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"Autologous fat transfer: Controversies and clinical applications in oral and maxillofacial surgery"

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Review Article

AUTOLOGOUS FAT TRANSFER: CONTROVERSIES AND CLINICAL APPLICATIONS IN ORAL AND MAXILLOFACIAL SURGERY

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Abstract
Autologous fat transfer is a technique widely used in cosmetic surgery to correct folds of the face. Autologous fat possesses many qualities of ideal filler, including its lack of immunogenicity, abundant supply, relatively low cost and potential for durable results, however, there exists a controversy concerning the optimal donor sites, the optimal techniques of harvesting, processing, injecting fat into the recipient sites and graft survival. In recent years there has been a renewed interest and more widespread clinical use of fat grafts in Aesthetic and Reconstructive Surgery, however, the scientific literature offers very few studies when concerning its use in the maxillofacial region. The aim of this scientific review is to focus on resolving the controversies surrounding autologous fat transfer and to highlight its possible clinical applications in the field of Oral and Maxillofacial Surgery.

Keywords: Autologous fat, Controversies, Clinical applications.

Introduction

Autologous fat transfer is a century old method for correcting contour of soft tissue defects. First described by Gustav Neuber in 1893 for correcting facial defects[1], it fell into disfavour in the 1950[s] owing to technical problems of harvesting and viability, especially after a study showed minimal graft survival 1 year post-transplantation[2]. The advent of liposuction in the early 1980[s] renewed interest in autologous fat injection[3], but the injected lipoaspirate continued to disappear almost completely despite numerous attempts. The problems of reabsorption were finally overcome in the 1990[s], when Sidney Coleman developed a new atraumatic technique for fat harvesting and placement that preserved the fragile adipocytes[4]. In the last 20 years, with the improvement in harvesting techniques, there has been a renewed interest and more widespread clinical use of fat grafts in Aesthetic and

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Reconstructive Surgery in general and in Cranio- Maxillofacial Surgery in particular.

Autologous fat possesses many qualities of ideal filler, including its lack of immunogenicity, abundant supply, relatively low cost and potential for durable results. Several investigators have reported short-term and long term viability of transferred fat[5-8]. However, the reports on different techniques for harvesting, processing and injecting fat are often contradictory. Although autologous fat grafting remains a valuable technique for volume and contour correction, there is justifiable concern due to the paucity of evidence based literature that addresses optimal techniques and long term outcomes.

In our opinion, relevant issues to be dealt with, with regard to autologous fat transfer in the cranio-maxillofacial region include donor site considerations, harvesting, processing, graft placement, need for overcorrection, and timing of subsequent injections, graft survival, complications and its clinical applications.

1: Donor Site Considerations

It has been a routine practice that the donor site for fat grafting is usually selected based on either the surgeons preference or the desired area is chosen by the patient. There is no conclusive evidence to claim that fat from specific donor site is optimal for specific facial region[9]. The most common donor sites include the extremities, trochanteric area, inner knee, dorsocervical fat pad and especially, the abdominal and flank sites[10]. The question of which is the best donor site to harvest fat grafts remains unclear as most of the previous studies[11, 12] have not detected significant differences in adipocyte viability between the donor sites. However, a recent study by Padoinet al[13] concluded that both the lower abdomen and inner thigh have higher concentration of processed lipoaspirate cells or adipose derived stem cells (ADSC) and that these areas may be the better donor sites of adult ADSC.

ADSC provide several benefits, they improve angiogenesis, graft vascularity and contribute to the adipocyte pool allowing fat grafts to maintain their volume[14]. With what we know about the potential role of ADSCs in autologous fat grafting, the lower abdomen and inner thighs should, therefore, be chosen as the better donor sites for fat transplantation. These donor sites are not only easily accessible by the surgeons with the patient in the supine position, but also scientifically sound because they have high concentrations of stem cells than other donor sites as long as patients have adequate amount of adipose tissue in those areas[15].

2: Harvesting

A critical review of scientific literature reveals numerous and sometimes contradictory approaches for fat harvesting.

2.1: Influence of local anesthesia on fat tissue:

Liposuction procedures mandate frequent use of adrenaline containing local anesthetic infiltration in order to prevent blood loss and to help post-operative analgesia. However the use of local anesthesia is somewhat controversial. Some clinicians believe that local anesthetics with or without adrenaline negatively impacts graft survival[16] whereas others believe that the vasoconstrictive action of adrenaline decreases donor site bleeding and potentiates graft survival as blood in the aspirate decreases adipocyte viability[17].

One of the more detailed studies assessing the effect of local infiltration showed that lidocaine inhibited human adipocyte lipolysis in tissue culture. However, the effect was found to be totally reversible once the agent has been washed out[18]. Recently, Shoshani showed that lidocaine (0.06%) with adrenaline does not alter the take of the fat grafts based on an in vivo volume and histological study[19].

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Therefore, based on the available literature, a commonly used tumescent solution with low concentration of lidocaine (0.05% or less) and only a short exposure to fat tissue (less than 20 minutes) can be used for analgesia of the fat graft donor site without much harmful effects to adipocytes or preadipocytes[20].

A commonly used solution by most surgeons is according to Coleman's recommendation of 0.5 % lidocaine with adrenaline (1:200000)[7]. However, the optimal solution has yet to be identified, as a recent study showed that the adipocyte viability varied between 90% and 20% depending on the local anesthetic used[21] indicating that more work in this area is required.

2.2: Method of Harvest

Syringe aspiration, vacuum extraction and surgical excision of fat have all been promoted in the literature as effective harvesting techniques. However, the optimal method of harvest of fat graft remains controversial. Obtaining fat by conventional liposuction under high negative pressures has been reported to cause 90% fat cell rupture[22]. When compared to excised adipose tissue, some authors claim a noteworthy decrease in adipocyte function in liposuction aspirates[23], whereas others claim a higher percentage of viable preadipocytes in liposuction aspirates than in excised fat[24].

In any case, syringe aspiration is currently the most popular fat harvesting method[10]. It combines the advantages of machine liposuction and surgical excision and at the same time, it does not have the burden of their disadvantages- respectively adipocyte destruction due to high negative pressure and disfiguring cicatrices. Furthermore, vacuum suction pressure employed can be manually controlled.

2.3: Cannulae and Syringe Size: A variety of cannulae have been used for fat harvesting[25-28], however, the proper size of the cannula and syringe used for syringe aspiration to harvest fat grafts also remains controversial The underlying principle is the atraumatic harvesting of adipocytes, to enhance adipocyte viability and hence graft survival.

A study by Erdim et al concluded that the use of larger cannulas for syringe aspiration appears to provide more viable adipocytes of the fat grafts based on the viable cell counts[29]. However, a comprehensive study conducted by Gonzalez et al concluded that the viability of fat grafts is significantly better when fat graft is harvested by 2mm diameter cannula with a blunt tip and several side holes connected to a 10cc syringe as compared to a 3mm diameter blunt tipped cannula connected to a 60cc syringe. They concluded that the larger size of cannula for syringe aspiration may not have very much advantage and the use of smaller syringes (10cc) is advisable to maintain a minimal negative pressure during harvesting[30].

Most surgeons use blunt 2 holed cannulas attached to 10 cc Luer-Lok syringes first described by Coleman. This technique is supported in the scientific literature[9, 26, 27, 31]. The cannula is pushed through 3 mm incisions and a gentle negative pressure is created by digital retraction of the syringe plunger. This slight negative pressure together with the curetting action of the cannula through the harvest site tissues allows small fat parcels to progress through the cannula and into the syringe[31].

3: Method of Processing

The product obtained by fat harvesting consists not only of morphologically preserved adipose structures but also of products of tissue disintegration which sets the need of subsequent specific purification. This stage of the surgical technique is still disputed and there are several known methods of its realization – decantation,

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filtration, centrifugation and washing with saline solution[32]. Filtration has already been denied for its traumatizing mechanical impact on fat cells and the too long exposition to air[33]. The method of decantation is also not preferred for its duration which prolongs surgical time. Nowadays the techniques of choice for most surgeons are centrifugation and washing with saline solution.

3.1: Centrifugation

Coleman emphasized the importance of centrifugation at 3000 rpm for 3 min in order to remove the non-living components like oil, blood, water and lidocaine from the suctioned aspirates[31]. Though there have been many controversial researches concerning its safety, optimal rpm and duration, the technique is proved to be atraumatic[34-36]. However recent studies have reported no significant differences in fat viability between centrifuged and non-centrifuged fat [10, 11, 37].

Nevertheless, centrifugation according to Coleman's protocol is recommended as it offers the following advantages:

1. It allows for a better adjustment of the injected adipose tissue because of interstitial fluid removal. Compression of adipose tissue sample prevents graft resorption and therefore avoids overcorrection or successive reinjections[38].
2. It creates a unique fraction of adipose stem cells potentially enhancing graft take[39].
3. It concentrates angiogenic growth factors like basic fibroblast growth factor, vascular endothelial growth factor in the middle portion of the centrifuge where adipose tissues are concentrated effectively separating them from oil or blood[40].

Since stem cells or angiogenic growth factors may play a role in fat graft survival, centrifugation according to Coleman's protocol appears to offer more benefits and should be a better choice for processing fat grafts.

3.2: Washing

In the literature, studies of graft washing have reproduced contradictory results. Its promoters claim that washing eliminates inflammatory components from the graft[41, 42] and leads to better graft quality as a result of increase in the viability of mesenchymal stem cells within washed adipose tissue[35, 42, 43]. Other studies oppose washing stating that it removes the fibrin content of the aspirate which is necessary for fat graft adherence[38]. Nevertheless, a review of scientific literature reveals that this is not a widespread method of graft preparation.

4: Method of Placement

This is one of the most important steps in fat grafting and constitutes a key to success and predictability [31, 44]. However, there appears to be no standardized technique on how fat grafts should be placed for soft tissue augmentation. The universally accepted technique is that by Coleman, and involves the production of multiple tunnels in which small fat parcels are deposited only during cannula withdrawal. This is thought of creating a large surface area of contact with the capillaries maximizing the graft survival[10, 45]

To optimize graft survival, damage to recipient tissue should be minimized. Blunt-tipped cannulas or small needles typically are employed; some authors contend that injection with a blunt-tipped cannula minimizes the risk for hematoma formation, but others prefer use of a needle because no incision site is necessary for the injections[8, 26, 46]. Coleman uses a 17 gauge blunt cannula with one hole at the distal end and advances it through 2 mm incisions but other authors also report favourable results using 14 gauge blunt tips or curved microcannula[8, 46].

5: Storage and Cryopreservation

Although literature reports that frozen fat can be reused[47, 48] and that freezing with cryopreservatives is superior to freezing

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without[49, 50], yet studies demonstrate that fat from fresh aspirate still gives the greatest number of viable adipocytes and preadipocytes[49]. A recent study revealed that storing fat at +4 ^{0}C provides the highest number of viable adipocytes for at least 2 weeks compared to dry frozen specimens (-20 ^{0}C and -80^{0}C) but the small sample size mandates more studies in this area[29].

6: Need for Overcorrection

Whether overcorrection would be necessary for fat grafting remain unclear. Since the viable fat grafts are only observed in the peripheral zone approximately 1.5 mm from the edge of the grafts and the percentage of graft viability depends on its thickness and geometrical shape[51, 52], overcorrection for "better" graft survival in the recipient site appears to be lack of scientific support. Therefore, significant overcorrection should be avoided at the present time until its necessity and safety can be confirmed by future studies.

7: Timing of subsequent injection

Additional procedures are always deemed necessary to achieve an optimal result since the overall take rate of fat grafting by even more experienced surgeons ranges from about 50 to 90% [7, 37, 53]. However, no scientific study has addressed the timing of subsequent fat grafting and therefore, only expert opinion has been mentioned in the literature regarding this specific issue. It has been described as "the timing of additional fat grafting sessions should be deferred until 6 months postoperatively to diminish the inflammatory response"[20].

8: Graft Survival

Although the clinical experience with fat grafts is remarkably positive, yet there is limited quality experimental evidence that proves that the transferred fat survives. Coleman believes that the graft volume stabilizes at 3-4 months, although a subtle volumetric decrease may occur upto 1 year; beyond that, he claims that the volume remains constant for 8-12 years[31]. Hörl et al[54]used magnetic resonance imaging to document volume changes after autologous fat graft survival for correction of facial defects. A reduction in graft volume of approximately 50% was demonstrated at 3 months, increasing to 55% at 6 months, and remaining stable thereafter until 12 months after reimplantation. Using a cell-labelling technique in rats, Rieck and Schlaak[55]demonstrated variable survival rates when fat was transferred to different recipient sites; when fat was injected into subcutaneous tissue, a 30% survival rate was noted at 6 months, but when fat was injected into muscle, only a 6% survival rate was noted at 6 months.

9: Complications

The complications although relatively low, appear to be related to surgeon's technique and experience. Possible donor site complications include liposuction deformities if the donor site is not correctly chosen, bleeding and bacterial infection predominantly staphylococcal that can be resolved with antibiotic therapy[10]. Possible complications at the recipient site include oedema and bruising that resolve within a month, undercorrection, overcorrection and contour deformities. Overgrowth of the graft is reported as a rare aesthetic complication[56, 57]. The few serious complications reported in the scientific literature include fat embolism due to intravascular injection with subsequent blindness, motor restriction, acute fatal stroke[58-60] and lipoid meningitis[61]. Complications like fat embolism due to intravascular injection are best avoided by using small blunt cannulas for soft tissue dissection and fat placement whereas infections are best prevented with meticulous asepsis.

10: Clinical applications in oral and maxillofacial surgery

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Possible clinical applications of autologous fat transfer in the craniomaxillofacial territory include:

1. Traumatic Defects

Autologous fat continues to be a gold standard for frontal sinus obliteration[62-64]. Literature also reports its use for treating post-traumatic enophthalmus[65, 66]. However, it is essential to be cautious when performing intra-orbital injections to avoid undue trauma that could lead to bleeding and retrobulbar hematoma with possible compression of the optic nerve[67]. In addition, use of autologous fat is documented for augmentation of the facial defect following traumatic atrophy[68] and to augment the cancellous bone in traumatic calvarial defects[69].

2. Head and Neck Reconstruction.

Fat grafting is usually performed as a touch up procedure well after primary cancer treatment and reconstruction have completed. The authors note that the areas grafted with fat appear softer and more pliable than those without[68]. Others believe that, for patients with poor tissue quality as a result of radiation damage, a gradual approach can be undertaken in which the first grafting procedure will improve the suppleness and flexibility and the subsequent procedure will help fill out the reconstruction[70]. Typically a 100 ml of harvested fat is considered to be more than enough material for a successful procedure.

3. Temporomandibular joint (TMJ) disorders.

The use of free abdominal fat into the joint space during open joint surgery is advocated to replace joint space after removal of the disc and associated capsule. In addition, the use of autologous fat grafts in the treatment of TMJ ankylosis is reported in the literature as early as 1913[71, 72]. The rationale for placing autologous fat grafts is to obliterate the dead space present around the joint prosthesis, thus preventing the formation and subsequent organization of a hematoma. Creating this physical barrier serves to minimize the presence of pluripotent cells and prevents the formation of extensive fibrosis and heterotopic calcifications. It may also isolate any residual reactive tissue from previous alloplastic failure to the periphery of the region, minimizing its formation around the joint components. The net result is a decrease in and perhaps elimination of the incidence of heterotopic bone formation and an improvement in jaw function[73].

4. Facial rejuvenation

Fat injections are more successful in facial areas due to the availability of a richer vascular supply[74]. Autologous fat transplantation is indicated for the correction of wrinkles, depressed or atrophic areas in the face[74] and volume loss in the aging process[75]. Today, with the advent of cosmetic surgery, fat grafts are also used as injectable fillers[76]. Besides the soft tissue augmentation effect, an improvement in the quality of aging skin has been reported. Longevity of the correction is unpredictable, depending on the harvesting and transfer techniques of the fat[77]. An unpredictable resorption rate is noted, especially in the peri-oral areas[78, 79].

5. Facial augmentation and enhancement of facial contours.

Coleman's technique of fat grafting or Lipostructure is most commomly advocated for augmenting facial soft tissues[67]. The areas of the maxillofacial region that are routinely augmented with favourable results are the malar region, the lips, nasolabial folds and the mental area. In addition, authors reports favourable results in treatment of facial lipoatrophy due to underlying HIV disease[80, 81].

6. Congenital Malformations.

Autologous fat may be useful to treat some congenital malformations (including facial asymmetry in patients with

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hemifacialmicrosomia) and the post-surgical sequelae of cleft lips.In patients with hemifacialmicrosomia, the traditional treatment programme includes distraction osteogenesis of the hypoplastic mandible at an early age, and LeFort1 osteotomy with sagittal splitting of the mandible and a contralateral costochondral graft and sliding genioplasty at completing of growth. In either case, the residual facial asymmetry, due to soft tissue deficit, can be corrected by repeated fat injections (at least 3 sessions at 4-month intervals, for a total of 60 cc), which lead to nearly normal symmetry and more predictable results than dermal fat grafts or use of implants[82, 83]. In the case of cleft lips, fat injections (generally two sessions for a total of 7-8 cc) can reduce scarring and increase upper lip volume[82].

7. Velopharyngeal insufficiency (VPI)

Velopharyngeal insufficiency (VPI) refers to the inability of the velum to close against the posterior pharyngeal wall during speech. This inability to close the Velopharyngeal port can ultimately lead to abnormal resonance, hypernasal speech, and decreased intelligibility. Autologous fat transfer offers an attractive option to augment the Velopharyngeal structures. It avoids the drawbacks of velopharyngoplasties like post-operative pain, bleeding, post-operative snoring and obstructive sleep apnoea and those of alloplastic implants for augmentation of posterior pharyngeal wall like extrusion, migration, foreign body or granuloma formation[82, 84].MRI scans demonstrate that the fat transfer results in a marked anterior displacement of the posterior pharyngeal wall and in so doing restores the velopharyngeal mechanism to competence[85].

Autologous fat injections presents a straight forward and minimally-invasive means of treating VPI that significantly reduces hypernasality and improves overall speech quality in paediatric and adult patients. However, a longer follow-up is needed to confirm these findings, and patients should be informed that multiple procedures might be needed to optimize the results.

8. Facial scarring as a result of burns

Facial scarring caused by burns poses both, an aesthetic as well as a functional challenge for improvement. However, it is observed that repeated fat injections (usually 2-3 sessions at 4-month intervals) can lead to better skin texture, scar quality and skin color, and also increase volume in retracted areas and re-establish gliding tissue, thus improving the contractures and limited mobility caused by fibrotic tissue and skin graft adhesions[82, 86].

9. Use in Postoperative Deformities.

9.1: Post Rhinoplasty Deformities.

Rhinoplastysequelae can be difficult to treat, especially in patients with thin skin. Adipose tissue, by virtue of its volumetric qualities and its action on skin trophicity, can be considered to be a gold standard implant[87, 88]. The most obvious indications are to correct the contours of the dorsum in the case of saddle nose deformity, camouflage cartilage or bone irregularities, or provide better skin texture in the case of atrophy or scarring. It may also improve airway obstruction when placed at the level of the nasal valve[82]. The quantity of adipose tissue injected ranges from 1 to 6 cc depending on the size of the deformation and the zone being injected[82, 88].

9.2: Post Tracheostomy Deformities.

Tracheostomy is a life-saving operation but may have bothersome sequelae. Because the defect resulting from tracheostomy is often allowed to repair spontaneously by secondary intention, hypertrophic scar formation is a frequent consequence. Furthermore, skin-to-trachea adhesions may develop, creating a "tracheal tug," that is, the skin movement in conjunction with the trachea, causing discomfort on swallowing[82, 89].

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Autologous fat injections can be used to improve the sequelae due to fibrotic bands between the skin and underlying tissue and correct hypertrophic scars. It can be considered as a valid alternative to major open surgery. The procedure is usually performed in 2-3 sessions. The first session with a total of 5cc of fat usually only corrects the depression and, if the tissue is still recessed, a further 3-4 cc can be delivered after 4 months to improve scarring retraction, increase tissue volume and restore eutrophic skin. After a further 4 months, the residual scar is excised to obtain a better aesthetic result as a final procedure[89].

9.3 Frey's Syndrome

The Frey syndrome, also called gustatory sweat syndrome or auriculotemporal syndrome, is characterized by a sweating and a flushing and/or an erythema of the cheek area during mastication after parotid surgery probably due to misdirected resprouting of the post-ganglionic parasympathetic fibres feeding the parotid gland to the cutaneous sweat glands[82]. The incidence of the subjective clinical occurrence of post-parotidectomy Frey syndrome is 10-40%[90]. Many forms of treatment have been proposed from local applications of anti-cholinergic medications to more invasive procedures like tympanic neurectomy or the interposition of an autologous graft (dermal, the temporoparietal fascia) to creating a barrier between the skin and the residual parotid gland. However, as the former are only partially and transiently effective in most cases, and the latter involve the risk of possible facial nerve injury, there is still no treatment of choice[90].

Autologous fat injections in the parotid area may be a minimally-invasive option as the fat would create a barrier between the skin and the residual parotid gland, and may prevent abnormal nerve neo-anastomoses to the sweat glands. In addition to being useful for treating the unpleasant salivary sweating and flushing typical of post-parotidectomy Frey syndrome, it could also have a positive aesthetic impact as it may fill the gap left by the excision of the parotid.

Favourable results have been documented by a recent study using autologous fat in excised form rather than injection form on 10 patients with Frey syndrome post-superficial or total parotidectomy[91].

9.4: Post Radiotherapy Effects.

The well-known dramatic consequences of radiotherapy on the head and neck lead to soft tissue deterioration and skin atrophy, particularly in children. Instead of invasive and often unpredictable major surgery, repeated fat injections (generally 2-3 sessions) can provide sufficient bulk to the affected side of the face. It is also useful in making the previously stiff and atrophied skin softer and more pliable, and improving its texture and color match[82].

Conclusion

An effort has been made to resolve most of the controversies surrounding autologous fat transfer and to present its possible clinical applications in the cranio-maxillofacial region. We hope that the surgeon will use the information presented in this review to choose a scientifically sound approach to fat grafting based on objective findings rather than anecdotal reports. The heightened interest in these procedures should instigate further investigation to refine surgical procedures and improve predictability. Autologous fat grafting definitely has a place to become a routinely performed procedure in the maxillofacial region in future.

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