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Use of placental tissues in periodontics: A review

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Abstract: *The goal of periodontal therapy is to reconstruct the lost tissues to a functional state that is similar or identical to the tissue that has been lost due to disease process. One of the oldest method used as a scaffold is the fetal membranes. The fetal membrane posses various properties which gives light towards its use in periodontal regenerative therapy.This paper reviews the historical background, properties and the application of placental membranes in periodontics.*
Keywords: *Chorion, Amnion, Periodontics, Gingival Recession*

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I. Introduction

The human placenta is a complex organ which starts developing within few days after fertilization and is very important for development and survival of the fetus throughout the gestation. Placental derived amnion and chorion membrane allografts have many unique properties that makes them a promising substitute in the field of periodontics. There is existence of pluripotent stem cells possessing the ability of trans differentiation to other cellular elements of periodontium making it a suitable candidate as a biological GTR in root coverage. Excellent revascularization of the placental membrane is another favourable property of this natural structure.[1] It also contains growth factors that may aid in the formation of granulation tissue by stimulating fibroblast growth and neovascularization.[2] Allografts derived from human placental membrane exhibit low immunogenicity and have shown the ability to reduce inflammation, pain, scarring and accelerated wound healing .[3] Beyond serving as a protective wound barrier, human fetal membrane provides a biological matrix supporting cell proliferation and tissue ingrowth.

II. History

Traditionally human placenta has been used in Chinese medicine for centuries. The Compendium of Materia Medica was published in 1593 by one of the first and greatest biologists and pharmaceutical experts of China, Li Shi-Zhen. In 1910, Davis reported that the use of amniotic membrane (AM) in skin grafting gave superior results than xenografts.[4] Shortly afterwards, Stern (1913) and Sabella (1913) reported the use of the AM for treating skin wounds. In the late 1930s, Brindeau (1934) and Burger (1937) reported the successful management of Mullerian agenesis with the use of amnion.[5,6] Dino et al. (1965) showed that AM could be sterilized and kept for 6 weeks at 4°C and can be safely used.[7] This was one of the first reports which suggested handling procedures for the AM, which in turn fueled even more interest among clinicians in using the AM for treating skin lesions.

The 1990s can be considered the beginning of modern history on the use of placental membrane in ophthalmology. In this decade, Dr. Tseng, an ophthalmologist from Miami, applied for Human Cell Tissue Products (HCT/P) regulatory status for the use of amniotic tissues in ocular repair which was rejected by the US Food and Drug Administration's (FDA) tissue reference group stating "Amniotic membrane for ocular surface reconstruction is considered a tissue under the current code of federal regulations (CFR) at 21 CFR Part 1270.[8] The twenty-first century marks another turning point in which the use of cells isolated from different placental regions are being progressively more investigated and used for their therapeutic potential.[9,10] These studies have paved the way for what are now considered established clinical uses and investigative clinical trials. Placental tissues, presently are an interesting therapeutic biomaterial currently used in the clinic.

III. Properties Of Placental Membrane

(a) Anti inflammatory and angiogenic: The exact mechanism of the anti-inflammatory properties of placental membrane is not clear. It is hypothesized that it decreases influx of inflammatory cells to the wound area and consequently reduces inflammatory mediators by serving as a barrier. A high molecular-weight glycosaminoglycan, hyaluronic acid, presents in large quantities in amniotic membrane and plays a vital role against inflammatory process. Other substances expressed in the amniotic membrane are low-molecular-mass elastase inhibitors which include secretory leukocyte proteinase inhibitor and elafin.[11] These inhibitors have antimicrobial actions in addition to their anti-inflammatory properties.

(b) Biomechanic Properties: An important property of placental membrane is its resistance to various proteolytic factors owing to the presence of interstitial collagens.[12] Elastin present in placental membrane is responsible for providing elasticity. It has multiple metabolic functions such as its role in water and soluble material transportation and production of bioactive peptides, growth factors, and cytokines.[9]

(c) Promotion of Epithelialization: Various growth factors produced by placental membrane can stimulate epithelialisation.[13] It can also promote expansion and maintenance of epithelial progenitor cells in vivo and can produce endothelin-1 and parathyroid hormone related protein. Placental membrane is an ideal tissue which facilitates the growth of epithelial cells, helping in their migration and differentiation.[14]

(d) Inhibits Fibrosis: Amniotic membrane reduces the risk of fibrosis by downregulation of transforming growth factor β and its receptor expression by fibroblasts. Therefore, scaffold of an placental membrane modulates wound healing by promoting reconstruction of tissues rather than promoting formation of scar tissue.[15]

(e) Lack of Immunogenicity: Occurrence of acute rejection after transplantation of placental membranes is negated by the fact that placental epithelial cells do not express HLA-A, HLA-B, HLA-D, and HLA-DR antigens but express HLAG on their surfaces. As tissue grafts of placental membrane materials present a low risk f immune rejection, they are considered to be bestowed with "immune privilege". [16]

(f) Antimicrobial and Antiviral Properties: Amniotic membranes also have the ability to produce β-defensins with the predominant type present in amniotic epithelium being β3-defensin.[11,17] Kjaergaard et al. in 2001 have also shown in vitro antimicrobial effects of the amnion and chorion against certain microorganisms. Its antiviral properties are exhibited by presence of cystatin E, the analogue of cysteine proteinase inhibitor.[18]

IV. Placental Membrane In Periodontics

Looking into placental membrane's various cell differentiation and proliferation properties, anti microbial properties, growth factors and many other advantages drew much attention towards its use in dentistry.

Pre clinical studies

1. Gomes et al. in 2001 studied the use of amnion grafts to line the floors of cortical bone defects and to cover the superficial surface of the defects. The authors concluded that the use of placental tissue grafts did not inhibit repair in guided bone regeneration and may have been beneficial for its antibacterial properties.[19]
2. Rinastiti M et al (2006) assessed histologically human amniotic membrane transplantation on rabbit's gingival wound. The results indicated that amniotic membrane transplantation may induce rapid epithelialization and promote rapid gingival wound healing in rabbits compared to secondary healing.[20]
3. Vilela-Goulart MG et al (2008) evaluated the effects of the homogenous amniotic membrane (HAM) as a biological dressing in the labial fornix region of inferior incisors in rats HAM showed not only no signs of rejection as well as an excellent tissue adherence to the ulcerated surface.[21]

Clincal studies

1. Kothiwale SV, Anuroopa P and Gajiwala AL (2009) compared the efficacy of demineralized freeze dried bone allograft (DFDBA) and bovine derived xenogenic bone graft (BDX) with amniotic membrane (AM) and concluded that both therapies resulted in significant reduction in PD and gain in CAL and significant bone fill.[22]
2. Gurinsky B (2009) obtained complete root coverage using amniotic membrane and also stated that amniotic membrane resembles oral mucosal basement membrane and contains different tyes of laminins which lays an important role in the adhesion of gingival cells.[23]
3. Velez I et al (2010) evaluated cryopreserved amniotic membrane (CAM) for helping cicatrization and wound healing after dental implant surgery. CAM was effective and supported the growth of the epithelium and facilitated migration and reinforced adhesion.[24]
4. Sikdar MA et al (2010) published a case report of excision of premalignant lesion- leukoplakia of the left buccal mucosa and defect reconstructed with human amniotic membrane graft (HAM) showed successful restoration without any complications.[25]
5. Kothari CR et al (2011) evaluated the clinical efficacy of amnion as a graft material for vestibuloplasty, concluded that amniotic membrane are viable material to cover the surface which prevented secondary contraction after vestibuloplasty, and maintained the postoperative vestibular depth.[26]
6. A case report published by Rosen PS (2011) treated an intrabony lesion with a mineralized bone allograft, recombinant PDGF, and a chorion-amnion barrier covered by a subepithelial connective tissue graft, and result was successful for correcting both the hard- and soft-tissue deformities around a maxillary canine.[27]
7. Wallace SC (2012) conducted a split mouth study comparing the efficacy of placental-derived membranes (PM) and acellular dermis matrix (ADM). Both materials were effective in gaining vertical root coverage and gain in clinical attachment level, but the acellular dermis matrix material showed a statistically significant greater amount of root coverage.[28]

8. Arai N et al (2012) reported the clinical usefulness of the hyperdry AM as an intraoral wound dressing material and suggested that the hyperdry AM is biologically acceptable and could be a suitable alternative for the repair of the oral mucosa.[29]
9. Singh H and Singh H (2013) presented a case report of root coverage of isolated gingival recession using coronally advanced flap with amnion membrane used as GTR membrane and concluded that the use of processed dehydrated allograft amnion showed increased tissue thickness, and increased attached gingival tissue and root coverage.[30]
10. Holtzclaw et al (2013) evaluated the efficacy of Amnion-chorion membrane (ACM) as GTR in the treatment of periodontal intrabony defects. The results showed a reduction in probing depth and gain in clinical attachment level at the end of 12 months.[31]
11. Suresh DK and Gupta A (2013) published a case report which shows the potential of human placental chorion membrane for root coverage and enhancement of gingival biotype and concluded that the rich content of various collagen and non-collagen proteins could have resulted in the enhancement of thin gingival biotype to thick biotype.[32]
12. Ghahroudi AA et al (2013) compare the efficacy of amnion allograft and connective tissue graft in root coverage and concluded that amnion allograft might be a suitable alternative to connective tissue graft in root coverage procedures.[33]
13. Gupta et al (2014) reviewed the use of amniotic membrane and concluded that human amniotic membrane could be a suitable material for use as an allograft.[34]
14. Shetty et al. (2014) compared usage of Platelet-rich Fibrin (PRF) and amniotic membrane in bilaterally occurring multiple Miller Class I recession and observed complete root coverage for both the membranes but the results were stable in the amniotic membrane-treated site at the end of seven months.[35]
15. Mehta TN et al (2014) [151] evaluated the efficacy of amnion and chorion membrane in the treatment of gingival recessions. Both membranes could be an alternative allograft material in the treatment of root coverage.[36]
16. Shah R et al (2014) published a case report where amnion allograft was used in the management of gingival recession. A complete coverage along with excellent esthetics and an improvement in gingival biotype was observed at 6 months postoperatively and concluded that the amnion allograft is well tolerated by the gingival tissues and results in excellent healing.[37]
17. Esteves J et al (2015) evaluated the efficacy of Human Chorion Membrane Allograft for Recession Coverage. The results showed statistically significant ($p < 0.001$) results at 3 and 6 months follow up. The mean percentage root coverage at the end of 6 months was 89.92±15.59% and 14 of 21 treated recession defects showed a100% root coverage. Nine sites which showed a thin biotype resulted into a thick biotype.[38]
18. Chakraborthy S et al (2015)[18] evaluated and compared the efficacy of amnion membrane and chorion membrane in combination with coronally advanced flap in the treatment of gingival recessions and reported that both membranes showed to be versatile allograft material to be used in the treatment of root coverage.[1]
19. A case report published by Mahajan R et al (2015) where gingival recession was treated ith GTR principle using amnion placental membrane. The results are encouraging and demonstrate that the amnion allograft is well tolerated by the gingival tissues and results in excellent healing in the treatment modality for root coverage of isolated buccal gingival recessions and amnion membrane has certain additive advantages over other membranes and can be used as an alternative to collagen membrane.[39]
20. Sharma A and Yadav K (2015) published a observational case series to evaluate the effectiveness, predictability and the use of amniotic membrane in the treatment of shallow-to-moderate isolated recession defects and concluded that autogenous graft tissue procurement significantly increases patient morbidity and long duration of surgery, while self‑adherent nature of amniotic membrane significantly reduces surgical time and easy to perform.[40]
21. Pundir AJ et al (2015) conducted a observational case series comparing amnion and chorion allograft for recession coverage. The results showed statistically significant ($p < 0.01$) improvements in all clinical parameters and nine out of twelve treated recession defects showed 100% root coverage and a thick gingival biotype.[41]
22. A comparative study conducted by Lafzi A et al (2016) comparing coronally advanced flap (CAF) plus amniotic membrane (AM) to CAF with connective tissue graft (CTG) in the treatment of Miller's class I and II gingival recessions and concluded that the results showed that application of AM instead of connective tissue decreased surgical operation time and patient discomfort but the amount of root coverage was not significantly different between the two methods.[42]
23. A case report published by Pai BS et al (2017) where amnion allograft was used in conjunction with coronally advanced flap has been used in the management of Class I Millers gingival recession showed excellent esthetics and an improvement in gingival biotype.[43]

V. Conclusion

Studies have shown encouraging results in periodontal regeneration and due to their various properties that enhances healing and epithelisation; use of placental membrane gives us a promising approach and an alternative allograft in periodontal regenerative therapy. The small sample size and short duration of most of the studies limits the long term stability, longitudinal randomized controlled clinical trials would give a better understanding of the long terms effect of these membranes.

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