

Original Article

Clinical Application of Amniotic Membrane as a Biologic Dressing in Oral Cavity and Pharyngeal Defects after Tumor Resection

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Abstract

Background: Oropharyngeal malignancies represent management challenges for the head and neck surgeons. Tumor resection and reconstruction with graft is the standard treatment. Split-thickness skin grafts are routinely used to cover the mucosal defects arising from resections. As amniotic membrane (AM) is used as a dressing substitute in burn, we decided to evaluate the efficacy of AM as a biologic wound dressing material for surgical defects of mucosa in the oropharyngeal region.

Methods: This was a single-institution prospective study which included 50 patients with primary oropharyngeal malignancy who underwent tumor resection between March 2010 and November 2011, and were up for two to 20 months after the surgical procedure.

We used amniotic membrane (AM) for dressing of the defects in the oral cavity and pharynx under general anesthesia. Efficacy of this procedure was assessed by rating of the pain and granulation tissue formation with surface epithelialization at the site of graft.

Results: The results were evaluated in the postoperative period. Forty males (80 %) and 10 females (20 %) were participated, age from 20 to 80 years with a mean age of 50 ± 10.41 years. The patients underwent partial glossectomy, or floor of mouth resection according to tumor location. Complete adherence of AM to the wound was detected in all cases. Allergy either systemic or local was not reported in any of the cases. The membrane was very effective in 40 patients, and effective in 10 cases.

Conclusion: Amniotic membrane (AM) can be used as a biologic dressing material for covering the mucosal defects in the oropharynx.

Keywords: Amniotic membrane, cancers, oral cavity

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Introduction

Neoplasm of the oral cavity and pharynx frequently cause significant soft tissue, bony, and skin defects which present reconstructive challenges. Tongue is the most common intraoral site of cancer in most countries with significant mortality and morbidity. Wide local excision is the surgical treatment of small tumors. In patients with large tumors which involve one quarter to one third of the lateral aspect of tongue, healing by secondary intention is an acceptable option. When tumor invades the floor of mouth, resection and reconstruction with graft is the standard treatment.^{1,2} This may result in functional impairment such as speech and swallowing.^{1,2} Objectives of reconstruction following surgery include adequate wound healing to facilitate postoperative radiation, to optimize function, and cosmetic appearance.^{1,2,3} Wound dressing prevents water loss, provides a wound covering, and promotes neovascularization with reepithelialization from the wound edge.⁴

In order to restore function and cosmesis, several techniques such as primary closure, skin grafts, local transposition of skin, and distant free vascularized flaps, have been developed to reconstruct oral and pharyngeal defects following surgery.^{1,3}

Primary closure is useful for relatively small oral cavity and oropharyngeal tumors. Split-thickness skin grafts (STSGs) are routinely used to cover mucosal defects arising from resections. Conventional STSGs are associated with donor site morbidity, including pain, infection, and hypertrophic scar formation. Mismatching in the color and texture of skin with tongue mucosa is another problem.^{1,3}

Human amniotic membrane (AM) has been used as a biomaterial for surgical reconstruction for nearly 100 years. In 1910, Davis⁵ was the first scientist to use AM in skin transplantation. Subsequently, it has been widely used as a surgical dressing in management of burns,^{6,7} surgical reconstruction of the bladder⁸ and vagina,⁹ and in the prevention of surgical adhesions.¹⁰

AM transplantation is also used in a wide variety of ocular disease as a temporary graft in order to promote ocular surface healing by suppressing inflammation, fibrosis, and neovascularization.^{11,12}

According to the above-mention points, the aim of this study was to evaluate the efficacy of AM as a biologic wound dressing material for surgical defects of mucosa in the oropharyngeal region.

Methods

A prospective study was conducted on 50 patients who underwent operative resection of primary intraoral tumors between March 2010 and November 2011, at the ENT Department of Khalili Hospital, affiliated to Shiraz University of Medical Sciences. The study was approved by the Ethical Committee of Shi-

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Figure 1. The patient with SCC of the tongue after one- month follow- up.



Figure 2. The same patient after 12- month follow- up.

raz University of Medical Sciences. Location of the primary lesion included tongue, floor of mouth, retromolar space, hard, and/or soft palate. In this study, we used AM for dressing of the defects in the oral cavity and/or pharynx after tumor resection.

The AM was fixed by suturing (Vicryle, 4.0 round) to the underlying mucosal membrane. The patients were followed up for two to 20 months with a mean time of 10 months.

Preparation of amniotic membrane (AM)

After informed consent, screening for potential risk factors such as cancer, infectious diseases, drug abuse, and sexual behavior was performed. The female donors were tested for hepatitis B and C, rapid plasma reagin for syphilis screening, and human immunodeficiency virus 1 and 2. In order to avoid any risk of transplanting infectious material, only amnion from cesarean sections was used with no history of premature rupture of membranes, endometritis, or meconium ileus. Immediately after delivery, under lamellar flow hood, placentas with adherent fetal membranes were washed with phosphate buffer saline (PBS); chorion and amnion were separated by blunt dissection and flattened onto a nitrocellulose membrane (Whatman, Schleicher, and Schuell Optitaran BA-S 85) with the epithelial surface up. The membrane with the filter was then washed three times with PBS containing 50 µg/mL

penicillin, 50 µg/mL streptomycin, and 2.5 µg/mL amphotericin B. Then, 10 × 10 cm pieces were made. Each of them was placed in 4 %, 8 %, and 12 % dimethyl sulphoxide (DMSO) PBS for five minutes and finally placed in a sterile vial containing 12 % DMSO medium (Sigma). Vials were frozen at -80°C in our “Amnion Bank”.^{11,13}

The criteria for judgment of AM

After surgery, the efficacy of this procedure was assessed by rating of the pain and granulation tissue formation with surface epithelialization at the site of graft. The criteria for judgment of AM dressing with respect to the results obtained were based on the scoring pattern that was used by Bessho and Murakami.^{14,15}

Pain relief was assessed subjectively based on patient's own statement at the end of the first week as good (none to mild), fair (moderate), or poor (severe). It was recorded on day 7 after the surgery when the patient was no longer taking analgesic medications.

Granulation tissue formation evaluated in the third week after surgery and categorized as good (entire wound), fair (nearly the entire of wound), or poor (inadequate). Surface epithelialization was noted at the end of the month and rated as good (entire wound), fair (nearly the entire wound), or poor (inadequate).

These criteria finally were judged as good, fair, or poor, which were given scores of 2, 1, and 0, respectively. Effectiveness was assessed by adding up the scores, and a value ranging from 8 to 10 was considered very effective; 5 to 7, effective; and 0 to 4, ineffective.^{14,15}

Reactivity/allergenicity of the material was assessed depending on the reactions elicited and was graded as none when no reactions were seen, moderate when few reactions were noted but resolved without any treatment, and severe when treatment was required. These were given scores of 2, 1, and 0, respectively. Finally, usefulness of the material was assessed by adding the scores for effectiveness and reactivity (effectiveness plus reactivity) and was graded as very useful (8 – 10 points), useful (5 – 7 points), or useless (0 – 4 points).

Results

The patients included 40 males (80 %) and 10 females (20 %), age from 20 to 80 years with a mean age of 50 ± 10.41 years. Squamous cell carcinoma (SCC) was reported in all patients (100 %). The anatomic location of tumors was: tongue in 34 cases (73 %), floor of mouth in six patients (13 %), five in buccal area (10 %), and two in retromolar area (4 %). The patients underwent partial glossectomy, floor of mouth resection, retromolar resection plus mandibulectomy according to tumor location. The mean time of hospitalization after surgery was three days (one to five days). On clinical follow-up, all patients had a good epithelialization (good), good pain relief, and good granulation tissue formation with surface epithelialization (Figures 1 and 2).

Complete adherence of AM to the wound was detected in all cases. None complained about the sensation of foreign body, and the patients were comfortable with intraoral grafting of AM. Allergy either systemic or local was not reported in any of the cases. Pain relief was good in all cases. Granulation and epithelialization were good in all 50 patients. The membrane was very effective in 40 patients, and effective in 10. The membrane was very useful in all patients.

Discussion

Surgery for tumors or traumatic lesions of the head and neck can cause significant soft tissue, bony, and skin defects. Although there has been progress with reconstruction of defects in the upper aerodigestive tract, but replacement of excised tissues with respect to tissue mobility is a challenging problem.^{1,3} Uncovered wounds are susceptible to infection and prone to scarring and contraction. The moist environment with saliva contamination interferes with healing process.^{16,17}

Autologous regional and distant flaps and/or skin graft are routinely used. Allograft donor is not suitable because of rejection after a short period of reconstruction.¹⁸ Different dressing materials have been used to cover defects after burn, denuded areas, or surgical defects temporary or permanently. A variety of materials have been evaluated for suitability as temporary or permanent cover after burns or surgical defects. Substances such as synthetic plastic, porcine xenograft, and artificial skin have been evaluated as wound cover.⁴

Other materials such as hyper dry AM, egg membrane, and alginate fiber dressing also were used as biologic dressing for covering defects in the mucosa or skin.^{19–22} In Rastogi, et al.'s study,

collagen membrane was used as graft material to repair defects of mucous membrane in the oral cavity. They recommended that collagen was an excellent material for graft wound healing.¹⁵ Skin graft is used as covering and reconstitution, but such graft used in the mouth will always retain the coloration of the skin and never attain the texture of the oral mucosa. Also, the growth of adnexal structures such as hair and sweat glands is unpleasure. In elderly patients the atrophic skin is unsuitable for this purpose.^{23,24}

In our study, we used fresh AM as a biodegradable wound dressing material for surgical defects in the oral cavity and pharynx. No special equipment or skills were required. Its application in the oral cavity is easy, and well tolerated with no adverse effects. In clinical follow-up, we had good outcomes without complication or tumor recurrence.

In comparison to skin graft, no growth of hair was identified. After local radiotherapy, less local contracture and speech impairment was noticed.

In a recent study which was performed by Shojaku, et al. usefulness of human AM patches as a dressing substitute for temporalis fascia graft was investigated in canal wall down tympanoplasty. Complete epithelialization of the mastoid cavity took place in all patients, as well as complete epithelialization of the AM graft was significantly faster than the fascia graft.²⁵

Now, in the 21st century, AM has gained importance because of its ability to reduce scarring and inflammation;²⁶ enhance wound healing and reepithelialization;²⁷ as well as its antimicrobial and anti-viral properties^{12,28} and low immunogenicity.²⁹ It has not been associated with graft rejection after transplantation.^{30,31}

In conclusion, AM can be used as a biologic dressing material for covering of the mucosal defects after tumoral resection in the oral cavity.

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