Heterogeneous acellular dermal matrix patch for repair of oral mucosal defects in 71 patients*

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Abstract

BACKGROUND: Recently, acellular dermal matrix allograft has been widely used in the repair of oral mucosal defects. But little information is about the heterogeneous acellular dermal matrix (HADM) patch for repair of oral mucosal defects.

OBJECTIVE: To investigate the efficacy and biosafety of HADM in the repair of oral mucosal defects.

METHODS: In total 71 patients with oral benign or malignant tumors who had oral mucosal or soft tissue defects following tumorectomy were included in this study. These patients comprised 37 males and 34 females, and were averaged 45 years (range, 20–70 years old). Of them, 42 suffered from benign tumors and 29 from malignant tumors. HADM patches were used for repair of oral mucosal defects. The survival, color, and texture of HADM patches were observed. Shrinkage rate of HADM patches was compared between regions without supports from hard tissues (cheeks, tongue, and mouth floor) and with supports from hard tissues (gingiva, hard palate).

RESULTS AND CONCLUSION: All 71 HADM completely survived. No necrosis and infection occurred. At 2 weeks after transplantation, (98.20±5.20) % of patch area survived. At 3 months after transplantation, patches showed similar color to surrounding oral mucosa and most patients had sense of tension to different extents. At 6 months after transplantation, cell creeping substitution and vascularization were successfully accomplished in the region of patch transplantation. Patches grew stably, with smooth pink appearance and good elasticity, and no further shrinkage. Patients felt normal. HADM patch shrank primarily at 2 weeks–1 month after transplantation, and tended to be stable at 3 months. There was no significant difference in tissue morphology between surgical region and normal tissue. The HADM shrinkage rate was significantly higher in regions without supports from hard tissues than regions with supports from hard tissues. These findings indicate that HADM patches have advantages in repair of oral mucosal defects including good histocompatibility, wide source, simple manipulation, and able to cover the wound surface in the early state, promote wound surface healing, and reduce scar formation, and can be used as an ideal material for repair of oral mucosal defects.

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Received: 2010-02-05
Accepted: 2010-03-25
(20100308003/GW)

Xue LF, Shang W, Feng YY, Jin XM Liu FT, Jia MY, Yuan RT, Bu LX. Heterogeneous acellular dermal matrix patch for repair of oral mucosal defects in 71 patients. Zhongguo Zuzhi Gongcheng Yanjiu yu Linchuang Kangfu. 2010;14(16): 3015-3018.

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INTRODUCTION

The conventional methods for repairing oral mucosal and soft tissue defects in the clinic are to use skin flap or free skin grafting. With the research progress in acellular dermax matrix, xenogenous acellular dermal matrix (XADM) have acquired good clinical efficacy in repairing oral mucosal and soft tissue defects caused by various factors, but little information is about the heterogeneous acellular dermal matrix (HADM) for repair of oral mucosal defects. Recently, we used HADM to repair oral mucosal and soft tissue defects and acquired satisfactory clinical efficacy.

SUBJECTS AND METHODS

Design

Case observation analysis.

Time and setting

This study was performed at the Department of Oral and Maxillofacial Surgery, Affiliated Hospital of Qingdao University Medical College between December 2006 and December 2008.

Subjects

In total 71 patients who received surgery at the Department of Oral and Maxillofacial Surgery in Affiliated Hospital of Medical College, Qingdao University between December 2006 and December 2008 were included in this study. These patients comprised 37 males and 34 females, and were averaged 45 years (range, 20-70 years old). Oral tissue defects were primarily the defects of mucosa and a part soft tissue caused by tumorectomy [benign (n = 42) or malignant (n = 29) tumors included]. Defect regions included those without supports from hard tissues, such as cheeks, tongue, and mouth floor, and those with supports from hard tissues, such as gingiva and hard palate. Defect area ranged 2 cm × 2 cm–5 cm × 5 cm.

Inclusion criteria

Confirmed by pathological examinations; all patients were informed of experimental and therapeutic regimen; surgical range not involving deep muscle.

Materials

HADM patch (trade name: heal mouth rehabilitation membrane) was made by Yantai Zhenghai Biotechnology Co.,Ltd., China. According to wound surface size, generally HADM patches with a size of 4 cm × 3 cm, 5 cm × 5 cm, and 6 cm × 4 cm were used (Figure 1).

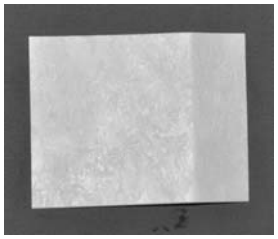


Figure 1 Heterogeneous acellular dermal matrix patch used in the surgery

Bovine skin tissue was subjected to acellular disposal, with three-dimensional structure of protein collagen retained, then prepared into HADM, freeze-dried, and packaged. HADM has one pyknotic surface and one porous surface.

Interventions

According to routine interventions, following focus removal and thorough basal surface hemostasis, tissue patches of proper sizes were taken, soaked in aseptic physiological saline, gas bubble-emitted, water renewed three times, at least 1 minute each, fully hydrated till semitransparent, soft, and no bubble status for future use. The scabrous basal surface was pasted to wound surface, with margin closely sutured and center perforated, and wrapped up with iodoform gauze. After surgery, oral cavity was kept clean and antibiotics were routinely used to prevent infection.

Postoperative observation

Observation of survival of HADM: Iodoform gauze was removed 2 weeks after transplantation. At 2 weeks, 1, 3, 6, and 12 months after transplantation, all patients were examined to observe the conjunction between HADM and surrounding tissue, and the texture, color, and elasticity of tissue in repair region. Calculation of shrinkage rate of HADM 1–6 months after transplantation: The shrinkage rate of DADM = (tissue area repaired–tissue area following shrinkage)/ tissue area repaired ×100%. ③ Comparison of shrinkage rate of HADM between regions without supports from hard tissue (cheek, tongue, mouth floor) and regions with support from hard tissue (gingiva, hard palate).

Design, enforcement and evaluation

This study was designed by the first author, performed and evaluated by all authors. All authors received professional training.

Statistical analysis

The shrinkage age of heterogeneous acellular dermal matrix patch was expressed as Mean ± SD. All data were statistically processed by the first author using SPSS 13.0 for Windows. Two sample *t*-test was used to determine if the difference in mean of data collected from the region without hard tissue supporting and the region with hard tissue supporting.

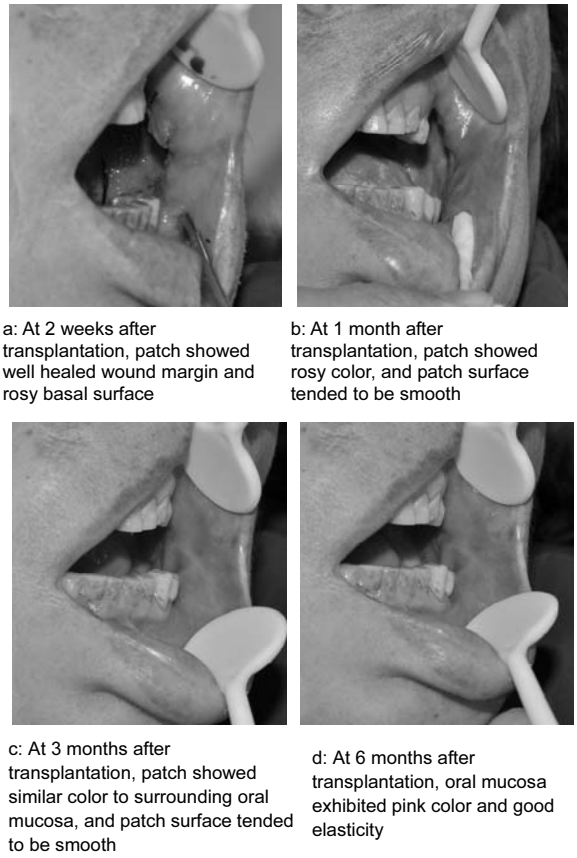
RESULTS

Quantitative analysis of participants

All 71 patients were included in the final analysis.

Survival of HADM patches

All transplanted patches survived, no necrosis and infection occurred. At 2 weeks after transplantation, (98.20±5.20)% of patch area survived, no obvious rejection was observed, wound margin well healed, and basal surface was rosy (Figure 2a). At 1 month after transplantation, patients did not have foreign body sensation and the restriction of mouth opening. The callus membrane on patch surface layer was basically ablated, patches showed rosy color and smooth surface (Figure 2b). At 3 months after transplantation, patches showed similar color to surrounding oral mucosa, flexible texture, and smooth surface (Figure 2c), and most patients had sense of tension to different extents. At 6 months after transplantation, cell creeping substitution and vascularization were successfully accomplished in the region of patch transplantation. Patches grew stably, with smooth pink appearance and good elasticity, and no further shrinkage (Figure 2d). Patients felt normal, and the restriction of mouth opening did not influence normal diet.



a: At 2 weeks after transplantation, patch showed well healed wound margin and rosy basal surface

b: At 1 month after transplantation, patch showed rosy color, and patch surface tended to be smooth

c: At 3 months after transplantation, patch showed similar color to surrounding oral mucosa, and patch surface tended to be smooth

d: At 6 months after transplantation, oral mucosa exhibited pink color and good elasticity

Figure 2 Survival of heterogeneous acellular dermal matrix patch at different time after transplantation

Shrinkage rate of HADM patch (Table 1)

Table 1 Shrinkage rate of heterogeneous acellular dermal matrix patches in repair of different oral mucosal defects ($\bar{x}\pm s$, %)

Region	*n*	Time after implantation (mon)			
		0.5	1	3	6
Without supports from hard tissues (cheek, tongue, and mouth floor)	39	4.12±0.79	4.68±1.13	6.39±1.40	6.96±1.21
With supports from hard tissue (gingiva, hard palate)	32	2.93±0.97[a]	3.64±0.83[a]	4.33±0.78[a]	4.74±0.81[a]
Total	71	3.58±1.06	4.44±1.25	5.56±1.55	5.95±1.52

[a]*P* < 0.01, *vs.* regions without support from hard tissues

HADM patch shrank primarily at 2 weeks–1 month after transplantation, with a shrinkage rate of (3.58±1.06)% at 2 weeks and (4.44±1.25)% at 1 month. The area of HADM patch was basically stable at 3 months after transplantation. HADM patches in different regions exhibited different shrinkage rates at 2 weeks–6 months after transplantation. The HADM shrinkage rate was significantly higher in regions without supports from hard tissues (cheeks, tongue, and mouth floor) than in regions with supports from hard tissues (gingiva, hard palate) (t = 4.25–15.73, P < 0.01; Table 1).

Host response of HADM

All patients were followed up for 1 year, and no infection or rejections were observed.

DISCUSSION

Related knowledge

Oral mucosal and soft tissue defects are commonly repaired by skin flap or free skin grafting, which needs to expand surgical range and increase wound area in other regions[1]. In 1995, Livesey *et al*[2] prepared acellular allograft dermal matrix, and Wainwright[3] successfully used acellular allograft dermal matrix in the management of full-thickness burns. Acellular dermal matrix allograft has been recently used to repair oral mucosal defects and some therapeutic effects are obtained[4-7].

Analysis on present results

We used HADM to repair oral mucosal defects and got satisfactory clinical efficacy. Heterogeneous bovine skin tissue was subjected to acellular disposal for removal of cells and other antigens, with three-dimensional structure of extracellular matrix and collagen fiber retained, prepared into HADM, and then transplanted into the recipients in the form of cytoskeleton, which induce cell growth and vascularization and promote tissue regeneration without transplantation rejection. Following transplantation into wound surface, the pyknotic surface of HADM provides natural plane for epithelial migration and benefits for rapid epithelization, and the porous surface retains the natural three-dimensional structure of skin tissue, with high porosity and proper aperture, which can regulate and induce cell in-growth and promote vascularization.

Wei *et al*[8-10] studied the biocompatibility of HADM in animals and found that HADM completely retained extracellular matrix components, removed immunogenicity, exhibited good histocompatibility, and had no obvious stimulating effects on oral mucosa. After transplantation, no abnormal epithelial proliferation, hyperkeratosis, ulcer, and basal cell changes[8-10] were found. Hou *et al*[11] used acellular dermal matrix allograft to repair soft tissue defects in oral cavity, and confirmed that acellular dermal matrix allograft exhibited good biosafety. These are similar to present results that all HADM patches survived, (98.20±5.20)% of patch area survived at 2 weeks after transplantation, and at 6 months after transplantation, cell creeping substitution and vascularization accomplished, HADM patches grew stably, with no further shrinkage, smooth and pink appearance, and good elasticity, indicating better biocompatibility of HADM and stronger healing capacity. HADM heal would help reduce scar formation. Granulation tissue and scar tissue histologically present with disordered arrange of collagen and lack of elasticity fiber. The three-dimensional structure of HADM porous surface leads fiber cells and newly formed collagen to weave into net-like structure, blocks the in-growth of fibrous connective tissue, thereby reduces contracted scar formation.

Domestic and foreign scholars reported that the absorption of biomembrane vascularization ranges between 3.2%–43.0%[12-14]. This shrinkage following repair would cause some influences on related functions, which should be well considered during surgical design[15]. In the present study, HADM patch shrank primarily at 2 weeks–1 month after transplantation, with a shrinkage age of (3.58±1.06)% at 2 weeks after transplantation, and (4.44±1.25)% at 1 month after transplantation, and tended to be stable at 3 months.

The present study results demonstrated that the shrinkage rate of transplanted HADM was obviously related to defect region, defect degree, defect size, and surrounding situations. The HADM shrinkage rate was significantly higher in regions without supports from hard tissues (cheeks, tongue, and mouth floor) than regions with supports from hard tissues (gingiva, hard palate). This occurs primarily due to a fact that HADM retains collagen bundle and elasticity fiber, and HADM binding to periosteum contributes to the creeping growth of fibroblasts on the periosteum, therefore, there is small shrinkage and no contracted scar after transplantation. Kirschner *et al*[16] used acellular dermal matrices to repair oronasal fistulae and found no obvious shrinkage formed after surgery. Li *et al*[17] used HADM to repair gingival soft tissue insufficiency in guiding bone regeneration surgery and found that alveolar crest width was increased. Xue *et al*[18] repaired tooth extraction wound using HADM and obtained similar clinical efficacy. The present results demonstrated that the shrinkage rate of HADM in the hard palate and gingival wound repair regions was lower than that in the cheeks, tongue, and mouth floor, which provides good conditions for tooth implantation following surgery, and the good anti-compression capacity of HADM benefits for bearing masticatory pressure and supporting movable dentures, especially provides good peripheral seal for complete denture and increases retention force. Defect area also influences the shrinkage rate of acellular dermal matrix, *i.e.*, smaller defect area would get lower shrinkage age of acellular dermal matrix, and high survival rate of acellular dermal matrix. Li *et al*[19] reconstructed oral mucosal defects using acellular dermal matrix in 82 patients and found that 60.0%–87.5% of patients who used less than half of acellular dermal matrix patches acquired excellent effects, and that the shrinkage rate of HADM increased with increasing defect area. The frequent activities of cheeks, tongue, and mouth floor result in incomplete attachment of acellular dermal matrix patches to wound surface basis and influence patch survival. Tissue patch repairing wound surface would lead to different extents of shrinkage[20], but it can cover the wound surface in the early stage, promote wound healing, and reduce scar formation. Mild restriction of mouth opening would be solved by long-term, effective mouth opening exercise.

Clinical fixation methods include iodoform gauze bandage, base plate fixation, and direct suture. These three methods have advantages and disadvantages. This study used iodoform gauze bandage, because this method can stably fix patches, make wound surface closely attached; in addition, iodoform

also exhibits anti-infection effects, effectively isolate the contamination of saliva and food in the oral cavity, and enhance the survival rate of patches.

Clinical significance

HADM patch exhibits better biocompatibility, high survival rate, and rapid healing. It can cover wound surface, promote wound surface healing, reduce scar formation, and be easily manipulated in repair of oral soft tissue defects, thereby, has great value in clinical application.

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异种脱细胞真皮基质组织补片修复口腔黏膜组织缺损 71 例⋆

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摘要

背景：近年来，同种异体脱细胞真皮基质组织补片已在口腔组织缺损修复中广泛应用，但有关异种脱细胞真皮基质组织补片修复口腔黏膜缺损的研究较少。

目的：评价异种脱细胞真皮基质在口腔黏膜组织缺损修复中的效果及生物安全性。

方法：选择口腔良、恶性肿瘤手术切除后遗留的黏膜及部分软组织缺损患者 71 例，男 37 例，女 34 例，年龄 45(20~70)岁；其中良性肿瘤 42 例，恶性肿瘤 29 例。采用异种脱细胞真皮基质组织补片修复口腔软组织浅层缺损。观察生物膜成活情况,颜色、质地，比较组织补片修复无硬组织支撑部位(颊、舌、口底)和有硬组织支撑部位(牙龈、硬腭)的收缩率。

结果与结论：71 例补片完全成活，未发生坏死、感染等并发症。植入后 2 周补片成活面积为(98.20±5.20)%，植入后 3 个月，补片颜色已与周围黏膜相近，大部分患者诉有不同程度的紧张感；植入后 6 个月补片植入区成功完成了细胞的爬行代替和血管化，生长稳定，无进一步收缩，弹性良好，患者感觉趋于正常。生物膜收缩发生在植入后 2 周~1 个月，植入后 3 个月后基本稳定，术区组织形态与正常组织相比无明显差异。无硬组织支撑部位(颊、舌、口底)的收缩率较硬组织支撑部位(牙龈、硬腭)收缩率大。说明应用异种脱细胞真皮基质组织补片修复口腔黏膜具有组织相容性好、来源广泛、操作简单等优点，能够起到早期覆盖创面，促进创面愈合，减轻瘢痕生成的作用，可作为口腔黏膜缺损修复的理想材料。

关键词：口腔黏膜组织缺损；异种脱细胞真皮基质；组织移植；补片；牙周与口腔组织再生修复材料

doi:10.3969/j.issn.1673-8225.2010.16.041

中图分类号: R318　文献标识码: A

文章编号: 1673-8225(2010)16-03015-04

薛令法，尚伟，冯元勇，金晓明，刘凤桐，贾暮云，袁荣涛，卜令学.异种脱细胞真皮基质组织补片修复口腔黏膜组织缺损 71 例[J].中国组织工程研究与临床康复，2010，14(16):3015-3018.

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(Edited by Liu L/Song LP/Wang L)