Effectiveness of Human Amniotic Membrane in Wound Healing

Gbeneol J. Tombari

Burns and Plastic Unit, Department of Surgery, Faculty of Clinical Sciences, College of Health Sciences, University of Port Harcourt, Nigeria.

E-mail: gbeneol.tombari@gmail.com

Tel:+2348033426025

ABSTRACT: The use of human amniotic membrane in wound treatment has earned historical background. The presence of key growth factors such as EGF, FGF, TGF, HGF, in amniotic fluid and membrane accounts for its clinical effectiveness and mechanism of action. This study examined the effectiveness of human amniotic membrane in wound healing and its implication in surgery. 65 patients who had wounds from surgery and other known and unknown sources were treated using human amniotic membrane. The results showed remarkable and quick improvement in the healing process which is indicative of its effectiveness as a treatment procedure. Human amniotic membrane can be used as a replacement therapy for quick wound healing in surgery and wound from other sources.

Key words: Effectiveness, Human Amniotic Membrane, Wound Healing,.

INTRODUCTION

Regenerative medicine involves the use of living cells to repair replace, or restore normal function of damaged or defective tissue or organs [1,2]. Amniotic membrane (AM) is a uniquely situated material for use as an allograft in wound management applied in its natural form, then later in preserved preparations.

The material is rich in collagen and various growth factors [31,32] that assist in healing process through a number of physical, biochemical and molecular biological pathways to promote regenerative healing while simultaneously reducing scar formation.

The clinical use of AM has a long history with the first reports on its application in treatment of skin burns and wounds more than a century ago [3-5]. These ground breaking studies played a significant role in advancing the use of AM in surgery, especially in areas such as reconstruction of the corneal and conjunctival surfaces, treatment of open ulcers and traumatic wounds, and skin transplantation [6, 7, 8, 9].

Egg membrane has also been used as home remedy for lacerations and wound management. It contains Type I, IV & V collagen and 90% protein. It acts as a temporary barrier to bacterial invasion, contracts while hardening, hence aids wound closure. A recent study by Zhang *et al* [36] has indicated that amniotic membrane-derived stem cell can help repair osteochondral defects at joints.

The shelf life of AM has been extended by irradiation, air-drying, lyophilization, cryo-preservation, and glycerol preservation techniques. These methods are expected to further expand the use of AM in ophthalmology to treat corneal, conjunctival and limbal lesions, burns, scars and defects as well as general surgery to reconstruct skin, genitourinary tract and other surfaces [9-15]. However, the efficacy of AM in clinical application can only be enhanced by retaining its biological properties in the long term. This issue is important because of the presence of key growth factors such as EGF, FGF, TGF, HGF, in AMs may account for their clinical effects and mechanism of action.

Currently, a series of standardized guidelines are being developed in a number of countries to optimize the production of surgically suitable AM from donor placenta.

MATERIALS AND METHODS

Surgical Technique and Treatment Plan

The application of human amniotic membrane was followed through the step by step procedure.

1. The length and breadth of the wound is measured
2. The wound is cleaned with normal saline
3. Amniotic membrane is carefully placed on the cleaned wound
4. Sulpha-2 (a petroleum jelly) is applied on the on the wound
5. The size of the wound is measured after one week
6. Neo-epithelium at the edge of the wound is examined which is an evidence of wound contraction
7. Podium iodine is applied to prevent infection

Table 1: A table showing wound progress using Amniotic Membrane

Day/ Parameters	At presentation	Week 1	Week 2	Week 3	Week 4	Week 5
Size Ap Lat						
Hypegrammilam Hypergrana		Flattened				
Discharge						
Slough		0	0	0	0	
Neo-epithelium (mm)						
Edge						
Sub-structure	Tendon, bone					

This has continuously followed a progressive trend, as such; Amniotic membrane is promising in chronic wound care.

DISCUSSION

The use of amniotic fluid- and membrane-derived cells as cell-based therapy for a variety of indications has been extensively explored in the past decade [33, 34]. Here, we briefly review the findings regarding the use of AM and AF in tissue engineering and cell replacement strategies in a number of injury and disease models.

Reports focusing on the physiological functions of fetal layers [35] have shown that amniotic membrane not only provides a physical support for the fetus, but also serves as a metabolically active filter through a direct interaction with amniotic fluid. In particular, the transport of water and soluble materials as well as the production of growth factors, cytokines, and other bioactive molecules are regulated by amniotic membrane [6]. In addition to its role during pregnancy, amniotic membrane allows the initiation and maintenance of uterus contraction at birth [16].

The translucent, avascular, low immunogenic, anti-inflammatory, antiscarring, and wound healing properties of amniotic membrane allow this material function beyond its role *in vivo* and assume a wide range of applications in

regenerative medicine [17, 7]. In fact, the clinical use of amniotic membrane has a long history, with the first reports on its application in treatment of skin burns and wounds more than a century ago [3–5].

Historically, HAM allograft have found for clinical utility over the last century in humans for treating ocular wounds (Fan et al., 2016), skin ulcerations, burns, and a variety of other wounds. [18-22, 36]. It is also effective in SS ulcers, as in the index patient.

It is expected that there should be amniotic membrane allograft incooperation into the wound bed within 1-2wks with some improvement in wound margins and depth within 2-3wks. [23] Similar findings were noted in this study. Chronic wounds, however, may still remain problematic and must still be closely followed.

In a retrospective analysis of 203 patients, Sheeham et all [24] concluded that if wound failed to resurface by at least 50% [Percent Area Reduction (PAR)] in the first 4weeks of therapy, the wound was unable to completely epithelialize in 12weeks, this representing a negative predictor of healing. It therefore becomes clear that advanced therapies such as HAM could be useful in facilitating a PAR of > 50% at 4 weeks accelerating healing.

Few weeks after application of AM on the index case, the ulcer was filled with healthy granulation tissue. The AM has been shown to possess anti-bacterial, anti-inflammatory, anti-adhesive and immunomodulatory properties which make it an ideal candidate for use in wound care for the treatment of venous leg ulcers. [25-30].

CONCLUSION

HAM as old as man, has up to 100 years of first usage. It may transfer diseases so advanced method of procurement and preservation are required.

It is also been proven to be hypoallogenic, antimicrobial, anti- scarring, anti-adherent and non-immunogenic.

REFERENCE

1. Chien KR. Regenerative medicine and human models of human disease. *Nature*. 2008;453(7193):302–305. [PubMed]
2. Polak DJ. Regenerative medicine. Opportunities and challenges: a brief overview. *Journal of the Royal Society Interface*. 2010;7(supplement 6):S777–S781. [PMC free article] [PubMed]
3. Davis J. Skin transplantation with a review of 550 cases at the Johns Hopkins Hospital. *Johns Hopkins Hospital Report*. 1910;15
4. Sabella N. Use of fetal membranes in skin grafting. *Medical Records—New York*. 1913;83, article 478
5. Stern M. The grafting of preserved amniotic membrane to burned and ulcerated surfaces, substituting skin grafts. A preliminary report. *JAMA*. 1913;60:973–994.
6. Mamede AC, Carvalho MJ, Abrantes AM, Laranjo M, Maia CJ, Botelho MF. Amniotic membrane: from structure and functions to clinical applications. *Cell and Tissue Research*. In press. [PubMed]
7. Parolini O, Soncini M, Evangelista M, Schmidt D. Amniotic membrane and amniotic fluid-derived cells: potential tools for regenerative medicine? *Regenerative Medicine*. 2009;4(2):275–291. [PubMed]
8. De Rotth A. Plastic repair of conjunctival defects with fetal membrane. *Archives of Ophthalmology*. 1940;23:522–525.
9. Meller D, Pauklin M, Thomasen H, Westekemper H, Steuhl KP. Amniotic membrane transplantation in the human eye. *Deutsches Arzteblatt*. 2011;108(14):243–248. [PMC free article] [PubMed]
10. Seitz B, Resch MD, Schlötzer-Schrehardt U, Hofmann-Rummelt C, Sauer R, Kruse FE. Histopathology and ultrastructure of human corneas after amniotic membrane transplantation. *Archives of Ophthalmology*. 2006;124(10):1487–1490. [PubMed]
11. Kitagawa K, Yanagisawa S, Watanabe K, et al. A hyperdry amniotic membrane patch using a tissue adhesive for corneal perforations and bleb leaks. *American Journal of Ophthalmology*. 2009;148(3):383–389.e1. [PubMed]
12. Kitagawa K, Okabe M, Yanagisawa S, Zhang XY, Nikaido T, Hayashi A. Use of a hyperdried cross-linked amniotic membrane as initial therapy for corneal perforations. *Japanese Journal of Ophthalmology*. 2011;55(1):16–21. [PubMed]
13. Dobreva MP, Pereira PNG, Deprest J, Zwijsen A. On the origin of amniotic stem cells: of mice and men. *International Journal of Developmental Biology*. 2010;54(5):761–777. [PubMed]
14. Seitz B, Das S, Sauer R, Hofmann-Rummelt C, Beckmann MW, Kruse FE. Simultaneous amniotic membrane patch in high-risk keratoplasty. *Cornea*. 2011;30(3):269–272. [PubMed]

15. Shojaku H, Takakura H, Okabe M, Fujisaka M, Watanabe Y, Nikaido T. Effect of hyperdry amniotic membrane patches attached over the bony surface of mastoid cavities in canal wall down tympanoplasty. *Laryngoscope*. 2011;121(9):1953–1957. [PubMed]
16. Toda A, Okabe M, Yoshida T, Nikaido T. The potential of amniotic membrane/amnion-derived cells for regeneration of various tissues. *Journal of Pharmacological Sciences*. 2007;105(3):215–228. [PubMed]
17. Niknejad H, Peirovi H, Jorjani M, Ahmadiani A, Ghanavi J, Seifalian AM. Properties of the amniotic membrane for potential use in tissue engineering. *European Cells and Materials*. 2008;15:88–99. [PubMed]
18. Hori, J., Wang, M., Kamuja, K., Takahashi, H., Sakuragawa, N. Immunological characteristics of amniotic epithelium. Cornea 25, S53 – S58 (2006).
19. Kang, J. W. et al. Immunomodulatory effects of human amniotic membrane – derived mesenchymal stem cells. J. Vet. Sci. 13, 23 (2012).
20. Zhang, S., He, H., Day, A. J. & Tseng, S. C. G. Constitutive expression of inter – a – inhibitor (IaI) family proteins and tumor necros is factor – stimulated gene – 6 (TSG – 6) by human amniotic membrane epithelial and stromal cells supporting formation of the heavy chain – hyaluronan (HC – HA) complex. J. Biol. Chem. 287, 12433 – 44 (2012).
21. Werber, B. & Martin, E. A prospective study of 20 foot and ankle wounds treated with cryopreserved amniotic membrane and fluid allograft. J. Foot Ankle Surg. 52, 615 – 621 (2013).
22. Basso, T. Use of dehydrated amniotic membrane allograft on recalcitrant lower extremity wounds. in The symposium of Advanced Wound Care (2014).
23. Stem M. The grafting of preserved amniotic membrane to burned and ulcerated surfaces substituting skin grafts. JAMA. 1913: 60(13): 973 – 974.
24. Sheehan P., Jones P., Caselli A., Givrini JM, Veves A. Percent change in wound area of diabetic foot ulcers over a 4 week period is a robust predictor of complete healing in a 12 week prospective trial. Diabetes Care. 2003: 26(6):1879 – 1882.
25. Rosenblum, B. Case series demonstrating the healing capability of diabetic foot ulcers using dehydrated amniotic membrane allograft. in The symposium of Advanced Wound Care (2014).
26. Peters, W. Clinical efficacy of dehydrated amniotic membrane allograft and off – loading on diabetic foot ulcers. in The symposium of Advanced Wound Care (2014).
27. Beless, D., Marcus, B. Dehydrated amniotic membrane allograft therapy for complicated non-healing wound: A promising therapy where other treatments have failed. in The symposium of Advanced Wound Care (2014).

28. Lintzeris, D., Yarrow, K., Johnson, L, White, A., Hampton, A., Strickland, A., Albert, K., Cook, A. Case series demonstrating the impact of dehydrated human amniotic membrane allograft on wound healing in acute and chronic wounds. in The symposium of Advanced Wound Care (2014).
29. Hori, J., Wang, M., Kamiya, K., Takahashi, H., Sakuragawa, N. Immunological characteristics of amniotic epithelium. Cornea 25, S53 – S56 (2006).
30. Kang, J. W. et al. Immunomodulatory effects of human amniotic membrane – derived mesenchymal stem cells. J. Vet. Sci. 13, 23 (2012).
31. Fan, J., Wang, M., Zhong, F. Improvement of Amniotic Membrane Methoth for the Treatment of Corneal Perforation. BioMed Res. Int. 2016: 1- 8
32. Fan, J., Wang, M., Zhong, F., 2016. Improvement of Amniotic Membrane Method for the Treatment of Corneal Perforation. BioMed Res. Int. 2016, 1–8. doi:10.1155/2016/1693815
33. Kang, N.-H., Hwang, K.-A., Kim, S.U., Kim, Y.-B., Hyun, S.-H., Jeung, E.-B., Choi, K.-C., 2012. Potential antitumor therapeutic strategies of human amniotic membrane and amniotic fluid-derived stem cells. Cancer Gene Ther. 19, 517–522. doi:10.1038/cgt.2012.30
34. Murphy, S.V., Atala, A., 2013. Amniotic Fluid and Placental Membranes: Unexpected Sources of Highly Multipotent Cells. Semin. Reprod. Med. 31, 62–68.
35. Uszyński, M., Uszyński, W., 2011. Coagulation and Fibrinolysis in Amniotic Fluid: Physiology and Observations on Amniotic Fluid Embolism, Preterm Fetal Membrane Rupture, and Pre-Eclampsia. Semin. Thromb. Hemost. 37, 165–174.
36. Zhijin Zhang, Linru Zeng, Jun Yang, Lin Guo, Qiao Hou, Fangbing Zhu, 2017. Amniotic membrane-derived stem cells help repair osteochondral defect in a weight-bearing area in rabbits. Exp. Ther. Med. 14, 187–192. doi:10.3892/etm.2017.4497