Adverse Effects of Calcium Hydroxylapatite as a Cosmetic Filler and Therapeutic Alternatives: A Systematic Review

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Abstract

Introduction: The use of calcium hydroxylapatite (CaHA) as a dermal filler has become a common procedure in facial aesthetic medicine due to its biostimulatory capacity and non-surgical lifting effect. However, its application may lead to adverse complications of varying severity, requiring proper management by healthcare professionals.

Objective: To conduct a systematic review of the adverse effects associated with the use of calcium hydroxylapatite as a cosmetic filler and the available therapeutic alternatives for their management.

Methods: A literature search was performed in PubMed, SciELO, Dialnet, and Google Scholar databases, following PRISMA methodology guidelines. Articles published in the last ten years, in Spanish and English, addressing adverse effects related to CaHA application and its treatment options were included. A total of 25 articles were selected after applying eligibility and exclusion criteria.

Results: The most frequently reported adverse effects include dermal nodules, erythema, ecchymosis, edema, and dysphonia, as well as major complications such as skin necrosis and vision loss. Therapeutic strategies described in the literature include the use of sodium thiosulfate ($Na_2S_2O_3$), dilutions with lidocaine and/or saline solution, combined techniques of collagenase ultraphonophoresis and thiosulfate diadynophoresis, as well as the application of vectorized patterns to optimize product distribution and minimize complications.

Conclusion: Calcium hydroxylapatite is a safe material when properly administered; however, its application requires a thorough knowledge of facial anatomy, proper injection techniques, and effective protocols for the prevention and management of complications. The dissemination of ev-

idence-based therapeutic strategies is essential to improve the safety of these procedures in clinical practice.

Keywords: Calcium hydroxylapatite; dermal fillers; complications; adverse effects; sodium thiosulfate; dilution; systematic review.

Introduction

Dermal fillers have become one of the most widely used non-surgical aesthetic procedures worldwide, particularly for the correction of nasolabial folds, lip augmentation, facial rejuvenation, nasal reshaping, and the treatment of minor defects (1–3). Among the materials used, calcium hydroxylapatite (CaHA) stands out for its biostimulatory capacity and lifting effect, making it a frequent option in aesthetic medicine.

Although the application of CaHA is considered safe when performed by trained professionals, it is not free from risks. Complications can be classified as early or late. Early complications include erythema, ecchymosis, edema, nodule formation, infections, necrosis, and skin blanching. Late complications include material migration, hypertrophic scars, telangiectasia, and granulomas (4–6).

Anatomical areas such as the nose, glabella, and periocular region are particularly susceptible to severe complications, including necrosis and visual disturbances. The safety of these procedures largely depends on the practitioner's anatomical knowledge, the injection technique, and the early identification of risk factors (1,5,7,8).

Given the growing demand for procedures involving calcium hydroxylapatite and the clinical relevance of its potential complications, this study aims to conduct a systematic review of the adverse effects associated with the use of CaHA as a cosmetic filler, as well as the therapeutic alternatives available for their management.

Materials and Methods

This study corresponds to a systematic review of the literature on the adverse effects associated with the use of calcium hydroxylapatite (CaHA) as a cosmetic filler, as well as the therapeutic alternatives for its management. The process was carried out following the guidelines of the PRISMA statement, which provides direction for the development of systematic reviews.

Eligibility Criteria

Original articles addressing complications or adverse effects arising from the application of calcium hydroxylapatite in aesthetic procedures, as well

as associated management strategies, were included. Studies published between 2013 and 2023, in Spanish or English, with full-text access were considered.

Theses, books, conference abstracts, editorials, documents without open access, and articles whose content was not directly related to the objectives of this review were excluded.

Information Sources and Search Strategy

The search was conducted in the PubMed, SciELO, and Dialnet databases, as well as in the Google Scholar search engine. The following English terms were used: "calcium hydroxyapatite," "filler," "facial," and "complication," combined using the Boolean operators AND and OR, according to the syntax of each database.

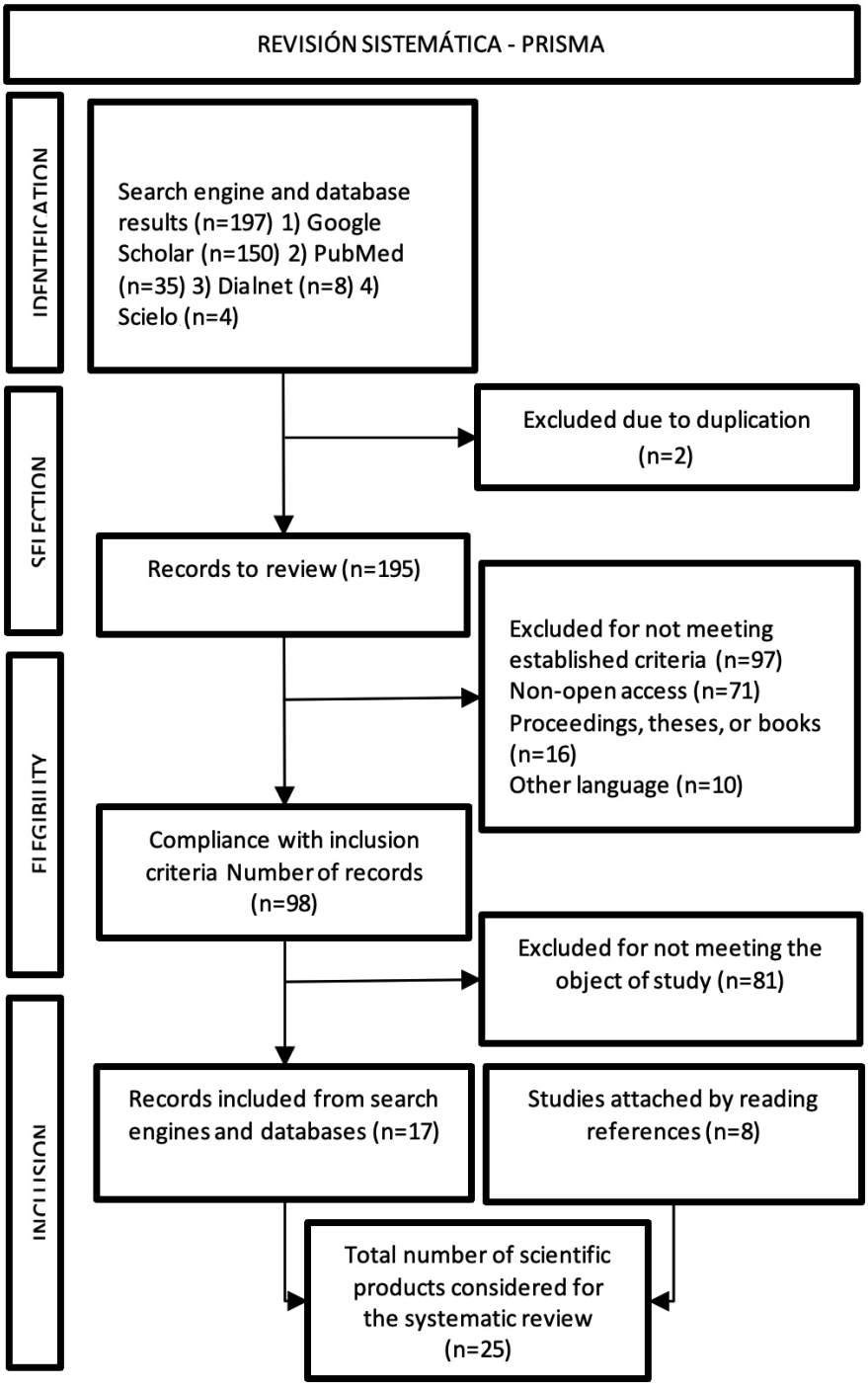
Filters were applied for date (last ten years), language (Spanish and English), and full-text availability.

Study Selection Process

A total of 197 records were initially identified: 150 in Google Scholar, 35 in PubMed, 8 in Dialnet, and 4 in SciELO. After removing duplicates (n = 2) and applying the inclusion and exclusion criteria, 17 articles were selected. In addition, 8 studies were retrieved through manual searching of the references of the selected articles, resulting in a total of 25 studies included in the review.

The selection process is summarized in Figure 1, according to the PRISMA flow diagram.

Figure 1. PRISMA flow diagram



In addition to the 25 articles selected through the application of inclusion and exclusion criteria in the systematic review process, 8 additional references were incorporated to support general concepts, contextualize the use of cosmetic fillers, provide complementary evidence on complica-

tions associated with materials other than CaHA, and substantiate aspects discussed in the introduction and discussion sections of this paper. These references are not part of the central corpus of the systematic review but were considered relevant to enrich the theoretical and clinical understanding of the phenomenon under study.

Results

From the total of 197 records identified in the databases and search engines, 25 articles were selected for this systematic review after applying the inclusion and exclusion criteria.

In general terms, calcium hydroxylapatite is a safe material when used appropriately. However, lack of technical expertise, insufficient knowledge of facial vascular anatomy, or inappropriate patient selection significantly increase the risk of adverse complications, some of which may lead to permanent sequelae.

The detailed information of the selected studies is presented in Table 1, which summarizes the main characteristics of each article, including author, country, year, and journal.

Table 1. Studies included in the systematic review on complications associated with the use of calcium hydroxylapatite as a cosmetic filler.

Author	Country	Journal	Año
Li et al. (9)	China	International Journal of Dentistry	2022
Zerbinati et al. (10)	Italy	Archives of Dermatological Research	2017
Mundada et al. (11)	Switzerland	Insights Imaging	2017
Cohen et al. (12)	Israel	BMC Ophthalmology	2016
Borrelli et al. (13)	United States	Ear, Nose & Throat Journal	2022
Chou et al. (14)	China	BMC Surgery	2015
Rullan & Lee (15)	United States	Cureus	2023
Viscomi (16)	Brazil	Clinical, Cosmetic and Investigational Dermatology	2022
Jang et al. (17)	China	Indian Journal of Dermatology, Venereology and Leprology	2016
Rullan et al. (18)	United States	Dermatología Cosmética, Médica y Quirúrgica	2024
Graivier (19)	United States	Aesthetic Surgery Journal	2021
Leupe & Menger (20)	Netherlands	B-ENT	2016
Vassallo (21)	United States	The Synapse	2018
Hiwa et al. (22)	India	International Journal of Clinical Studies & Medical Case Reports	2022
Halepas et al. (23)	United States	Journal of Oral and Maxillofacial Surgery	2022
Singh et al. (24)	United Kingdom	Aesthetic Surgery Journal	2018
Faria et al. (25)	Brazil	Surgical & Cosmetic Dermatology	2020
Sosa et al. (26)	Spain	Dermatología Revista Mexicana	2022
Liu et al. (27)	Taiwan	Annals of Plastic Surgery	2020
Tran & Lee (28)	United States	Journal of Dermatology and Skin Science	2021
Van Loghem et al. (29)	Netherlands	Journal of Cosmetic Dermatology	2020
Aksenenko et al. (30)	Russia	Journal of Clinical and Aesthetic Dermatology	2022
Virdi & Spotswood (31)	Canada	Plastic and Reconstructive Surgery	2022
Yutskovskaya et al. (32)	Russia	Dermatologic Clinics	2024
Lee et al. (33)	Korea	Journal of the Korean Society of Laryngology, Phoniatrics and Logopedics	2018

The studies included report multiple adverse effects derived from the use of calcium hydroxylapatite (CaHA) as a cosmetic filler, which are grouped into two main categories: early complications and late complications.

Early complications

Early complications, occurring within the first weeks after the procedure, include:

- Mild local reactions: erythema, edema, ecchymosis, and transient pain (9,10,15).
- Formation of superficial or deep dermal nodules, generally associated with inadequate techniques or injection in incorrect planes (11,17,18).
- Acute inflammatory reactions, such as facial cellulitis and severe upper airway edema (13,17).
- Acute vascular compromise, manifested in some cases by ocular pain, blurred vision, ptosis, nausea, headache, and, in the most severe cases, partial loss of vision (12,14,27).

Late complications

Late complications, appearing weeks to months after the procedure, include:

- Foreign body granulomas and persistent nodular reactions (20,26).
- Migration of the filler material, resulting in asymmetries or alterations in facial contour (21).
- Hypertrophic scars or localized fibrosis, especially in areas of repeated injection or inadequate management of complications (20,26).
- Functional complications, such as dysphonia secondary to infiltration in cervical regions or involvement of nearby structures (13).

Severe complications documented

In particular, several studies report serious adverse events associated with CaHA use, including:

- Unilateral blindness, linked to embolization of periocular arterial branches (24,27,28).
- Cutaneous necrosis, usually secondary to vascular obstruction or injection in inappropriate planes (24,31).
- Airway compromise due to severe edema (13).

Therapeutic alternatives described

The reviewed articles propose different therapeutic strategies for managing these complications, notably:

- Infiltration of sodium thiosulfate ($Na_2S_2O_3$) as a CaHA-reducing agent in cases of nodules or severe side effects (18,19).
- Dilution of CaHA with lidocaine and/or saline solution, which decreases viscosity and improves distribution, thereby reducing the risk of complications (23,25).
- Use of combined techniques, such as collagenase ultraphonophoresis and thiosulfate diadynophoresis, for the treatment of granulomas and persistent nodules (30).
- Application of vectorized patterns, which optimize injection techniques by adjusting the volume and distribution of the material according to the patient's anatomical characteristics (25).

Discussion

The findings of this systematic review confirm that although calcium hydroxylapatite (CaHA) is a widely used and generally safe material as a cosmetic filler, it is not free from complications, some of which may be severe and carry the potential for permanent sequelae. The most frequently reported complications in the literature include dermal nodules, edema, erythema, and ecchymosis, which are usually transient and manageable when identified early. However, more severe adverse events have been documented, such as cutaneous necrosis, dysphonia, and, in isolated cases, partial or total vision loss, generally associated with vascular occlusion secondary to injection in high-risk anatomical areas such as the glabellar region, nose, or periocular area (12,14,24,27,28).

These results are consistent with previous reviews and international consensus statements warning about the risks of filler materials, particularly in procedures performed by professionals lacking specialized training in facial anatomy and advanced injection techniques (29). A relevant aspect identified in this review is the growing body of evidence on specific therapeutic alternatives for managing CaHA-associated complications. Sodium thiosulfate ($Na_2S_2O_3$) stands out as a chemical dissolution agent in cases of nodules, granulomas, or vascular events, as well as the use of complementary techniques such as collagenase ultraphonophoresis and thiosulfate diadynophoresis, which have shown effectiveness in the treatment of persistent complications (18,19,30).

Similarly, the reviewed literature supports the practice of diluting CaHA with lidocaine and/or saline solution, which decreases the product's viscosity and allows better control of its distribution, thereby reducing the incidence of complications (23,25). The use of vectorized patterns is another emerging strategy that optimizes treatment planning and precision in product administration (25).

Despite these strategies, prevention remains the main tool to avoid complications. Appropriate patient selection, precise understanding of facial vascular anatomy, mastery of injection techniques, and early recognition of complication signs are key factors in ensuring procedural safety.

Study limitations

This study presents some limitations inherent to the review design. The inclusion of Google Scholar as a data source, although useful for broadening the search, may incorporate literature of lower scientific rigor. In addition, the methodological heterogeneity of the included studies—ranging from case reports to clinical series of varying sizes—limits the possibility of establishing incidence rates or conducting a quantitative meta-analysis.

Clinical implications

The findings of this review reinforce the need for specialized training for professionals performing aesthetic procedures with calcium hydroxylapatite. Likewise, it is essential that clinics and aesthetic centers have complication management protocols in place and access to therapeutic agents such as sodium thiosulfate.

Future research directions

Prospective studies with larger sample sizes are needed to assess the actual incidence of complications associated with CaHA, as well as the efficacy and safety of the different therapeutic strategies available. Moreover, direct comparisons between CaHA and other filler materials, such as hyaluronic acid, in terms of safety and long-term outcomes, would be valuable.

Conclusions

Calcium hydroxylapatite (CaHA) is a widely used material in non-surgical aesthetic procedures due to its biostimulatory capacity and facial lifting effect. However, its application is not free of risks, and the complications reported in the literature include both mild and transient events—such as edema, erythema, and dermal nodules—as well as major complications, notably cutaneous necrosis and vision loss, mainly associated with injections in areas of high vascular risk.

Therapeutic strategies identified in the literature include the use of sodium thiosulfate, dilution techniques with lidocaine or saline solution, and combined procedures such as collagenase ultraphonophoresis and thiosulfate diadynophoresis, as well as the implementation of vectorized patterns to improve product distribution and reduce complications.

The findings of this review highlight the importance of specialized training in facial anatomy and injection techniques, as well as the need for prevention and complication management protocols in centers offering these procedures.

Large-scale clinical research is recommended to assess the efficacy and safety of current therapeutic strategies and to conduct systematic comparisons between calcium hydroxylapatite and other filler materials in terms of outcomes, safety, and complication profiles.

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