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RESEARCH ARTICLE

HYALURONAN AND ITS ROLE IN PERIODONTAL HEALING.

Dr. Mohamed Haris. P. M.
Senior Lecturer, Department of Periodontology, Malabar Dental College and Research Centre, Manoor, edappal, Malappuram, Kerala, India.

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Abstract

Hyaluronan(Synonyms- Hyaluronic acid (HA), Hyaluronate)is a naturally occurring linear polysaccharide with a high molecular weight. It is a member of glycosamine family and present in the extracellular matrix of the connective tissue, synovial fluid, skin, periodontal tissues and many other organs and tissues of the body. Hyaluronan is naturally synthesized by a class of integral membrane proteins called hyaluronan synthases, and it is degraded by a family of enzymes called hyaluronidases. This molecule is a key component in the series of stages associated with the wound-healing process in both mineralized and non-mineralized tissues. It has unique properties which also helped in the treatment of inflammatory process especially in medical areas such as dermatology, ophthalmology, rheumatology. It has shown anti- inflammatory,anti-oedematous, and anti- bacterial effects for the treatment of periodontal diseases. This review highlights the potential role of hyaluronan in periodontal tissue healing and as an aid to the treatment of periodontal diseases.

Introduction:-

Hyaluronan(HA) is a non-sulphated polysaccharide component of the glycosaminoglycan family with a high molecular weight.[1,2]They are present in the extracellular matrix of connective tissue, synovial fluid, embryonic mesenchyme, vitreous humor, skin, and also in other organs and tissues of the body. Chemical structure of HA contains repeating units of d- glucoronic acid and N–acetyl- d- glucosamine.[3] Hyaluronan is established in all periodontal tissues, mostly prominent in the non-mineralized tissues such as gingiva and periodontal ligament; it is present in small quantities in mineralized tissues such as cementum and alveolar bone. Besides high levels of hyaluronan are present in circulating blood serum and hyaluronan has been found in almost all gingival crevicular fluid(GCF). However, hyaluronan is absent in GCF samples from patients with acute necrotizing ulcerative gingivitis, due to the high levels of bacterial enzymic activity (hyaluronidases) related to this condition. It can only reappear in the GCF following the patients undergoing metronidazole treatment and the decrease in bacterial numbers.[2] In the presence of endotoxin; it is also produced by fibroblasts and it plays an important anti-inflammatory role throughout the inhibition of tissue destruction and helps in healing. Hyaluronan also has been accepted for the treatment of inflammatory process in medical areas, for example orthopedics, dermatology and ophthalmology and even applied in radioepithelitis, osteoarthritis of the knee and rheumatoid Arthritis and cataract surgery. [4] Hyaluronan has also undergone studies in the field of tissue engineering thus showing a main role during organogenesis,cell migration and development .[5]

Corresponding Author:- Mohamed Haris. P. M.
Address:- Senior Lecturer, Department of Periodontology, Malabar Dental College and Research Centre, Manoor, edappal, Malappuram, Kerala, India.

History:-

In 1934, Hyaluronan was discovered by Karl Meyer and his colleague John Palmer and they isolated a previously unidentified chemical substance from the vitreous body of cows eyes. They found that the material contained two sugar molecules, one of which was uronic acid.The term is derived from "hyalos", which is the Greek word for glass and uronic acid. Then commercially in 1942 when Endre Balazs used for a patent to use it as a substitute for egg white in bakery products. In the 1950s hyaluronan was initially applied medically for humans as a vitreous substitution or replacement during eye surgery.[6]

Properties of Hyaluronan[3]:-

- Hygroscopic nature
- Viscoelastic properties
- Bacteriostatic effect
- Biocompatibility and non- antigenicity
- Anti- inflammatory
- Anti- oedematous
- Antioxidant

Main applications of hyaluronan [3,5]:-

- Used as a dermal filler in the field of cosmetic dermatology.
- While undergoing surgery the application of Hyaluronan can prevent the scar formation in surgical wounds.
- Due to the exogenous effect it is beneficial in wound healing
- In the field of orthopedics it is used for the treatment osteoarthritis of the knee and rheumatoid arthritis.
- In ophthalmology it is applied for the treatment of cataract and xeropthalmia.
- Hyaluronan has also been investigated and used in the field of tissue engineering.
- Modifications to Hyaluronan consists of esterification and cross- linking to provide some structure and rigidity to gel for the cell- seeding function.
- Hyaluronan , recently has been explored as a drug delivery agent for various routes of administration, including ophthalmic, nasal, pulmonary, parenteral, and topical.

Hyaluronan and periodontal healing:-

Series of stages are related along with the wound healing process in both mineralized and non-mineralized tissues.[2] They are Inflammation, Granulation tissue formation, Epithelium formation and Tissue remodelling.[3]

Inflammatory phase

- It prevents periodontal pathogenic proliferation
- Improved inflammatory cell and extracellular matrix cell infiltration into the inflamed site
- Increase in proinflammatory cytokine production by inflammatory cells and extracellular matrix cells.
- Maintains the stability of granulation tissue matrix
- Scavenger reactive oxygen species, for example superoxide radical (O2) and hydroxyl (OH) species.
- Inhibits the inflammatory cell-derived serine proteinases

Granulation phase

- Organization of the granulation tissue matrix
- Extracellular matrix cell proliferation
- Inflammatory cell and extracellular matrix cell migration
- Blood vessel formation (angiogenesis)

Epithelium formation

- Migration and proliferation of keratinocyte.[2]

Bone regeneration:-

Bone regeneration can be accelerated with hyaluronan by:

- Chemotaxis
- Proliferation and
- Successive differentiation of mesenchymal cells.

Hyaluronan as a potential aid to periodontal treatment:-

Hyaluronan has played a multifunctional role in the wound healing process in accordance with the similar mechanisms of healing that potentially occurs within the periodontal tissues. It is non-toxic,biocompatible, biochemical and physiochemical properties and the application of exogenous hyaluronan or hyaluronan based biomaterials ie.applied topically to inflamed periodontal sites that have beneficial effects in modulating and accelerating the host response.

High molecular weight hyaluronan based gel (GENGIGEL®) that is applied topically that potential to induce the periodontal healing in patients with inflammed periodontal diseases. In addition to the gel,there is three-dimensional scaffold containing the hyaluronan-based biomaterial, HYAFF® that helps in tissue engineering technology by periodontal surgical procedures to increase gingival attachment during gingival augmentation. Hyaluronan based biomaterial, cross-linked hyaluronan, has been used as a carrier of the recombinant bone regenerating extracellular matrix component, bone morphogenic protein-2 (BMP-2), while undergoing alveolar ridge augmentation.[2]

Review of Literature:-

Engström et al.[7] had investigated the anti-inflammatory effect and the effect on bone regeneration of Hyaluronan(HA) in surgical and nonsurgical groups in the patients with chronic periodontitis. In the surgical group, a bioabsorbable membrane was used for both test and control sites, and HA was placed in the infrabony pocket of the test site. In the non-surgical group, the periodontal pockets were scaled and the HA was administered three times with an interval of 1 week in the test pockets. They observed the difference in bone height between test and control sites in the surgical group after 12 months, less than 1 mm, which was only detectable on radiographs. No statistical difference was found on radiographs in the non-surgical group, where as a decrease in bone height was found for both groups after scaling. Probing depth reduction after the surgical treatment, as well as after Scaling and root planing, was there as expected. The result showed that HA in contact with bone and soft tissues had no influence on the immune system in this study.

Gontiya et al.[8] investigated the clinical and histological outcomes of local subgingival application of 0.2% HA gel as an adjunct to SRP in chronic periodontitis patients.They concluded that subgingival placement of 0.2% HA gel along with SRP provides a significant improvement in gingival parameters, but no additional benefits were found in periodontal parameters. Histologically, experimental sites showed reduced inflammatory infiltrates, but the results were not statistically significant.

Fujioka-Kobayashi M et al.[9] investigated the effect of HA on PDL cell compatibility, proliferation, and differentiation in vitro.They concluded that both non-cross-linked and cross-linked HA maintained high PDL cell viability, increased proliferation, and early osteogenic differentiation. However, HA was consistently associated with a significant decrease in late osteogenic differentiation of primary human PDL cells.

Conclusion:-

Hyaluronan has shown anti- inflammatory, anti- oedematous, and anti- bacterial effects and it plays a vital role in the treatment of periodontal disease.Initial studies indicated that it can act as a mediator for periodontal tissue healing and as an aid to periodontal disease treatment.Further long term based research and large-scale randomized controlled clinical trials have to be carried out on hyaluronan and hyaluronan-based materials to evaluate the true benefits.

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