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COLLAGEN MEMBRANE – A BIOLOGIC MUCOSAL SUBSTITUTE FOR INTRAORAL DENUDED AREAS

Dental Science

Endla Varun Kumar — Assistant Professor, Department of oral and maxillofacial surgery, Maharaja institute of medical sciences, Vizianagaram.

Neelima Chembolu* — Reader, Department of Oral and Maxillofacial Surgery, Malla Reddy dental college for women and hospital, Hyderabad, Telangana. India. *Corresponding Author

Bal Reddy Patlola — Prof & Head, Department of Oral and Maxillofacial Surgery, Government Dental College and Hospital, Hyderabad, Telangana, India. 500012.

Dharavattu Prabhakar — Post graduate endodontics Sri sai dental college Srikakulam

Durga Bhavani Domothota — Student, Gitam dental college and hospital, Visakapatnam.

ABSTRACT

Background & Objectives: Oral and maxillofacial surgical procedures often can produce open wounds. Oral mucosal or skin grafts are used to cover the open wounds to prevent microbial infection, excessive fluid loss, foreign material contamination and wound contracture optimize the rate of healing. In this study collagen sheet was used to cover the wounds intraorally for its effectiveness & usefulness in promoting wound healing.
Methods: Evaluation of collagen sheet as biological dressing material was used in 20 patients for intraoral denuded areas following excision of premalignant lesions & conditions such as leukoplakia, lichen planus and oral sub mucous fibrosis. The efficacy of collagen membrane in promoting haemostasis, relieving pain, inducing granulation, preventing infection, assisting in rapid epithelization at wound site and minimizing scar were assessed.
Results: Collagen for intraoral wounds is proved to be very effective & very potent in promoting haemostasis & relieving pain. In none of the cases any adverse reaction to the collagen was observed proving its safety as a biological dressing.
Conclusion: It is an effective biological dressing in promoting hemostasis, relieving pain, preventing wound contamination and induces granulation tissue and epithelization thereby reduces degree of scarring and tissue contracture and avoiding second surgical site.

KEYWORDS

Wound, Wound Healing, Dressing Material, Grafts, Collagen, Collagen Membrane.

INTRODUCTION

The healing wound is an overt expression of an intricate and tightly choreographed sequence of cellular and biochemical responses directed towards restoring tissue integrity and functional capacity following injury. Wound healing at multiple levels i.e; biochemical, physiologic, cellular and molecular level provides the surgeon with a framework for basing clinical decisions aimed at optimizing the healing response. It allows the surgeon to critically appraise and selectively use the growing array of biologic approaches that seek to assist healing by favourably modulating the wound microenvironm ent.[1]

The existence of a variety of wound types with varied healing modes and phases led to the evolution of different types of wound dressings. Wound dressings before 1960s, were considered to be passive products that had a minimum role in the healing process. Development of a wound dressing from the traditionally passive to more functionally active dressing through interactions with the wounds they cover, create and maintain a moist healing environment & facilitate healing.

Oral and maxillofacial trauma & surgical procedures often produce open wounds. Oral mucosa or skin grafts are used for this purpose. These grafts require a second surgical procedure. Oral mucosa is an excellent intraoral graft material, but its availability is limited. Split-thickness skin grafts are available but they contain adnexal structures, and express different pattern of surface keratinization leading to the development of abnormal tissue texture in the oral cavity that could interfere with the function.[3]

Bovine derived xenogenous collagen, a biologic plastic, was found to be ideal dressing which can be moulded like wax into desired forms. The high level of tolerance of xenogenous collagen by tissue and its successful use as a temporary cover for burns has prompted the use of xenogenous, cross linked collagen sheet to cover wounds in oral mucosa. Because of its easy availability, method of extraction, purification and low antigenicity, it has been used in many clinical conditions as temporary dressing materials with favourable results.

The denuded areas confined as secondary defects of the oral mucosa, occur after the excision of oral lesions such as benign lesion, reactive proliferations, premalignant lesions and conditions and some excisional biopsy wounds. Only those lesions that were sufficiently large and could not be closed primarily were taken for study with the following objectives i.e to evaluate the clinical efficacy of collagen as a biodegradable dressing material for surgical defects of oral mucosa[2].

MATERIAL AND METHODS

A total of 20 patients, 18 males and 2 females were taken for the study. Patients ranging in the age group between 20-60 years were included in the study. The cases selected were in good health, none of the patients presented with evidence of systemic or frank oral infection. Informed consent was taken. The studies were confined to the denuded areas in oral cavity, which resulted from excision of premalignant lesions and conditions. Diabetic patients, patients on steroidal therapy, pregnant, smokers & alcoholics were excluded from the study. Xenogenous collagen membrane was used for the study. Ethical committee clearance was taken for the study. The collagen used in this study was a purified bovine (Serosa) reconstituted collagen. Purified collagen is free from other components normally associated with it in its native state. Reconstituted collagen is the reassembled individual triple helical molecules with or without their telopeptide extensions, brought into solution and then regrouped into the desired form. This study was done in case of resultant defects of the oral mucosa, which occur after excision of premalignant lesions and other conditions, such as leukoplakia, lichen planus & oral sub mucous fibrosis [fig 1]. Only those lesions that were sufficiently large and could not be closed primarily were included in the study.

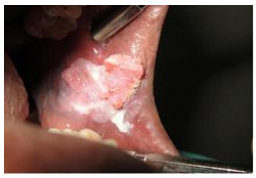


Fig 1: Preoperative lesion.

SURGICAL PROCEDURE

Excision of lesions was carried out under local anaesthesia[fig 2]. Collagen membrane removed from aluminium pouch was thoroughly washed in sterile saline solution (in order to remove the preserving medium), was cut in slight excess of the wound size and the collagen membrane was stabilized by 3-0 silk at the periphery of the defect and few quilted sutures in the center of the membrane over the defect [fig 3].

Fig 2: Surgical defect Fig 3: On 1st postoperative day

No pressure dressing was used. None of the patients were prescribed antibiotics, but were given only analgesics [Paracetamol 500mg] for 48hrs post operatively. The sutures were removed on the 5thpost operative day [fig 4]. The collagen sheet showed certain degree of sloughing & disintegration after 7 days. In the 2nd week, most of the collagen sloughed off the surface. The remnants of collagen were removed by irrigation with normal saline. Healing of the lesion after 1 month and 3 months respectively is shown in figures 5, 6.

Fig 4: Adherence of collagen on 5th postoperative day

Fig 5: After one month

Fig 6: After 3 months

The criteria for judgment were the haemostatic effects, pain relief, granulation, epithelization and contracture of the wound. They are evaluated on the day of surgery, after 24 hrs, 3rd, 5th day, 7th, 10th postoperative day and then 2nd week, 1 month, 3 months. It was judged as good, fair or poor and was scored as 2, 1 and 0 respectively. Results are obtained based on the scoring pattern used by Bessho etal[15]. Using this scoring pattern, the effectiveness and usefulness of collagen membrane were evaluated in this study.

Effectiveness (E) was assessed by adding up the scores, Values ranging between 8-10 are considered very effective, 5-7 as effective and 0-2 as ineffective. Usefulness (U) of the material was assessed based on the scores of effectiveness & reactivity noted; as being very useful (9-12) points + no reactions), useful (5-8) points + no reactions) and not useful (0-4 points + mild to severe reactions) [table 1].

Table 1: Criteria for Judgement of Collagen Membrane: (Good=2, Fair=1, Poor=0)

1. Hemostatic effect:
No bleeding – good
Slight bleeding, no hemostasis required- fair
Bleeding that required hemostasis- poor

2. Pain relief:
None – good
Slight- fair
Required analgesics- poor

3. Granulation:
Entire wound-good
Nearly entire wound-fair
Inadequate- poor

4. Epithelization:
Entire wound-good
Nearly entire wound-fair
Inadequate- poor

5. Contracture:
Little or more-good
Slight<50%-fair
Serious >50%- poor

Effectiveness [E]	Reactivity [R]	Usefulness [U] = [E] + [R]
Very effective score 8-10	None none	Very useful 9-12 points, no reactions
Effective Score 5-7	Slight few, did not require treatment	Useful 5-8 points, no reactions
Ineffective score 0-4	Severe required treatment	Not useful 0-4 points, mild to severe reactions

RESULTS

Twenty patients with a mean age of 35 years 6 months were enrolled in the study. Collagen membrane was used as a dressing material for intraoral wounds after excision of four cases of leukoplakia, 10 cases of oral submucous fibrosis and two cases of lichenplanus at various intraoral sites such as buccal mucosa, retromolar region, gingivobuccal sulcus and tongue was done.

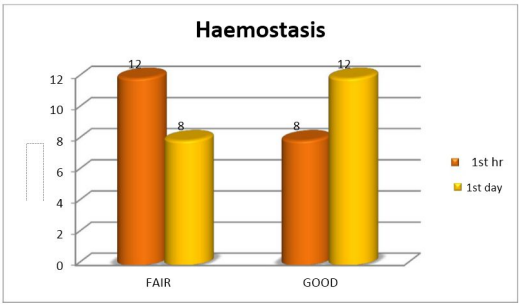
Table 2: Assessment of patient in postoperative period.

Post-operative period	Parameters assessed
On the day of surgery	Hemostasis and reactivity of the collagen
3rd postoperative day	Pain Reactivity of the collagen
5th postoperative day	Adherence of collagen to wound Pain Reactivity of collagen
7th postoperative day	Lysis of collagen membrane
10th postoperative day	Lysis of collagen membrane Granulation tissue formation
End of 2nd week	Granulation tissue formation
After one month	Epithelization Contracture of wound
After 3rd month	Contracture of wound

Table 2 shows the following developments in the cases after surgery.

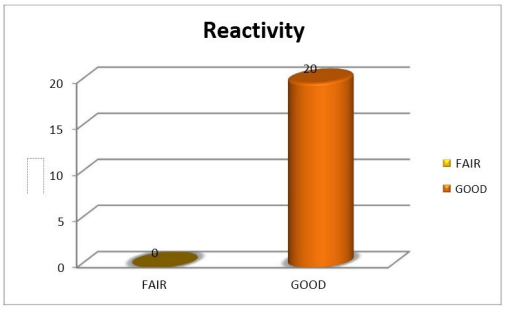
1. Haemostasis: [Graph 1]: In 1st hour 8 patients rated good (40%) & 12 patients rated fair (60%) during 1st hour. During 1stpost op day 12 patients rated good (60%) & 8 patients rated fair (40%).

GRAPH 1: ASSESSMENT OF HAEMOSTATIC EFFECT



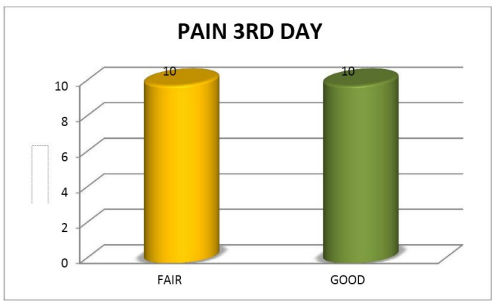
2. Reactivity: [Graph 2]: None of the patients showed any type of reactions with collagen membrane on oral mucosa.

GRAPH 2: ASSESSMENT OF REATIVITY



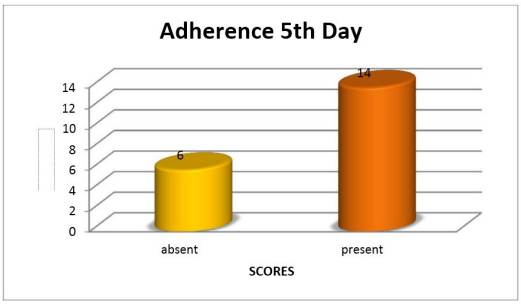
3. Pain Relief: [Graph 3]: Pain was rated as good in 10 cases (50%) & fair in 10 cases (50%) during 3rd post op day.

GRAPH 3: ASSESSMENT OF PAIN RELIEF



4. Adherence: [Graph 4]: Collagen membranes adhere to the underlying wound bed in 16 patients (80%) and have failed to adhere in 4 patients (20%) on 5th post operative day. No patients reported with infection.

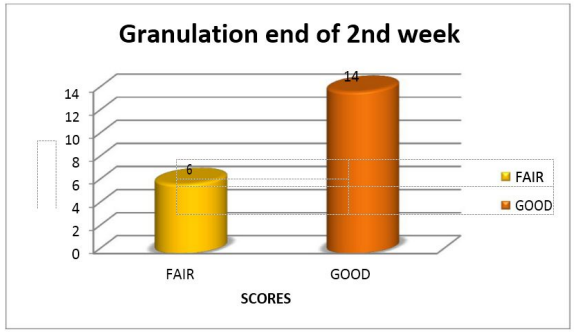
GRAPH 4: ASSESSMENT OF ADHERENCE



5. Collagen lysis: Post operatively 60% of patients showed complete lysis on 10th day.

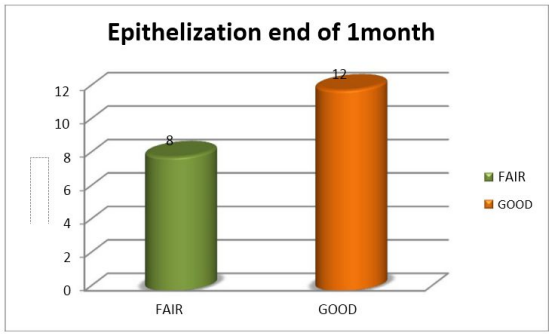
6. Granulation tissue: [Graph 5]: The presence of granulation tissue was assessed by the end of 2nd week. Granulation tissue was good in 14 cases (70%) & fair in 6 cases (30%).

GRAPH 5: ASSESSMENT OF GRANULATION TISSUE



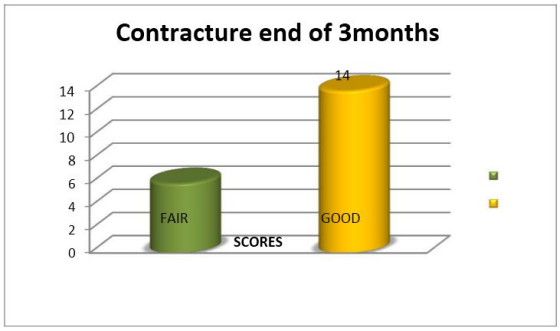
7. Epithelization: [Graph 6]: Epithelization was good in 12 cases (60%) & fair in 8 cases (40%) after 1st month.

GRAPH 6: ASSESSMENT OF EPITHELIZATION



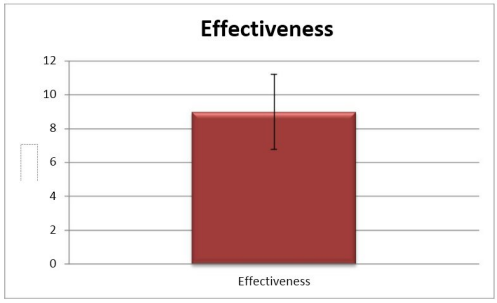
8. Contracture of wound: [Graph 7]: Contracture was measured by the difference in amount of mouth opening preoperatively and postoperatively after 3 months and rated as good in 14 cases (70%) were little or no contracture occurred & fair in 6 cases (30%).

GRAPH 7: ASSESSMENT OF CONTRACTURE



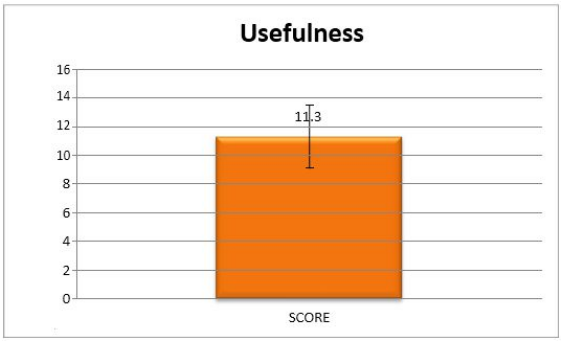
In the present study effectiveness of collagen membrane as a dressing material for intraoral wounds was scored to be very effective in 16 cases (80%) and effective in 4 cases (20%) [Graph 8].

GRAPH 8: ASSESSMENT OF EFFECTIVENESS



Usefulness of the material was graded as very useful in 16 cases (80%) and useful in 4 cases (20%) [Graph 9].

GRAPH 9: ASSESSMENT OF USEFULNESS



DISCUSSION

Raw wounds of the oral cavity heals by granulation tissue and epithelization, but sets problems as oral environment is always moist with salivary secretion and food ingestion and bacterial contamination. This is compounded by constant movements of cheek and tongue, which may interfere with graft adherence and acceptance. The risk of infection in the oral cavity is quite high resulting in scar contraction. The oral cavity is highly sensitive to any residual scarring, which may undergo ulceration and could be a constant source of irritation to patients wearing dentures[7,11].

Wounds that are left uncovered are prone to infection and scarring with additional clinical problems. It has been well documented that the incidence of infection & degree of contraction are greatly reduced in wounds which were dressed with biologic materials rather than left exposed or dressed with non-biologic material during healing. It's a proven fact that grafted wound heals faster with less complications than open wounds. Various defects in oral mucosa are covered with skin graft, mucosal graft or with xenogenous bovine collagen membrane.

A mucosal graft is an excellent intraoral graft material, but its availability is limited. Skin graft is the next choice, but when grafted in the mouth it becomes macerated, never attaining the texture or the resiliency of oral mucosa, also associated with growth of adnexal structures like hair and sweat glands. Dermis consists almost entirely of collagen and as an autogenous dermal graft it has been shown to be successful. However all these grafts require a second surgical intervention & are associated with donor site morbidity[3,8].

In the present study collagen was used as an alternative graft material to cover the raw areas during the initial phase of healing. It was observed that xenogenous collagen membrane had good conformability in lining mucosa i.e. it was supple & adapted to the wound no matter what the contour was.

Twenty patients between the age group of 20-60 years with mean age of 35years 6 months were enrolled in the study. Collagen membrane was used as a dressing material for intraoral wounds resulting from excision of oral premalignant lesions and conditions such as leukoplakia, oral sub mucous fibrosis, and lichen planus. The intraoral sites included were 14 buccal mucosa, 2 retromolar region, 2 gingivobuccal sulcus and 2 on the tongue.

The role of collagen membrane in haemostasis was explained in the ultra-structural study conducted by Zuker and Mason[4]. The normal sequence of interactions of platelets with collagen involved were a) the adhesion of platelets to collagen fibers, b) the release reaction, and c) platelet aggregation brought about by released platelet products. The interaction with collagen and certain other fibrillar connective tissue constituents is a vital component of the haemostatic reaction and Mason and Read[5] demonstrated that Microfibrillar collagen triggered adhesiveness of platelets and stimulated the "release phenomenon," producing aggregation of nearby platelets. In the present study collagen membrane showed good haemostatic effect in almost all the cases of application. These results were in accordance with the study conducted by Saroff etal[9], Uannai et al. & Alexander[6] who showed that microfibrillar collagen produced rapid & effective haemostasis and was superior to Gelfoam and to Surgicel as a topical haemostatic agent in oral wounds.

In our study no one showed any adverse reaction to the collagen membrane proving its safety as a biological dressing material. The collagen did not cause any adverse reaction and may have been responsible for the clinical impression of slightly more rapid healing. This was in accordance with the study of Marvin & Levin[20] by healing of the oral mucosa with the use of collagen artificial skin and Gupta[7] as collagen sheets were found to be as good biological dressing material in case of raw wounds.

Whereas in study of Lee et al[22] adverse reactions were seen as to the cell response to exogenous collagen starts shortly after the material is kept in contact with tissues, evoking a local and fast inflammatory response. This is not accordance with present study.

Pain being subjective, variations may be seen on the raw wounds of oral cavity. In this study the pain relief was rated as good in 50% and fair in 50% by 3rd post operative day. This result was in accordance with the study of Rajendra etal[16] where collagen was used to cover the raw area providing the coverage for sensitive nerve endings thereby diminishing degree of pain.

The adherence of collagen membrane is initially due to fibrin collagen interaction and later due to fibrovascular ingrowth into the collagen membrane. The present study revealed good adherence of the collagen membrane to the wound bed in 80% and failed to adhere in 20% of the cases, which were in accordance with the study done by Bhatnagar, Krishnan & Goel[8] and Sanjay et al[21], all collagen membranes, with time, slowly underwent collagenolysis and were eventually sloughed off. However, despite weakening by collagenolysis, collagen membranes were robust enough to resist masticatory forces for a sufficient time, to allow granulation tissue to form, which appeared uniform and clinically healthy. Whereas the study of Dharmdas et al[19] on patients with oral sub mucosal fibrosis, no adherence was seen in few cases because of restricted mouth opening which was not in accordance with the present study.

In the present study granulation tissue was rated as good in 80% and fair in 20%. This results were in accordance to study of Mitchell[10] where collagen forms a little excess of granulation tissue which was possibly the reason that minimal scarring of the soft tissue after healing.

In the present study, the results obtained for epithelization were good in 60% and fair in 40% which were in accordance with Omura & Mizuki[14] and Bessho & Murakami[15] who used a newly developed collagen for mucosal substitute on oral defects. The cellular tufts of fibroblasts and capillaries had infiltrated into the collagen. The infiltrated collagen matrix became a new connective tissue that re-epithelized rapidly by migrating peripheral epithelium 4-5 weeks after application.

Shoba[18], and Rajendra and Shankaramba[16] also evaluated the role of collagen in pre-prosthetic surgery (vestibuloplasty) as a biological dressing material. They found that it promoted rapid epithelization and prevented wound contracture.

In the present study, contracture was found good in 60% and fair in 40% which were in accordance to the studies of Fujioka and Fujii[13], Shinya et al[17] where artificial dermis was used for the repair of oral mucosal defects, and investigated for the incidence of postoperative scar contracture and studied factors related to cicatrisation by reducing the minimum diameter of the artificial dermis which may contribute to a decrease in scar contracture.

In the present study epithelization and contracture were rated as good to fair respectively. Similar results were reported by Shoba[18] to evaluate the epithelization and contracture, the results obtained are accordance with our study.

In the present study the effectiveness and usefulness were evaluated. The mean value for effectiveness was 9 and for usefulness the mean value was 11.3 which was in accordance to the study of Khanna[12] who evaluated the effectiveness and usefulness of collagen membrane as a dressing material in covering raw area created after excision of oral conditions and concluded that the material had advantages over other techniques used in promoting haemostasis, epithelization, granulation, and preventing the degree of swelling, contracture and donor site morbidity. Similar studies were also conducted by Omura et al[14], Bessho and Mukakami[15] and Sanjay[21].

Thus, collagen membrane obtained xenogenously fulfilled all the requirements of an ideal graft and can be used as an alternative to grafts. Because of the simple chair side application and good tolerance of the membrane by oral tissues, collagen membrane can be advocated as a temporary biological dressing material in oral cavity. It is an alternative to autologous grafts rather than being a replacement of other grafts used in oral mucosa and can be viewed as a satisfactory additional armamentarium to oral surgeons.

CONCLUSION

Purified bovine 'serosa' reconstituted collagen used in the present study is said to be a near ideal biological dressing material used for intraoral denuded areas following excision of small lesions as it is readily available, no second surgical site, easily reconstituted, remains moist, supple and intact, most biocompatible, better cosmesis. It also promotes hemostasis, reduces postoperative pain, prevents wound contamination, withstands masticatory trauma, induces granulation tissue formation and epithelisation. All these make the collagen membrane the most useful material for intraoral dressing.

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