Research Article

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Lipostructure Plus Platelet Rich Plasma Injections for Enophthalmos Treatment in Patients Carrying Prosthetic Eye- Safety and Efficacy

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Abstract

Purpose: *To describe one-year functional and aesthetic outcomes in patients with post-enucleation enophthalmos who underwent lipostructure plus platelet-rich plasma injections.*

Materials and Methods: *26 patients treated with orbital lipostructure and three platelet rich plasma injections at 1, 2 and 6 months after surgery were retrospectively assessed. Photographs of all patients were taken preoperatively and at 1 and 12 months after surgery. The area of each eye lid esthetic unit/subunit was calculated, both in frontal and profile images. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, Illinois, USA). Paired t-test was used to compare the unit/subunit areas before and after surgery. Differences were considered significant when P <0.05.*

Results: *Comparing baseline to 1-month images, an improvement of the enophthalmos appearance was observed in all patients. Analysis of each single esthetic units was performed, with an overall unit area reduction of 19.8%. Comparing the two postoperative images, the overall amount of resorption was 12.75%. The surgical procedure appeared to be well tolerated in all cases. Minor complications regarding the lower eyelid were recorded in 6 cases.*

Conclusions: *lipostructure plus platelet rich plasma injections proved to be a valid and effective option for the treatment of post enucleation socket syndrome.*

Keywords: Enophthalmos, Lipostructure, Platelet rich plasma, Post enucleation socket syndrome, Prosthetic eye.

Introduction

Orbital volume decrease and enophthalmos display variable clinical pictures and may require different surgical treatments.

Enophthalmos, superior eyelid ptosis, inferior eyelid laxity, tilting of the prosthesis and in most cases ageing and deterioration of the periocular region are classically recognized as the post-enucleation socket syndrome (PESS) [1,2]. In recent decades, the most frequently used surgical approaches for PESS treatment included dermo-fat graft, implant of alloplastic tissue on the orbital floor, refilling of the orbital eyelid fold with macro/micro fat graft [3-8].

In order to reduce the rate of complications frequently reported using other techniques (fat migration, inflammation and rejection), we decided to treat our patients modifying the Coleman's technique [5,9]. In 1926, Miller described for the first time the use of autologous fat as filler for face and neck [10]. Later, Coleman brought further improvements conceiving a new technique that involved withdrawal, centrifugation and subsequent copious and reproducible re-injection of autologous fat in the periorbital region [11-13].

Other complementary procedures such as reconstruction of the lower fornix, canthopexy, lower eyelid spacer implant and eyelid ptosis correction may be further associated in order to improve the stability of the prosthesis [14-17]. However, these surgical procedures are often not sufficient to completely solve the enophthalmos, the absorption of fat and subsequent modifications and have the disadvantages to be hugely invasive, surgically complex, involve sutures and scars and have high recurrence rates. In fact, the fat transplantation, especially when grafted with macro-structure features, has a resorption rate greater than 50% over time [18-20].

The evolution of regenerative medicine and tissue reconstruction has significantly increased the interest regarding the use of adipose tissue. In its cellular form, fat tissue represents ideal filler with numerous advantages: widely available, autologous and therefore not immunologically active, non-carcinogenic, non-allergenic, inexpensive and with bio-stimulation and bio-restructuring properties, as confirmed by the discovery of adipocyte derived mesenchymal stem cells [21,22].

The authors describe the results obtained with autologous fat graft modifying the Coleman technique to retrieve orbital volume in patients with ocular prostheses.

Materials and Methods

Patients

We retrospectively analyzed twenty-six (26) patients, 16 women and 10 men with a mean age of 53 years (range 32-62) who referred to our clinic for evaluation and management of post-enucleation enophthalmos. Between February 2013 and March 2015, all patients underwent orbital autologous fat graft (lipostructure) on the orbital floor, into the intraconal portion and inside the superior retro-septal space. This study was approved by the Ethical Review Board of the University of Pisa (Comitato Etico, Pisa University, Pisa, Italy) and was performed in adherence to the tenets of the Declaration of Helsinki; all patients signed an informed consent form.

Inclusion criteria were: post enucleation enophthalmos, 12-months follow-up and complete integration of the prosthetic implant. Patients with metabolic syndrome, cigarette smoking (> 20 cigarettes per day in the last 10 years), alcohol abuse, maxillary sinusitis and previous radiation therapy, psychological problems during pregnancy or lactation and with severe cardiovascular diseases were excluded from this study.

Photographic analysis technique

All patients were pre- and postoperatively photographed using standard techniques for digitized medical photography. In all acquisition, the same ambient light levels, flash intensity and distance between the patient and the camera lens were respected. To avoid the confounding effect of postoperative edema, the photographs were taken at 1 month and 1 year after surgery. The analysis of postoperative morphological variations may be challenging without performing magnetic resonance imaging. Therefore, the authors decided to considering the eye lid aesthetic units and the modifications of these regions compared with the contralateral ones [23,24].

All images were processed using AutoCAD 2017 software (Autodesk, San Rafael, CA, USA). To be comparable, the images were resized using the scale tool; then the eye lid units were identified (lower lid unit; upper lid unit; lateral canthal subunit; medial canthal subunit) [23]. The area of each unit/subunit was calculated using the area tool, both in frontal and profile images (Figure 1). Comparing baseline to 1-month images the volume increase due to fat autograft was calculated. The amount of resorption was calculated comparing the two postoperative photographs. Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, Illinois, USA). Paired t-test was used to compare the unit/subunit areas before and after surgery. Differences were considered significant when $P < 0.05$.

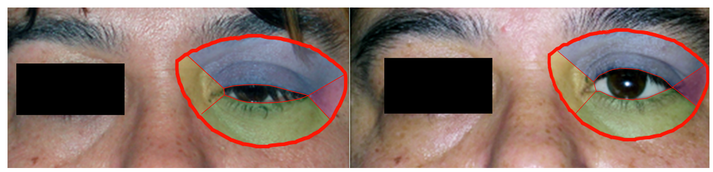

Figure 1: Preoperative (left) and 1 year postoperative (right) images. To be comparable, the images were resized using the scale tool of AutoCAD 2017 software (Autodesk, San Rafael, CA, USA); then the eye lid units were identified (lower lid unit = green; upper lid unit =light blue; lateral canthal subunit = violet; medial canthal subunit = yellow). The area of each unit/subunit was calculated using the area tool.

Anaesthetic technique for the donor site

Local anaesthesia involved the injection of large volumes of dilute lidocaine and epinephrine solution (for vasoconstriction) in the subcutaneous fat as long as the areas become literally tumescent ("tumescent anaesthetic technique") [25]. The purpose of this anaesthetic technique is to create a wide anesthetized surface and a widespread capillary constriction, which allow a better canalization of the suction cannula. The anaesthetic mixture was a Klein's modified solution: levobupivacaine 0.5% (Chirocaine® 5mg/ml, Abbvie S.r.l., Aprilia, LT, Italy) + epinephrine (Adrenalina, Fisoppharma, Salerno, Italy) 1: 100,000 diluted to 50% with Ringer lactate.

Harvesting, purification and transfer of autologous fat

Through a small suture-less umbilical access with a diameter of 3 mm, 10 ml of abdominal fat tissue was aspirated using a standard technique [11]. To isolate the supernatant (lysate of fat cells), 20 washes with Ringer's lactate were performed, and then the infranatant (blood and aesthetic) laid down and was subsequently eliminated. This modified technique differs from the one described by Coleman that provides for the purification and selection of lipocytes by centrifugation at 3000 rpm for 3 minutes. The purified fat graft was then transferred into 2.5 ml Luer Lock syringes. The washing and the transfer of the fat were simplified thanks to the use of three-way diverters commonly employed for vitreo-retinal surgery.

Anaesthetic technique of the receiving site

Mepivacaine 1% (Carbocaina, AstraZeneca, London, UK) was used to perform a nerve block of the infra- and supra-orbital, infra- and supratrochlear nerves.

Injection of the autologous fat preparation into the receiving site
An average volume of 2.5 ml of purified fat was injected into the anophthalmic orbit by means of a blunt tip cannula (25 gauges). The cut did not require stitches and was closed with steri-strips (3M Company, Minnesota, USA). Through an incision along the inferior orbital rim, the cannula was inserted and pushed up to the orbital plane and fat micro-boluses were released on various levels during the retrograde movement of the cannula. About 2/3 of the total fat amount were injected on the orbital floor and the remaining 1/3 on the upper eyelid fold posteriorly to the orbital septum.

Management of the postoperative period

During the postoperative phase, 2 mm of platelet rich plasma (PRP), obtained by patient's venous blood sample, was injected into the orbit at 1, 2 and 6 months after surgery.

Results

Comparing baseline to 1-month images, an improvement of the enophthalmos appearance was observed in all patients. Analyzing the single esthetic eye lid units, the grater area reduction was measured in the upper lid unit (29.34% P = 0.007, paired t test), followed by the lateral canthal subunit (21.01% P = 0.012), the lower lid unit (19.78% P = 0.02) and medial canthal subunit (9.09% P = 0.043). The overall esthetic unit area reduction was 19.8%. Comparing the two postoperative images, the amount of resorption was 16% in the upper lid unit (P = 0.023, paired t test), 14% in the lateral canthal subunit (P = 0.034), 13% in the lower lid unit (P = 0.027) and 8% in the medial canthal subunit (P = 0.032). The overall amount of resorption was 12.75%.

Minor complications regarding the lower eyelid were recorded in 6 cases: formation of oily cysts in 2 cases (one of them developed liponecrosis), hardened cystic formations in 3 cases as a result of a specific scar reaction and orbital fat increase in 1 case. All these patients underwent surgical removal of the cysts and/or the exceeding fat through a lower transconjunctival access with a complete resolution of the complication issue. At final follow-up visit, all patients were satisfied for the aesthetic result.

Discussion

The use of adipose tissue in ophthalmic plastic reconstructive surgery dates back to the late 19th century. It is important regenerative bio stimulating and bio-restructuring properties are related to the presence of adipocyte derived mesenchymal stem cells which legitimized its widespread application [21,26,27]. Up to 1977, the donor fatty tissue used to be collected with a surgical excision. This method, however, was burdened with a high rate of resorption and periodic re-implants were needed. Later, Illouz conceived and developed the lipoaspiration via cannulas (numerous variants were ideated by different surgeons), which led to a significant lengthening of graft survival [28,29]. In 1997, Coleman introduced the "lipostructure technique" based on an atraumatic manipulation of the collected adipose tissue [11], this procedure required the aspirated fat to be reduced in microscopic lobules, centrifuged and grafted into the recipient tissue on various levels to recreate a real tissue structure. The deposition fat tissue on various layers aims to provide the maximum contact surface with other well-vascularized tissues from which the graft can draw nourishment, initially for imbibition and subsequently forming new vascular connections, thus allowing an improvement in the survival rate [30]. If the fat graft were implanted in large quantities and in macro-structure, only a small portion of the transplanted fat cells would be in contact with vascular structures, while the other would develop apoptosis, necrosis and resorption [19]. This is the primary limitation of dermo-fat graft and lipofilling procedures that can only be used for small fillings. The authors modified the Coleman technique using a syringe with a 25 Gauge blunt tip and a retrograde release system at various levels to further reduce the trauma in the area of the implantation and increase the contact between the implanted tissue and the vascular orbital structures. Furthermore, the repeated washings used in the decantation technique have the advantage of better complying with the cell structures and be feasible in the absence of centrifugation systems.

Ultrastructural studies of the lipoaspirate showed the presence of multipotent stem cells (AMSC, Adipose Mesenchymal Stem Cells), derived from the vascular-stromal fraction [13,27]. The AMSC are able to differentiate into bone, cartilage, muscle, heart, endothelial or nerve cells depending on the scaffold [21,27,31]. These findings enhanced the importance of associating the use of the platelet rich plasma (PRP) in order to increase the stability and the viability of the fat graft [32]. Platelets in fact play a fundamental role in modulating the biological phenomena of the tissues thanks to their ability to release growth factors, including platelet-derived growth factor (PDGF), transforming growth factor β (TGF β), insulin like growth factor 1 (IGF-1), fibroblast growth factor (FGF), epidermal growth factor (EGF) and in particular vascular endothelial growth factor (VEGF), the most important factor of vascular growth stimulation [33]. The alpha granules contained in the platelets are also a source of cytokines, chemokines and many other proteins variously involved in stimulating cell proliferation and maturation, in modulating inflammation and activating other cells, thus regulating the tissue homeostasis and regeneration processes [33-35].

In orbital implants, the PRP improves the vascularization of the receiving site leading to an increased adipocytes engraftment; it rebalances the extracellular matrix and optimizes the efficiency decreasing the absorption of fat [36].

These findings made it possible to expand the indications for the use of lipostructure, considering it as a regenerative procedure of tissue bio-restructuration.

Conclusion

In conclusion, the lipostructure technique plus PRP injections for the treatment of post-enucleation enophthalmos appeared to be safe, effective and stable during 12-month follow-up. None of the patients required alloplastic materials implant (silicon, hydroxyapatite fillers, collagen or cross-linked hyaluronic acid), thus eliminating the risk of rejection, hypersensitivity reactions or the formation of reactive nodules and complications related to them (cuts, sutures, scars, need to carry the prosthesis for prolonged periods). Further studies using magnetic resonance imaging will be useful to implement the knowledge of the vascularization process of the fat graft inside an anophthalmic orbit.

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