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BILAYERED COLLAGEN MEMBRANE : AN ORAL MUCOSAL SUBSTITUTE IN INTRA ORAL SOFT TISSUE DEFECTS

Dentistry

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ABSTRACT

Bakground And Objectives:- Few oral surgical procedures including wide excision of lesions may result in soft tissue defects which require grafting. Autogenous skin graft or mucosal graft are used to cover the defect but they show donor site morbidity. Xenograft overcomes this demerit. In this study collagen sheets was used to cover such wound and its effectiveness and usefulnessin promoting wound healing was evaluated. **Methods:-** in present study, 30 patients were taken up for evaluation of bilayered collagen membrane as biological dressing material for intraoral denuded areas. Lesions included were erythroleukoplakia, fibroma, giant cell granuloma, oral submucous fibrosis, etc. Evaluation was based on subjective parameters. The criteria for judgement of collagen dressing was based on the scoring pattern of Besho k et al. **Results:-** Amongst 24 males and 6 females 76.6% showed good hemostatic effect, satisfactory pain relief in 43% patients. In 24-25 cases adequate granulation and epithelisation occurred. None of the cases showed any adverse reaction. Collagen membrane proved to be very effective in 24 cases(80%). **Conclusion:-** Collagen membrane proved to be a efficacious substitute of autogenous soft tissue grafting. It reduced the degree of scarring and tissue contracture significantly.

KEYWORDS

Bilayered collagen membrane, wound healing, mucosal substitute, dressing material, xenograft.

INTRODUCTION

The existence of various oral and maxillofacial lesions often produces open wounds after the surgical procedures. These include excision of nonhealing ulcer, premalignant lesion, mucoceles, fibrotic band in sub mucous fibrosis ,traumatic tissue loss and burns etc. Few of these wounds can be primarily closed and they heal by primary intention where as few larger defect that cannot be closed primarily result in loss of mucosal cover. If not covered with suitable graft or mucosal barrier, this increases the risk of infection, morbidity and results in increased scarring and secondary deformity [1]. Therefore variety of dressing material have been evolved and evaluated for their suitability to treat denuded area and surgical defect.

From the use of fresh meat and honey to the use of antibiotic films, synthetic plastics, porcine xenograft, artificial skin and many other materials have been evaluated and studied in attempt to develop ideal wound cover[2].

Skin grafting to cover the cutaneous defect was first started by Reverdin in 1871[3]. A major milestone in the development of skin substitute was the introduction of the invitro technique by Rheinwald and Green that involved the culturing of human keratinocytes into epithelial sheets suitable for auto graft.[4]. Oral mucosa is considered to be an appropriate graft material for intraoral defect but s available in limited supply. Availability is not the limitation with split thickness skin graft but contains adnexal structures, express different pattern of keratinisation resulting in abnormal tissue texture [5].

With the advent of synthetic wound dressing many newer material have been introduced which at present have reached up to tissue engineered skin substitute.

In this study bilayered collagen membrane have been used as a surgical dressing material for intraoral denuded areas. The aim of this study is to evaluate the efficacy of collagen membrane as a biological dressing material and to evaluate short term and long term complication including allergic reaction, infection etc.

This study was based on clinical parameters and was intended to make the technique as simple as possible.

MATERIALAND METHODS

This clinical study was carried out in 30 patients ranging in age group between 16 to 65 years. It was a prospective controlled clinical trial. The study was confined to the denuded areas in intraoral regions which resulted from tissue loss from trauma or excision of lesions including leukoplakia fibroma mucocoele etc (table 1, graph1, fig 1). The cases selected were in good health. Medically compromised patients and uncooperative patients were excluded from the study.

Xenogenous collagen membrane used in this study is a bilayer collagen membrane. This absorbable atelocollagen membrane is a sterile pliable, porous, scaffold agent made of highly purified atelocollagen derived from porcine skin.

The membrane is white in colour and covered with transparent silicon sheet on one side. This silicon sheet acts as carrier and aids in securing it to the soft tissue defects with the help of sutures.

- The collagen membranes come in varying dimension of 30x40mm, 70x50mm
- It is sterilized by gamma irradiation.

Surgical Technique

After getting clearance from ethical committee of the institute, study was carried out in 30 patients. Relevant history was taken from the patients and careful clinical examinations were done. After taking informed consent local anesthesia was injected. Margins of lesion was marked and excised (Fig 2).

Sterile collagen membrane was cut according to the wound size and sutured to the edges of the wound by the use of Black silk or vicryl sutures (Fig 3). A few quilting sutures were also given.

The collagen sheet showed certain degree of sloughing & disintegration after 7 days. After one week transparent silicon sheet was removed (Fig 4). The patient was kept on follow up after 7 days, 1 month & 3 months (Fig 5, Fig 6).

The criteria for judgement of collagen dressing membrane with respect to the results obtained is based on the scoring pattern which was used by Bessho K. et al in their study of a new bi-layer artificial dermis for vestibular extension(table 2)[20]. Using this scoring pattern, the Effectiveness, Reactivity and Usefulness of collagen membrane were evaluated in this study.

The criteria for judgment were the haemostatic effects, pain relief, granulation, epithelization and contracture of the wound, it was judged as good, fair or poor and was given the scores of 2, 1 and 0 respectively.

The Effectiveness (E) was assessed by adding up the scores and the value ranging between 8-10 was considered very effective, 5-7 as effective and 0-2 as ineffective.

Finally usefulness (U) of the material was assessed based on the scores of effectiveness & reactivity noted; as being Very useful (8-10 points + no side effects), Useful (5-7 points + no side effects) or Useless (0-4 points + side effects).

RESULTS

The study was designed to evaluate the clinical efficacy of collagen. Thirty patients between the age group of 20-60 years (24 males & 06 females) were enrolled in the study(table 3, graph 2). The intraoral site included buccal mucosa, gingivobuccal sulcus, tongue, upper and lower lip & maxillary defect.

Manipulation of collagen membrane was good while using intraorally as it could be easily secured to the tissue Good haemostasis was noted in 23 cases (76.67%) out of 30 and fair haemostasis in 7 (23.33%) patients. Pain relief was rated on 3rd post op day as good in 13 cases (44%) & was fair in 15 cases. It was poor in 02 cases(6.67%) where the collagen membrane failed to adhere to the underlying wound bed. Infection was not seen in any of the cases. (table 4 and graph 3)

In 24 cases (80%) granulation and epithelialisation were rated as good & there was little or no contracture. In these cases the Collagen membrane was in contact with the wound bed during the initial healing phase.. Contracture was confirmed by judging the resiliency of mucosa and mouth opening.

In this study on an average the adhered collagen underwent lysis/ sloughing off on the 8th day

In the present study when using collagen for dressing intraoral wounds, it proved to be very effective in 24 cases (80%), effective in 6cases (20%). In none of the cases any adverse reaction to the collagen was observed proving its safety as a biological dressing. It was regarded as very useful in 26cases (86.67%), useful in 4 cases (13.33%)(table 4, graph 4)

DISCUSSION

Large denuded intraoral areas heal by secondary intention in which wound contraction and reepithelisation are the two important event[6]. In first week of healing wound shows no change in size known as lag phase. Then wound enters the exponential phase where wound contraction occurs at constant rate[7]. Healing depends on the depth of the injury. Deeper wound take more time to heal as it requires more granulation tissue formation. Denuded areas continuously tend to loose surface fluid and electrolyte as intact skin barrier and keratin is absent to prevent it. The keratin layer of skin serve as effective antimicrobial barrier. The layer of collagen is required as a scaffold for the orderly ingrowth of epithelium. Denuded area are devoid of this resulting in extensive scar and keloids[8].

An ideal soft tissue graft should promote haemostasis, relieve pain, facilitate granulation tissue formation, resist infection, prevent tissue reactions, and promote rapid epithelisation[9].

With time various material acting as oral substitute were involved satisfying the ideal requirement.

Other than oral mucosa, split thickness skin grafts was used as graft material. The collagen based bilayer membrane was developed by yannas et al as artificial skin in burns[10]. In 1910 Davis was the first to advocate the use of amniotic membrane in skin transplantation[11]. In 1990 this was brought to be used in maxillofacial surgery[12] . Various oral substitute were prepared using invitro culturing techniques[5]. Dermal substitute “integra ” developed by Burke and Yanna has been applied in oral cavity[13].

Other oral mucosal equivalent are “apligraft ” (still under experiment)[14]. De-epidermised dermis and cultured oral mucosa keratinocytes from buccal mucosa and hard palate was studied in Korea [15]. Oral keratinocytes seeded onto the human cadaveric dermal matrix , alloderm have also been used as mucosal equivalents[5]. Tissue engineered oral mucosa are now been developed. Most of these are not available readily or few are under experimental trials.

The most easily and commercially available is bilayered collagen membrane as mucosal equivalents. Peacock, Seigler used collagen sponges in treatment of liver disease and proved its excellent haemostatic properties[16]. Hyder PR et al used freeze dried cross linked bovine type I collagen for guided tissue regeneration in surgical treatment of periodontal diseases[17].

Miami M Beghe studied the role of collagen in wound repair, its interaction with platelets and fibronectin, its scaffold role for fibroblast proliferation[18]. Feinbergs, Mc Donel EJ used preformed collagen sheets as a disc replacement after TMJ surgery in white rabbits[19]. Omura S et al used bilayer membrane as mucosal substitute in oral defects of cancer patients[10].

Bessho K, Murakami K used it for vestibular extension[20]. Collagen membrane has been used for correction of maxillary sinus membrane perforation[21]. It has also been used for reconstruction of buccal defect following fibrotic band excision in oral submucous fibrosis.

In this study xenogenous bilayer membrane derived from porcine skin is used. This collagen membrane is covered with transparent silicon sheet on one side that act as carrier and improves the handling properties.

30 patients were included in this study for clinical evaluation of collagen membrane. Good haemostasis was achieved in 76.6% patients. Similar study was conducted by Saroff et al who highlighted the interaction of platelets with microfibrillar collagen[22]. It was stated that collagen acted as a chemotactic factor for platelets influencing there adhesion and aggregation.

In this study 43.3 % patients had good pain relief that is, no analgesics were required after third post operative day . Only in two patients pain control was poor. This could be attributed to the lack of adherence of membrane to the underlying soft tissue resulting in prolonged exposure of nociceptive receptors. Although the pain is multifactorial, it also correlates with the level of tissue damage.

In 24 patients healthy granulation tissue covered the entire wound and was graded as good response. Unhealthy granulation tissue meant to be tissue with inflammatory redness, that bleeds on slightest provocation. Rastogi S et al[2] conducted a similar study and noted healthy granulation tissue in all 60 patients at the end of second post op week.

While the study of vestibular extension by in 50 patients Few variations were seen in the study carried out by Bessho K et al[20] for vestibular extension in 50 patients. It was found that granulation tissue formation was good in 36 patients and fair in 14 patients.

Satisfactory epithelisation was seen in 83% cases when evaluated after 30 days. The variability in the healing time can be attributed to the difference in size of wound and depth of defect. Good epithelial resiliency was achieved without any limitation of mouth opening in 80% cases owing to minimal or no tissue contracture.

This collagen membrane was found to be biocompatible in all cases as there was no allergic response noted. In 28 out of 30 patients good adherence of the collagen membrane was achieved . The adherence is due to fibrin collagen interaction and fibrovascular ingrowth.

After evaluating all the clinical parameters including haemostasis, pain relief granulatrion tissue formation, epithelisation, it was found that collagen sheet was very effective in 80% patients. Therefore this xenogenous collagen can be successfully used as an oral mucosal substitute and can be advocated as temporary biological dressing material in orofacial region.

CONCLUSION

Clinically this bilayered collagen membrane proved to be a biocompatible surgical material. It is well tolerated with no adverse effect . normal mucosal texture was seen to be restored in 1 month . Therefore it can be successfully used as an alternative mucosal replacement in various intra oral defects.

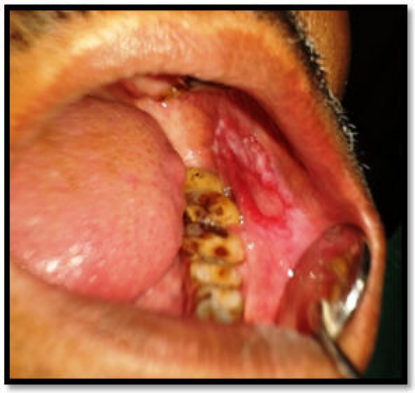


Fig 1:- erythroleukoplakia patch present on Left buccal mucosa

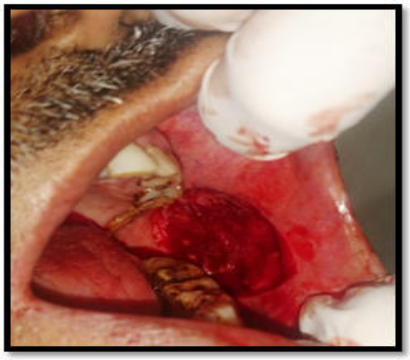


Fig 2:- excision of lesion

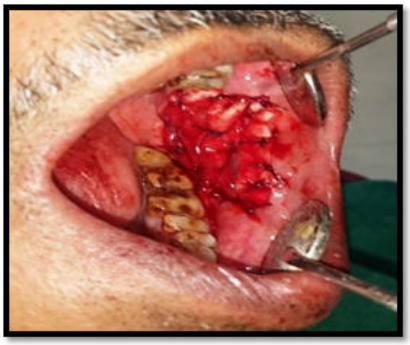


Fig 3:- bilayered collagen membrane secured to The surgical defect

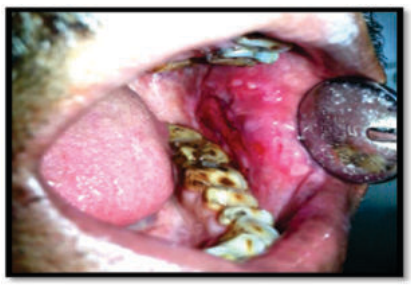


Fig 4 :-1 week post op showing showing granulation tissue formation

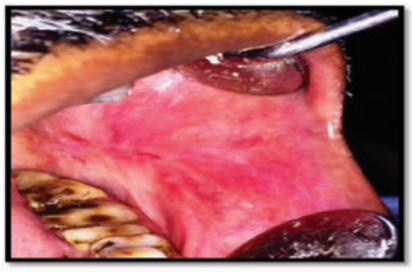


Fig 5:- one month post op showing Healthy epithelisation

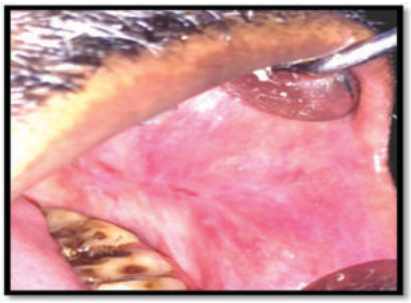


Fig 6:- Healing after three months Healthy epithelisation

Table 1: Distribution of study subjects according to type of lesion.

Characteristics	
Age	
Mean ± SD (years)	37.77 ± 11.86
Min-Max (years)	18-57
Gender	
Male {n (%)}	24 (80.00)
Female {n (%)}	06 (20.00)

Table 2:- Criteria For Judgement Of Membrane

Score	Definition
Haemostatic effects (day after operation):	
Good	No bleeding
Fair	Slight bleeding, no haemostasis required
Poor	Bleeding that required haemostasis
Pain relief (day after operation):	
Good	None
Fair	Slight
Poor	Required analgesics
Granulation (month after operation):	
Good	Entire wound
Fair	Nearly the entire wound
Poor	Inadequate
Epithelization (month after operation):	
Good	Entire wound
Fair	Nearly the entire wound
Poor	Inadequate
Contracture (month after operation):	
Good	Little or none
Fair	Slight (< 50%)
Poor	Serious (50% or more)
Effectiveness (after a year):	
Very effective	Score 8–10
Effective	Score 5–7
Ineffective	Score 0–4
Safety (after a year):	
None	None
Slight	Few, did not require treatment
Severe	Required treatment
Usefulness (after a year):	
Very	8–10 points, no side-effects
Useful	5–7 points, no side-effects
Useless	0–4 points, side-effects

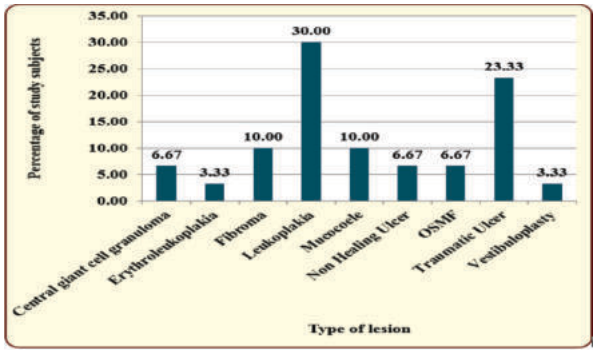
Table 3: Characteristics of study subjects(n=30).

Characteristics	
Age	
Mean ± SD (years)	37.77 ± 11.86
Min-Max (years)	18-57
Gender	
Male {n (%)}	24 (80.00)
Female {n (%)}	06 (20.00)

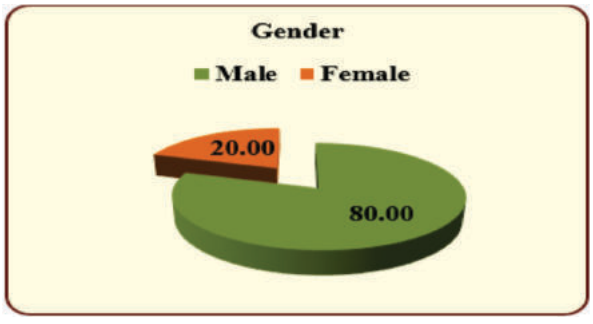
Table 4:-Judgement of membrane according to clinical parameters

Criteria	Judgement of Success			Total n (%)
	Good n (%)	Fair n (%)	Poor n (%)	
Haemostatic Effect	23 (76.67)	07 (23.33)	00 (0.00)	30 (100.00)
Pain Relief	13 (43.33)	15 (50.00)	02 (06.67)	30 (100.00)
Granulation	24 (80.00)	06 (20.00)	00 (0.00)	30 (100.00)
Epithelializati on	25 (83.33)	05 (16.67)	00 (0.00)	30 (100.00)
Contracture	28 (93.33)	02 (06.67)	00 (0.00)	30 (100.00)
	Very Effective n (%)	Effective n (%)	Ineffective n (%)	Total n (%)
Effectiveness	24 (80.00)	06 (20.00)	00 (0.00)	30 (100.00)
	None n (%)	Moderate n (%)	Severe n (%)	Total n (%)
Reactivity	30 (100.00)	00 (0.00)	00 (0.00)	30 (100.00)

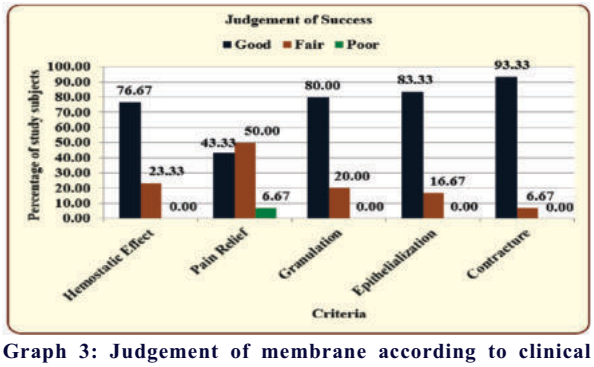
	Very Useful n (%)	Useful n (%)	Useless n (%)	Total n (%)
Usefulness	26 (86.67)	04 (13.33)	00 (0.00)	30 (100.00)
	Good n (%)	Fair n (%)	Poor n (%)	Total n (%)
Comfortability	29 (96.67)	01 (3.33)	00 (0.00)	30 (100.00)
Biodegradability	30 (100.00)	00 (0.00)	00 (0.00)	30 (100.00)
Biocompatibility	30 (100.00)	00 (0.00)	00 (0.00)	30 (100.00)
	Present n (%)	Absent n (%)	-	Total n (%)
Adherence	28 (93.33)	02 (06.67)	-	30 (100.00)



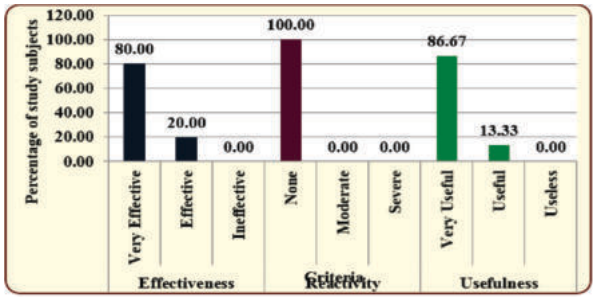
Graph 1: Distribution of study subjects according to type of lesion.



Graph 2: Gender distribution (in percentage) of study subjects.



Graph 3: Judgement of membrane according to clinical parameters



Graph4: Judgement of membrane.

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