injected material:* excessive volumes put pressure directly on the lymphatic vessels if the material is injected either superficially or deep in the *septum malaris*.

-*Elasticity (G') properties of the filler:* elasticity is the capacity of a material to return the force applied

to it. An example of material with high G' is gelatin, which deforms slightly when force is applied to it, and a material with low G' is cocoa spread, which deforms easily and permanently when force is applied to it. It is preferable to use *fillers* with low G' because they offer less resistance to applied force, less extrusion force, less tissue stretching, a softer feel and are less palpable. The greater the elasticity of the *filler*, the greater the risk of compression of lymphatic vessels and edema formation.

-Patient propensity: patients with previous malar bags, a history of malar edema after excessive intake of salt or alcohol or when getting up in the morning, are patients with diminished lymphatic transport capacity so they are more at risk of presenting malar lymphedema after treatment.

Recommendations in the treatment of tear troughs

It is recommendable to make a supraperiosteal injection (avascular space) to reduce the risk of compression of lymphatic vessels, lymphedema, ecchymosis, visible material and embolism, as mentioned previously. Injection of small *bolus* of 0.05 cc of product prevents the appearance of lymphedema and nodules. The nodules in this region are more visible and palpable because the skin of the lower eyelid is extremely thin, so it is important to prevent their appearance.

Moreover, it is not advisable to vigorously massage the area after injection because massaging can move the *filler* superficially through the needle tracts and lead to inappropriate placement of the product even though it was initially injected correctly.

Correct patient selection is also important. Patients suspected of being at greater risk of lymphatic insufficiency in this region should not be candidates for treatment. Nevertheless, if the decision is taken to treat these patients, the safest approach would be to perform the procedure with a small volume of product and in various sessions to avoid saturating lymphatic transport capacity due to lymphatic vessel compression.

It is also necessary to choose the right products, which must offer low elasticity and be resorbable, such as hyaluronic acid with low cross-linkage or semi cross-linked, or collagen. Permanent products must be avoided in this region because they increase the risk of complications such as granulomas, product migration, chronic reaction to a foreign body and visible or palpable material.

The choice between cannula or needle depends on the physician preference, but generally less bruising and ecchymosis occur with cannula. Bruising may also cause lymphatic vessel compression and greater risk of edema, so the technique should be as atraumatic as possible. Cannula also minimizes the risk of intravascular injection and embolism. It is also advisable not to inject medially in the inner canthus to avoid lesions to the angular vessels.

Whenever the purpose of treatment is to restore volume in the midface together with treatment of the tear trough, it is recommendable to start by treating the midface. With aging, facial fat compartments atrophy and lower migration of facial fat occurs, increasing the distance between the eyelid and cheek fat compartments, leading to the appearance of the tear trough. Restoring volume in the midface rejuvenates the face and reduces the distance between the eyelid and cheek fat compartments, thus partially correcting the tear trough. This reduces the amount of product required to treat tear troughs, and also reduces the risk of complications, which are difficult to treat; hence, the most important thing is to prevent their occurrence[7].

Malar edema is a complication poorly tolerated by patients that can last months or even become permanent and cause disfiguration. There is no effective treatment, but it can be improved with postural measures (sleeping with the head elevated), lymphatic drainage, radiofrequency, restricting salt and alcohol intake, administration of oral corticosteroids or intralesional hyaluronidase. Injecting intralesional corticosteroids in the lower eyelid is not recommended because, given the thinness of the skin in this region, a skin atrophy can occur.

Personal technique

The personal technique recommended for filling *tear trough* and palpebromalar groove would be the use of a 25G x 38 mm cannula. The cannula is inserted through a puncture hole made with a 23G needle into the skin. The entry point of the cannula is located at the intersection between the line passing through the lateral *limbus* of the iris and the line marked by the tear trough. From this point of entry, both the tear trough and the palpebromalar groove can be filled. After introducing the cannula, resistance to the passage of the cannula should be noted; the cannula should pass through this resistant layer until it reaches the safe supraperiosteal layer. Once the cannula has been inserted into the deep layer, it should be moved medially, injecting small amounts in a fan shape, in the form of *bolus* or using the retro-tracing technique. From the same entry point, the cannula is removed and inserted laterally at supraperiosteal level to fill the palpebromalar groove in a similar way (Figure 9). It is not advisable to inject more than 0.5 cc per side in the same session; it is preferable to repeat the treatment after one month if more volume is needed. Natural results can be achieved with good technique (Figure 10 and Figure 11). Another technique is to make the entry point of the 25G x 40 mm cannula from the nasolabial folds, at a point located one cm to one side and one

cm below the nasal ala, injecting the *filler* in vertical strokes, perpendicularly to the tear trough (Beut-Jelks technique)[8]. This technique can be used to correct the tear trough and restore volume in the deep medial fat compartment of the cheek from the same point of entry.

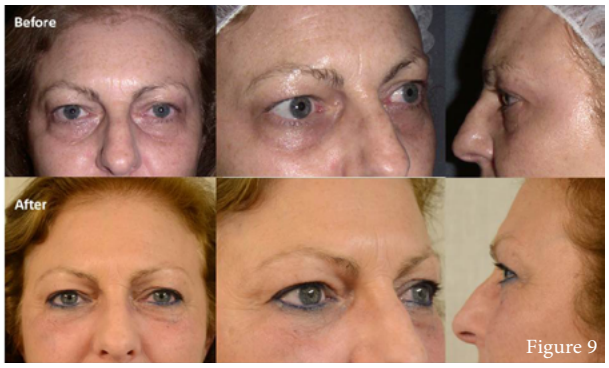

Figure 9 - Female patient aged 59 before (top) and after (bottom) filling of the tear trough with Teosyal Redensity II (Teoxane laboratoires, Geneva, Switzerland)

Figure 10 - Female patient aged 42 before (top) and after (bottom) filling of the tear trough with Teosyal Redensity II (Teoxane laboratoires, Geneva, Switzerland)

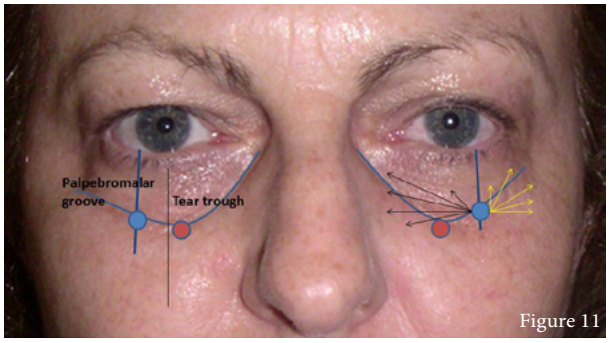

Figure 11 - Marking used in the personal technique for filling the tear trough. The entry point (blue circle) is at the intersection between the line of the lateral *limbus* of the iris and the line of the tear trough. The red circle indicates the location of the infraorbital *foramen*. The black arrows indicate the direction of the material deposits in the tear trough. The yellow arrows indicate the direction of the deposits of the material in the palpebromalar groove. The lacrimal groove or tear trough goes from the inner canthus to the mid-pupil line and the palpebromalar groove is lateral to the mid-pupil line

Summary

The anatomical features of the tear trough make it a particularly delicate area when injecting *fillers*. The injection technique must be based on good anatomical knowledge of the region, a refined and atraumatic technique with supraperiosteal injection of resorbable products with low elasticity, in moderate volumes and adequate selection of patients not prone to lymphatic insufficiency. If these principles are followed, satisfactory results will be achieved by minimizing the occurrence of complications.

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Complications and adverse effects of mesotherapy and of microinjections of drugs and mixtures of compounds into the skin: Systematic review

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ABSTRACT

Background and Objective: Some complications of mesotherapy for medical-aesthetic purposes have been known since the 1980s. The objective of this study is to set out the risks, complications and adverse effects associated with the microinjection of products into the skin using microneedles.

Methods: A search for and selection of original articles in the Medline database by two experts, with concordance confirmed using the kappa coefficient. A complementary search for information using Google Scholar. Systematic analysis of the information contained in the selected studies.

Results: Good concordance was obtained in the information selection (kappa coefficient = 0.86). 53 original articles were analysed: 34 case reports, 9 short case series (n = 2-14) and 10 clinical studies (n≥15). Numerous local, systemic, non-infectious and infectious complications were counted and evaluated, including 9 epidemic outbreaks by atypical mycobacteria.

Conclusion: Complications can be avoided or reduced by limiting interventions to properly trained doctors, selecting indications in the clinical context of patients, using authorised, sterilised products and guaranteeing the necessary asepsis measures throughout the entire microinjection procedure.

Keywords
Mesotherapy, intradermotherapy, safety, side effects, complications, systematic review

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Introduction

The technique involving direct injections of medications into the skin was first described by the French physician Michel Pistor in 1952. He coined the term "mesotherapy" which translates as "treatment of the mesoderm". Mesotherapy, also known as intradermotherapy, does not mean the treatment of any particular condition; it simply describes a method of drug delivery through the skin.

Most authors consider mesotherapy to be the use of intracutaneous or subcutaneous injections containing mixtures of compounds to treat local medical and cosmetic conditions, although there is no absolute agreement on considering all microinjection techniques as mesotherapy. By definition, the concept of mesotherapy includes the injection of any kind of substance into the skin or dermis using microneedles[1,2].

Irrespective of the type of technique or substance, the risks and complications of microinjections into the dermis were reviewed as early as the 1990s[3-5]. However, the boom in mesotherapy for aesthetic purposes, together with the appearance of epidemic outbreaks by atypical mycobacteria, secondary to mesotherapy, justify an in-depth review of the subject using current data.

The Spanish Society of Aesthetic Medicine (SEME) considers that mesotherapy could be effective in the treatment of certain aesthetic conditions, such as cellulitis or localised adiposity, provided that it is performed by qualified doctors using the correct equipment and in a suitable clinical environment. It is a technique, either manual or using automated systems, for the injection of substances. The objective is to introduce drugs or homoeopathic products intradermically to achieve a medical or aesthetic result. The introduction of substances into the skin, whether manually using microneedles or using modern microinjection guns, always entails risks.

These risks depend on the nature and pharmacological activity of the substance that is injected, and on the injection procedure itself, which should guarantee perfect asepsis conditions in certain key points.

As the automated injection of substances into the skin appears somewhat simple and that it can be performed by anyone, many aesthetic professionals who are not doctors also apply these treatments for aesthetic purposes.

The SEME, echoing the recommendations of other scientific and medical organisations, warns of the risks associated with the application of any kind of injection of substances into the skin by professionals who are not M.D.

A systematic review of the literature concerning the risks, complications and adverse effects of techniques for the microinjection of substances into the skin is presented here.

Material and methods

A search and selection was carried out of scientific publications mentioning in their title or abstract some type of risk, complication or adverse effect of mesotherapy and techniques for the microinjection of products into the skin or dermis was carried out. Only texts containing primary original information were included, which had been published in indexed journals subject to a review process. The criteria for the exclusion of articles were: opinion articles, author reviews, systematic reviews, meta-analysis, consensus documents and any other kind of secondary information.

Medline is nowadays considered to be the most comprehensive international database in terms of specialised medical contents and is the most consulted database by clinical researchers providing the greatest amount of reliable clinical information. The search for and selection of articles was performed by two experts in medical documentation, based on recommendations on how to carry out this type of study[6-9]. A data dump of the Medline information was performed, with an auxiliary search in Google Scholar. The intention was to include other possible primary texts that were considered of special interest and excluded from Medline. Key words and descriptors used were: *mesotherapy, intradermotherapy, microinjection, safety, side effects and complication*. The most productive selection strategy was the reading of titles and abstracts of 197 articles found by using the key word "*mesotherapy*". The degree of concordance in the independent selection of articles, by both experts, was evaluated by using Cohen's kappa coefficient. The complete text of the selected articles was requested and they were ordered chronologically from the oldest to the newest, in order to facilitate a historical overview of the various adverse events and complications that had been reported. The following was considered for the data exploitation: 1) type of study 2) author affiliation and origin of cases, 3) type of risk, complication or adverse effect reported, 4) number of registered cases and 5) principal data from each study to enable a global study of all of them.

Results

A good concordance was confirmed in the selection of publications by both experts (Cohen's kappa coefficient = 0.86). A total of 53 articles containing original, well-documented information in complete texts were obtained for analysis[10-62]. Two publications that appeared in two different journals commenting on the same cases but with different focuses and that had previously been included were excluded. Out of the 53 articles found, 34 were related to single clinical case reports (case reports, letters to the editor or comments

with few cases and only one well-defined case study), 9 articles were short case series covering between 2 and 14 patients and 10 articles were clinical studies with samples of 15 or more patients. Out of these 10 clinical studies, 9 were retrospective studies on outbreaks of atypical mycobacterial infections secondary to mesotherapy. The remaining clinical study was a pilot trial on efficacy, containing a few irrelevant adverse effects. No randomised or controlled trials with adverse effects were found.

The information from the 9 retrospective studies concerning epidemic outbreaks was evaluated as a whole, while attempting to find similarities between them. All of them concerned outbreaks of non-tuberculous mycobacteria, due to failings or shortcomings in the application, which could be prevented[24,27,29,38,43,45,46,48,53]. Tables 1 and 2 show the basic data of all the analysed studies in chronological order to facilitate a historical evaluation of how the various complications have occurred. The references found extend throughout the period between 1984 and 2016, with those that appear after 2005 being more frequent, meaning that over half of the references are after 2008.

It was observed that mesotherapy is practised in many parts of the world and that alarms regarding adverse effects come from a wide range of geographical locations. The initial cases came from France, and then later also came from other European Union countries such as Spain and Italy. The outbreaks of infections by atypical mycobacteria were only recorded in Latin America and in Mediterranean Europe (Tables 1 and 2). Cases of adverse effects were not reported from Anglo-Saxon countries, except for relatively isolated cases in the USA.

The best documented complication of mesotherapy is infection by non-tuberculous atypical mycobacteria, which are aggressive and difficult to treat [10,11,15,16,18,20,22,24,27,29,35,38,41,43,45,46,48,52,53].

They cause serious skin and subcutaneous cellular tissue conditions, including nodules, abscesses, fistulas and residual scarring, especially in aesthetic

Year	Country	Complication/Adverse Reaction	Cases	Ref.
1984	France	Cutaneous infection (NTM-Mycobacterium spp)	2	10
1987	France	Cutaneous infection (NTM-Mycobacterium spp)	1	11
1987	France	Severe intolerance reaction	1	12
1992	France	Liquenoid eruption	1	13
1994	Italy	Urticarial reaction	1	14
1997	France	Cutaneous infection (NTM-Mycobacterium spp)	1	15
2001	Spain	Cutaneous infection (NTM-Mycobacterium spp)	3	16
2001	Italy	Isomorphic Koebner phenomenon in psoriasis	1	17
2002	France	Cutaneous infection (NTM-Mycobacterium spp)	2	18
2004	France	Urticaria pigmentosa	1	19
2004	USA	Cutaneous infection (NTM-Mycobacterium spp)	1	20
2005	Korea	Subcutaneous nodules and fat necrosis	1	21
2005	Belgium	Cutaneous infection (NTM-Mycobacterium spp)	1	22
2005	Brazil	Abdominal haematoma	1	23
2006	Venezuela	Cutaneous infection (NTM-Mycobacterium spp)	49	24
2006	P.Rico	Systemic lupus erythematosus	1	25
2006	USA	Panniculitis	1	26
2007	Colombia	Cutaneous infection (NTM-Mycobacterium spp)	15	27
2008	Spain	Sporotrichosis	1	28
2008	Perú	Persistent cutaneous abscesses	35	29
2008	USA	Multifocal scalp abscess and scarring alopecia	1	30
2008	USA	Granuloma annulare	1	31
2008	S.Arabia	Facial cutaneous ulcers	1	32
2008	USA	Delirium with psychotic features	1	33
2008	USA	Non-infectious granulomatous panniculitis	2	34

Table 1 - Complications and adverse effects reported between 1984 and the middle of 2008. It shows the year of publication, the origin of the authors and patients, the number of cases included in each study and the bibliographical reference number

Year	Country	Complication/Adverse Reaction	Cases	Ref.
2008	Spain	Cutaneous infection (NTM-Mycobacterium spp)	2	35
2008	Brazil	Factitious thyrotoxicosis	1	36
2009	USA	Orbital fat inflammation	1	37
2009	Argentina	Subcutaneous nodules (NTM-Mycobacterium spp)	19	38
2009	Turkey	Cutaneous granulomatous reaction	1	39
2009	USA	Disfiguring scarring	1	40
2009	Italy	Nodules, abscesses and sinuses (NTM)	1	41
2009	Brazil	Patchy alopecia	2	42
2009	France	Cutaneous infection (NTM-Mycobacterium spp)	16	43
2009	Italy	Lymphoadenopathy due to Pseudomona aeruginosa	1	44
2010	Spain	Cutaneous infection (NTM-Mycobacterium spp)	39	45
2010	Venezuela	Cutaneous infection (NTM-Mycobacterium spp)	68	46
2010	Spain	Panniculitis	3	47
2010	Colombia	Cutaneous infection (NTM-Mycobacterium spp)	29	48
2010	Turkey	Panniculitis in a case of Behcet's diseases	1	49
2010	Greece	Urticaria	1	50
2010	Colombia	Cutaneous tuberculosis (M. tuberculosis)	6	51
2011	Thailand	Cutaneous infection (NTM-Mycobacterium spp)	1	52
2011	Spain	Cutaneous infection (NTM-Mycobacterium spp)	17	53
2011	Spain	Systemic symptoms (rash, drowsiness, itching…)	7	54
2011	Spain	Multiple subcutaneous nodules	1	55
2012	Brazil	Oleoma	1	56
2012	Serbia	Severe acute caffeine poisoning	1	57
2013	Italy	Mild adverse reactions	15	58
2013	France	Nicolau syndrome	1	59
2014	Mexico	Supurative granuloma due to Nocardia brasilensis	1	60
2015	Turkey	Frontal edema	1	61
2016	Turkey	Panniculitis	1	62

Table 2 - Complications and adverse effects reported between the middle of 2008 and July of 2016. It shows the year of publication, the origin of the authors and patients, the number of cases included in each study and the bibliographical reference number

intervention areas such as the abdomen, the buttocks and hips. Table 3 shows the mycobacterium species that have been isolated from injuries secondary to mesotherapy, many of them causing major aesthetic damage (M. abscessus, M. chelonae and M. fortuitum)[24,27,29,35,43,46-48,52,53,48]. Cases of cutaneous tuberculosis by Mycobacterium tuberculosis have also been confirmed[51]. Non-mycobacterial infections are due to inoculation using microneedles of other microorganisms, such as Sporothrix schenckii[28], pseudomona[44] and nocardia[60]. Other cutaneous-subcutaneous tissue conditions, due to infection or not, include nodules, granulomas, panniculitis, fat necrosis, lichenoid eruptions, oleomas and Nicolau dermatitis, among others (see complications and references shown in Tables 1 and 2). The corresponding original articles show illustrative photographs and specify the details of each case. There are also many complications from mesotherapy in hair treatments. For example, persistent edema of the forehead after mesotherapy using minoxidil[61], or cases with a worse prognosis such as multifocal abscesses with subcutaneous fat necrosis and cicatricial alopecia[30]. Some injected substances include mixtures of natural extracts from plants, homoeopathic products, vitamins, vasodilators, finasteride and minoxidil. Duque-Estrada et al. describe a severe case of cicatricial alopecia after the injection of only homoeopathic agents[42].

Although one of the objectives of mesotherapy is to reduce systemic complications associated with drugs, some mesotherapy cases have caused generalised disorders. The described disorders include cases of weakness, rashes, drowsiness and itching[54], urticaria[50], systemic lupus erythematosus[25],

delirium and psychosis[33], thyrotoxicosis factitia[36] and caffeine intoxication[57]. It has also been suggested that mesotherapy could be associated with graver complications in patients with autoimmune diseases, especially with Behçet's disease[49].

Regarding the 9 studies concerning post-mesotherapy outbreaks of atypical mycobacteria[24,27,29,38,43,45,46,48,53], the following results were obtained:

1. The existence of epidemic outbreaks of non-tuberculous atypical mycobacteria after mesotherapy treatments was confirmed, with a proven cause-and-effect relationship, in Venezuela[24,46], Colombia[27,29], Peru[29], Argentina[38], France[43] and Spain[45,17]. Spain is the European country with the highest number of cases in these outbreaks, according to the information on Medline.
2. The reason for the mesotherapy treatment in all outbreaks was to reduce cellulitis or localised obesity.
3. The injected products were unknown products, homoeopathic products or unauthorised substances. In Venezuela the substance is known as "Lipoescultor" and contains plants, algae, minerals and salts usually used in homoeopathy. Homoeopathic products were injected in Spain.
4. The characteristics of the injuries were the same in all the studies (granulomas, abscesses and ulcers) without response to the antibiotic treatment.
5. The injuries were located in the injection sites, generally the abdomen, hips, buttocks and legs, in the form of abscesses and suppurative ulcers.
6. The laboratory analyses were positive for non-tuberculous mycobacteria, often isolating the species (references included in Table 3).
7. In general the patients had attended the same centre and the same product had been applied to them.
8. In most cases the therapist was the same.
9. The genetic epidemiological studies of the microorganisms showed that all the patients had the same source of infection in common, which did not come from the environment.
10. The studies that completed the research concluded that the injected products were not authorised, were probably contaminated and/or the hygiene measures were inadequate.
11. Various authors have stated that it is necessary to intervene because new preventable outbreaks are predicted. The best way to do so is by using authorised products applied by doctors trained in the technique and guaranteeing the sterility and asepsis conditions at all times.

Mycobacterium specie	References
Mycobacterium abscesus	24, 35,46,47,52,53.
Mycobacterium chelonae	24, 27, 29, 43, 48.
Mycobacterium fortuitum	11, 16, 24, 41, 45.
Mycobacterium bovis	15, 18.
Mycobacterium cosmeticum	20, 24
Mycobacterium peregrinum	24
Mycobacterium simiae	24
Mycobacterium immunogenum	38
Mycobacterium frederiksbergense	43
Mycobacterium tuberculosis	51

Table 3 - Isolated mycobacterium species from cutaneous and subcutaneous injuries caused by mesotherapy. The species Mycobacterium cosmeticum was identified for the first time from a cutaneous infection caused by mesotherapy and was particularly aggressive

Discussion

The main limitation of this study is the lack of other valid publications, those not included in databases or those are included in databases other than Medline, which have not been considered. Recognising this limitation, this review is the broadest review of complications from mesotherapy carried out to date in terms of number of original articles included in the references.

Complications from mesotherapy are an ongoing problem considering that most of them have been reported since 2008. Injected products, including homoeopathic products, can cause a wide range of adverse reactions that are localised or systemic in isolated cases. Complications can exceptionally arise in ideal application conditions, depending on the particular characteristics or hypersensitivity of patients. These cases can rarely be prevented and that is why it is important to assess the benefit/risk of mesotherapy interventions, always in the clinical context of patients. It is important to bear in mind that patients with autoimmune diseases could have more complications due to different immunological responses to exogenous substances, including homoeopathic substances[25,49].

There has been awareness of soft-tissue infections by non-tuberculous mycobacteria since the first references found in 1984. In epidemiological terms, isolated cases or short case series at different times cannot be considered as equal to dozens of cases in a short period of time with a common infectious source. That is, infections caused by atypical mycobacteria are relatively frequent as isolated cases, due to a regular shortcoming in a treatment, or because the risk of infection also exists when things are done correctly. Some single cases presented as abscesses or granulomas or other types of injuries, where there has been no cultivation or identification of germs, could well relate to atypical mycobacteria. This is one of the risks of mesotherapy. Cases of mycobacterial epidemic outbreaks are different and action can be taken against them, because they are a consequence of using

unauthorised products, probably poorly sterilised, and/or a lack of hygiene in one or more of the steps of the application technique. The chain of infection from mycobacteria to a successive series of patients in a short period of time is related to a lack of knowledge and hygiene[24,27,29,38,43,45,46,48,53].

In Latin America and Mediterranean Europe, mesotherapy is usually used to treat skin infections and aesthetic conditions such as keloids, alopecia areata and diffuse alopecia, and especially for cellulitis and localised obesity. Often the doctors who treat complications in patients are not the same therapists that have applied mesotherapy, have no knowledge of the products that have been injected and end up lost in a single research study that is hindered when the "therapists" involved are not doctors.

In the cases of Latin American countries, the most commonly injected substances include vasodilators, lipolytics (carnitine, aminophylline), minerals, vitamins and natural extracts from plants (artichokes, centella asiatica) alone or combined with local anaesthetics (lidocaine or procaine)[24]. Venezuela is the country with most reported cases. The therapists were doctors, cosmetologists and people without any licence[24], and many of the products injected were not submitted to any quality control inspections.

Venezuelan doctors have investigated these outbreaks in depth, both clinically and in laboratories[24,46]. The inoculated mycobacterial species have also aroused the interest of the Center for Disease Control and Prevention (CDC, Atlanta, USA) regarding Mycobacterium cosmeticum, an isolated species that was first identified from a post-mesotherapy cutaneous infection in a Venezuelan patient and is particularly aggressive[20].

The clinical experience in Venezuela with atypical mycobacteria is described by Rivera Olivero et al., emphasising the difficulties and the delay in the definitive diagnosis experienced by patients. He also warns against this practice when it is performed inadequately in unsuitable conditions, using products that do not have health permits and unqualified therapists[24]. This is echoed by Da Mata Jardín et al., who describes in great detail the essence of these outbreaks in terms of their epidemiology and their laboratory analysis[46].

In February 2005, when epidemic outbreak cases were still unknown, the Virginia Department of Health (USA) and the CDC reported an accumulation of cutaneous adverse reactions secondary to mesotherapy treatments performed by a therapist without medical qualification in the district of Columbia (USA). An investigation was carried out and 20 affected patients were interviewed.

16 of them reported adverse reactions in one or more injection sites, in 14 cases the adverse effects lasted longer than three days and 11 of them still presented the injuries at the time of the interview. Said injuries consisted of redness, swelling and, in some cases, ulcers. Based on the interviews with the affected patients, it was recorded that the interventions were performed with a lack of hand hygiene, a failure to disinfect the skin using an antiseptic and a failure to use gloves. At that time the therapist could not be found. The patients stated that the injected substance contained plant extracts, liquid "graphites", procaine and other substances.

Apart from procaine, none of the substances reported by the affected patients was authorised by the FDA for injection. Injury samples could only be obtained in a few cases and laboratory cultures were inconclusive[63]. In the light of the current experience, the clinical and epidemiological characteristics of the case suggest that it must have been an outbreak of mycobacteria.

Mesotherapy for medical-aesthetic purposes must be exclusively applied in accordance with medical procedures, because the indication and application of the treatment, ensuring asepsis measures during interventions and the treatment of possible complications are all medical actions.

The Italian Society of Mesotherapy (SIM) has made a similar recommendation, with a reminder that the application of mesotherapy requires a clinical diagnosis and informed consent, which records the potential benefits, limitations and possible risks, however slight they may be, and regardless of the injection method used[64,65].

Taking into account that the vast majority of the adverse effects of mesotherapy are not reported, these data are just the tip of the iceberg. It has been demonstrated that mesotherapy is not a harmless procedure, that there are serious risks that are not sufficiently taken into account and that certain cases could represent a public health problem. Any microorganism is potentially inoculable by using microneedles and any substance could cause local or generalised adverse reactions in predisposed patients.

Health authorities and political bodies need to remain alert concerning the risks to public health represented by the practice of mesotherapy without the necessary health, hygiene and medical training measures.

The Spanish Society of Aesthetic Medicine (SEME), along with other similar European medical societies, stresses the need to act against cases of professional encroachment in a manner that is consistent with the potential damages that can be caused and that are included in this review.

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The effects of weight loss on oedematous fibrosclerotic panniculopathy and body composition: a review

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ABSTRACT

Adipose tissue acts as an endocrine organ. Adipocytes represent the primary cell type of adipose tissue and they are responsible for storing excess calories, as triglycerides, in their cellular lipid droplets, without the common lipotoxicity experienced by other cells under such circumstances. Oedematous fibrosclerotic panniculopathy (cellulite) is a modification of the topography of the skin that happens mainly in women on the pelvic region, lower limbs and abdomen. It is characterized by a padded or 'orange peel' aspect. In females, fat cell chambers, "papillae adiposae", are sequestered by connective tissue septa, positioned in a radial and arched manner and fix the dermis to the muscle fascia. The subcutaneous fat cell chambers swell into the dermis, there by changing the cutaneous surface appearance. Oedematous fibrosclerotic panniculopathy may be classified into four grades according to histopathological and clinical changes. Many people confuse cellulite with obesity. This is mistaken; in obesity, only adipocyte hypertrophy and hyperplasia are observed, while in oedematous fibrosclerotic panniculopathy, there are a lot of structural modifications in the dermis, microcirculation and inside the adipocytes. The purpose of this review is to highlight the need to further study the long-term effects of a low calorie diet and the resulting change in body composition and oedematous fibrosclerotic panniculopathy.

Keywords
Cellulite, body composition, weight loss

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Introduction

The prevalence of obesity is increasing in the industrialized world, so that the World Health Organization considers obesity as a "pandemic" in rich populations. A large number of studies investigate the maintenance of body composition. Systems that control food intake and/or energy expenditure are able to influence body weight. Several substances influence food intake. The "glucostatic hypothesis"[1] emphasizes the role of blood glucose, considering that an increase in glucose blood level induces a reduction of food intake. Leptin, which is a peptide secreted by white adipose tissue, acts on the hypothalamic areas inducing a reduction in food ingestion. This is in agreement with the "lipostatic hypothesis"[2] of food intake. Gastrointestinal hormones can induce a decrease in food intake; this influence is known as the "hypothesis of gastrointestinal control of food intake"[3]. The autonomic nervous system is involved in the control of eating behaviors through influences exerted on the production and loss of heat. Thus, the control of body temperature is strictly associated with the control of body weight; this is in agreement with the "thermoregulatory hypothesis"[4] of food intake. Adipose tissue acts as an endocrine organ by producing various signalling cytokines called adipokines (including leptin, free fatty acids, tumour necrosis factor-, interleukin-6, C-reactive protein, angiotensinogen, and adiponectin). Adipocytes represent the primary cell type of adipose tissue and are responsible for storing excess calories, as triglycerides, in their cellular lipid droplets, without the common lipotoxicity experienced by other cells under such circumstances. Adipocytes exist in a spectrum of subtypes, identified as white or brown cells. White adipocytes constitute the classical fat cell and represent the majority of cells in both visceral and subcutaneous adipose depots. Brown adipocytes encompass smaller brown fat depot that plays a role in thermogenesis in most mammalian species. Edematous fibrosclerotic panniculopathy (Cellulite) is a modification of the topography of the skin that happens mainly in women on the pelvic region, lower limbs and abdomen. It is characterized by a padded or 'orange peel' aspect. Oedematous fibrosclerotic panniculopathy (PEFS) affects 85% of postpubertal female subjects[5], the high incidence and skin appearance that goes with it make it a distressing condition, both from an aesthetic and self-esteem point of view, for the feminine world. PEFS treatment is a priority for the cosmetic and pharmaceutical industries[5,6]. Products[7,8], supplements[9,10], and massage techniques[11,12] expect to treat cellulite, presumably by decreasing the appearance of the dimpled, granulous skin.

Many factors are also thought to influence the formation of PEFS; a genetic predisposition, along with hormonal influences, structural adipose differences, and inflammation may all contribute. It is thought that in PEFS the adipose cells are arranged in chambers surrounded by bands of connective tissue called septae, which span to connect muscle to the inferior portion of the dermis. The adipose cells that are encased within the perimeters of this area expand with water absorption, thereby stretching the connective tissue. This connective tissue can contract and thicken, holding the skin at a nonflexible length, while the surrounding tissue continues to expand with weight, or water gain. This expansion results in skin dimpling and 'orange peel' appearance, mainly in the pelvis, thighs, and abdominal areas.

Nomenclature

The term 'cellulite' was for the first time used in the 1920s to describe the anti-aesthetic modification of the skin's surface. Since then, other more descriptive names have advanced; these include nodular liposclerosis[13], edematous fibrosclerotic panniculopathy (PEFS)[14], panniculosis[15], gynoid lipodystrophy (GLD)[16] and others. Etymologically, cellulite is termed as a localized metabolic disorder of the subcutaneous tissue, which provokes a modification in the female body shape.

Physiopathology and Etiology

The irregular cutaneous surface texture is assigned to the three-dimensional (3D) architecture of the hypodermal connective tissue[17,18,19]. In females, fat cell chambers, "papillae adiposae", are sequestered by connective tissue septa, positioned in a radial and arched manner and fix the dermis to the muscle fascia. The subcutaneous fat cell chambers swell into the dermis, thereby changing the cutaneous surface appearance[20].

Traditionally, there are three principal theories for cellulite etiology. The first regards the architectural subcutaneous tissue (ST) differences between genders and the modifications in the connective tissue (CT). The second, is based on vascular changes and the presence of edema in the intercellular matrix of the affected areas. The third, considers the presence of a chronic inflammatory process secondary to the hormonal activity of the menstrual cycle as the principal cause. A fourth line of research regards genetic influences[21,22,23].

PEFS anatomy and grading

The topographic appearance of PEFS is multifactorial in nature. The overall contour deformity is that of skin depression admixed with lax inelastic epidermis. The area of PEFS can comprise isolated depressions or a cluster of such that leads to an overall rippled

appearance. The depressed areas can be either ovoid or linear in shape. Ovoid areas of cellulite tend to be more prominent on the buttocks or posterior thigh regions. PEFS can be broken down into 3 main structural components: (1) adipocytes and collections of fat cells that are arranged in clusters surrounded by bands of connective tissue; (2) these connective tissue septae, which connect underlying muscle to the subdermal layer; (3) cells held within the perimeters of this area expand and stretch the connective tissue. Eventually, this connective tissue contracts and sclerosis holds the skin at a nonflexible length, while the surrounding tissue continues to expand with weight, or water gain. Authors described an anatomic hypothesis of PEFS based on gender-related differences in the structural characteristics of dermal architecture. They reported that dermal septae of affected women are thinner and more radially oriented than those of unaffected men; this facilitates herniation of adipose tissue into the dermis.

Classification

The physical examination should be done with the patient standing to account for the force of gravity and any asymmetry should be meticulously noted. When examining the area of PEFS, the pinch test can be used, or the patient can contract the muscles in the area, to accentuate the dimpling of the PEFS. The pinch test is done by pinching the area of interest between the thumb and index finger. Tangential lighting can also aid in the visualization of PEFS because this allows for more inspection of contour irregularities. Baseline body weight and body mass index should be recorded.

Also circumferential measurements of the area being evaluated (bilateral thighs, hips, or waist) may be taken. Even depths of individual PEFS depressions can be measured at baseline to compare after treatment.

PEFS may be classified into four grades according to histopathological and clinical changes[13].

Grade I

The patient is asymptomatic and there are no clinical alterations. Ahistopathological evaluation, there may be raised thickness of the areolar layer, raised capillary permeability, capillary ectasia, diapedetic microhemorrhages, adipocyte anisopoikilocytosis, and fusiform microaneurysms within the postcapillary venules.

Grade II

After cutaneous compression or after muscular contraction, there is decreased elasticity, pallor, and decreased temperature. There are no relief modifications at rest. Histopathologically, hyperplasia and hypertrophy of the periadipocyte and pericapillary argentaffin fibril framework happens along with capillary dilatation, increased thickness of the capillary basement membrane and microhaemorrhages.

Grade III

A padded skin and/or an ‘orange peel’ aspect is evident at rest; palpable sensation of thin granulations in the profound levels; pain to palpation; reduced elasticity; decreased temperature and pallor. Histopathologically there is: fatty tissue disassociation and rarefaction ensued by encapsulation of little collections of degenerated adipocytes, forming micronodules; sclerosis and thickening of the internal layer of little arteries; dilation of venules and little veins; formation of numerous microaneurysms and hemorrhage inside the fatty tissue; neoformation of capillaries; obliteration of the border between the dermis and subcutaneous tissue, ensued by a rise in the volume of the fatty micronodules, which are ordinarily dysmorphic; and sclerosis with inclusion of adipocytes inside the connective tissue of the deep dermis.

Grade IV

There are the equal characteristics as in grade III with more palpable, visible and painful nodules, adherence to the profound levels and an obvious wavy aspect of the cutaneous surface. Histopathologically, the lobular structure of the fatty tissue has vanished and some nodules are encapsulated by dense connective tissue. Diffuse liposclerosis (followed by important microcirculatory modifications), telangiectasias, microvarices and varices, and epidermal atrophy complete the microscopic painting.

Relation with BMI and weight loss

People often confuse cellulite with obesity, and this is mistaken; in fact in obesity, only adipocyte hypertrophy and hyperplasia are observed[24], while in PEFS, there are a lot of structural modifications in the dermis, microcirculation and inside the adipocytes. These, in turn, may be linked to additional morphological, histochemical, biochemical and ultrastructural alterations[25,26]. PEFS occurs in lean and obese women and men[27]. Weight gain, however, can accentuate the look of cellulite. Lola K. et al.[28] observed that PEFS severity, measured by expert image evaluation or quantitative surface roughness parameters, was significantly linked to the body fat in the interested region, the architecture (surface area) of the dermal-subcutaneous border, and the tissue mechanical properties (compliance, stiffness).

The body mass index and related anthropomorphic parameters (weight, thigh circumference) were strongly associated with cellulite severity. The observed aspect of PEFS, i.e., PEFS severity as valued by surface roughness parameters, derived upon the percentage of fat in the thigh and surface area of the dermal-subcutaneous junction. The study of Smalls et al.[29] demonstrates that in the majority of subjects studied there was a betterment in cellulite with weight loss, but the condition worsened for others. Betterment was linked to significant reductions in weight and percentage of thigh fat, significantly higher starting body mass index, and significantly higher initial severity. PEFS worsened with a significantly smaller starting body mass index, smaller reductions in weight and no change in the percentage of thigh fat, and significant rise in tissue compliance.

Different parts of the body respond differently to weight loss (ie, abdominal vs. femoral). Mauriège et al.[30] showed very interesting findings about adipose tissue; their research was focalized on the response to a low-calorie diet and its effects on adrenoreceptor (AR) sensitivity on adipocytes of the abdominal and femoral regions in both males and females. Their work demonstrated that there is an overall important decrease in fat cell weight in both sexes by 15% to 20% after an average 10-kg weight loss. Basal lipolysis, maximal lipolytic response to isoproteronol (a b-AR agonist), and dobutamine and procaterol (b1- and b2-AR agonists, respectively) as well as the maximum antilipolytic results of epinephrine (a2-AR agonist) were equal before and after weight loss. But, both b1- and b2-AR lipolytic sensitivities and overall b-AR density were increased in both males and females after weight loss; this result was more evident in the subcutaneous abdominal adipose tissue as compared to femoral adipose tissue. a2-AR antilipolytic sensitivity was decreased in adipose cells from both regions in women, but only in abdominal adipose cells in men, even though a2-AR density stayed unchanged. Furthermore, femoral adipocytes are larger in women than in men. In their work, Mauriège et al.[30] showed that this difference loses its significance after weight loss, because adipose cell size decrease was found to be the same order of magnitude in both genders.

Conclusions

We need further studies to investigate the effects of a low-calorie diet over a long period of time and what effect that diet will have on cellulite and femoral adipocyte a2-AR density and sensitivity.

It is, therefore, necessary to take into account the assessment of the effects of long-term maintenance of weight reached by individuals with higher BMI, as well as, an evaluation of the effects of a change in eating habits on individuals with low BMI, leading to a change in body composition and/or PEFS without necessarily having a weight loss.

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Assessment of the effects of aesthetic medicine treatments on self-esteem, anxiety, and depression levels: a naturalistic cohort study

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ABSTRACT

Evidence has been accumulating that aesthetic medicine treatments improve psychological measures like mood, self-esteem and perceived quality of life. We aimed at testing the effects of aesthetic medicine interventions on psychological function of women undergoing such interventions. We here report the results of our longitudinal prospective, observational study that we conducted from November 2015 to April 2016 on female outpatients undergoing filler, botulin toxin (BoNT-A), skin biostimulation, or peeling. To assess the effect of these treatments on self-esteem anxiety and depression, we administered the Rosenberg Self-Esteem Scale (RSES), the State-Trait Anxiety Inventory Y1 (state anxiety) and Y2 (trait anxiety) and the Beck Depression Inventory II (BDI-II), respectively, at baseline (T0), one month (T1) and three months (T2) after initiation of treatment. At endpoint, 35 women had completed the study. RSES scores increased, with a trend at T1 (p=.069) that became significant at T2 (p=.047). STAI-Y1 scores dropped significantly baseline to T1 and to T2. BDI-II scores also dropped significantly from baseline to T1 and to T2. Aesthetic medicine interventions were associated with significant increasing improvement on self-esteem, anxiety and depression.

Keywords
Self-esteem, depression, anxiety disorders, filling with hyaluronic acid, type A Botulinum Toxin

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Introduction

Patients undergoing aesthetic medicine treatment reappraise their body image and self-awareness[1], thus re-establishing their psychophysical balance and improving perceived self-image. This translates into increased self-esteem, self-confidence and sense of mastery, that in turn positively affects mood and perceived quality of life[2]. In fact, low self-esteem was found to represent a risk factor for depression in a sample of male and female adolescents and young adults[3].

Patients who were receiving aesthetic treatment showed improved self-esteem and quality of life *vs.* placebo[4], as well as mood, that was better in those undergoing botulinum neurotoxin type A (BoNT-A) treatment of glabellar frown lines compared to those undergoing filler or peeling treatment[5].

BoNT-A has also been used to treat depression. In a pilot study, 8 out of 10 Major Depressive Disorder (MDD) patients who received glabellar BoNT-A added on ongoing antidepressant treatment, showed significant reduction of their depressive symptoms[6]. Further randomised controlled studies confirmed the positive effect on mood of glabellar BoNT-A in patients with MDD with an unsatisfactory response to antidepressants[7-9]. Both response (45.7% *vs.* 10.7%) and remission (30.5% *vs.* 6.7%) rates were higher with BoNT-A, compared to placebo[9]. Mood improved with BoNT-A in MDD patients both when administered as monotherapy[8] and as add-on in MDD treatment-resistant patients[10].

Baseline agitation, as assessed with the corresponding item 9 of the Hamilton Depression Rating Scale (HRDS), was found to constitute a reliable predictor of positive clinical response to BoNT-A, and this was speculated to be due to reduced facial expression of negative emotions associated with agitation[11].

The positive effect of aesthetic treatments on self-esteem, as assessed through the Rosenberg Self-Esteem Scale, proved to be long-lasting, as it was present even when the effects of BoNT-A and hyaluronic acid were reduced, three and six months later[12]; furthermore, self-esteem improvements correlated with decreases in depressive symptoms, both clinician-rated (HRDS) and self-rated (Beck Depression Inventory), and with global clinical rating (Clinical Global Impressions Scale).

The main mechanism explaining the "antidepressant" effect of BoNT-A is facial feedback (FF). It is hypothesised that contracting specific facial muscle groups through the stimulation of proprioceptive nerve fibres, delivers motor, cutaneous or vascular signals to the brain, thus modulating emotional experience and positively or negatively affecting emotional perception[13,14]. For example, Strack et al.[13] showed that contracting facial muscles by holding a pen with one's teeth, like when a person is smiling, made people to rate the vision of a cartoon as more amusing.

A recent review suggested that BoNT-A inoculated into the glabellar corrugator, procerous and frontal muscles, which are involved in negative emotions, like anger, sadness, worry and fear, may improve depression[15]. Such treatment would impair intense frowing, leading to decreased FF, thus allowing the patient to feel less sad[16]. In turn, this would translate into social situations with more favourable responses by others that would further enhance patient's wellbeing, as reflected in increased self-esteem, improved mood and lower anxiety. Improved affective state is supported also by animal research; in fact, 5 U/kg BoNT-A inoculation in rat whisker pad was followed by increased striatal noradrenaline and hypothalamic serotonin concentrations[17].

We here report results of a cohort study we conducted in a group of female patients undergoing selected aesthetic medicine treatments, assessing their effect on self-esteem, depression and state anxiety.

Materials and Methods

The study has been carried out consecutively on women between 18 and 65 years of age referring to the outpatient Aesthetic Medicine service of the Fatebenefratelli Hospital of Isola Tiberina, Rome, Italy (SAMEst) or private offices of aesthetic medicine specialists, between November 2015 and April 2016. Patients were either naive to aesthetic treatments or had in the past received such treatments; however, at recruitment they had not received any such treatment for at least 6 s.

Treatments were either hyaluronic acid fillers, BoNT-A, or cutaneous biostimulations (including peeling). The study was naturalistic and longitudinal in nature, involving assessments at baseline (enrolment, T0), one (T1) and three (T2) months after initiating treatment.

Exclusion criteria included male gender, pregnancy, lactation, psychiatric disorders, including somatoform disorders, ongoing psychoactive drug intake, substance or alcohol use disorder, general medical conditions, cancer, or conditions for which aesthetic medicine interventions were contraindicated.

Psychometric rating scales

Rosenberg Self-Esteem Scale (RSES)

This is a 10-item, self-rating scale assessing global self-esteem; higher scores are related to higher self-esteem. The scale has been prepared by Morris Rosenberg in 1965; it investigates a person's favourable or unfavourable attitude towards him/herself[18] and is considered the standard scale for measuring the self-esteem construct[19]. Its Italian version has been

validated in the late nineties[20]. Normal values range from 25 to 35.

State-Trait Anxiety Inventory, Forms Y1 and Y2 (STAI-Y1 and -2, respectively)

20 items each, which measure state and trait anxiety, respectively; higher levels correspond to worse anxiety. The test contains straight and reverse items. The STAI has been developed by Charles D. Spielberger et al.; its first version dates back to 1970[21] and its revision that we used here was developed by the principal author more than a decade after[22].

In both versions, the 1 scale refers to state anxiety and the 2 to trait anxiety. An Italian adult population scored 36.0 (SD=9.7) on state anxiety and 36.5 (SD=9.6) on trait anxiety in the Italian validation of the tool[23]. This population has been stratified in three trait anxiety layers, i.e., less than 35 (low levels of anxiety), between 35 and 43 (medium levels), and more than 43 (high levels of anxiety)[24].

Beck Depression Inventory II (BDI-II)

This is a 21-item rating scale of depression, whose total score is obtained by adding scores of all items; higher scores indicate worse depression. It has been developed by Aaron T. Beck in the early sixties and explores the psychological and somatic aspects of depression with particular reference to the former[25], differently from the clinician-rated Hamilton Depression Rating Scale[26].

This scale showed an elevated internal consistency in adolescent and adult samples[27]. Scores between 0 and 13 indicate no depression, 14-19 are mild, 27-29 moderate, and 30-63 are severe depression. A score above 16 is the cut-off for clinical alertness.

Design of the study

At T0, all patients were explained the purpose and methods of the study and signed free, informed consent for participation in the study. Their sociodemographic and historical data were recorded on a datasheet. On this occasion, the patients completed self-rated scales, i.e., the RSES, the STAI-Y1 and -Y2, and the BDI-II.

At T1 and T2 patients completed only RSES, STAI-Y1, and BDI-II. The study received approval by the local ethical committee (Parere etico comitato etico Fatebenefratelli 2/2014).

Statistical analysis

To choose the statistical testing we first subjected our data to the Shapiro-Wilk Normality Test; normality was found only for RSES data and not for all other tests, hence we applied non-parametric tests. To evaluate the effect of aesthetic treatments on the continuous variables represented by scores on each scale, we performed Repeated-Measures ANOVA with one within-subjects factor and then Student's t-test for RSES data and Friedman's non-parametric analysis of variance for correlated measures to evaluate the progression of the curves of each scale and then Wilcoxon's paired rank-sum test, two-tailed, for the comparisons between each successive timepoint with baseline, and time for STAI-Y1 and BD-II data. We performed Bonferroni correction for each RSES analysis, thus setting appropriate p values to account for multiple comparisons. Spearman's ρ was used to compute correlations. Statistical significance was set at $p<.05$. For statistical analyses we used the IBM® SPSS® Statistics 19 software.

Results

Fifty-six consecutive outpatients were enrolled and received one of the aforementioned aesthetic medicine treatments. Of these, only 35 (57.1%) completed the study. All 21 patients who dropped out were reluctant to continue and most were vague about their decisions. Twenty drop-out patients left the study at T1 and one at T2. Table 1 shows sociodemographic data of the initial sample.

Age, years (SD), range	**49.75 (9.286), 23-65**
Marital status	
Single	12
Married/living together	29
Divorced/separated	12
Widowed	3
Education	
Middle school	2
High school	14
College/University	40
Employment status	
Executive	7
Employee	19
Freelance	19
Student	1
Housewife	7
Retired	2
Unemployed	1

Table 1 - Sociodemographic data of included outpatients (N=56 women)

Our patients scored in the normal range on the RSES across all time points; however, while at T0 they scored on the average at the exact median of the scale, at the three-month follow-up they scored a little higher than the median, nearer to the upper limits of the norm.

At baseline, 13 of the 56 enrolled patients scored low on trait anxiety (23.2%), 26 scored medium

(46.4%), and 17 (30.3%) scored high on trait anxiety.

At T0, 10 patients scored above the clinical alarm of 16 on the BDI-II, which was in the mild range in four of them, moderate in one, and severe in five patients. Two of these patients did not return at follow-up, but in all others there was a significant decline in BDI-II scores, with final scores lower than the clinical alarm cut-off.

On the Repeated-Measures ANOVA, the significance for the self-esteem curve toward increase was slightly above the statistical cut-off (F=2.94; p=.057). Applying the t-test, the mean scores on the self-esteem scale (RSES) went from 30.73 (SD=5.5) at T0 to 32.69 (SD=4.09) at T1 and to 32.91 (SD=4.19) at T2 (Figure 1). The increase in self-esteem was slightly above p cut-off at T1 (t=-1.84; p=.069) and became significant at T2 (t=-2.01; p=.47).

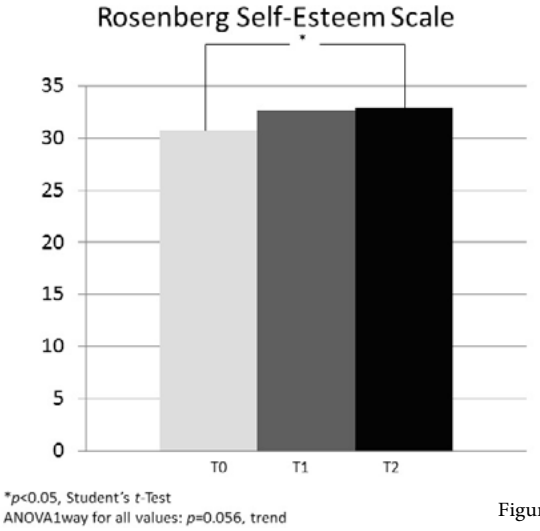

Figure 1

Figure 1 - Mean scores on the RSES of the completers (N=33) during the study

The anxiety curve was significant on Friedman's test (F=10.65; p=0.005). On the Wilcoxon paired test, all comparisons were statistically significant. The reduction from baseline vs. T1 was very significant (Z=-2.79; p=0.0053), as were the baseline vs. T2 and T1 vs. T2 STAI-Y1 score drops (Z=-3.3191; p=0.0009, and Z=-2.185; p=0.029, respectively).

The depression curve was also significant on the Friedman test (F=23.917; p=0.000006) and similarly, BDI-II score drops were significant in all timepoint comparisons. On the Wilcoxon, the BDI-II baseline vs. T1 comparison yielded a Z-value of -3.1353 (p=0.0017), at the baseline vs. T2 comparison the significance was even higher (Z=-4.254; p<0.00000001), and at the T1 vs. T2 comparison somewhat less than the other two (Z=-2.7245; p=0.00652).

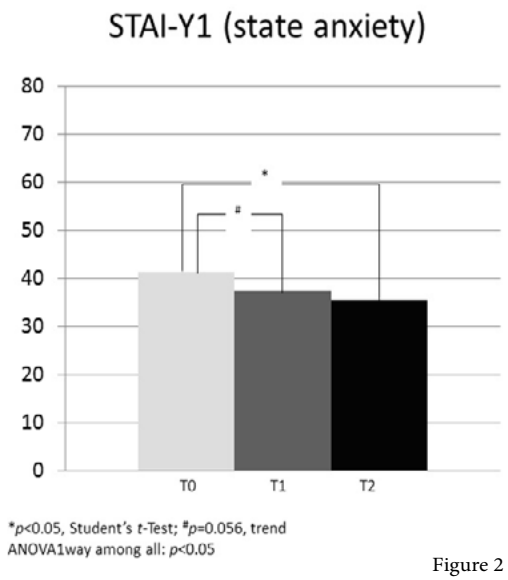

Figure 2

Figure 2 - Mean scores on the STAI-Y1 of the completers (N=33) during the study

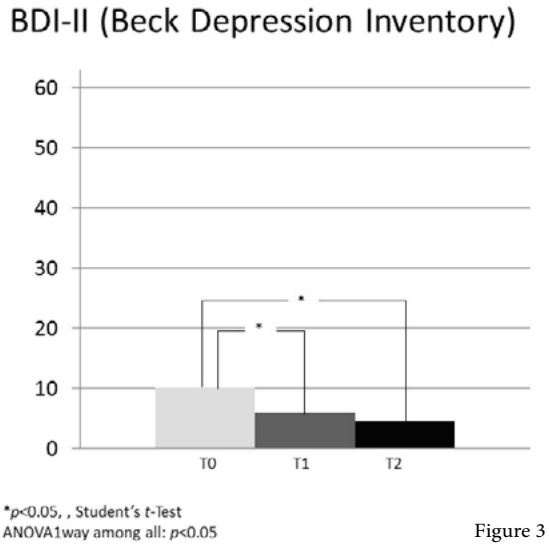

Figure 3

Figure 3 - Mean scores on the BD-II of the completers (N=33) during the study

Age did not correlate with baseline scores on the RSES (Pearson's r=-0.122; p=0.485, n.s.), STAI-Y1 (Pearson's r=0.031; p=0.857, n.s.), STAI-Y2 (Pearson's r=0.113; p=0.519, n.s.), BDI-II (Pearson's r=0.187; p=0.282, n.s.), RSES at T1 (Pearson's r=-0.231; p=0.182, n.s.) and T2 (Pearson's r=-0.079; p=0.652, n.s.), BDI-II at T1 (Pearson's r=0.271; p=0.116) and T2 (Pearson's r=0.153; p=0.380), but correlated positively with STAI-Y1 at T1 (Pearson's r=0.394; p=0.019). Other correlations were carried out with the Spearman' coefficient and are shown in Table 2.

Instrument	RSES BL	RSES T1	RSES T2	STAI-Y1 BL	STAI-Y2	STAI-Y1 T1	STAI-Y1 T2	BDI-II BL	BDI-II T1	BDI-II T2
RSES BL	1	0.72*	0.33	-0.46*	-0.69*	-0.40*	-0.07	-0.55*	-0.46*	-0.25
RSES T1	0.72*	1	0.66*	-0.18	-0.45*	-0.63*	-0.41*	-0.23	-0.57*	-0.24
RSES T2	0.33	0.66*	1	0.011	-0.16	-0.59*	-0.67*	0.02	-0.46*	-0.24
STAI-Y1 BL	-0.46*	-0.18	0.011	1	0.68*	0.22	0.13	0.73*	0.41*	0.45*
STAI-Y2	-0.69*	-0.45*	-0.16	0.68*	1	0.44*	0.10	0.72*	0.58*	0.44*
STAI-Y1 T1	-0.40*	-0.63*	-0.59*	0.22	0.44*	1	0.68*	0.28	0.68*	0.39*
STAI-Y1 T2	-0.07	-0.41*	-0.67*	0.13	0.10	0.68*	1	0.06	0.51*	0.47*
BDI-II BL	-0.55*	-0.23	0.02	0.73*	0.72*	0.28	0.06	1	0.57*	0.58*
BDI-II T1	-0.46*	-0.57*	-0.46*	0.41*	0.58*	0.68*	0.51*	0.57*	1	0.70*
BDI-II T2	-0.25	-0.24	-0.24	0.45*	0.44*	0.39*	0.47*	0.58*	0.70*	1

Table 2 - Correlations between psychometric instruments used in this study (Spearman's *rho*)

Abbreviations: BDI-II, Beck Depression Inventory, II version; BL, baseline; RSES, Rosenberg Self-Esteem Scale; STAI, State-Trait Anxiety Inventory-Y1, State, -Y2, trait; T1, one month after initiation of treatment; T2, three months after initiation of treatment.

*p<0.05

As expected, there were strong intercorrelations between the same test at different time-points and depression correlated with anxiety, while self-esteem correlated negatively with anxiety and depression.

Discussion

In this study we investigated the effects of aesthetic medicine interventions on psychological functioning in women, particularly focusing on self-esteem, anxiety and depression. We found significant effects on all measures at the third month of follow-up, with depression responding also quicker than the other measures. The positive effects were not significant at the one-month follow-up for self-esteem, but became so at the end of the treatment, while anxiety and depression dropped significantly from baseline to both follow-ups. Our data appear to be in line with what found in literature.

The dimensions we explored were all intercorrelated, positively or negatively, according to whether improvement was intended as an increase or decrease of scores on the employed scales, at each timepoint. So self-esteem increased as depression and anxiety decreased. We also obtained a positive correlation between age and anxiety one month after treatment initiation. It should be recalled that moderate anxiety is a predictor to positive response to treatment[28]. Self-esteem was found to be negatively correlated with anxiety and depression also in a study on healthy blood donors that used the same scales as we used here[29]. Another study on Chinese prisoners that used the same scales for self-esteem, anxiety and depression, found that music therapy treatment affected concomitantly all three scales[30]. Self-esteem had a moderation effect on both depression and anxiety in a large Hungarian study of internet problem users[31], and was found to reduce both negative affective states in a meta-analysis[32]. However, the relationship could also be the other way round, as an aesthetic surgery intervention was found to reduce anxiety and depression, which in turn increased self-esteem[33]. Also, effective psychotherapy increased self-esteem and decreased anxiety and depression in a non-psychotic psychiatric sample[34].

Taken together, these literature data agree with our results in that positive treatment effects are associated with favourable simultaneous improvements on all dimensions explored in this study, which we found to be strongly intercorrelated.

Limitations: we here had a high drop-out rate that limit the validity of our conclusions. Since all patients were appropriately explained the study aims and signed free, informed consent, we have no explanation for their subsequent reluctance to continue the study. Another limitation deriving from the relatively small sample size is that we could not perform a valid logistic regression that could allow us to speculate the mediating effects of each dimension involved. A recent study investigating the moderating effects of anxiety, affect, self-esteem and stress on depression found that anxiety partially mediated the effects of both stress and self-esteem on depression, stress partially mediated the effects of anxiety and positive affect on depression, stress mediated the effects of self-esteem on depression, and a significant interaction between stress and negative affect, and between positive affect and negative affect on depression[35]. We did not use a scale to evaluate stress or positive or negative affects, so we cannot compare our results to those of this study; however, the role of positive affect on such outcomes in aesthetic medicine interventions has already been

underlined previously[5,16]. Finally, the distribution of STAI and BDI scores failed normal distribution and obliged us to use non-parametric tests, the results of which are not as strong as those of parametric tests.

Conclusions

Aesthetic medicine treatments are associated with increasingly improved self-esteem and reduced anxiety and depression levels. Positive results are present after one month of treatment and after three months. Depression responds faster and more consistently than anxiety, and both than self-esteem. Our results need to be replicated on wider samples.

Disclosure of interest

All authors have no conflict of interest; the study has not been supported by any public or private agency.

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Courses and Congresses

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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
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Portuguese Society of Aesthetic and Anti-Aging Medicine
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www.spme2016.com
secretariado@spme.pt

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12th National Congress of the Italian Academy of Aesthetic Medicine
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Contents