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Hyaluronic Acid in Periodontics: An Emerging Adjunct for Periodontal Regeneration – A Review

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Abstract: Hyaluronic acid (HA) is a natural substance found in connective tissues and is important for keeping tissues moist, helping cell movement, and promoting wound healing. Because of its anti-inflammatory, antibacterial, and healing properties, HA has gained interest as an additional aid in periodontal treatment. Studies suggest that HA can improve healing, reduce inflammation, increase patient comfort, reduce periodontal pockets, and support healing after periodontal surgery. However, differences in HA concentration, methods of application, and study designs make it difficult to draw strong clinical conclusions. Overall, hyaluronic acid appears to be a useful and promising adjunct in periodontal therapy, but more well-designed, long-term clinical studies are needed to confirm its benefits and establish standard treatment guidelines.

Keywords: *Hyaluronic Acid, Hyaluronic Acid for Gingivitis, Hyaluronic Acid for Periodontitis, Periodontal Therapy.*

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I. INTRODUCTION

Hyaluronic acid (HA), also called hyaluronan or hyaluronate, is a naturally occurring substance in the human body. It is widely used in skin care, joint treatments and dentistry because of its ability to support tissue healing, reduce inflammation, and maintain moisture. In dentistry, HA has gained attention due to its important role in the extracellular matrix (ECM), synovial fluid, and wound healing processes [1].

HA is present in synovial fluid, saliva, serum, and gingival crevicular fluid. It forms a major part of the ground substance of both mineralized and non-mineralized tissues, with higher levels in soft periodontal tissues such as the gingiva and periodontal ligament than in hard tissues like alveolar bone and cementum. Cells such as fibroblasts, chondrocytes, and osteoblasts produce HA. Through its involvement in cell migration, proliferation, and tissue hydration, HA plays a key role in maintaining periodontal health [2].

Because of its anti-inflammatory, analgesic and regenerative properties, HA has been used in wound and ulcer healing, as an adjunct to scaling and root planing, and in the management of periodontal diseases. Its applications have also been explored in implant dentistry, oral surgery, and oral hygiene products. However, it remains important to determine whether HA represents a true therapeutic benefit or is mainly a marketing trend, highlighting the need for evidence-based evaluation.

II. HISTORY OF HYALURONIC ACID

Hyaluronic acid was discovered in 1934 by Meyer and Palmer at Columbia University. It was first taken from the jelly-like substance inside a cow's eye. The name comes from the Greek word *hyalos*, meaning glass, and its uronic acid component. At the time of its discovery, its medical and dental importance was not yet understood [3].

- *The Essence of Hyaluronic Acid: Structure, Nature, and Synthesis*

Hyaluronic acid (HA) is a naturally occurring, high-molecular-weight glycosaminoglycan that is non-sulfated in nature. It is made up of repeating units of N-acetylglucosamine and glucuronic acid linked by β-1,3 and β-1,4 bonds, forming a long, linear chain [4]. This structure

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allows HA to bind large amounts of water and maintain tissue hydration and integrity.

HA is continuously broken down and renewed in the body. Its turnover occurs mainly through local metabolism and lymphatic drainage. Once HA enters the bloodstream, most of it is removed by the liver with only a small amount excreted by the kidneys. HA has a short half-life, ranging from a few hours to a few days, and is mainly degraded by enzymes called hyaluronidases or by reactive oxygen species [5,6,7].

Due to its chemical structure and the presence of acid groups, HA can be easily modified for clinical use. These properties make HA suitable for applications in periodontal therapy, especially in drug delivery systems aimed at reducing inflammation and promoting tissue regeneration [8].

➢ *Hyaluronic Acid: A Key Ingredient in Periodontal Treatment*

Hyaluronic acid (HA) has been widely used in medicine and was first introduced in dentistry in 1997 by Vangelistic et al. and Pagnacco et al. [7]. HA is a major component of the ground substance and plays an important role in maintaining tissue health by interacting with growth factors, regulating osmotic pressure, and improving tissue lubrication.

Due to its properties [Figure 1] such as hydration, biocompatibility, anti-inflammatory action, tissue regenerative ability, analgesic effect and biodegradability, HA has several applications in dentistry especially in periodontal therapy [9]. Although HA shows promising benefits in improving treatment outcomes, its use should be guided by strong scientific evidence and well-designed clinical studies.

Fig 1 Properties of Hyaluronic Acid

➢ *Hyaluronic Acid in Routine Dental Practice*

Hyaluronic acid (HA) is a promising material in modern dentistry because of its healing and regenerative properties. It helps in periodontal wound healing, treatment of gum recession and regeneration of bone defects. HA supports cell growth, reduces inflammation, improves blood vessel formation and promotes collagen and new bone formation. Because of these benefits, HA can improve periodontal treatment outcomes when used in routine dental practice [10,11].

➢ *Efficacy and Safety of Hyaluronic Acid in Scaling and Root Planing*

Scaling and root planing (SRP) is one of the most commonly performed dental procedures and is essential for maintaining periodontal health. It works by removing plaque and calculus from above and below the gingival margin, thereby reducing harmful bacteria in periodontal pockets and improving gingival health. Studies have shown that hyaluronic acid (HA) is naturally present in gingival tissues [12]. When HA is used along with SRP, it can enhance the healing response [13]. Clinical studies have reported that adding HA to SRP results in greater reductions in bleeding on probing and probing pocket depth compared to SRP alone [14]. This improvement may be due to the presence of HA in periodontal pockets for several days after treatment [9], during which it promotes tissue healing by stimulating fibroblast activity and increasing collagen production [15], helping the gingiva reattach to the root surfaces [14].

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However, it is important to understand that HA does not replace SRP. SRP remains the primary and most important treatment for periodontal disease. Hyaluronic acid should be used only as an adjunct to SRP, with the aim of improving healing and enhancing overall treatment outcomes.

➢ *Periodontal Regeneration*

Local drug delivery (LDD) is a useful treatment for periodontal pockets that remain after scaling and root planing (SRP), especially during the maintenance phase. Fibroblasts play an important role in periodontal healing, and hyaluronic acid (HA) supports their activity by promoting cell growth, movement, collagen formation, and the release of growth factors needed for tissue repair. HA also helps in extracellular matrix remodeling and shows anti-inflammatory and antimicrobial effects [16].

HA is gaining importance as an LDD because it is effective against periodontal pathogens with minimal systemic effects [15]. It is used as an adjunct to both nonsurgical and surgical periodontal therapy [14]. However HA is effective only after proper plaque removal and SRP and it cannot replace mechanical therapy. Clinical studies by Shah et al. (2016) and Chauhan et al. (2013) reported reduced probing pocket depth and improved clinical attachment levels when HA was used after nonsurgical periodontal therapy [17,18]. HA remains in periodontal pockets for several days, allowing slow and sustained drug release [5,19]. Although results are promising, further histological studies are needed to confirm true periodontal regeneration.

➢ *Treating Black Triangles with Hyaluronic Acid*

Hyaluronic acid (HA) injections have shown promising results in the treatment of black triangles by promoting blood vessel formation and papillary regeneration. HA interacts with growth factors, maintains tissue hydration, and improves lubrication, all of which help preserve tissue structure and support the regeneration of the interdental papilla [8]. Due to its strong water-binding ability, HA attracts and retains water, leading to tissue swelling and volume gain, which helps fill the missing papilla. The nonsurgical injection of 0.2% HA is a minimally invasive approach that increases interdental papilla volume while reducing postoperative discomfort. This method improves aesthetics and periodontal appearance with good patient acceptance [17,18,20,21]. However, although results are encouraging, further long-term studies are required to address existing limitations and confirm its effectiveness.

➢ *Gingival Recession Treatment with Hyaluronic Acid*

Gingival recession is a common clinical condition seen even in individuals with good oral hygiene and often leads to aesthetic concerns and dentinal hypersensitivity. Studies have shown that hyaluronic acid (HA) improves the strength of healing tissues and increases periodontal ligament cell viability. When used along with surgical root coverage procedures for single Miller Class I recession defects. HA helps promote cell migration, differentiation, and tissue repair, leading to predictable and safe outcomes [22,23]. However, HA should be considered only as an adjunct as its benefits are additive to conventional surgical techniques and not a replacement for them.

➢ *Hyaluronic Acid in Implant Dentistry*

Hyaluronic acid (HA) shows promising potential in implant dentistry by improving both osseointegration and soft-tissue integration. The use of HA-coated implant surfaces or HA-based bone graft materials may enhance the long-term success of dental implants. HA influences mesenchymal stromal cells and pre-osteoblasts by promoting their growth and differentiation into bone-forming cells, thereby supporting bone regeneration and osseointegration [24].

HA regulates bone formation through its physical properties and by interacting with cell surface receptors such as CD44, which supports osteogenic activity, and RHAMM, which regulates cell movement. Its effect also depends on molecular weight, with high-molecular-weight HA enhancing osteogenic gene expression and low-molecular-weight HA promoting cell proliferation [25,26]. Although current findings are encouraging, further clinical studies are needed to determine optimal dosages, delivery methods, and long-term effects of HA on osseointegration [24].

➢ *Managing Oral Wounds and Ulcers with Hyaluronic Acid*

Oral ulcers are common lesions of the oral mucosa, usually caused by trauma, biting, sharp teeth, faulty restorations or burns from hot food. Hyaluronic acid (HA)–based gels have been shown to be effective in the management of oral ulcers by reducing erythema, exudation, ulcer size, pain, and healing time [27,28,29]. High-molecular-weight HA has anti-inflammatory and immunomodulatory properties, promotes cell migration and maintains tissue hydration, creating favourable conditions for wound healing. HA interacts with cell receptors such as CD44, RHAMM and ICAM-1 which support cell movement, proliferation, and tissue repair.

Clinical studies by Kapoor et al. and Nolan et al. reported faster healing and reduced pain in patients with recurrent aphthous ulcers treated with HA compared to placebo [30]. HA also promotes angiogenesis, fibroblast activity and extracellular matrix formation, all of which accelerate oral wound healing [31,32]. Histological studies have shown increased blood vessel formation without adverse inflammatory reactions, confirming the safety and effectiveness of HA in oral mucosal healing [33,34].

➢ *Hyaluronic Acid in Tissue Engineering*

Hyaluronic acid (HA) and its derivatives are widely used in tissue engineering as scaffold materials due to their excellent biocompatibility, controlled cross-linking ability and suitable porosity which support cell attachment, growth and differentiation. HA-based scaffolds provide a favourable environment for cell infiltration and blood vessel formation while maintaining necessary mechanical strength. Because HA meets key requirements such as biocompatibility, biodegradability and cytocompatibility it has been extensively studied and successfully applied in tissue engineering particularly in cartilage regeneration [35].

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➢ *Future Applications of Hyaluronic Acid*

Hyaluronic acid (HA) shows great potential in various areas of dentistry, including periodontal therapy, implantology, wound healing, orthodontics, caries prevention and cosmetic procedures. In the future, HA may be used as a stable drug delivery system, help in tissue and bone regeneration, improve implant stability and promote soft-tissue healing when combined with growth factors. Its role in aesthetic dentistry further highlights its wide application in dental care [36].

III. CHALLENGES IN USING HYALURONIC ACID IN DENTISTRY

Hyaluronic acid (HA) has a wide range of applications in dentistry, including periodontal therapy, implantology, wound healing, orthodontics, caries prevention and aesthetic procedures. It helps promote soft-tissue healing, supports tissue and bone regeneration and may improve implant stability. In the future, HA can be used as a stable local drug delivery system and in combination with growth factors to enhance healing outcomes. Its growing role in aesthetic dentistry further highlights its importance in modern dental care [36].

➢ *Standardization of Hyaluronic Acid Formulations*

Hyaluronic acid (HA) is available in many formulations and molecular weights, which can affect its clinical effectiveness. The lack of standardized HA products makes it difficult to compare research findings and draw clear conclusions about its benefits in dentistry. Regulatory approval of HA-based products also varies between regions. In Europe, medical devices are classified into four risk categories, while in the United States the FDA uses a three-class system. Many HA-based products are considered high-risk devices and require strict safety and efficacy testing. Differences in regulatory systems can affect product availability, cost and clinical use. Understanding these regulatory challenges is important for the wider acceptance and safe application of HA-based treatments in dentistry [41].

➢ *Durability and Biodegradability*

Hyaluronic acid (HA) breaks down naturally in the body, which raises concerns about how long it remains effective in dental treatments. The main challenge is to develop HA-based materials that last long enough to support healing while still maintaining their structure and therapeutic effects.

➢ *Local Delivery Methods:*

Successful therapeutic application of hyaluronic acid (HA) requires accurate and sustained delivery at the treatment site. In the oral cavity, factors such as salivary flow, mastication and continuous tissue movement make local retention difficult. Designing delivery systems like gels, films or scaffolds that can adhere to oral tissues and provide controlled, slow release of HA is technically challenging. Inadequate stability or premature loss of HA from the site may reduce its clinical effectiveness, highlighting the need for improved local delivery formulations.

➢ *Immunogenic Reactions:*

Although hyaluronic acid (HA) is generally biocompatible and safe, higher doses, repeated applications or long-term use may induce immune reactions in some patients. These reactions are often related to formulation impurities or degradation products rather than HA itself and may present as localized inflammation, swelling or hypersensitivity. Further research is needed to better understand these responses and to develop safer, high-purity HA formulations.

➢ *Regulatory Approval and Guidelines:*

The regulatory approval of hyaluronic acid (HA)–based dental products remains a complex and time-intensive process, largely due to rigorous safety and efficacy requirements. The establishment of well-defined clinical guidelines, supported by high-quality evidence and close collaboration among researchers, clinicians and regulatory authorities are essential to facilitate standardized clinical application and ensure optimal patient outcomes.

➢ *Patient Education and Awareness:*

Patients should be provided with clear, accurate and understandable information regarding the benefits, possible risks and expected clinical outcomes of hyaluronic acid (HA) therapy. Proper education helps address patient concerns, improves compliance and builds trust and acceptance toward this treatment approach.

IV. SUMMARY AND CONCLUSION:

Hyaluronic acid (HA) is more than just a marketing product and has shown real value in dentistry. It is used in a wide range of dental procedures from routine periodontal treatments to advanced surgical procedures. HA helps to improve wound healing, reduces inflammation, maintains tissue moisture, and supports tissue repair and regeneration, making it a useful aid in dental care. However, its routine use in dentistry is still limited by factors such as a lack of long-term clinical evidence, variations in formulations, difficulties in local delivery, possible immune reactions and regulatory concerns. Further research and well-defined clinical guidelines are needed to overcome these challenges. With proper scientific evidence and standardized protocols, HA has strong potential to improve treatment outcomes and overall patient care in dentistry.

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