Curr Otorhinolaryngol Rep (2015) 3:42–45
DOI 10.1007/s40136-014-0074-5

Complications of Facial Fillers

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Published online: 5 February 2015

Abstract One of the cornerstones of modern facial esthetics is the use of facial fillers. We now recognize that loss of volume is a key aspect of the aging face. In addition to elastosis and rhytidosis, volume rejuvenation is essential to create a natural, harmonious facial appearance. The vast majority of facial filler applications are safe and allow for consistent results. That being said there are a variety of off-label uses of filler as well as expanded indications and usage. No procedure is without complications and the purpose of this article is to evaluate the recent literature and report on the latest findings of complications from facial fillers.

Keywords Complications · Facial fillers · Hyaluronic acid · Calcium hydroxyapatite

Introduction

One of the cornerstones of modern facial esthetics is the use of facial fillers. We now recognize that loss of volume is a key aspect of the aging face. In addition to elastosis and rhytidosis, volume rejuvenation is essential to create a natural, harmonious facial appearance. The vast majority of facial filler applications are safe and allow for consistent results. That being said there are a variety of off-label uses of filler as well as expanded indications and usage. No procedure is without complications and the purpose of this article is to evaluate the recent literature and report on the latest findings of complications from facial fillers.

This article is part of the Topical Collection on *Soft-Tissue Augmentation in Facial Plastic Surgery.*

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Injection Technique

Hexsel et al. [1••], looked at injection-related side effects and complications using a cannula versus a standard needle for soft tissue augmentation of nasolabial folds. In a level 1 evidence prospective double-blind randomized, controlled clinical trial Hexel et al. injected 0.5 mL of hyaluronic acid to bilateral nasolabial folds using a cannula or needle with a standardized injection technique (linear retrograde injection) in 25 women with grade 2–3 according to the modified Fitzpatrick Wrinkle Scale (MFWS) for both nasolabial folds. Standard photographs were taken, each participant was issued a diary to record adverse events, the nasolabial folds were evaluated according to the MFWS and the investigator and participants completed the Global Aesthetic Improvement Scale (GAIS) for each side of the face; follow-up visits were at 3, 7, and 90 days post-procedure. On the day of injections, participants reported significantly less pain, edema, redness, and fewer hematomas on the side injected with the cannula. The blinded investigator's opinion on the day of injection also supported a significantly reduced intensity of hematoma, redness, and pain at the site of injection with a cannula compared to that injected with a standard needle. At all post-treatment visits there were no significant differences concerning reported side effects. Both methods demonstrated improvement from baseline at 3 days post-procedure according to the MFWS, and there was no difference between the two injection methods in GAIS evaluated according to the blinded investigator's judgment and

participant's opinion at day 3. No differences in improvement were found at days 7 or 90 post-procedure. This article demonstrated fewer immediate side effects of treatment with use of a cannula to inject hyaluronic acid filler as compared to the standard treatment with a needle. Although study numbers were low, this evidence gives support to the use of cannula injection technique where applicable.

Injection technique is essential to deliver filler with the minimum of local tissue trauma. Injection technique and fundamentals are also essential to prevent major complications from filler. Kim et al. [2], described a case of unilateral blindness and panophthalmoplegia after injection of hyaluronic acid into the nasal dorsum. This level 4 evidence case report describes a young woman who received a hyaluronic acid containing filler injection into her nasal dorsum for dorsal augmentation and experienced sudden periocular pain and complete vision loss in her right eye. She subsequently developed ptosis and panophthalmoplegia. Axial diffusion-weighted brain MRI demonstrated multifocal punctate high-signal intensity lesions in both frontal areas. Care must be taken with injection placement and pressure when injecting dermal filler into the forehead and nose due to arterial anastomoses and potential for obstruction of the ophthalmic artery or its branches. Nasal augmentation is technically an off-label use for many types of filler. While commonly utilized in this area—it is essential that providers detail all risks, benefits, and possible complications prior to treatment.

Underscoring the potential for post-procedure issues Kim et al. [3], reported a case of accidental intravascular injection of hyaluronic acid filler that led to visual loss and cerebral infarction. This level 4 evidence case report describes a 23-year-old male patient who suffered a right ophthalmic artery occlusion and multifocal infarcts to the right frontotemporoparietal region after injection of hyaluronic acid for augmentation rhinoplasty. Of note, during the injection the patient initially reported severe dizziness but after a brief pause the injection was continued and the patient suddenly experienced severe pain, loss of right eye vision, and dilation of the right pupil. He developed right-sided facial paralysis and left limb paralysis and subsequently received tissue plasminogen activator but the ophthalmic artery did not recanalize. Follow-up CT demonstrated right intracranial hemorrhage and subarachnoid hemorrhage with midline shift ultimately necessitating a decompressive craniectomy. This case highlights the risk of ophthalmic artery/cerebral infarction with dermal filler injections. Physicians should be aware of the potential for accidental intravascular injection and discontinue the procedure if any dizziness, headache, or severe pain is reported. Furthermore, the failed thrombolytic therapy and occurrence of intracranial hemorrhage after administration of tissue plasminogen activator suggests that standard thrombolytic treatment may not be sufficient when arterial occlusion/cerebral infarction is caused by dermal fillers such as hyaluronic acid.

Not all serious complications are recognized at the outset. Tracy et al. [4], reported a case of tissue necrosis after receiving calcium hydroxylapatite filler injection. The level 4 evidence case report describes a 41-year-old woman with a past medical history of rhinoplasty surgery, and multiple prior dermal filler injections to the melolabial folds who received bilateral CHA injections to the melolabial folds and suffered swelling and skin changes to the left alar crease. After initial treatment for presumed infection and subsequent treatment for presumed herpes zoster, she was evaluated at an outside institution (Tzanck smear negative) and found to have frank tissue necrosis with diffuse inflammation and fibrinous exudate. After debridement and daily wound care, the wound healed by secondary intention with subsequent pulsed dye laser therapy to reduce scarring and hyperpigmentation. This case demonstrates the potential for tissue necrosis secondary to either direct embolization of vasculature or compression of local vasculature with filler product. If symptoms suggestive of tissue ischemia are present during or soon after facial filler injection, immediate steps should be taken so as to prevent tissue necrosis. This report highlights the need for providers to know the signs of tissue ischemia and have a plan to treat the affected area. Immediate treatment and initiation of care can significantly reduce tissue damage.

Delayed and Inflammatory Reactions

Permanent soft tissue filers are used less frequently in the United States but have a major presence world wide. It is essential to understand the potential risks associated with this category of fillers. Kadouch et al. [5], examined delayed-onset complications of permanent soft tissue filler injections to the face, specifically monitoring the type of adverse events and factors that may influence onset with the aim of proposing a therapeutic strategy for such complications. The study was a level 4 evidence prospective case series of 85 patients with delayed-onset complications (complications that begin 2 weeks or more after injection of filler). Complications were categorized as non-inflammatory nodules, low-grade inflammation, abscess formation, or migration. Of the 85 patients, the majority (66 patients) had delayed-onset complications after polyalkylimide gel (PAIG) injections. Other permanent fillers studied included hydroxyethyl methacrylate (HEMA)/ethyl methacrylate (EMA), polymethyl methacrylate (PMMA), polyacrylamide hydrogel (PAAG), and liquid injectable

silicone. Time to onset for the delayed-onset complications varied from 1 month to 10 years with a mean onset of 38 months. The most common complications were low-grade inflammation (40 %), migration (40 %), and non-inflammatory nodules (39 %). Abscess formation at the site of filler deposition occurred in 29 % of patients and only occurred in patients injected with PAIG. The majority (72 %) of complications occurred spontaneously, 13 % of patients experienced complications after a visit to a dentist or oral hygienist and 12 % of patients experienced an inflammatory response after additional filler injections. Invasive treatment including intralesional corticosteroid injection, evacuation of filling material, excision of filling material, and incision and drainage of abscess was required in 60 % of the patients. Notably, the study included 34 HIV-positive patients who received PAIG to treat combination antiretroviral therapy-induced facial lipoatrophy. These patients were significantly overrepresented in the abscess formation subgroup. This study not only demonstrated the varied time frames and complication types for delayed-onset complications of permanent soft tissue filler injections but also suggests that characteristics of the filler and patient immune status may influence the type of complication.

One of the complications of any type of filler can be an inflammatory nodule. These can occur many weeks or even months after the initial injection. Ledon et al. [6], examined the etiology of inflammatory nodules for various dermal fillers and their treatments. The article was a level 4 evidence literature review that systematically discussed inflammatory nodule formation for each class of soft tissue filler in use today. Ledon et al. assert that nodules that appear immediately are likely secondary to uneven filler placement whereas nodules that appear days to weeks later and present with erythema and pain are likely secondary to infection. Both nodule presentations may be secondary to any filler type although polyacrylamides, due to their high biocompatibility that may allow low virulence bacteria to flourish, are the most commonly infected filler implants. Nodules that appear weeks to months later that may be palpable, not visible, and present with pruritus and erythema may be secondary to hypersensitivity reactions. Such reactions most commonly occur with collagen, hyaluronic acid, or poly-L-lactic acid and may be treated with antibiotics alone or in combination with hyaluronidase, corticosteroids, surgical drainage, or excision. Nodules that appear within weeks to months after injection and present with pain/erythema may be secondary to development of a sterile abscess, which may be found secondary to the use of hyaluronic acid. Polyacrylamide use may precipitate nodules that appear weeks to months later and present with induration/erythema secondary to infection and require broad-spectrum antibiotics and, occasionally, excision of the material. Polyacrylamide filler use may also precipitate firm, mobile, and photosensitive nodules months to years later that are present as cysts requiring similar treatment. Nodules presenting months to years later with gross disfigurement, pain, and pruritus may be secondary to a foreign body granuloma or chronic, low-grade infection. Such nodules are most commonly found after injection of PMMA, silicone, or hyaluronic acid with acrylic hydrogels. Intralesional steroids, oral antibiotics, or surgical excision are all potential treatments depending on the dermal filler used. Finally, use of autologous fat transplant may precipitate soft, non-tender nodules months to years later that are secondary to lipohypertrophy and may be corrected surgically. The treatment modality chosen for inflammatory nodules after soft tissue filler use should be determined on an individual basis according to the filler used, time frame of presentation, and symptomatology.

Pathology

Understanding the origin of soft tissue filler complications may shed light on their treatment or even their prevention. Faria et al. [7], reported the use of fine needle aspiration cytology (FNAC) to identify adverse reactions to cosmetic dermal filler. In a level 4 evidence case report, Faria et al. describe a patient with history of a dermal polymethyl methacrylate (PMMA) injection who presented with a painful, hardened nodule in her perioral region present for 2 years. Using FNAC with a 24-gage needle, the nodule cytology findings were consistent with a foreign body reaction caused by dermal applications of PMMA. This diagnosis was confirmed with histologic examination of the intraoral excisional biopsy. This case report demonstrates that fine needle aspiration cytology is a viable method of diagnosing adverse reactions to facial cosmetic dermal fillers. The advantage of FNAC is that it is a minimally invasive method of differentiating nodule formation due to an adverse reaction to facial filler that may preclude biopsy with potential for scar formation.

Eversole et al. [8], examined pathology specimens from patients who experienced dermal filler foreign body reactions after undergoing injection lip augmentation. The study was a level 4 evidence case series examining the histopathologic features in twelve cases of perioral foreign nodules that presented as submucosal plaques, nodules or swellings attributable to reactions to dermal fillers. Reactions to six different fillers were identified: bovine collagen, hyaluronic acid, hydroxyapatite, poly-L-lactate, liquid silicone, and hydroxyethyl methacrylate. Eversole et al. found unique histomorphology which may identify the dermal filler involved in the foreign body reactions: cross-

linked collagen, human and bovine, demonstrates eosinophilic coagulum, basophilic lakes are found with all hyaluronic acid polymers, spheroid filler particles identify hyaluronate polymers with hydroxyapatite, and broken-glass like particles identify poly-L-lactate (refractile under polarized light) or hydroxyethyl methacrylate, (non-refractile under polarized light). Host responses to the fillers were also classified. The bovine collagen demonstrated foreign material without inflammatory reaction. Hyaluronate filler lesions showed either the foreign material without inflammatory reaction or the foreign granuloma with epithelioid histiocytic/multinucleated giant cell response. The hydroxyapatite, poly-L-lactate, liquid silicone, and hydroxyethyl methyacrylate all contained a host response classified as a foreign body granuloma with epithelioid histiocytic/multinucleated giant cells. This study demonstrated distinctive histomorphologic features of dermal filler injectables and accompanying foreign body reactions that may be used by pathologists to identify the inciting material in dermal filler reactions.

Conclusions

Soft tissue fillers are an essential part of the armamentarium of any facial cosmetic practitioner. Rejuvenation of facial volume is critical for achieving natural, balanced results. The general and recommended use of FDA-approved facial fillers is quite safe with a low overall complication rate. This review of the current literature highlights the importance of certain rare complications. Also a close connection between injection technique and eventual outcome is demonstrated. Lastly insight is shed on the molecular mechanism for inflammation and local tissue reaction to more permanent fillers.

Compliance with Ethics Guidelines

Conflict of Interest Benjamin Marcus and David Hyman declare no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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