Available online at www.sciencedirect.com
ScienceDirect
British Journal of Oral and Maxillofacial Surgery 46 (2008) 649–652
BRITISH Journal of Oral and Maxillofacial Surgery
www.bjoms.com

Use of allogenic acellular dermal matrix in prevention of Frey's syndrome after parotidectomy

Wei Min Ye, Han Guang Zhu, Jia Wei Zheng *, Xu Dong Wang, Wen Zhao, Lai Ping Zhong, Zhi Yuan Zhang

Department of Oral and Maxillofacial Surgery, College of Stomatology, Ninth People's Hospital, School of Medicine, Shanghai Jiao Tong University. Shanghai 200011, China

Accepted 7 November 2007
Available online 10 June 2008

Abstract

Objective: To evaluate the use of an allogenic acellular dermal matrix (ADM) as an interpositional graft to prevent Frey's syndrome after parotidectomy.
Method: We studied a total of 168 patients with benign parotid gland tumours, including 89 patients with pleomorphic adenoma; 45 with Warthin tumour; 17 with basal cell adenoma; and 17 with miscellaneous tumours. The patients were divided into two groups: the first (control $n = 104$) had superficial or partial parotidectomy alone, and the second (experimental $n = 64$), had superficial or partial parotidectomy with simultaneous placement of an ADM graft. All patients were evaluated for gustatory sweating by clinical examination. For objective assessment, 60 patients (30 from each group) were randomly selected for a starch-iodine test.
Results: Subjectively Frey's syndrome was recorded in 63 patients (61%) from the controls and one patient (2%) from the ADM group. Objectively Frey's syndrome was found in 24 patients from the control group (23%) and 2 patients from the ADM group (2%). Salivary fistulas developed in 18 patients from the control group (17%), but in only 1 patient from the ADM group (2%). Both differences were $P < 0.05$, but there was no significant difference between superficial parotidectomy and partial superficial parotidectomy ($P = 0.714$).
Conclusion: The use of acellular dermal matrix (ADM) as an interpositional graft is an effective way of preventing Frey's syndrome after parotidectomy.

Keywords: Acellular dermal matrix; Parotidectomy; Frey's syndrome

Introduction

Gustatory sweating, or Frey's syndrome, is a common complication of parotidectomy. The clinical signs include flushing and sweating in the parotid region while eating. It often adversely affects patients' daily life. The reported incidence of Frey's syndrome varies substantially, ranging from 1.7% to 98%.[1–3] To prevent it, many treatment methods such as temporalis myofascial flap, femoral fascia as an interpositional physical barrier, and implants, have been reported. However, additional surgical donor sites, the longer operating time, and the corresponding complications might lead to other problems. In recent years, an acellular dermal matrix (ADM) has been used as a barrier or implant to prevent Frey's syndrome, with relatively satisfactory results.[4] From January 2004 to April 2005, 64 patients with parotid tumours had ADM inserted in our department. We report the preliminary clinical outcomes of its use in preventing Frey's syndrome after parotidectomy.

Patients and methods

The study included 168 patients with benign parotid tumours who were treated between January 2004 and April 2005 in the Department of Oral and Maxillofacial Surgery, College of Stomatology, Ninth People's Hospital, School of Medicine,

* Corresponding author. Tel.: +86 21 63121780; fax: +86 21 63136856.
E-mail address: zhjw@omschina.org.cn (J.W. Zheng).

0266-4356/$ – see front matter
doi:10.1016/j.bjoms.2007.11.006

Shanghai Jiao Tong University. Of these, 89 had pleomorphic adenomas; 45 had Warthin tumours; 17 had basal cell adenomas; and 17 had miscellaneous tumours. Their ages ranged from 18 to 67 years (mean 42). Before the operation, the patients were examined thoroughly, and signed informed consent after detailed explanation of the operation. They were then divided into 2 groups: 104 patients (control group) had superficial or partial parotidectomy alone, while 64 patients (ADM group) had superficial or partial parotidectomy with simultaneous insertion of an ADM between the parotid masseter fascial flap and the residual parotid tissue. The size of the ADM graft depended on the amount of tissue required to restore the normal facial contour. All patients were examined for the development of Frey's syndrome; the starch-iodine test was also used in 30 selected patients from each group.

Material

RENOV tissue sheets purchased from Beijing Qing Yuan Wei Ye Bio-tissue Engineering Co., Ltd. were used. Each package contained one piece of freeze-dried acellular human dermis, which is fabricated by a proprietary method of processing human skin from cadavers who had no infectious diseases (including AIDS). RENOV tissue has been approved by the Chinese Food and Drug Agency for clinical applications. It is aseptic, and free of the cells responsible for the antigenic response to allograft skin. The material is available in many different sizes and shapes. A 6 cm × 8 cm sheet was used for single-layer grafts, and larger sheets were used for folding grafts.

Surgical technique

The preauricular–submandibular S-shaped incision was used in all patients. The skin flap was raised above the parotid fascia and beyond the tumour in all cases to ensure complete exposure of the tumour. Superficial parotidectomy was done in a standard manner. Partial superficial parotidectomy is similar to superficial parotidectomy with the exception that fewer branches of the facial nerve are dissected and less normal parotid tissue is removed.[5] In partial superficial parotidectomy only the tumour-bearing area of the gland's parenchyma was excised, with identification of the main trunk and preservation of the branch of the facial nerve that was adjacent to the site of the tumour with no need for more extensive dissection.[6] After complete removal of the tumour and the involved parotid tissues, an ADM of a given size was rehydrated to fill the space in patients in the ADM group. The ADM was fixed to the surrounding tissues to prevent loosening and displacement. For patients with major postoperative tissue deficiency, larger ADMs were selected and folded into several layers to fill the space and achieve facial symmetry (Fig. 1A–D). Suction drainage was used routinely in all patients postoperatively to prevent haematomas or seromas. The suction tubes were inserted between the remaining parotid beds and the ADM in this group.

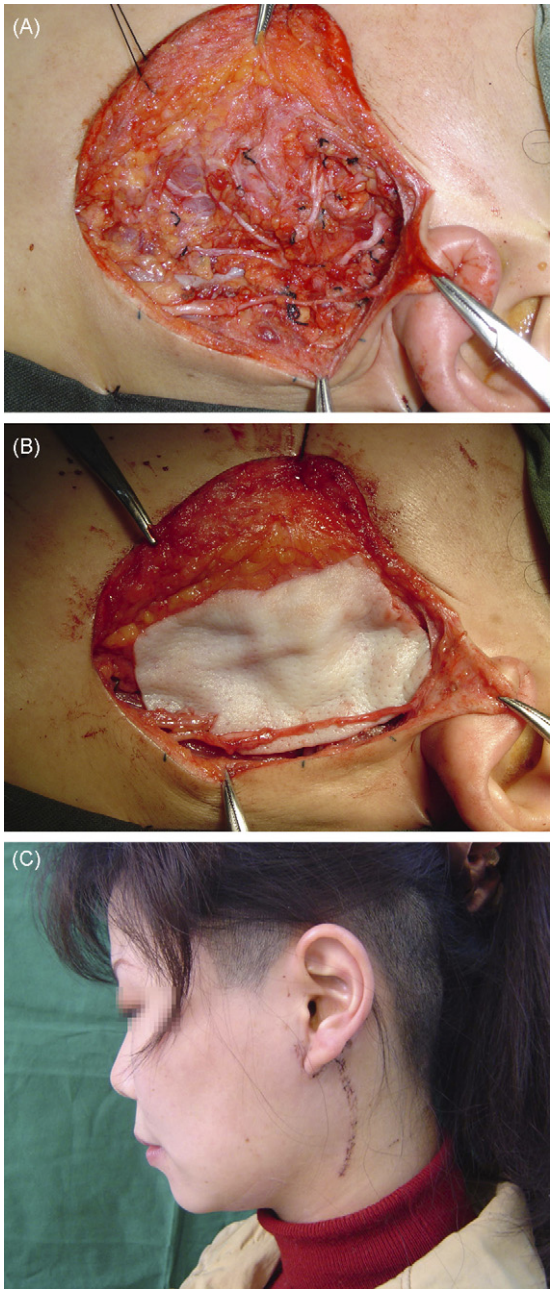

Fig. 1. Superficial parotidectomy in a patient with pleomorphic adenoma.
A. Surgical field after parotidectomy with preservation of the facial nerve.
B. Insertion of two layers of acellular dermal matrix.
C. Lateral view postoperatively.

All the patients were followed up for 11–27 months postoperatively (median 16 months). To evaluate Frey's syndrome and other complications, they were examined by the senior surgeons. For objective assessment, 60 patients (30 from each group) were randomly selected for a starch-iodine test, which was done in a routine manner.

Table 1
Results of starch-iodine test for Frey's's syndrome in 60 patients

Pathological type	Group 1 (control)			Group 2 (ADM)			*P* value
	Number	Subjective	Objective	Number	Subjective	Objective	
Pleomorphic adenoma	17	12	15	18	1	1	<0.001
Warthin tumour	6	3	3	4	0	0	0.091
Basal cell adenoma	5	3	4	7	0	1	0.023
Miscellaneous	2	1	2	1	0	0	0.083
Total	30	19	24	30	1	2	<0.001

Table 2
Results of starch-iodine test for Frey's syndrome between different surgical techniques in 60 patients

Surgical type	Group 1 (control)			Group 2 (ADM)			*P* value
	Number	Subjective	Objective	Number	Subjective	Objective	
Superficial parotidectomy	9	5	7	8	1	1	0.714
Partial superficial parotidectomy	21	14	17	22	0	1	
Total	30	19	24	30	1	2	

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS Inc., Chicago) was used for the chi square test. Probabilities of less than 0.05 were accepted as significant.

Results

During the follow-up period, 63 patients from the control group (61%) and one patient from the ADM group (2%) complained of symptoms of Frey's syndrome. From the results of the starch-iodine test, 24 patients in the control group and 2 patients in the ADM group had Frey's syndrome. In addition, 18 patients in the control group and 1 patient in the ADM group had developed a parotid fistula. The incidence of Frey's syndrome was significantly different between the 2 groups ($P = 9.9510^{-9}$, $P < 0.001$) (Table 1), but no significant difference was found between superficial parotidectomy and partial superficial parotidectomy ($P = 0.714$) (Table 2).

Discussion

One of the mechanisms of Frey's syndrome is the aberrant regeneration of two different nerves. Injuries or defects in the parotid fascia after parotidectomy may expose the postganglionic parasympathetic nerve fibres that may misconnect with the nerve fibres that innervate the subcutaneous sweat glands, resulting in abnormal secretions from those glands. The clinical signs include flushing and sweating of the parotid region during eating. The reported incidence of Frey's syndrome is around 20%–98%. Overall, the subjective and objective incidences are 38% and 86%, respectively.[1,3] In the present groups, 104 were not given an ADM graft. Their subjective and objective incidences were 61% and 80%, respectively. This high incidence has attracted widespread attention, and in-depth studies have been conducted by many research workers.

Many materials, including autologous adipose tissue, temporal fascia, fascia lata femoris, and sternocleidomastoid myocutaneous flaps, have been used as barriers to isolate misconnected nerve fibres between the postganglionic parasympathetic nerve fibres and the nerve fibres that innervate the subcutaneous sweat gland, effectively lowering the incidence of Frey's syndrome. However, adipose tissue is easily absorbed. The amount of tissue in the nearby sternocleidomastoid myocutaneous flap is not enough to cover the wound surface completely. Among other factors, this shortage of fascial tissue makes it impossible to fill the depression and restore the facial contour. Additional donor sites, the longer operating time, and the corresponding complications at the donor site, made acceptance by patients impossible.[2,3,7,8] Some researchers also gave botulinum toxin type A locally to treat Frey's syndrome, which was extremely effective. However, the mean period of efficacy was only 17 months, and the outcome was uncertain.[9,10] For patients in whom synthetic materials were used, the wound surface remained unhealed for a long time, and the tissue was rejected. Since materials such as ADM have been used, these problems have been relatively unknown.

ADM is derived from allograft skin after screening for HIV, HBV, HCV, human T-lymphangiotrophic virus type I, and syphilis. All the cellular constituents of the epithelium and dermis are removed by a series of treatments so that no immune response is elicited during implantation of an allograft. Type IV collagen, which has biochemical and structural effects, is then preserved within the dermal matrix to block the misdirected in-growth of nerve fibre effectively.[11] This tissue sheet has the following advantages: it has a low likelihood of rejection and is available in abundance, is easy to procure, is easily fixed and shaped, and is an excellent mate-

rial to fill postoperative tissue defects and restore the facial contour. The operating time is short, and injuries from the second surgical field can be avoided. No tissue was rejected in the present series. All the wounds healed primarily, and the facial contour was restored.

Sixty-four patients had an ADM graft. The subjective and objective incidence rates of Frey's syndrome were 1.6% and 6.7%, respectively. The incidence was remarkably less, and the results were similar to those reported by Dulguerov et al.[3] Two patients developed Frey's syndrome at the margins of the operative field, probably because the implanted ADM did not completely cover the deficient parotid fascia. In this study, one salivary fistula was noted in the ADM group, while 18 cases developed in the control group ($P = 0.002$). This difference was thought to be related to the use of the ADM graft. The operative area in patients with grafts was fully in contour and symmetrical, with fine scars, while control patients' scars were noticeable, locally depressed and with wrinkled skin. We propose that when it is used intraoperatively the ADM should completely cover the wound surface. Irrespective of the size of the postoperative deficit in tissue volume, it should be completed. A suction drainage tube is routinely placed between the parotid bed and the ADM. It is best if its two sides extend beyond the margins of the tissue sheet so that the suction may promptly eliminate the dead space and drain the empyema thoroughly. When the postoperative drainage volume for 24 hours is less than 10 ml the suction tube can be removed, and a pressure dressing applied for about a week. The presence of a salivary fistula may be related to the site of the drain, the timing of its removal, and the continuous application of local compression after removal of the tube.

The ADM graft can effectively control the occurrence of Frey's syndrome after operations for parotid tumours. It is also one of the effective methods of correcting postoperative depression in the operative parotid region.

References

1. Tugnoli V, Marchese Ragona R, Elropra R, et al. The role of gustatory flushing in Frey's's syndrome and its treatment with botulinum toxin type A. *Clin Auton Res* 2002;**12**:174–8.
2. Upton DC, McNamar JP, Connor NP, Harari PM, Hartig GK. Parotidectomy: ten-year review of 237 cases at a single institution. *Otolaryngol Head Neck Surg* 2007;**136**:788–92.
3. Dulguerov P, Quinodoz D, Cosendai G, Piletta P, Marchal F, Lehmann W. Prevention of Frey's syndrome during parotidectomy. *Arch Otolaryngol Head Neck Surg* 1999;**125**:833–9.
4. Govindaraj S, Cohen M, Genden EM, Constantine PD, Urken ML. The use of acellular dermis in the prevention of Frey's's syndrome. *Laryngoscope* 2001;**111**:1993–8.
5. Hancock BD. Clinically benign parotid tumours: local dissection as an alternative to superficial parotidectomy in selected cases. *Ann R Coll Surg Engl* 1999;**81**:299–301.
6. Papadogeorgakis N, Skouteris CA, Mylonas AI, Angelopoulos AP. Superficial parotidectomy: technical modifications based on tumour characteristics. *J Craniomaxillofac Surg* 2004;**32**:350–3.
7. Ahmed OA, Kolhe PS. Prevention of Frey's's syndrome and volume deficit after parotidectomy using the superficial temporal artery fascial flap. *Br J Plast Surg* 1999;**52**:256–60.
8. Rubinstein RY, Rosen A, Leeman D. Frey's syndrome: treatment with temporoparietal fascia flap interposition. *Arch Otolaryngol Head Neck Surg* 1999;**125**:808–11.
9. Arad-Cohen A, Blitzer A. Botulinum toxin treatment for symptomatic Frey's's syndrome. *Otolaryngol Head Neck Surg* 2000;**122**:237–40.
10. Laccourreye O, Akl E, Gutierrez-Fonseca R, Garcia D, Brasnu D, Bonan B. Recurrent gustatory sweating (Frey's syndrome) after intracutaneous injection of botulinum toxin type A: incidence, management, and outcome. *Arch Otolaryngol Head Neck Surg* 1999;**125**:283–6.
11. May JS, McGuirt WF. Frey's's syndrome: treatment with topical glycopyrrolate. *Head Neck* 1989;**111**:85–9.