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ORIGINAL ARTICLE

Evaluation of Bovine-Derived Collagen Membrane in Oral Surgical Mucosal Defects

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Abstract
Background The overall purpose of this clinical study is to evaluate the effectiveness of bovine-derived collagen in surgical oral mucosal defects.
Patients and methods The study model included thirty-two patients who underwent surgery for benign and malignant lesions of oral cavity in the Indira Gandhi Medical College and Research Institute, Puducherry, India—from 2012 to 2018. The surgical oral mucosal defects had been reconstructed with a commercially available bovine-derived type I collagen [Surgicoll-Mesh, 0.5 mm thick] membrane. The clinical effectiveness of this collagen membrane was evaluated using parameters like haemostasis, pain, epithelialisation, granulation tissue formation and mouth opening as the functional test parameter.
Results The clinical outcome results documented proved that the bovine-derived collagen membrane showed excellent significant results with respect to haemostasis, pain relief, epithelialisation and granulation tissue formation.

Keywords Collagen membrane · Submucous fibrosis · Oral cancer · Contracture · Wound healing

Introduction

Oral surgeries of premalignant and malignant lesions result in large mucosal defects. These oral mucosal defects need a temporary dressing material to deal with bleeding, post-operative pain, masticatory stress and infection. Skin grafts, buccal fat pad, nasolabial graft and tongue flap were commonly used. The problem of skin graft is the presence of adnexal tissue and donor site morbidity. Buccal fat pad is difficult to handle and suture. The xenograft, bovine-derived collagen membrane (0.5 mm), serves to be a user-friendly and reliable option for dealing with oral mucosal defects.

Patients and Methods

Thirty-two patients who underwent oral mucosal resections for benign, premalignant and malignant lesions of oral cavity were included in the study. Among 32 patients, 8 were female and 24 were male. Appropriate consent was obtained from the patient. Premalignant lesions like leukoplakia and oral submucous fibrosis (OSMF), benign lesions like mucocele and fibromas and malignant lesions were included. The patients in age group of 18–65 were included in the study. Patients with diabetes mellitus and chronic kidney disease were excluded from the study. Patients with mucosal defects were reconstructed with type I reconstituted collagen (bovine) under LA/GA appropriately. Patients were evaluated for haemostasis, post-operative pain, epithelialisation, granulation tissue formation and contracture. This is based on Bessho et al. [1] scoring criteria for mucosal healing.

Surgical Procedure and Post-operative Care

Appropriate surgical resections were done for benign, premalignant and malignant lesions of the oral cavity. Haemostasis is achieved in the surgical defects. Surgicoll-

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Mesh (collagen membrane) was soaked in normal saline for minimum 5 min for imbibing water. This makes the membrane soft and supple and mimics the native skin graft. The membrane is adapted to the mucosal defect and trimmed to appropriate size. No special surgical stent was required as the graft can be easily trimmed with scissors. The collagen membrane is secured on the edges of wound with 3-0 Vicryl sutures. Quilt sutures is done for fixing the collagen membrane in the centre and in the periphery. Quilting was done to secure the graft and to handle the drainage of the wound. Patients were advised for naso-gastric tube feeding for 3 days in case of large defects. Patients were reverted to oral feeding from 3rd post-op day. This protocol was followed only for larger defects especially in oral cancer surgeries. Gargling with saline and betadine from 2nd post-op day was advised. On the 7th post-op day, the membrane usually undergoes resorption or disintegration with a good epithelial tissue formation underneath.

Scoring Criteria (Based on Bessho et al. [1])

A. Haemostasis

2—Good—no bleeding or bleeding stops within 5 min
1—Fair—slight bleeding, no intervention required, haemostasis took longer period, i.e. > 5 min
0—Poor—intense bleeding that required intervention for achieving haemostasis

B. Pain being subjective, assessed on the 3rd post-operative day, based on patients own words:

2—Good (none to mild)
1—Fair (moderate)
0—Poor (severe)

C. Presence of granulation tissue noted at the end of one month:

2—Good (entire wound)
1—Fair (nearly the entire wound)
0—Poor (inadequate)

D. Epithelialisation noted at the end of the month:

2—Good (entire wound)
1—Fair (nearly the entire wound)
0—Poor (inadequate)

E. Contracture of the wound at the end of 1 month:

2—Good (none)
1—Fair (< 50%)
0—Poor (severe, i.e. > 50%)

F. Effectiveness of the membrane after 3 months

8–10—very effective
5–7—effective
0–4—ineffective

Results

A. Haemostasis:

2 (Good)—26 patients
1 (Fair)—6 patients

B. Pain on 3rd post-op day

2 (Good)—22 patients
1 (Fair)—10 patients

C. Presence of granulation tissue after 1 month

2 (Good)—28 patients
1 (Fair)—4 patients

D. Epithelisation after 1 month

2 (Good)—30 patients
1 (Fair)—2 patients

E. Contracture

2 (Good)—20 patients
1 (Fair)—8 patients
0 (Poor)—4 patients

F. Effectiveness was assessed at 3 months.

Very effective (8–10)—26 patients
Effective (5–7)—6 patients
Ineffective (0–4)—0 patients

Discussion

Oral surgical defects were commonly reconstructed by split thickness skin graft, buccal fat pad [3, 4], nasolabial grafts [5] and tongue flaps. The gold standard method for reconstruction of oral mucosa was split thickness skin graft. The skin graft has the layer of epidermis and little dermis. It also bears the adnexal tissue. An ideal oral epithelial graft should have stratified epithelium with underlying dense connective tissue, i.e. lamina propria. The skin graft is much thicker than the oral epithelium. Studies show that skin graft undergoes contracture and rejection [6].

Healing of oral cavity wound needs special care as the wound is exposed to masticatory stress, saliva and compounded by multiple oral microbial infections. This risk of infection leads to scarring and contraction of the mucosa. Contraction further leads to the reduction in mouth opening. A search of ideal dressing material/graft was always seen in the evolution of maxillofacial surgical procedures.

Autografts such as split thickness skin grafts, nasolabial flaps, tongue flaps and buccal fat pad were extensively used over years. It is documented that temporary cover of oral wound by dressing material reduces infection and scarring than left exposed. Dressing creates a physiological interface between the wound and oral environment and permits healing of vestibule [7] (Figs. 1, 2).

Nasolabial flaps many times do not provide adequate tissue for covering the defect. In addition, it leaves a scar on the face. Buccal fat pad is not a reliable option as the tissue is not firm when subjected to masticatory stress. Tongue flaps provides a reliable pedicle of tissue with predictable healing, but the need for second surgery and patient discomfort is the greatest setback of this flap. Further the size of the available tissue is less in the case of buccal mucosa reconstruction in OSMF cases and in oral cancer cases (Tables 1, 2).

Surgicoll-Mesh is an implantable biocompatible type I collage mesh. The mesh becomes supple and easy to handle just like natural tissue when hydrated with normal saline. Surgicoll-Mesh is free from contaminants like lipids

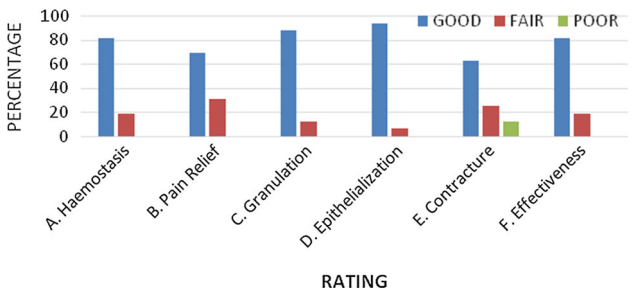


Fig. 1 Clinical study results of the present study

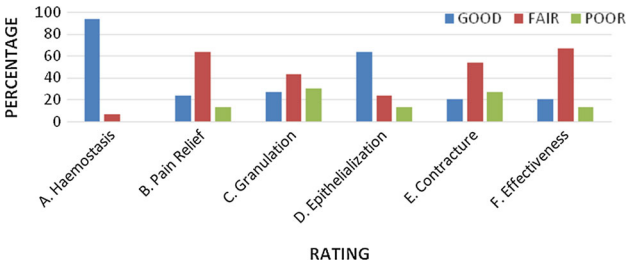


Fig. 2 Previously reported study results [2]

and immunogenic proteins. The product is derived from US-patented technology, and we found no allergic reactions in all the patients operated and used. The mesh comes in various dimensions: 5 × 5 cm, 5 × 10 cm and 10 × 10 cm. The ideal dimensions that we used for oral applications were 5 × 5 cm, 5 × 10 cm, 10 × 10 cm and 10 × 15 cm sizes of 0.5 mm thickness.

The applications of collagen membrane in other surgical disciplines include third-degree burns, synovial tissue implants, muscle flap reinforcement and colon, rectal, urethral and vaginal prolapse, and more commonly used in hernia repair, coverage over bone, tendon, cartilage and joint space.

The product's biochemistry and micro-porosity enhance rapid cell penetration and neo-vascularisation. High-purity type I collagen membrane induces chemotaxis and haemostasis, resists masticatory forces and allows rapid epithelisation and granulation tissue formation [8]. Collagen is considered as an important element in all stages of wound healing [9]. Collagen plays an integral part during each phase of wound healing. More than its excellent haemostatic feature, the native type I collagen's surface chemistry; when exposed to the cells of the open wounds, it activates the wound repair. Several experimental results suggest that collagen is an ideal material for tissue regeneration compared to other non-biological wound healing materials.

Collagen membrane is a specific activator of platelets and causes platelet aggregation over the biomaterial. Thus, it strengthens the clot. Collagen causes chemotaxis, cell aggregation and adhesion and release reaction of platelets [9]. Collagen has chemo tactic effect to endothelial cells and fibroblasts, due to this inflammation and pain is significantly reduced [10].

Collagen causes early migration of fibroblasts, leading to good granulation tissue formation.

Our results showed good granulation tissue formation except in four cases of carcinoma which involved more than half of the width of buccinator muscle.

Collagen stabilises the blood clot and aids in epithelialisation. Rapid epithelisation and control of infection reduce scarring. Epithelialisation and excellent colour

Table 1 Clinical effectiveness of collagen membrane

Present study	Percentage					
	A. Haemostasis	B. Pain relief	C. Granulation	D. Epithelialisation	E. Contracture	F. Effectiveness
Good	81.25	68.75	87.5	93.75	62.5	81.25
Fair	18.75	31.25	12.5	6.25	25	18.75
Poor	0	0	0	0	12.5	0.00

Table 2 Study by Poornima et al. [2]

Study by (Poornima et al.)	Percentage					
	A. Haemostasis	B. Pain relief	C. Granulation	D. Epithelialisation	E. Contracture	F. Effectiveness
Good	93.3	23.3	26.6	63.3	20	20
Fair	6.6	63.3	43.3	23.3	53.3	66.67
Poor	0	13.3	30	13.3	26.6	13.33

match have been achieved in 4 weeks post-operative in all our patients except four cancer patients who involved both mucosa and buccinator. So, scarring was more in these patients and it led to trismus. All other patients had near-normal mucosa and no complaints of trismus.

Overall experience with the collagen membrane in our institute is good with respect to wound healing, reduction in pain and decreased scar formation. Within 1 week, 75% of this study patients reverted back to normal eating habits. This is in accordance with Shanmugam et al. [11]. The collagen is stable and seems to be sufficiently thick (0.5 mm thickness), and we do not need any further reinforced collagen membrane grafts. Even in mucosal defects which are more lateral (i.e. in buccal mucosa), there is no damage to the membrane during mastication.

No allergic reaction was reported in any of our cases, proving that it is a safe biological membrane. This in accordance with the findings of Ragavendra Reddy et al. [12], Shoba Natraj et al. [13] and ESGorell et al. [14]

Let us analyse the possible reasons for the relatively better clinical outcomes of the present study. Surgicoll-Mesh product, as declared by its manufacturer, possesses high bioactivity as a result of its highly purified, US-patented, non-cross-linked native type I collagen. Besides these features, its nanotechnology of controlled phosphorylation of selected amino acids (serine, tyrosine, threonine, hydroxylysine and hydroxyproline [15]) maximises wound healing process by cell signalling that influences the migration of inflammatory cells to the wound bed [16]. This phosphorylated collagen clinically shows previously to render unique abilities in the growth of soft or hard tissue as needed by the physiological system. Phosphorylation of native un-cross-linked pure type I collagen exposes multiple free binding sites which allows the collagen–connective tissue framework to develop quickly. This proper alignment and binding of collagen fibres cause the maturation process to accelerate wound healing and faster tissue regeneration. Surgicoll-Mesh, clinically proved to invite the neo-vascularisation within 4–5 days upon surgical application, is based on the predicate device clinical data.

In conclusion, precise clinical data analyses of regenerative medical device products are more difficult compared to drugs, as the biological characteristics of such devices are attributable to heterogeneous biological cells. However, with the available clinical data comparison, it is quite obvious that the overall effectiveness of Surgicoll-Mesh collagen sheet, when compared with such reported similar earlier studies (Poornima et al. [2]), has significantly shifted the curve from the rating fair to good. More studies should be conducted with more number of patients to further strengthen the clinical findings of this study.

Results

The collagen membrane (0.5 mm thickness) was used as temporary dressing material on oral mucosal defects. The membrane is proved to be effective in terms of patient compliance and healing. Collagen membrane is a handy and reliable option that ensures predictable healing. Most of the patients reverted back to normal feeding habits on the first post-operative week as the patients have not experienced any burning sensation on the oral wound. The thickness of the material obviates the need for the stent as well as reinforcement of the membrane. The hypoallergenic collagen membrane is strongly recommended for all

oral mucosal defects for a complaint-free post-operative period.

Compliance with Ethical Standards

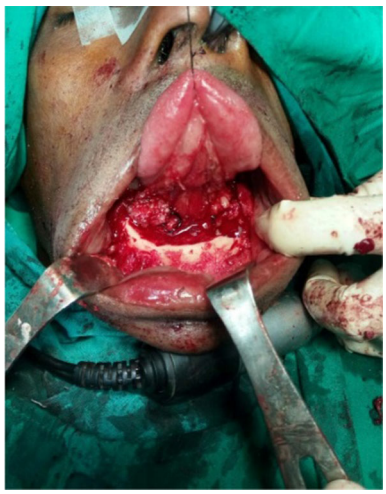
Conflict of interest All authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

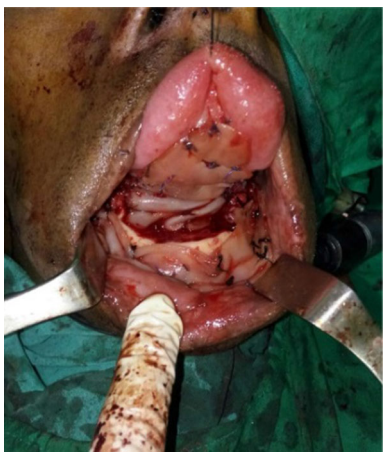
Informed Consent Informed consent was obtained from all individual participants included in the study.

Appendix

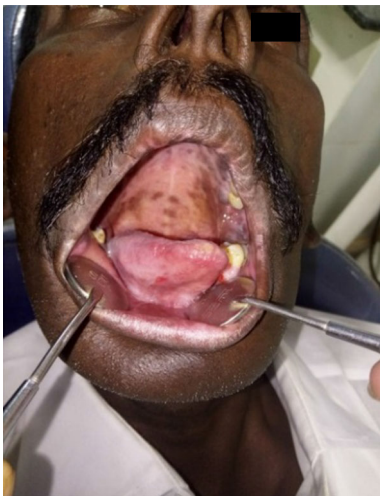
Patient-1:



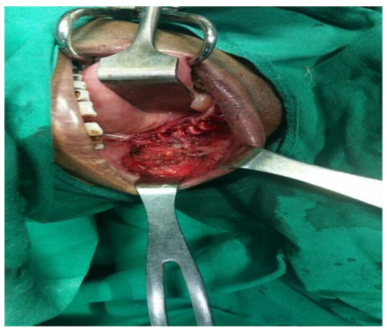
Surgical defect



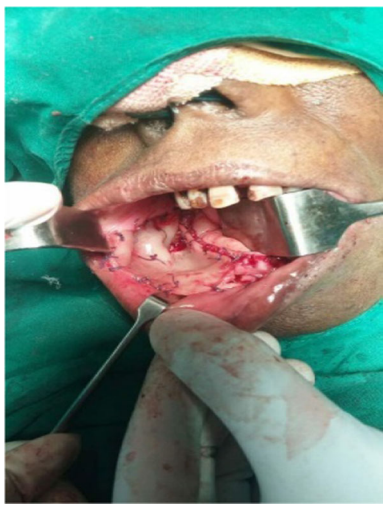
Application of collagen membrane



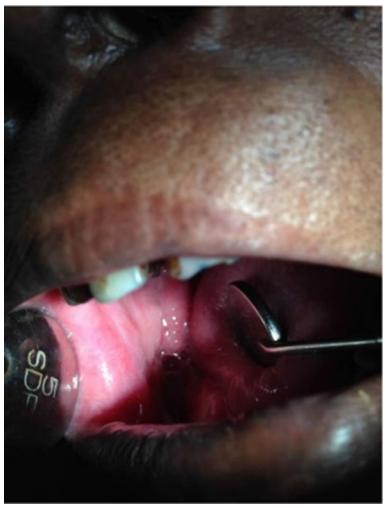
Two months post-op after surgery
Patient-2:



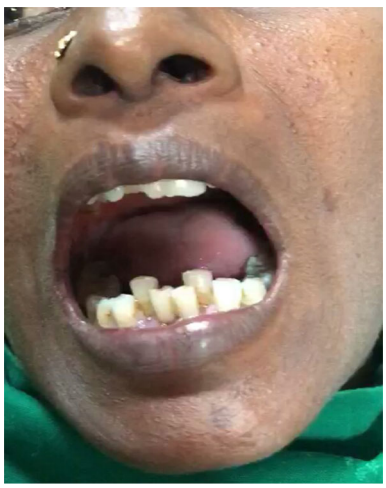
Surgical defect of verrucous carcinoma



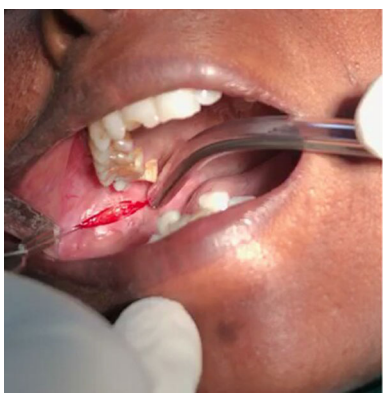
Application of collagen membrane 1



Post-op 2 months with good healing of the surgical site
Patient-3:



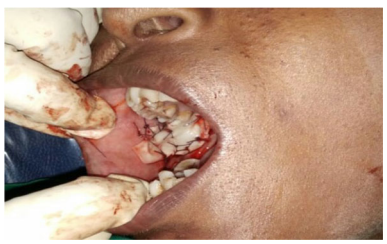
Pre-op mouth opening



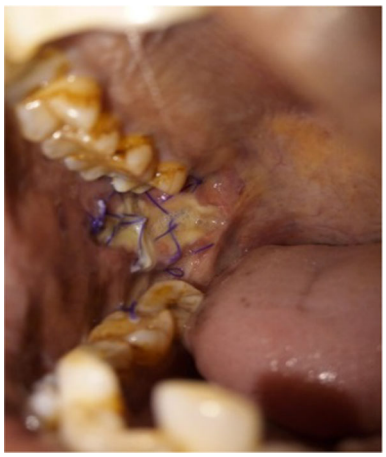
Incision

Collagen (Surgicoll-Mesh) prior to application

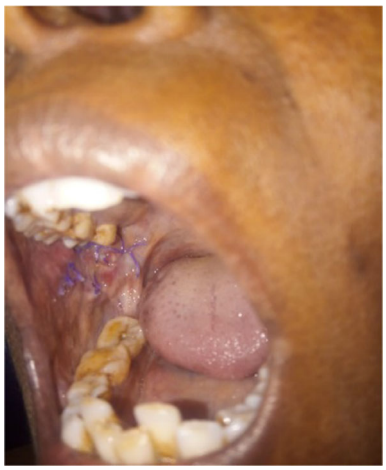
Preparation for applying collagen



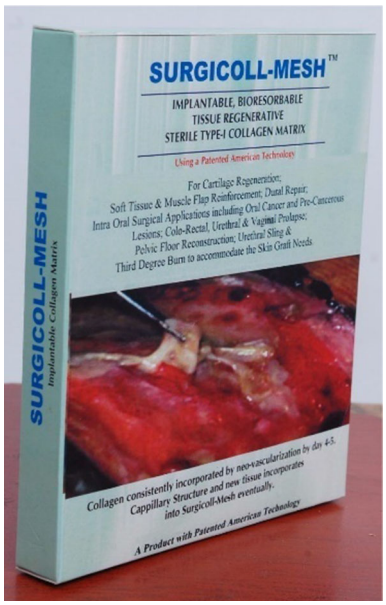
Surgical application of type I collagen sheet



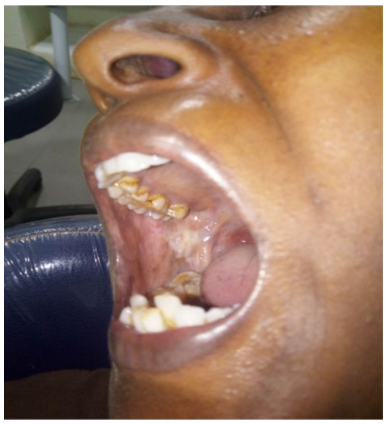
Fourth day after surgery



Seventh day after surgery



Surgicoll-Mesh product box image



Post-op after 3 months

Mouth opening after 3 months

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