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RESEARCH ARTICLE

HYALURONIC ACID AND ITS APPLICATION IN PERIODONTAL THERAPY: A REVIEW

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ABSTRACT

Hyaluronic acid is a high molecular weight polysaccharide, which plays a major role in the functioning of extracellular matrices. Its presence has been found in connective tissues and is particularly concentrated in synovial fluid, the vitreous fluid of the eye, umbilical cords. Also it is found in periodontal tissues including mineralized and non mineralized tissues with a greater concentration in non mineralized tissues, such as gingiva and periodontal ligament. Due to its role in inflammatory and healing mechanisms, use of hyaluronic acid has been applied in various fields like ophthalmology, Dermatology, Orthopedics, etc in various therapeutic procedures. Recently hyaluronic acid has been applied in various periodontal procedures for its therapeutic properties. The aim of present review, article is to discuss application of hyaluronic acid in various periodontal procedures.

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INTRODUCTION

Hyaluronic acid is a naturally occurring polysaccharide of the extracellular matrix of connective tissue, synovial fluid and various tissues. It was first discovered by Meyer *et al.* in 1934 at Columbia university in New York, where hyaluronic acid was isolated from vitreous jelly of cows eyes (Vedamurthy, 2004). The isolated substance was named Hyaluronic acid as it was derived from Greek word hyalos (glass) and contained two sugar molecules one of which was uronic acid. Hyaluronic acid is a high molecular weight polysaccharide with a molecular weight of 10000 to 10000000 Daltons. It is a polymer made of repeated disaccharide units of N-acetyl glucosamine and D-glucoronic acid. (Necas, 2008) (Figure 1) The estimated total amount of Hyaluronic acid present in human body is about 5g. Most cells are capable of synthesizing Hyaluronic acid and synthesis takes place in cell membrane. The turnover of Hyaluronic acid in the tissues occurs by either lymphatic drainage to the blood stream or by local metabolism. (Fraser *et al*., 1997) Hyaluronic acid is being used in various branches of medical field. A viscous solution of sodium hyaluronate is used during surgical procedures on the eye, for example for cataract extraction. Introduction of the solution into the anterior or posterior chamber via a fine cannula or needle allows tissues to be separated during surgery and protects them from trauma.

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Sodium hyaluronate eye drops 0.1% are also used for the relief of dry eye and as a contact lens lubricant. Sodium hyaluronate is given by intra-articular injection in the treatment of osteoarthritis of the knee. Doses vary according to the preparation used, but are of the order of 20 to 25 mg once weekly for 5 weeks or up to 30 mg once weekly for 3 or 4 weeks. It are generally recommended that the treatment course for any individual joint should not be repeated within 6 months. Sodium hyaluronate is also used during arthroscopic procedures to flush out irrigating solutions and act as a temporary substitute for synovial fluid. Hyaluronic acid is applied topically to promote wound healing.

Zinc hyaluronate has also been used. A film containing sodium Hyaluronate and carmellose is used to prevent surgical adhesion. Sodium hyaluronate has also been used in the management of lesions of the oral mucosa. Hylans, which are polymers derived from Hyaluronic acid, are used similarly for osteoarthritis and wound care. Sodium hyaluronate instilled intravesically has been used as a temporary replacement of the glycosaminoglycan layer in the bladder for the symptomatic treatment of interstitial cystitis. Topical formulations of Diclofenac in Hyaluronic acid are used in the treatment of actinic keratosis but distinguished from an oral formulation of isofagomine tartrate under investigation for use in Gaucher disease. Hyaluronic acid has been used as a dermal filler for the correction of moderate to severe facial wrinkles and folds

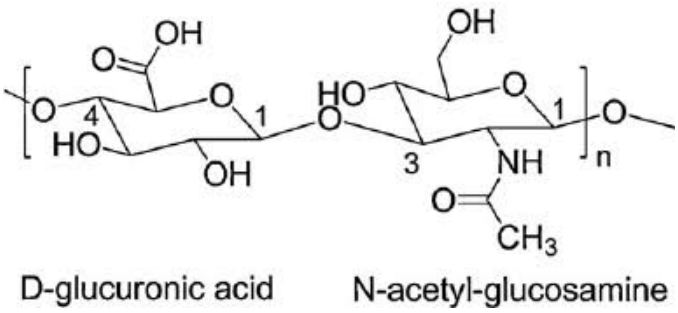

Figure 1. Structure of hyaluronic acid

Influence of Hyaluronic acid on Healing

Hygroscopic nature

Hyaluronan is highly hygroscopic and this property is believed to be important for modulating tissue hydration and osmotic balance. (Sutherland, 1998) When Hyaluronic acid is incorporated into aqueous solutions, hydrogen bonding takes place adjacent to carboxyl and N- acetyl groups. This helps to maintain conformational stiffness and to retain water. Because of its hygroscopic properties, hyaluronan significantly influences hydration and the physical properties of the extracellular matrix. As a physical background material it has functions in shock absorption, space filling and protein exclusion.

Viscoelastic property

Hyaluronic acid through its viscoelastic property influence cell functions that modify the surrounding cellular and extracellular environments. The viscoelastic property may influence the penetration of viruses and bacteria which influences healing [(4)]

Bacteriostatic effect

A clinical application of Hyaluronic acid membranes and gels and sponge during the surgical therapy may reduce the bacterial contamination of surgical wound site, thereby lessening the risk of post surgical infection and promoting predictable regeneration. (Pirnazar *et al*., 1999)

Anti – inflammatory

Hyaluronic acid exerts the anti-inflammatory effect due to its action as a scavenger by draining prostaglandins metalloproteinase's and other bio active molecule. (Laurent *et al*., 1995)

Antiedematous

The anti edematous effect of hyaluronic is due to osmostic property which indirectly helps in tissue healing. (Laurent *et al*., 1995)

Anti-oxidant

It is believed that hyaluronic acid may act as an antioxidant by scavenging ROS and helps in stabilizing the granulation tissue matrix. (Waddington *et al*., 2006)

Use in Periodontal Therapy

Soft tissue defects

Hyaluronic acid can be used to treat soft tissue gingival defects. The healing properties of hyaluronic acid help in healing and regeneration of soft tissue in a more natural process. Recently Dr. William Becker has used Hyaluronic acid in treatment of papillary deficiencies adjacent to dental implants and teeth. On injecting a minute quantity 0.2 ml of hyaluronic acid for three times an improvement up to 97% was noticed. Patients were followed from 6 to 25 months and treatment outcome was satisfied. A similar study was carried out by Dr.Mansouri in 11 patients and similar results were found (William Becker, 2010; Sadat Mansouri, 2013). Also Hyaluronic acid application can be done in cases of implant surgery in cases of in adequate flap closure. After implant placement and before flap closure hyaluronic acid when applied directly or along with the sutures, helps in adequate approximation of flaps and minimizes soft tissue defects and infection and ensuring optimum esthetics around implants.

In Gingivitis

Gingivitis is an inflammatory disease of the periodontium that does not result in clinical attachment loss. It is a reversible disease. The treatment is aimed primarily at elimination of etiological factors to reduce inflammation there by allowing gingival tissues to heal. It is proposed that Hyaluronic acid topically when used on gingival tissues acts as a barrier to plaque bacteria and due to its various properties helps in maintenance of healthy gingiva.

The topical application of a high-molecular weight exogenous hyaluronan based gel has been proposed to have some potential in inducing periodontal healing in patients with gingivitis, during randomized, controlled double blind studies conducted by Vangelisti *et al*and Pagnacco *et al*. (Vangelisti *et al*., 1997) Also Dr. Yashika Jain carried out a study on gingivitis subjects and treated them with use of 0.2% Hyaluronic acid gel topically as an adjunct scaling and root planing and concluded that hyaluronic acid is effective in treatment of gingivitis. (Yashika Jain, 2013) (Figure 2)

Figure 2. Application on soft tissue

In treatment of Bony Defects

Periodontal Bony defects are a common clinical challenge in dental practice. These lesions can be approached by resection, which aims to surgically eliminate the pocket, or by regenerative techniques, which promote re growth of the lost periodontal tissue. Hyaluronic acid accelerates bone regeneration by means of chemotaxis, proliferation and successive differentiation of mesenchymal cells. (Mendes *et al*., 2008) Recently Dr. Leonardo carried out a study on 19 infrabony defects and one mandibular molar furcation. The flap surgery was carried out and after thorough debridement hyaluronic acid in the form of fibers was packed into defect completely and subjects were followed after one year. It was concluded from the study that Hyaluronic acid posses the potential of bone regeneration and is a promising method for treatment of intra bony defects. (Dr. Leonardo, 2009)

In Guided Tissue Regeneration and Guided Bone Regeneration

Topical application of hyaluronic Acid as an adjunct to periodontal therapy can be effective in treatment of bony defects and guided bone regeneration. It is claimed that hyaluronic acid gel when applied topically on bone grafts before wound closure enhances healing and osteoblastic formation. It is reported that when hyaluronic acid used in treatment of grade II Furcation can be effective when used along topically along with the membrane. Dr. S. Harveen Kalra carried out a study using hyaluronic acid gel in conjunction with amnion membrane in grade II furcation cases. The author concluded that on follow up of 6 months there was obvious fill in defect of furcation area and hyaluronic acid gel when used in guided bone regeneration was effective. (Harveen Kalra, 2015)

In Ridge Augmentation

Wherever possible, the dentist should focus treatment efforts on ridge preservation and prevent ridge defects from occurring. This is especially important in the anterior aesthetic zone of the dental arches. In cases of ridge collapse the ridge augmentation procedures are carried out. It is usually indicated in cases of implant therapy where adequate vertical ridge is height is required for implant placement to achieve primary stability. The ridge augmentation procedures involve use of regenerative procedures aimed to increase the vertical bone dimension of the ridge. It is proposed that Hyaluronic acid used along with bone regenerative materials helps in fastidious augmentation through its healing properties there by reducing time for implant placement.

Socket Preservation

Following the extraction of a tooth the alveolar bone undergoes remodeling. Early changes primarily result in a loss of bone width. However, pathology, infection and or preexisting osseous defects can result in vertical bone loss as well. Socket bone grafting, often termed socket preservation, can be useful in maintaining alveolar bone dimensions and ridge contour. Socket grafting may be performed for dental implant placement or ridge preservation. Recently Dr.kotsakis described flapless technique "socket plug" technique using collagen sponge for socket preservation post extraction. (Kotsakis, 2014) (Figure 3) It is proposed that when collagen sponge was moistened with Hyaluronic acid gel and grafted in extraction socket proved better results than collagen sponge used alone. (Figure 4)

Figure 3. Used in socket preservation

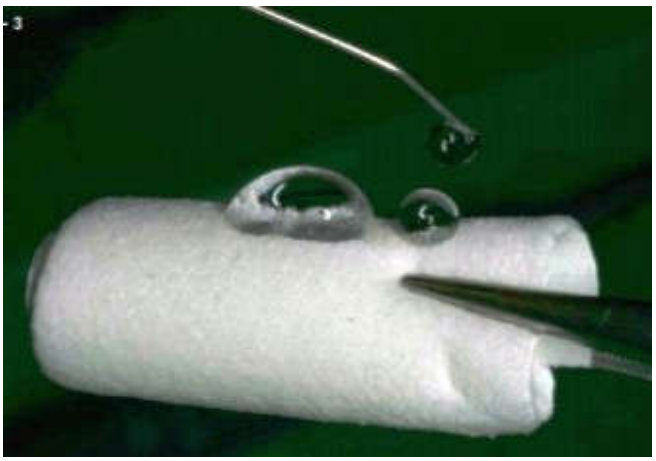

Figure 4. Hyaluronic acid mixed with collagen plug

In Sinus Lift Procedures

Sinus lift procedures are indicated in implant therapy. Post extraction due to resorption of the alveolar bone in the maxillary premolar and molar region, the floor of the maxillary sinus approximates crest of alveolar ridge. This results in a decreased vertical ridge dimension and therefore creates a contraindication for implant placement. For primary stability and success of implant it is proposed that a minimum height of 12mm is required. In such floor of sinus is elevated to required level and grafted with bone materials. (Figure 5) Recently Dr. Michael claar carried out sinus lift procedures with bone regenerative procedure followed by immediate implant placement. He used Hyaluronic acid gel during procedure and concluded that use of Hyaluronic acid had a positive impact on healing. (Micheal clear, 2013)

The primary benefits of using Hyaluronic acid are

- Stabilization of granules: Precise application of bone granules is made much easier as viscous gel structure of the preparation prevents displacement.
- Formation of protective barrier: The beneficial effect arises as a result of high viscosity of the gel which directly covers the wound like a biological membrane. This minimizes the risk of bacterial contamination. (Figure 6)

Figure 5. Use of hyaluronic acid in sinus lift procedure

Figure 6. Hyaluronic acid mixed with bone graft

Conclusion

As it is evident Hyaluronic acid has an influencing potential on healing, its application in therapy of various periodontal inflammatory conditions should be implemented. Also due to its various properties which help in regeneration of both hard and soft host tissues it should be used as an adjunct to various regenerative materials in regenerative procedures. Due to limited research data it is difficult at present to conclude its safety. There are various products of Hyaluronic acid indicated for dental procedures which are available in the market. But only few are approved by FDA.

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