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REVISIÓN SISTEMÁTICA DE LA COMPARACIÓN ENTRE EL ÁCIDO HIALURÓNICO Y EL HIDROXIAPATITO DE CALCIO EN LA TERAPIA DE REEMPLAZO DE VOLUMEN FACIAL

SYSTEMATIC REVIEW OF THE COMPARISON OF HYALURONIC ACID AGAINST CALCIUM HYDROXIAPATITE IN FACIAL VOLUME REPLACEMENT THERAPY

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Systematic Review of The Comparison of Hyaluronic Acid Against Calcium Hydroxiapatite in Facial Volume Replacement Therapy

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ABSTRACT

A study was carried out whose objective was to carry out a review of the clinical literature to compare the utility of hyaluronic acid versus calcium hydroxyapatite in facial volume replacement therapy. A search was carried out in the databases: Sciencedirect, Springer, and Wiley Science with the keywords: "hyaluronic acid facial", "hyaluronic acid filler", obtaining 854 results from clinical studies. Of which were evaluated by a group of experts, reducing the number of articles to 126, later only those studies that had full text access were collected, obtaining a total of 17 studies included in the hyaluronic acid section. For the consultation of studies of calcium hydroxyapatite, the same databases as the hyaluronic acid section were carried out with the keywords: "calcium hydroxylapatite facial", "calcium hydroxylapatite filler", obtaining 154 articles, of which were Selected by the group of experts 68 articles, of which 11 studies were selected to which full text was accessed. For qualitative analysis, the extraction domains included: main author, year of publication, number of patients, assessment method, patient satisfaction, clinical results. We concluded that the use of hyaluronic acid is slightly superior in terms of clinical results of facial volume replacement therapy.

Keywords: hyaluronic acid, replacement therapy, hydroxyapatite filler

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Revisión Sistemática de la Comparación entre el Ácido Hialurónico y el Hidroxiapatito de Calcio en la Terapia de Reemplazo de Volumen Facial

RESUMEN

Se llevó a cabo un estudio cuyo objetivo fue realizar una revisión de la literatura clínica para comparar la utilidad del ácido hialurónico frente al hidroxiapatito de calcio en la terapia de reemplazo de volumen facial. Se realizó una búsqueda en las bases de datos: Sciencedirect, Springer y Wiley Science con las palabras clave: "ácido hialurónico facial", "relleno de ácido hialurónico", obteniendo 854 resultados de estudios clínicos. De estos, fueron evaluados por un grupo de expertos, reduciendo el número de artículos a 126, posteriormente se recopilaron solo aquellos estudios que tenían acceso al texto completo, obteniendo un total de 17 estudios incluidos en la sección de ácido hialurónico. Para la consulta de estudios de hidroxiapatito de calcio, se realizaron las mismas bases de datos que en la sección de ácido hialurónico con las palabras clave: "hidroxiapatito de calcio facial", "relleno de hidroxiapatito de calcio", obteniendo 154 artículos, de los cuales fueron seleccionados por el grupo de expertos 68 artículos, de los cuales se accedió al texto completo de 11 estudios. Para el análisis cualitativo, los dominios de extracción incluyeron: autor principal, año de publicación, número de pacientes, método de evaluación, satisfacción del paciente, resultados clínicos. Concluimos que el uso del ácido hialurónico es ligeramente superior en términos de resultados clínicos en la terapia de reemplazo de volumen facial.

Palabras claves: acido hialuronico, terapia de reemplazo, relleno de hidroxiapatito

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INTRODUCTION

The usefulness of facial fillers dates back to the 19th century, when the German physician, Dr. Franz Neuber, first described autologous fat as a soft tissue filler for cosmetic deformity. [1] The Food and Drug Administration (FDA) approved since 1980 the use of fillers for cosmetic use in nasolabial folds and lips. [2]

Procedures based on the use of filling materials are indicated in all patients, regardless of age, who present accentuated signs of aging in the region of the upper lip, lower lip, flattening of the upper lip with alteration of the philtrum pillars, furrows nasolabial and labial commissures, with or without alterations of the mandibular contour, especially in Glogau grade I, II and III patients. [3] The choice of injection and filling technique should always be determined based on in-depth consultation, individual patient examination, and occasionally patient preference. [4]

Hyaluronic acid

Hyaluronic acid is a natural polysaccharide present in the extracellular fluid of all living beings, identical in all species and in all tissues, therefore it does not generate immunological activity. The body content of hyaluronic acid in an adult is approx. 15 grams, with a daily replacement of 2 grams. 56% of the body's hyaluronic acid is found in the skin. [5]

Rheology

There is growing interest in the biophysical characteristics of fillers used for soft tissue augmentation. These characteristics reflect unique manufacturing processes and the resulting physicochemical structures. They confer specific flow-related (rheological) properties, including elasticity, measured as elastic modulus; and viscosity, measured as complex viscosity or viscous modulus. Rheological properties have been used as a scientific basis for the selection of appropriate fillers for specific clinical applications (rheological adaptation). [6]

Hyaluronic acid crosslinking

To overcome the limited shelf life of hyaluronic acid caused by its rapid enzymatic degradation in vivo, a cross-linking process was discovered in the 1960s that produces intermolecular bonds between hyaluronic acid macromolecules. It stabilizes the superstructure of this otherwise linear macromolecule. Today, hyaluronic acid fillers are derived from biotechnological processes using

streptococcal biofermentation and are generally cross-linked with a binding agent, 1,4-butanediol diglycidyl ether. [7] Hyaluronic acid dermal fillers are generally divided into two categories, monophasic or biphasic, based on variations in crosslinking. Monophasic hyaluronic acid fillers are more cohesive, may last longer, and may not migrate as much after your injection. [8]

Mechanism of action

One gram of hyaluronic acid can bind up to 6 L of water, and this binding occurs through the formation of a hydrogen bond with the carboxyl group of the hyaluronic acid molecule. At physiological pH, the hyaluronic acid molecule attracts water, causing it to swell. Water molecules bind to N-acetyl and carboxyl groups; It should be taken into account that the units of the molecules are repeated, the longer the molecule, the more places it has for the water molecules to join and therefore the greater the hydration and turgor capacity it will have. [9]

Hyaluronic acid properties

A very important property of hyaluronic acid gels is that they act as a single unit, this forms a physical and chemical barrier against enzymatic degradation and free radicals, this property being greater in cohesive gels, which due to their high viscosity they tend to stick together and remain in the area where they were implanted without showing migration. Another important property of the same is the absorption of water since this maintains the volume for a time despite the degradation of the material; however, the absorption of water in general is not very high because the product is already saturated in water. [10]

Complications of hyaluronic acid fillers

Ecchymosis is the usual problem when using fillers in the facial area, even if it has been worked with previous anesthetic infiltration. The edema, which is generated by the trauma when injecting, adds to that produced by the application of the product. [11] Ecchymosis and edema can be minimized by stopping aspirin, NSAIDs, supplements containing ginkgo biloba, vitamin E, omega-3s, fish oil, ginseng, kava-kava, and St. John's wort at least one week before process. [12]

Lumps, asymmetries, or contour deformities that occur in the early post-treatment period may respond to massage. [13] Also, all hyaluronic acid gels are clear and can result in a slightly visible blue cast injected too superficially; what can be treated with hyaluronidase. [14] Vascular compromise after soft

tissue augmentation with fillers is a major concern, since frank intravascular injection or, less commonly, arterial compression can prevent blood flow through the arteries supplying the skin or even the eye. [15]

Hyaluronidase

Hyaluronidases are actually a family of enzymes that catalyze the hydrolysis of hyaluronic acid. Hyaluronidase has been shown to be effective in vivo in reducing the amount of hyaluronic acid present in non-aesthetic results. [16]

Calcium hydroxyapatite

Calcium hydroxyapatite (CaHa) is the main biomineral component found in human hard tissues, that is, teeth and bones. Its stoichiometry is represented by the formula (Ca10 (PO4) 6 (OH)). It is composed of calcium and phosphorus present in the ratio (Ca / P) of 1.67. [17] Dissolution of CaHA releases calcium and phosphate ions, which are safely removed through the body's normal physiological excretory processes. [18]

This product is especially recommended for the correction of severe facial folds and major maxillofacial defects related to volume loss or lipoatrophy, that is, the loss of facial fat in people with human immunodeficiency virus. After a subcutaneous injection of CaHA, the carrier gel is resorbed in 2 to 3 months and is replaced by the long-term deposition of new collagen, which surrounds the CaHA microspheres that remain at the injection site. [19] While the first instructions for using CaHA were limited to the mid-dermis to treat wrinkles, practitioners have consistently expanded the injection depths to the deep dermis and up to the supraperiosteal to structurally lift and contour the face. [20] Radiesse, trade name for CaHa, is composed of CaHa microspheres suspended in a 70% aqueous gel vehicle composed of 6.4% glycerin and 1.3% sodium carboxymethylcellulose. [21] Radiesse is currently the only FDA-approved filler with a jawline indication. Radiesse is the injection of choice for the jawline because it can define and correct volume through periodic, subcutaneous injections. [22]

Action mode

When injected, the gel that carries the CaHA microspheres fills the areas that have lost volume, providing a lifting effect shortly after treatment and giving immediate volume. The benefits develop over time as the CaHA microspheres stimulate the body's collagen production in the skin. [23] In the

skin, calcium hydroxyapatite results in active physiological remodeling of the extracellular matrix by stimulating a 2-step process, whereby type I collagen gradually replaces type III collagen. [24] CaHa has the ability to stimulate long-term physiological remodeling of the extracellular matrix. Specifically, it has shown an effect on collagen, elastin, and fibroblasts. [25]

The longevity of CaHA is the result of its dual mechanism of action. The product is composed of uniform and smooth synthetically produced CaHA microspheres (25-45 µm diameter) suspended in a sodium carboxymethyl cellulose gel in a ratio of 30% microspheres to 70% gel by volume. In the first phase, the soluble carrier gel evenly distributes the CaHA microspheres at the injection site and provides immediate volume correction. During the second phase, the gel gradually dissipates, leaving the CaHA microspheres at the injection site where they stimulate the production of endogenous collagen and dermal fibroblasts. [26]

Injection Considerations

Although a 25 G to 27 G needle is recommended based on the product label, a 27 G (1 / 2–1 1/2 inch long) needle is more than sufficient. If the tip of the needle is visible after percutaneous insertion, the needle is likely too shallow and placement must be deeper to ensure subdermal injection. [27]

Injection protocol

On the upper face, sunken temples and the area above the eyebrows (front concavity) can contribute significantly to an aged appearance. Adding a small amount of CaHA to this area provides a very subtle forehead lift by restoring volume to a small pad of fat located directly below the brow. In the middle part of the face, restoring volume to the cheekbone and the sunken area under the cheekbone (submalar hollow) returns the face to a more youthful heart shape (youth triangle) and is a subtle way to make a patient look and feel younger. The use of calcium hydroxyapatite for chin augmentation alters the projection of the chin and reduces marionette lines, providing noticeable improvements in an individual's appearance. In the mentum, a multilevel approach is also recommended, where supraperiosteal placement is combined with dermal / subdermal placement. [28]

Complications of the facial application of calcium hydroxyapatite

Calcium Hydroxyapatite filler has an excellent safety record. [29] The side effect profile of calcium hydroxyapatite is often transient and mild, and includes postprocedural swelling, bruising, erythema,

and discomfort. Cases of granuloma formation have been reported. [30] The use of calcium hydroxyapatite fillers in areas with a thinner dermis, such as the nasal dorsum and tear canals, increases the risk of the product accidentally showing through the skin. [31] The formation of cords and papules are usually noticeable at the time of filling, but after 1 or 2 days they become more evident, leaving a raised, shiny whitish cord or papule. The treatment, once detected, consists of applying pressure so that the product is distributed in the tissue or it comes out through the puncture site. Both complications are caused by a very superficial application, but especially by an excess of filling, and if they are not treated they are usually visible for weeks to months. The lower eyelid area deserves special care, where the application of the filling, if it has not been uniform, can leave an irregular area with a cobbled appearance. [32]

Nodule formation after injection of some other CaHa fillers, particularly in the lip, presents complications due to incorrect injection procedures related to superficial placement of too large volumes. This is usually the result of the clinician's degree of experience with the material. If CaHA filler is injected into the middle or superficial dermis, it will result in visible nodules. The nodules can be removed by puncture immediately prior to adhesion of the microspherules to the adjacent stroma. [33]

Complications prophylaxis

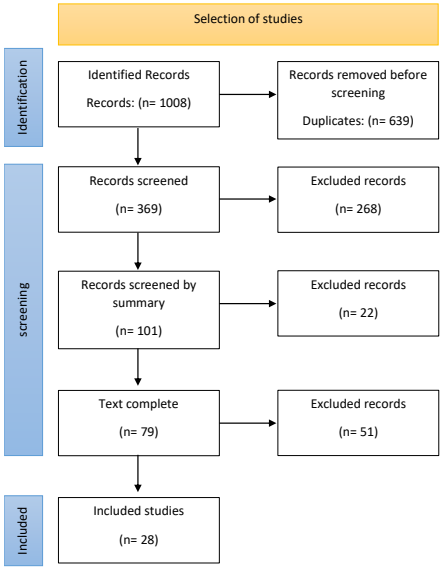
When assessing site-specific risk, the lips are the most likely to develop nodules due to the thin mucosa, the greatest amount of bacterial flora, and the greatest mobility of the perioral region. [34] Various techniques have been suggested for the prevention of vascular complications. These techniques can be divided into 2 categories: 1) reduce the risk of intra-arterial puncture, and 2) in case of intra-arterial puncture, reduce the risk of high-speed, high-volume injection. It is good practice to retract the plunger before injection, although high viscosity fillers such as CaHa may not allow retrograde visualization. [35]

The objective of the study was to carry out a review of the clinical literature to compare the utility of hyaluronic acid versus calcium hydroxyapatite in facial volume replacement therapy.

MATERIAL AND METHODS

A search was carried out in the databases: Sciencedirect, Springer, and Wiley Science with the keywords: "hyaluronic acid facial", "hyaluronic acid filler", obtaining 854 results from clinical studies. Of which were evaluated by a group of experts, reducing the number of articles to 126, later only those studies that had full text access were collected, obtaining a total of 17 studies included in the hyaluronic acid section. For the consultation of studies of calcium hydroxyapatite, the same databases as the hyaluronic acid section were carried out with the keywords: "calcium hydroxylapatite facial", "calcium hydroxylapatite filler", obtaining 154 articles, of which were Selected by the group of experts 68 articles, of which 11 studies were selected to which full text was accessed.

PRISMA diagram of the record selection process



Data extraction

The data extraction method of the studies that met the selection criteria was the use of a data collection form. For qualitative analysis, the extraction domains included: main author, year of publication, number of patients, assessment method, patient satisfaction, clinical results.

RESULTS

Table 1: Hyaluronic Acid Review

Main author	Year	Number of patients	Assessment method	Patient satisfaction	Clinical results
Denton [36]	2007	18	Photographic analysis and 7-point Likert scale	Significant improvement between 1 month and 12 months (p = 0.0466)	Significant improvement between month 1 and 12 (p = 0.3693)
Hersant [37]	2017	31	FACE-Q scale	Not reported	Significant improvement at 6 months compared to baseline (44.3 6 1.9 at baseline versus 52 6 3.17 at 6 months (p = 0.03)
Solish [38]	2018	30	2D motion videos	Satisfaction in 84.3%	93.3% improvement
Black [39]	2017	31	Merz Aesthetic Validated Assessment Scales, Lemperle Facial Wrinkle Scales, 4-point likert scale	Improvement in lip (88%), cheek (94%), nasolabial folds (65%), melolabial folds (80%) and forehead (71%).	The 5 areas studied showed significant improvements (p <0.01)
Ho [40]	2017	19	Carruthers Lipoatrophy Severity Scale (CLSS) and Global Aesthetic Improvement Scale (GAIS)	Improvement reported, but not accounted for	Improvement reported, but not accounted for
Ho [41]	2016	19	Carruthers Lipoatrophy	Not reported	100% improvement in GAIS scale

			Severity Scale (CLSS) and Global Aesthetic Improvement Scale (GAIS)		
Vitagliano [42]	2010	208	5-point Likert scale	Satisfaction with the results in 87.5%	Not reported
Pignatti [43]	2011	54	Ultrasonographic measurement and Global Aesthetic Improvement Scale, VAS-face scale and Freiburg test	GAIS improvement: 87.5%, VAS-Face: 77.9%, Freiburg: 93.6%	Cheek soft tissue thickness increased significantly from 9.45 to 13.12 mm (p <0.0001)
Huang [44]	2020	6	GAIS Scale, Photographic Evaluation	GAIS scale improvement by 67%	Photographic analysis did not reveal significant changes.
Hoffmann [45]	2009	70	Facial Volume Loss Scale and GAIS	88% reported a very significant improvement	The mean scores on the Facial Volume Loss Scale decreased significantly (p <.001)
Iannitti [46]	2014	60	Wrinkle Severity Rating Scale	Not reported	Improvement in the Wrinkle Severity Scale (p <0.001)
Choi [47]	2015	66	Wrinkle Severity Rating Scale and GAIS Scale	There was no significant improvement	Significant improvement in Wrinkle Severity Rating Scale
Sood [48]	2011	10	Photographic records	100% satisfaction	Not reported
Wu [49]	2016	88	Wrinkle Severity Rating Scale and Global Aesthetic Improvement Scale	GAIS improvement of 60.9%	Improved Wrinkle Severity Rating Scale of 100%

Xi [50]	2019	27	Standardized marginal reflex distance 2 (MRD2)	Not reported	MRD2 improvement of 1.19 mm at 9 months
Reuther [51]	2009	19	Ultrasonographic measurement and use of cutometer to assess skin elasticity	Not reported	Significant changes in skin elasticity ($p < 0.05$)
Baspeyras [52]	2013	55	Cutometry and ultrasonography	Not reported	The thickness of the skin increased significantly ($p = 0.008$). The elasticity of the skin improved for up to 2 months, after which the effect disappeared.

Table 2: Review of calcium hydroxyapatite

Main author	Year	Number of patients	Assessment method	Patient satisfaction	Clinical results
Alam [53]	2011	3	Photographic record	Satisfaction not quantified	Not reported
Alam [54]	2007	22	Telephone interview	Duration of effect more than 12 months	Not reported
Kerscher [55]	2018	22	Global Aesthetic Improvement Scale (GAIS) and Merz Aesthetic Scale (MAS)	50% satisfaction	Mas scale score decreased by at least 1 point in 89%.
Moers [56]	2007	60	Wrinkle Severity Rating Scale and GAIS Scale	GAIS improvement by 79%	31% improvement in wrinkles
Bass [57]	2010	117	Lemperle Rating Scale and Global Aesthetic	94.6% improvement in GAIS	Average increase of 1.23 points on the Lemperle scale

			Improvement Scale (GAIS)		
Roy [58]	2006	82	5-point Likert scale	Average score of 4.9	Average score of 4.6
Berlin [59]	2008	5	Biopsy at 6 months	Not reported	Type I and Type III collagen deposition
Jansen [60]	2006	609	5-point Likert scale	Average score of 3.94	Not reported
Tzikas [61]	2008	1000	Photographic record	88% satisfaction	Not reported
Silvers [62]	2006	100	Global Aesthetic Improvement Scale (GAIS) and Facial Lipoatrophy Severity Scale	91% improvement	91% improvement
Carruthers [63]	2008	30	Global Aesthetic Improvement Scale (GAIS) and photographic record	100% satisfaction	80% improvement in GAIS scale at 3 months. Significant increase in the thickness of the skin of the cheeks

DISCUSSION

It is appreciated that both fillers have similar effectiveness profiles. Unfortunately, few studies use an objective means to assess the changes produced by the intervention; In the few cases where there was an objective assessment, a 100% superiority was shown with the use of hyaluronic acid reported by Ho et al (40), while for the use of calcium hydroxyapatite Carruthers et al [63] reported an improvement of only 80%.

In addition to the clinical changes, a superiority in the use of hyaluronic acid is shown due to the fact that, as it is a material that is absorbable by the body. The need to correct hyaluronic acid filler overfilling should be rare, but at a time when injectable fillers are achieving a longer duration of action, even to the point of permanence, it is reassuring to know that a reasonably longevity filler exists. which can be completely reversed if you wish. [64]

In contrast to the characteristics of calcium hydroxyapatite, which is a material resistant to degradation by the body. [65] However, the use of a filler material with a longer duration may be desirable, despite the lack of an effective method of correcting excess material in certain areas of the face, such as those in proximity to bony protrusions.

CONCLUSIONS

The use of hyaluronic acid is slightly superior in terms of clinical results of facial volume replacement therapy.

This systematic review compares the effectiveness of hyaluronic acid and calcium hydroxyapatite in facial volume replacement therapy. The findings suggest a slight superiority of hyaluronic acid in terms of clinical outcomes. Hyaluronic acid's efficacy in improving appearance and patient satisfaction is well-documented, reflecting a general trend in the literature towards preference for this material.

In contrast, calcium hydroxyapatite, while also effective, shows limitations in terms of reversibility and adaptability. These factors are critical in facial filler procedures. The flexibility and reversibility of hyaluronic acid are highly valued in clinical practice.

It's crucial to note that while hyaluronic acid is generally the preferred choice, the selection of material should be based on an individual assessment of patient needs and expectations, as well as the specific characteristics of each substance. The choice of the right filler is a complex process that should consider both the physical properties of the material and the aesthetic and clinical demands of the procedure.

In summary, this systematic review supports the use of hyaluronic acid over calcium hydroxyapatite for facial volume replacement therapy, aligning with the current trend in literature and clinical practice. However, the importance of careful material selection, based on an individualized approach and a thorough understanding of each substance's properties, is emphasized.

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