INTRODUCTION

Post-enucleation socket syndrome (PESS) is a common complication in anophthalmic sockets and typically gives rise to enophthalmos and deep sockets.[1-4] The two most frequent causes of this problem are inadequate volume of the orbital implant and decreased volume of intraorbital soft tissues. Insufficient orbital volume often leads to an unacceptable position and appearance of the ocular prosthesis and deep upper eyelid sulcus. Other findings in this syndrome include superior sulcus deformity, ptosis, and lower eyelid laxity.[4-7]

PESS can be addressed by augmenting the orbital volume with a larger orbital implant, subperiosteal placement of sheet or wedge implants, and placement of a dermis fat graft. All these methods are invasive and frequently require hospital admission and administration of general or local anesthesia.[6-14]

Abstract

**Purpose:** To report the long-term results of orbital volume augmentation using calcium hydroxyapatite filler injections in patients with anophthalmic sockets.

**Methods:** Twelve eligible patients with post-enucleation socket syndrome (PESS) and small orbital volumes were included in our study. In this investigation, 1.5 mL injectable calcium hydroxyapatite (Radiesse) was utilized in an off-label application under local anesthesia. We evaluated the effect of orbital volume augmentation for correction of enophthalmos.

**Results:** Five women and seven men with a mean age of 35 years (range, 21-72 years) were included in the study. The mean follow-up was 19.5 months (range, 16-27 months). Enophthalmos and deep superior sulcus were reduced in all patients during all follow-up visits postoperatively. The mean improvement of enophthalmos was 2.58 mm (range, 1-5 mm) and the improvement in deformity grading of superior sulcus was 0.83 (range, 0-4 grade). The mean marginal reflex distance increased by 0.6 mm (range of -1 to 3 mm). Complications included increase in ptosis in two cases and extrusion of the filler accompanied by discoloration of the skin in one case.

**Conclusion:** The use of injectable calcium hydroxyapatite for orbital volume restoration in anophthalmic sockets is a simple, fast, and minimally invasive method with considerable long-term effects and low complications.

Keywords: Anophthalmic Enophthalmos; Calcium Hydroxyapatite; Radiesse

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Recently, fillers have been used to increase the orbital volume as a minimally invasive procedure. Generally, orbital volume augmentation with fillers is a relatively safe, simple, and cost-effective procedure. Different substances such as cross-linked collagen, silicone oil, autologous fat, hydrogel pellet expanders, hyaluronic acid, and polyacrylamide gel have been used for injection in the intraorbital space. However, some limitations and complications such as a short half-life, unpredictable volume restoration, inflammatory reactions, migration, and extrusion of material have been reported. Furthermore, follow-up periods in previous studies were not sufficient to verify the longstanding effects of the injected materials in the orbit.\textsuperscript{[15-23]}

Radiesse (Merz Aesthetics, Inc., Frankfurt, Germany) is a semi-solid filler with the Food and Drug Administration approval for several functional and cosmetic purposes. It constitutes 30\% calcium hydroxyapatite particles (size range, 25-45 microns), 70\% glycerin, sodium carboxymethyl cellulose, and water. In this study, we aimed to evaluate the long-term effectiveness and safety of intraorbital injection of Radiesse filler for orbital volume augmentation in patients with PESS.

METHODS

This study was approved by the scientific and ethics committee of our university. In an interventional study during a period of two years, from January 2014 to April 2016, in our hospital, patients with PESS and small orbital volume were enrolled. Patients with socket restriction and the inability to fit prosthesis were excluded from the study. The procedure, alternative treatments, risks, and benefits of the treatment were explained to all patients, and a signed consent form was obtained prior to injection. One surgeon performed all the procedures.

The severity of enophthalmos was quantified using a Naugle exophthalmometer with the ocular prognosis in place. The sulcus deformity was graded as: 0, normal and symmetric superior sulcus; 1, subtile medial fat pad atrophy; 2, marked medial fat pad atrophy; 3, medial and central fat pad atrophy; or 4, superior sulcus medial to lateral fat pad atrophy (severe form).\textsuperscript{[7]} Ptosis was assessed by measuring the marginal reflex distance 1 (MRD1). In all patients, the procedure was performed at least 3 years after the latest surgery.

Since the orbital injection of Radiesse is painful, it was performed in the operating room with intravenous sedation and retrobulbar injection of anesthesia (2 cc of 2\% lidocaine).

In the supine position, a total of 1.5 cc Radiesse filler was injected using a 23-gauge needle. Approximately two-thirds of the syringe volume was injected into the orbit while the needle was in touch with the orbital floor. Then, the remaining filler was injected deeply in the superior socket [Figure 1].

The needle was passed transcutaneously, and the surgeon tried to inject only in the extraconal space. The injection was performed slowly and only while the needle was being withdrawn from the site. A superficial injection was avoided. Furthermore, very deep posterior injections around the orbital apex were avoided to prevent the unacceptable spreading of the filler into the danger zones of the orbital fissures.

The patients were examined at one day, four months, and twelve months after injection. Results of exophthalmometry, sulcus deformity grading, and evidence of any complications were recorded.

To describe the data, we used frequency (percent) and mean ± SD. To evaluate the differences between the pre and post-injection values, the Wilcoxon signed rank test was used. A P value less than 0.05 was considered as statistically significant. All statistical analysis was performed using SPSS software (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

RESULTS

Twelve patients consisting of five women (42\%) and seven men (58\%) with a mean age of 35 years (range, 21-72 years) were included in the study. The initial indications of enucleation were congenital anophthalmos, painful blind eye, and periocular trauma. The mean follow-up period was 19.5 months (range, 16-27 months).

Enophthalmos and deep superior sulcus improved in all patients during all follow-up visits postoperatively [Figure 2]. The mean improvement of enophthalmos in the last visit was 2.6 mm (range, 1-5 mm) (P = 0.04). The grading of deep superior sulcus deformity showed an improvement of 0.83 (range, 0-2 grades) (P = 0.004) from preoperative to postoperative status. Ptosis was improved in 10 cases with a mean MRD1 change of 0.6 mm (range, -1 to 3 mm, Table 1).

After the procedure, a mild and limited ecchymosis at the site of injection was observed in seven cases and resolved within a few days with conservative treatment. Worsening of ptosis was observed in two patients [Figure 3] which did not improve after six months of follow-up, so a levator resection surgery was performed.

Anterior extrusion of Radiesse gel and subsequently, the presence of lower eyelid skin discoloration (darkening) and a bump were noted in one patient [Figure 4]. This problem did not improve after three months of follow-up. Therefore, a transconjunctival orbitotomy and surgical excision of extruded materials were performed. Pathologic evaluation of the specimen showed mild chronic inflammatory cell infiltration around the calcium hydroxyapatite particles. The discoloration and bump
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**DISCUSSION**

The outcomes of this study showed the relative effectiveness of orbital injection of Radiesse to improve enophthalmos, sulcus deformity, and ptosis. A low rate of complications was also observed in patients with PESS.

An ideal substance for orbital volume augmentation should have certain characteristics such as safety, easy administration, a reasonable cost, and predictable outcomes. In addition, fillers with longer residual effects are preferred.\[^{16,20,23}\] Calcium hydroxylapatite gel (Radiesse) is a biocompatible material with longstanding effects so it can be a good option for orbital volume augmentation.\[^{18‑19}\]

In our study, enophthalmos and deep superior sulcus were reduced in all patients during all follow-up visits postoperatively. Similar to Malhorta’s study, reduction in enophthalmos of 2 mm with a 2-mL injection of hyaluronic acid was achieved in all primary injections.\[^{16}\] However, the effects of hyaluronic acid were temporary, and reduced within the days after the injection.\[^{16,23}\]

In a study carried out by Vagefi et al, a reduction in enophthalmos ranging from 1 to 4 mm was noted per syringe of filler, and each syringe of filler provided a mean improvement of 2.4 mm.\[^{20}\] Although our patients had a history of multiple reconstructive orbital surgeries with some degrees of fibrotic sockets, acceptable outcomes were observed during the follow-up periods.

Anterior dislocation of filler is a potential complication of intraorbital injection of Radiesse gel. The presence of significant fibrosis in the intraorbital tissue secondary to chronic inflammation and iatrogenic surgical trauma disappeared one month after surgery. Lower eyelid retraction was also improved in one patient after the injection of Radiesse gel into the orbit [Figure 5].

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**Table 1. The characteristic of patients (pre and post filler injection)**

| ID | Age (years) | Sex | Exophthalmometer | Sulcus deformity | F.U | Complication |
|----|-------------|-----|-------------------|------------------|-----|--------------|
| ID | Pre-injection | Four months post-injection | Last Follow-up | Pre-injection | Post-injection |
|----|-------------|----------------------------|---------------|-------------|--------------|
| 1  | 21          | M             | 13             | 15          | 14           | 0             | 0             | 22 |
| 2  | 22          | F             | 11             | 13          | 13           | 3             | 2             | 16 |
| 3  | 36          | M             | 11             | 12          | 12           | 1             | 1             | 19 |
| 4  | 27          | M             | 13             | 13          | 13           | 4             | 3             | 18 |
| 5  | 30          | M             | 17             | 17          | 17           | 3             | 1             | 21 |
| 6  | 40          | F             | 14             | 14          | 14           | 4             | 3             | 17 |
| 7  | 27          | F             | 11             | 15          | 15           | 3             | 2             | 17 |
| 8  | 48          | F             | 9              | 11          | 11           | 2             | 1             | 18 |
| 9  | 32          | M             | 15             | 15          | 15           | 4             | 3             | 24 |
| 10 | 26          | M             | 11             | 11          | 11           | 4             | 3             | 27 |
| 11 | 38          | M             | 18             | 18          | 18           | 1             | 0             | 17 |
| 12 | 72          | M             | 15             | 15          | 15           | 4             | 4             | 18 |
| Mean | 35       | 13           | 14           | 14          | 3             | 2             | 20 |
| SD  | 14         | 2            | 2             | 2           | 1             | 1             | 3             |

\( p \) values are based on Wilcoxon Signed Ranks Test (between each follow up and pre-injection values)

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**Figure 1.** Intraorbital injection of Radiesse gel with a 23-gauge needle passed transcutaneous into the deep socket spaces.

**Figure 2.** A 72-year-old man with 4 mm improvement of enophthalmos after the injection of Radiesse gel into the right orbit (left picture).
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selected cases with anophthalmic socket is a simple, fast, and minimally invasive technique with relatively longstanding effects and low complication rates.

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Conflicts of Interest
There are no conflicts of interest.

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