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ROLE OF AMNIOTIC MEMBRANE IN ORAL AND MAXILLOFACIAL SURGERY: A REVIEW

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Abstract
The amniotic membrane (AM) is considered an important potential source for scaffolding material. Amniotic membrane is the inner most lining of the human placenta that is normally discarded after parturition and is composed of a single epithelial layer, a thick basement membrane and an avascular stroma. The membrane has numerous growth factors, proteins and stem cell reserves that help in accelerating wound healing with regeneration of the lost tissues. In addition, the AM has other biological properties important for tissue engineering, including anti-inflammatory, anti-microbial, anti-fibrosis, anti-scarring, as well as reasonable mechanical property and low immunogenicity. The preserved human amniotic membrane is a novel tissue engineered biomaterial that is recently tried in field of medicine and dentistry to regenerate the lost tissues and accelerate repair. This review paper unfolds the inherent structure, properties, mechanisms and the applications of this neglected tissue that makes it a potential material for regeneration especially in the field of oral and maxillofacial surgeries.

KEYWORDS: Amniotic membrane, Oral surgery, Dentistry.

INTRODUCTION

Regenerative medicine is a new field primarily based on the concept of transplanting exogenous or stimulating endogenous stem cells to generate biological substitutes and improve tissue functions. Recently, amnion derived cells have been reported to have multipotent differentiation ability, and these cells have attracted attention as a novel cell source for cell transplantation therapy.[1]

Davies in 1910 was the first to advocate the amniotic membranes in skin transplantation. Following this, several studies of its use as a biological material for dressing burns, non-healing skin ulcers and as an aid to physiological wound healing appeared. In addition, this versatile material has been used in surgical procedures of oral cavity. The early 1990s can be taken as a suitable starting point in tracing the modern history of the use of amniotic membranes in Oral and Maxillofacial Surgery.[2]

History

Historically, natural amniotic membranes have been successfully used for wound and reconstructive purposes since the early 20th century. The first reported use of fetal membrane as skin substitute was by Davis in 1910. In 1913, Salbella presented the first clinical report of successful use of amniotic membrane in the treatment of skin ulcerations.[1]

In oral surgery, Lawson first used amniotic membrane with a pectoralis major muscle flap for intraoral lining in 1985.[3] Lai et al. used a single layer of fresh amnion for the surgical treatment of oral submucous fibrosis in 1995. The use of amnion in vestibuloplasty has been reported by Guler et al (1997) and Samandari et al (2004). In 2009, Gurinsky described the use of amnion allograft in the treatment of gingival recession. In 2010, Kesting and Denys evaluated the use of multilayer human amniotic membrane (HAM) as a grafting material for the repair of midpalate oronasal fistulas in seven Berlin minipigs. More recently, Tuncel and Ozgenel studied the efficacy of HAM as an interpositional material in the prevention of temporomandibular joint (TMJ) reankylosis in a randomized rabbit Model.[4]

Amniotic membrane as a source of stem cells for TE

Amniotic cells have several characteristics that make them a great source of stem cells for TE. Similar to the three germ layers of the embryo, including the ectoderm, mesoderm, and endoderm; the amniotic epithelium derives itself from the epiblast prior to gastrulation. This would suggest that the amniotic epithelium might retain a reservoir of stem cells all throughout pregnancy.[5]

Clonogenicity is the ability of a single cell to form a cloned colony and is a key defining function that demonstrates the self-renewal properties of stem cells.

Amniotic cells are clonogenic and their cloning efficiency is comparable to some HESC lines (Human embryonic stem cells).[5]

Basic Structure of Amnion Membrane

The human placenta is a complex organ starts developing within a few days after fertilization and is very important for the development and survival of the fetus throughout the gestation. It is about 10-15 micrometer thick which consists of two fetal membranes; the inner amniotic membrane and the outer chorion. The AM encases the amniotic fluid and fetus, and is highly flexible because of which it is easily be separated from the chorion. AM have two types of cells with different embryological origins: amnion epithelial cells derived from embryonic ectoderm and amnion mesenchymal cells from embryonic mesoderm. At ultra-structural level AM is a thin, tough, transparent, avascular composite membrane composed of three major layers: a single epithelial layer, a thick basement membrane, and an avascular mesenchyme consisting mainly of collagen. The amniotic epithelial cell layer is a single layer of flat, cuboidal and columnar cells that are in direct contact with the amniotic fluid. It is from this layer that amniotic Mesenchymal stem cells are isolated and stored to be used for regenerating tissues. There are no nerves, muscles, or lymphatics in the amniotic membrane.[3]

Bourne described the amnion as consisting of five layers from within outward,[2,6]
(a) epithelium;
(b) basement membrane;
(c) compact layer;
(d) fibroblast layer; and
(e) spongy layer.

The epithelial layer

Consists of a single layer of amniotic membrane epithelium. These cells are polygonal in shape and vary from columnar over the placenta to cuboidal or flat away from the placenta.

The basement membrane

Is a thin layer composed of reticular fibers. It is closely adherent to the amniotic epithelium from which multiple processes interdigitate into it.

The compact layer

Is a dense layer almost totally devoid of cells and consists mainly of a complex reticular network.

The fibroblastic layer:- is the thickest layer of the amnion and consists of fibroblasts embedded in a loose network of reticulum.

The outermost spongy layer

Forms the interface between the amnion and chorion and consists of wavy bundles of reticulum bathed in mucin.

Another unique characteristic of amniotic membrane is its lack of immunogenicity. The tissue does not express the usual major histocompatibility antigens such as HLAA, B or D, as a result, amniotic membrane does not induce immunological rejection after its transplantation. The membrane, especially the epithelium, also produces various growth factors including basic fibroblast growth factor, hepatocyte growth factor, and transforming growth factor. They aid in neoangiogenesis.[7]

Fresh versus preserved amniotic membrane

Both fresh and preserved amniotic membrane has been found to function equally well when transplanted. However, there are certain concerns when using fresh amniotic membrane. Ideally, serologic tests on the maternal donor must be done both at the time of procurement of the donor tissue and again six months later. This dual testing eliminates the slightest risk of disease transmission. With the fresh amniotic membrane the time interval from tissue procurement to transplantation is short and prevents repeat testing of the donor.[2]

The viability of amniotic epithelial cells may be associated with low-grade inflammatory response. The drawback with the preserved amniotic membrane is the need for a -70^0 refrigerator, which precludes its use outside big institutions.2

Uses of the Amniotic Membrane

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. This may result in functional impairment such as speech and swallowing. Objectives of reconstruction following surgery include adequate wound healing to facilitate postoperative radiation, to optimize function, and cosmetic appearance. Wound dressing prevents water loss, provides a wound covering, and promotes neovascularization with reepithelialization from the wound edge.[8]

Human amniotic membrane has been used as a biomaterial for surgical reconstruction for nearly 100 years. Subsequently, it has been widely used as a surgical dressing in management of burns, surgical reconstruction

of the bladder and vagina, and in the prevention of surgical adhesions.[9]

Amniotic membrane had used as a graft or a dressing in different surgical subspecialties reported in early literature. Normal amniotic membrane is 0.02-0.5 mm thick, which is equivalent to 6-8 cells, and has an average surface area of 1600 sq cm. Harvesting the HAM is a simple procedure and it does not require any special arrangements. After harvesting the HAM, it is sterilized by Gamma radiation and oven dried.[10]

Though the amniotic membrane has been used in general surgery for a long period of time, it use in dentistry especially in oral and periodontal surgeries is increasing with promising results.

Its biological properties of rapid re-epithelialization, vascularization and formation of granulation tissue makes AM a good biological dressing. These fetal membranes are being used as a graft or dressing in the management of burns; in the reconstruction of the oral cavity, bladder, and vagina; tympanoplasty; arthroplasty and so forth. Its adhesive and tight contact with the injured surface promotes hemostasis and good pain relief due to exposition of nerve fibres.[3]

Good biocompatibility and mechanical properties like permeability, stability, elasticity, flexibility, plasticity, and resorbability also makes it a promising scaffolding material in tissue engineering as in cell adhesion and the potential for delivery of biomodulatory agents such as growth factors and genetic materials. This amnion membrane is an excellent micro carrier for culture technique as it involves a development of a three dimensional space that is suitable for the growth and proliferation of embryonic stem cells (ESCs).[3]

Guler et al in 1997 concluded that grafts of amniotic membrane are better than other grafts for mandibular vestibuloplasty. Samandari MH et al suggested the use of amniotic membrane graft in oral surgery. Being readily available, inexpensive, easy storage, this allograft has almost no antigenicity with potential antibacterial properties and ability to enhance epithelialization, HAM may be suited for temporary or long-term coverage of mucosal defect. Prasad et al have suggested the use of amniotic membrane for extra and intra oral ulcers. Though the skin graft are widely used, but in intra oral environment the presence of adnexal structure like hair, the texture and resiliency are compromise for it to be called the ideal substitute.[10]

In study by Khademi B et al[8], 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.[8]

AM may be used as alternative treatment to manage wounds in the oral cavity like the tongue, buccal mucosa, vestibule, palatal mucosa, and floor of the mouth. Antiinflammatory and antiscarring property of AM have shown decreased necrosis and rapid healing of ulcers with herpes simplex virus (HSV), varicella zoster virus–infected tissues, erythema multiforme major (Stevens-Johnson syndrome) and cervical necrotizing fasciitis.[3]

Various materials have been used to cover the denuded periosteum after mandibular vestibuloplasty, such as mucosal and skin grafts.

The use of amniotic membranes offers the advantage that the thicker intact membrane can be handled more easily and remains on the wound longer than amnion by itself.[7]

Lawson in 1985 studied the use of amniotic membrane along with pectoralis major muscle for oral cavity reconstruction. He concluded that placement of amnion over the deep aspect of the muscle that is exposed in the oral cavity resulted in a more rapid formation of mucosa. When muscle was used without amniotic membrane, the healing process usually took twice as long. Also, when amnion was not used, one saw a significant amount of wound contracture. Lawson suggested that amnion enhanced re-epithelialization of the oral cavity and reduced the contracture effects in moderate-sized defects.[7]

Numerous techniques for oronasal fistula repair have been described, including tongue flaps, mastoid fascia grafts, auricular cartilage transplantation, bone grafts, distraction osteogenesis, and free flap transfer. However, no standard techniques have been presented, and up to 65 percent of oronasal fistulas are reported to reappear.[11]

Amniotic membrane is useful for oronasal fistula repair. It prevents donor-site morbidity and is easy to harvest, economically reasonable, and available in large quantities. The multilayer technique and protective plates solve the problem of mechanical instability.[11]

CONCLUSION

Clinical acceptability and applicability of HAM as a good grafting material for oral cavity reconstruction will ensure a reliable, available and easily affordable option for surgeons and patients.

The use of this novel biological membrane is rising in various fields of in tissue engineering, medicine, regeneration biology and stem cell research. However, further research and long term clinical trials investigating the full potential of this potential stem reservoir are still warranted to strengthen the fact amniotic membrane is indeed a reservoir for regeneration and repair.

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