MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2025.1.385.389

OPEN ACCESS

Key Words
Oral submucous fibrosis, tissue engineering, scaffold

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Received: 18 November 2024
Accepted: 20 December 2024
Published: 31 December 2024

Citation: Dr. Anusha kollu, Dr. R. Sudhir, Dr. Nandha kishore and Dr. M. Yashwanth, 2025. Triple Regimen for Oral Submucous Fibrosis: Our Institutional Experience in a Series of 10 Cases. Res. J. Med. Sci., 19: 385-389, doi: 10.36478/makrjms. 2025.1.385.389

Triple Regimen for Oral Submucous Fibrosis: Our Institutional Experience in a Series of 10 Cases

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ABSTRACT
Conventional treatments for oral submucous fibrosis were usually prolonged, with a impractical remission mainly due to relapse or poor patient compliance. Mainstay of treatment is concentrated on attempts to improve mouth opening and relieve the associate symptoms by medical and surgical means. 10 patients diagnosed with oral submucous fibrosis were included in the study, all the patients were subjected to triple regimen and followed over a period of 6 months. Amnion with its exceptional wound modulating properties have explored its potentiality in the field of regenerative medicine by acting as a natural scaffold for wound healing, adding on triple regimen made it an excellent candidate for tissue engineering. The purpose of the present study is to call the attention towards the capacity of triple regimen for the successful outcome in the cases of oral submucous fibrosis.

INTRODUCTION

Modern world has many incidents happening around which induce a lot of tissue damage and dysfunction. Primary response to the injury is seen at micro environment cell level, when extensive injury has occurred and is beyond the level of cell response medical intervention is obligatory. One mode of medical management is to replace the damaged tissue with an acceptable substitute, which can have a natural or synthetic background. Tissue engineering acts as a strategic alternative with promising results and eliminates the limitations of synthetic substitute. The word tissue engineering is first introduced by Langer and Vacanti in 1993 and defined it as field concerned with biological substitutes that maintain, improve, or restore tissue functions in order to cope up with the problem related to tissue damage[1]. In tissue engineering the cells are engulfed in a scaffold which are slowly released and replaced by natural tissue, as the cells are being used and later on, they are replaced and enhances the function is always under the scope of tissue engineering. Various inner body cavity membranes can be used as tissue engineering structures which includes peritoneum, pericardium, omentum, pleura and amniotic membrane[2]. Amnion is a thin, avascular, resistant and transparent membrane surrounding and protecting the foetus during the term of pregnancy. Amnion is the fantastic substance in the field of regenerative medicine with an era of history and remarkable results. Amnion is the inner layer of placenta which has unique source of stem cells and collagen with an additional functions including[3]. (Table 1).

Table 1: Functions of Amniotic Membrane

AMNION FUNCTIONS
Analgesic effect
Angiogenic effect
Antibacterial effect
Anti-inflammatory effect
Mechanical effect
Non immunogenic effect
Reduced scarring effect
Neo epithelization effect

With no less importance amniotic membrane acts as a biodegradable scaffold with wide range of application with few added materialistic problems like transmission of infectious diseases. Application of amnion with proper precautions and safety criteria makes the amnion a useful adjuvant in day-to-day practice, hereby we display series of cases in which amnion has been used as a graft material in combination with systemic supplements and pharmacological drugs for an effective molecular prevention.

MATERIALS AND METHODS

Ten Patients suffering from oral submucous fibrosis diagnosed clinically and pathologically were included and treated in our hospital. our patients had varying degrees of inability to open mouth, the main criteria adopted for grading of OSF was presence of clinical blanching, palpable bands and reduced inter incisal opening to 20-25mm were included. A detailed personal history, routine blood investigations and radiographs were obtained from all the patients to rule out any systemic diseases. Patients with pericoronitis and any acute infections were excluded from the study. Before the surgical procedure all the patients were asked to cease the habits, quarter of the patients in the study group were ready to give up betel nut chewing than to stop drinking alcohol or tobacco chewing, patients with this mind set were fully informed especially not to raise their expectations for a complete cured final outcome. All the patients were gone through triple regimen which includes vitamin B supplements with a daily dose of 200mg, buflomedil hydrochloride 450mg three times daily, initiated one week prior to surgery. Amnion was used as graft material in all the cases and medication was extended till six months of the post operative period.

Amnion Processing: The placenta was retrieved intact post vaginal delivery and processed under sterile conditions. The chorioamnion membrane was stripped from the placenta and under lamellar flow hood in a clean room and sterile conditions the chorion and amnion were separated. The amnion was cleaned to clear it from blood clots and then washed in balanced salt containing pencillin, streptomycin and amphotericin, later the membrane is preserved in 2 lakh IU of crystalline pencillins at 4 degree C. In all the cases membranes were collected one day prior to surgery and were made still in the pencillins for 24 hours. Serological tests were repeated prior and for every three months post operatively for all the subjects to detect any infections, if any, occurring during the window period.

Surgical Procedure: The choice of anesthesia was general for all the subjects. Fibrous bands were excised bilaterally in all the subjects exposing the underlying muscle. Repair of the defect was then done using amnion with the pre measured split. All the patients were encouraged to be under nasogastric feeding for a period of week.

Clinical Parameters: The clinical parameters were pain which is subjective, swelling and inter incisal opening which were objective. Pain was recorded using VAS scale on 1st, 3rd, 5th and 7th post operative day as per the criteria laid by Izumi *et al*: pain gradually reduced in all the cases at the end of 20 days of post operative period. Swelling was recorded on post operative days according to scoring criteria given by Siddiqui *et al*: in all the cases there was a peek in the swelling on 3rd day and gradually decreased. With regards to mouth opening, at the end of six months all the patients

showed a satisfactory gain in their inter incisal opening.

RESULTS AND DISCUSSIONS

Table 2: Mean Age Group of the Patients

Mean Age	SD	P value
33.00	8.89	0.575., NS

Table 3: Mouth Opening

Time	Mean ± SD
Pre-op	21.40 ± 2.88
Intra-op	37.00 ± 4.12
1 week	35.00 ± 4.53
1 month	32.60 ± 4.93
3 months	33.00 ± 4.53
6 months	34.20 ± 4.44

Table 4: Graft Adaptation and Success

	Adaptability and success		
Good	Fair	Poor	Total
3(60%)	2(40%)	-	5
5(100%)	-	-	5
8	2	-	10

Table 5: Improvement in Weight Gain

	Weight gain		
2kgs	5 kgs	10	Total
5(100%)	2(40%)	3 (60%)	10

Table 6: Daily Dosing of the Supplements

Vitamin	Function	Daily dose
B1 (Thiamine)	carbohydrate metabolism	1mg /day
B2 (Riboflavin)	mucosal integrity	2mg/day
Nicotinic acid	Nerve function and mucosal integrity	20mg/day

Fig. 1: Pre Operative Mouth Opening

Fig. 2: Post Operative Mouth Opening

The mean age group was 33 years with a strong predilection for the male patients (Table 2). Seven out of ten patients in the present study complained of trismus and burning sensation on intake of food, rest of the patients had no added complaints. Betel nut chewing, alcohol consumption were present in all the cases, additional habit of smoking was observed in two cases. Buccal mucosa was affected bilaterally in all the cases and all were managed by amnion as a graft bilaterally. Pre operatively B complex and vasodilator was supplemented for the entire patient range, and there was a drastic change in all the patients in regards to burning sensation without any change in trismus. Pre operative mouth opening was 21+/-2mm with a drastic increase at the end of 6 months to 34+/-4mm which was the success showed by the triple regime in our study (Table 3) (image 1 and 2). Adaptability of the graft was satisfactory for all the cases, there is a biological bond which is formed between the muscle bed and the amnion, thus the fibro elastic biological bond makes the adaptability a success. (Table 4). There was a significant weight gain recorded in all the patients mainly due the diet modifications and the supplements, although the symptoms were relieved with an adequate weight gain, long term supplementation were required to maintain a persistent outcome (Table 5). AM acts as a rich scaffold of proteins and growth factors making it an gold standard structure in the field of regenerative medicine. With a growing interest in the field of tissue engineering and regenerative medicine lot of modifications have been done for AM for its better service to the mankind. Growth and development of cells always takes place in a well organised three dimensional matrix where there is a proper cell to cell and cell to matrix adhesion for a better expression of its properties which is evident in a amnion. AM was first used in the medical world as a component of tissue engineering and medicine by Davies et al in 1910 as a skin transplant. Further on AM is utilized as transplant in conditions of skin burns, lining for urinary tract, oral cavity, stomach and orbit. Antimicrobial property of AM prevents bio film formation and makes it more interesting material in areas of microbial load like oral cavity, urinary tract and orbital areas. AM is rich in biological growth factors like epithelial growth factor (EGF), tumour growth factor beta(TGF-BETA) along with structural proteins, keratinocytes, fibroblasts which all supports in healing of chronic non healing wounds[4]. There are various enlisted biological and physiological properties of AM which includes:

- **Anti-Inflammatory Effect:** AM acts as scaffold and traps the inflammatory cells and deliver them to pro apoptotic agents and suppresses the inflammation and acts as a biological agent.
- **Antibacterial Effect:** AM secrets natural barriers like defensins, cystatin and elafins which act as a barrier and prevent bacterial infiltration.
- **Non Antigenic and Anti-Immunogenic Effect:** AM lacks antigens, blood vessels, nerves and lymphatic chains in its structure making them low to non-immunogenic agent.
- **Anti-Scarring Effect:** reduced proteases activity due to secretion of tissue inhibitors gives AM an anti-scarring effect.

- **Neo Epithelization:** this is due to the growth factors secreted by the amnion
- **Cell to Cell Adhesion:** AM acts as reserve for hyaluronic acid and proteins like fibronectin, collagens and proteoglycans.
- **Anti-Oncogenic Property:** due to the presence of pro apoptotic agents like interleukins and endostatin[5].

In physiological delivery the placental portion has found to have more amounts of cell lines with an increased expression of TGF and EGF which supports a good healing in chronic wounds on the other hand caesarean delivery has reportedly less TGF and are found to be more useful in ophthalmological applications. In our study all the amnions are obtained post physiological delivery for a enhanced healing[6]. AM contains collagen type IV, V and VII in its basement membrane which resembles the basement membrane of the oral cavity and has a properties of epithelial cell migration, de-differentiation, cell-cell adhesion and prevents apoptotic cell death and facilitates satisfactory healing in chronic non healing lesions like oral submucous fibrosis. Post-surgical scarring in OSMF cases leads to decrease in the inter incisal opening and thus leads to altered patient compliance, this biological process of scar formation is well inhibited by the suppression of tumour growth factors 1, 2 and 3 thus preventing fibroblasts proliferation and migration. This property makes the AM a step ahead to other materials in aspect of neo bands formation which is well seen in our series of cases where there is adequate mouth opening achieved in post operative follow up period[7]. Anti-inflammatory effect is essential for healing in chronic wounds, staffing of neutrophils and inhibition of interleukins gives AM this unique property and thus improving the outcome which is clearly evident in our study. Foetal hyaluronic acid which is present in AM suppress the signalling of fibroblasts and prevents the conversion of fibroblasts to myofibroblasts and thus inhibits scarring which is a useful mechanism required in oral submucous fibrosis and made it as an important tool in our present study[8]. Anti-microbial effect of AM is an important feature required in oral cavity as microbial load is more in around the surgical site, AM had been found to have antimicrobial effect against staphylococcus aureus, E coli and pseudomonas and the close adhesion of the membrane to the recipient site also acts as affective physical barrier for bacterial adhesion[9]. AM has attractive mechanical properties which makes it a key element in the field of tissue engineering AM has viscoelastic behaviour which is responsible for its highly stretch resistance with an added intrinsic mechanical property making it more useful in our field where there are pounding stretch forces acting upon it. Clonogenicity property of AM that is the ability of cell to form a cloned colony is a key defined function which helps in replacing the AM with the local tissue and thus maintains the naturality and tissue integrity. Degenerative and precancerous changes in the oral cavity are clearly due to some form of long term persistent mild injury., formerly believed due to local irritant like betel nut chewing which is evident in our cases as an etiological agent, adding to it there can be existence of intrinsic factors produced due to deficiency of essential vitamins. B complex is considered to be one of the prime vitamin to maintain the mucosal integrity in the oral cavity, the best known vitamin B fractions are thiamine , riboflavin and nicotinic acid[10]. (table 6). One of the most important responses following vitamin therapy is weight gain which is clearly seen in our cases by 52%. Malnutrition is evident in patients with oral submucous fibrosis mainly due to discomfort and difficulty in consuming food, while these obstacles play a prominent role and missed in day to day practice we have incorporated vitamin supplements as an essential component of regenerative medicine in our study. there is no laboratory test devised to furnish the accurate requirement of vitamin B requirement in oral submucous fibrosis, but the patient do manifest local symptoms which almost and always improves with administration of B complex substitutes to the dietary chart. Alcohol is oxidised in our body to produce energy and replaces the daily caloric requirement and thus leading to vitamin deficiencies, all the subjects involved in the study group were chronic alcoholics and thus made us to change the dietary chart. Deficiency symptoms recur once the vitamin supplements were stopped apparently due to little storage of excess vitamin B in our body, this is the reason why it made us to effectively incorporate supplements as a regular routine for an extended duration[11]. A close monitoring of different school of thoughts reveals the presence of local ischemic changes in submucous fibrosis primarily due to artero and atherosclerosis and secondarily due to local tissue fibrosis. Conventional therapies yield a good result through a proper blood circulation thus failing to yield good results, for this reason we have incorporated a peripheral vasodilator buflomedil hydrochloride with the conventional therapy to achieve a enhanced results[12]. The encouraging results made us to do the prompt change in the treatment strategy for submucous fibrosis, which even further requires a close call in all the cases.

CONCLUSION

amnion is always a suitable material in the field of medicine, with a growing interest in its application in the field of tissue engineering lot of modifications are done for AM as it is more accessible and cost effective.

The changes in the treatment regime shortened the duration, effectiveness and satisfaction both for the patients and clinician without any relapses and side effects.

Declaration of Competing Interest: None declared.

Ethical Clearance: Declared.

Patient Consent: Obtained.

REFERENCES

1. Langer, R. and J.P. Vacanti, 1993. Tissue Engineering. Science, 260: 920-926.
2. Inci, I., A.N. Dizaji, C. Ozel, U. Morali, F.D. Guzel and H. Avci, 2020. Decellularized inner body membranes for tissue engineering: A review. J. Biomater. Sci., Polym. Edition, 31: 1287-1268.
3. Fénelon, M., S. Catros, C. Meyer, J.C. Fricain and L. Obert et al., 2021. Applications of Human Amniotic Membrane for Tissue Engineering. Membranes, Vol. 11 .10.3390/membranes11060387.
4. Gicquel, J.J., H.S. Dua, A. Brodie, I. Mohammed and H. Suleman et al., 2009. Epidermal Growth Factor Variations in Amniotic Membrane Used forEx VivoTissue Constructs. Tissue Eng. Part A, 15: 1919-1927.
5. Mamede, A.C., M.J. Carvalho, A.M. Abrantes, M. Laranjo, C.J. Maia and M.F. Botelho, 2012. Amniotic membrane: From structure and functions to clinical applications. Cell Tissue Res., 349: 447-458.
6. Brown, G.L., L.B. Nanney, J. Griffen, A.B. Cramer and J.M. Yancey et al., 1989. Enhancement of Wound Healing by Topical Treatment with Epidermal Growth Factor. New Engl. J. Med., 321: 76-79.
7. LEE, S.H. and S.C.G. TSENG, 1997. Amniotic Membrane Transplantation for Persistent Epithelial Defects With Ulceration. Am. J. Ophthalmol., 123: 303-312.
8. Solomon, A., et al., 2001. Suppression of interleukin 1alpha and interleukin 1beta in human limbal epithelial cells cultured on the amniotic membrane stromal matrix. Br. J. Ophthalmol., 85: 444-449.
9. Inge, E., Y.P. Talmi, L. Sigler, Y. Finkelstein and Y. Zohar, 1991. Antibacterial properties of human amniotic membranes. Placenta, 12: 285-288.
10. RUFFIN, J.M., 1941. The diagnosis and treatment of mild vitamin deficiencies. J. Am. Med. Assoc., Vol. 117 .10.1001/jama.1941.02820440001001.
11. Jolliffe, N., 1941. 1. newer knowledge of the vitamin B complex, Bull.N.Y.Acad.Med., Vol. 195.
12. Sharma, J.K., et al., 1987. 1. clinical experience with the use of peripheral vasodilator in oral disorders. Int .J. Oral Maxillofac.Surg., 16: 695-699.