Hyaluronic Acid Effect on Periodontal Parameters: Review

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Abstract

The periodontal apparatus requires the body's hyaluronic acid for extracellular matrices to function properly. It supports the processes underpinning the inflammatory and wounds heal processes. Hyaluronic acid is found in periodontium in varying concentrations, with higher concentrations found in non-mineralized structures like gingiva and periodontal ligament and reduced concentrations found in mineralized tissues like cementum and jaw bone. Recent research indicates that hyaluronic acid has the capacity to control periodontal tissue repair and therapy of periodontal disorder. For both deepest periodontium and peripheral gum, hyaluronic acid encourages symptomatic alleviation. The purpose of the current review was to look into the usage of hyaluronic acid in periodontal treatment and the publications that currently support it.

Keywords: hyaluronic acid, periodontitis, gingivitis, regeneration

Introduction:

The disaccharide polymer which is the member of the glycosaminoglycan category is hyaluronic acid. Hyaluronic acid is a key compound of extra-cellular matrix and is found within human connective and epithelial tissue(s) in a large molecular-weight state (104-107 Dalton) (1). The one of more prevalent glycos-aminoglycans in an extra-cellular matrix is a hyaluronic acid, often known as hyaluronan (2). Haluronic acid removed first from the hyaline of eye of cow in 1934 (3). The Greek word hyalos, which means "glazier," gave rise to the acronym " hyaluronic acid " which included 2 sugar molecules, one of which is uronic acid. Additionally, those linear polysaccharides demonstrate a large number of repeating disaccharides units (4). Remarkably, a seventy kg grown individual has about fifteen gramme of hyaluronic acid in his body (5). The majority of body cells are able to produce hyaluronic acid, this production happens within cells membrane. A protein linked to the plasma membrane produces HA there. Secretion of synthesized hyaluronic acid towards extracellular environment is straight. In the existence of endotoxins, fibroblast also generates it (6). Hyaluronic acid is being utilized to treat chronically inflammatory disorders. Moreover, periodontal diseases affect the periodontium and are the inflammatory condition. Very little hyaluronic acid is present in the calcified alveolar jaw bone and the cementum of the periodontal apparatus, but an extracellular matrix of gingiva and the periodontal ligaments require it (5). Due to the subsequent effect on receptors of HA, that are involved in the cellular migrations, an angiogenesis, and an inflammation, healing of wound is expedited after treatment by hyaluronic acid. Hyaluronic acid eases discomfort in deeper periodontal parts as well as peripheral gingiva (7). In both a mineralized and non-mineralized periodontal structure, hyaluronic acid plays a crucial role in the mechanisms of an inflammation, granulation tissue development, and epithelial remodeling process during recovery of the chronic wounds (8). Additionally, several periodontal therapies including a non-surgical and a surgical remedy, as well as hard and soft tissues regeneration, have made advantage of this wound-healing property of hyaluronic acid. Additionally, hyaluronic acid controls inter cellular-matrix exchanges, and are essential for cell signaling, and hemostasis. Additionally, hyaluronic acid affects the movement of nutrients and waste (9). Furthermore, hyaluronic acid can be employed in periodontal investigations since it has a wide range of uses, vastly are enumerated in this paper.

Characteristics of HA:

Utilizing its physical, chemical, and biological features hyaluronic acid performs a number of functions in the body. Those biological activities range from fundamental structural responsibilities in an extracellular matrix to regulation over tissue macro- and microenvironments, impacts on the cell behaviors, and the developmental regulations. Effects of those hyaluronic acid activities on gene expression are also directly receptor-mediated (10, 11).

1. **Hygroscopic nature:** One of the compounds in environment which has the uttermost hygroscopic is hyaluronic acid. Hydrogen bonding between adjacent carboxyl and N-acetyl groups occurs when hyaluronic acid is dissolved in water; this property enables hyaluronic acid to maintain conformational rigidity and to hold onto water. Up to six Liters can be held in 1 gramme of hyaluronic acid. As the background physical substance, it serves as space filler, lubricant, shock absorber, and a protein excluder (12).
2. **Viscoelastic properties:** By preserving gaps and shielding the surfaces, hyaluronan, a viscoelastic material, aids in periodontal regenerating processes. By being aware of its viscoelastic properties, hyaluronic acid can affect how cells behave, changing the intracellular, an extracellular, and macro-environments around them. In the treatments of periodontal disease, viscoelastic qualities of the materials may impede the invasion of bacteria and viruses (12).
3. **Biocompatibility and non-antigenicity:** Due to its excellent biocompatibility and lack of immunogenicity, hyaluronic acid is used in a variety of medical procedures, as the augmentation of joints fluid in rheumatoid arthritis, assistance in surgery of eye, speed up the rebuilding of bone, and periodontal structure. Cross linking and esterification are modification made to hyaluronan to give rigidity like gel and structure for cell-seeding reasons. These bio-polymers promote the development of mesenchymal stem cell; chondrocyte and fibroblast are fully bio-degradable (13).
4. **Antioxidant:** Hyaluronan, therefore, may play a slightly paradoxical function in controlling an inflammatory response by sweeping reactive oxygen species and serving as an anti-oxidant. Hyaluronan may therefore aid in stabilizing the matrices of the granulation tissue (13).
5. **Anti-oedematous:** Osmotic activities of hyaluronic acid may possibly be connected to its anti-oedematous effects. It can be utilized as an addition to mechanical therapy because of its qualities that speed up tissue recovery (14).
6. **Anti-inflammatory:** Because of whisk function of an exogenous hyaluronan, that drains metalloproteinases, prostaglandins, and other bioactive compounds, hyaluronic acid seems to have anti-inflammatory impact (13).
7. **Bacteriostatic effect:** New research on regenerative surgical methods suggests that reducing bacterial onus at the wound site may promote regenerative treatment's clinical result. The highest bacteriostatic impact is produced by the greater percentage of lower and medium molecular weight hyaluronic acid, especially on strains of *Staphylococcus aureus*, *Prevotella oris* and *Aggregatibacter actinomycetemcomitans* that are frequently present in lesions of gingiva and periodontal wounds. By using hyaluronic acid gel, membranes, and sponges in surgical operation, it may be possible to lower the chance of postoperative infections and encourage highly predicted regeneration (15).

Synthesis of HA:

In contrast to other glycosaminoglycans hyaluronic acid charged glycosaminoglycan negatively. Mammals' cellular plasma membranes are where hyaluronic acid production takes place; Golgi apparatus is frequently site of glycosaminoglycan synthesis (9). Hyaluronic acid has high molecular weight between 103 and 104 kDa, a length between 2 and 25 μm, and it has no sulphate groups (10). The largest quantities of hyaluronic acid are found in umbilical cord, synovial fluid, epidermis and another tissues, whereas the fewest quantities are found in blood serum (16). Either lymphatic outflow into the blood circulation or regional metabolism is responsible for the transformation of hyaluronic acid contents in the tissues. A regional metabolism accounts for 20 to 30 percent of hyaluronic acid

transformation in the joints and skin, while lymphatic routes evacuate the remaining percentage. About 85 to 90 percent of it is removed in the liver after it passes through the blood circulation. Only 1 to 2 percent of the 10 percent that the kidneys expel is found in the urine. No matter how it is eliminated hyaluronic acid has a tissue half-life that spans from few hours to two or three days. (17).

Role of hyaluronic acid healing of wounds:

Owing to its chemical and physical properties and lack of immunogenicity, hyaluronic acid has been employed in medical field for many years in its greatly pure state. Due to its substantial water retention capacity, hyaluronic acid influence and enhances tissues regeneration, limiting the formation of dead skin and scarring (18, 19).

In addition to many other tissues, cartilages use it as a building element. Proteins containing a variety of glycosaminoglycans are interacted with hyaluronic acid to create proteoglycans. Infiltrating extra cellular matrix and cells of inflammation both grow, aiding inflammatory process. As result, hyaluronic acid has the capacity to affect the microenvironment around cells, which may have an influence on behavior of cells (17). Hyaluronic acid participates in a variety of cell processes that speed up tissue repair, including proliferation of cell, motility, and recognizing. Thence, the cells of tissue repairing can colonize hyaluronic acid more easily (20). It was suggested that hyaluronic acid induces angiogenesis, thence in the bone matrix, there was increasing the rate of wound healing. hyaluronic acid is angiogenic when with low molecular weights, but become anti-angiogenic at higher molecular weights (21). Results of previous studies demonstrated that exogenous hyaluronic acid exerted satisfying wound healing benefits (22, 23, 24). hyaluronic acid has the potential to be used in tissue engineering because it is a crucial component of cell motility, evolution and organo-genesis (25). The crosslinking and esterification of hyaluronic acid are two changes that produce the gel-like structure and stiffness for cells seeding. These bio-polymers promote the growth of fibroblasts, chondrocytes, and mesenchymal stem cells because they are biodegradable (26). Hyaluronic acid is thus utilised as dermal filler in cosmetic dermatology (27). A chemo-therapeutic substance called hyaluronic acid has been used to treat gingivitis. Additionally, the osseointegration of dental implants suggests that hyaluronic acid is involved (28). When a wound is healing, high molecular weight hyaluronic acid promotes osteo-induction or the creation of bone (29). In directed guided bone regeneration and tissue engineering, it may therefore show promise as a biomaterial scaffold (30). Following hyaluronic acid treatment, extraction socket wounds heal more quickly (31). Furthermore, a variety of microorganisms in the planktonic phase showed dose-dependent bacteriostatic effects when exposed to hyaluronic acid (32). An essential component of hyaluronic acid signalling is the molecular weight of hyaluronic acid. It is noteworthy that hyaluronic acid activates various signalling pathways depending on the molecular weight (33).

Hyaluronan interacts with cell receptors to cause cellular responses. Notably, hyaluronic acid signaling involves a wide variety of cell receptors. CD44 is the most prevalent receptor for hyaluronic acid signaling (34). As CD44 in fibroblasts is necessary for emigration towards the damaged area, CD44 signaling is important for wound repair (35). Noticeably, CD168, also known as the receptor for hyaluronan-mediated motility (RHAMM), is important for signaling. For tissue regeneration and inflammation, RHAMM-hyaluronan interactions are essential (36). Innate immune response, tissue metabolism, and tissue haemostasis are all regulated by toll-like receptors (37). Defesins, which have antibacterial capabilities and use cell-regenerative stimuli, are produced as a result of toll-like receptors (38).

Role of hyaluronic acid in periodontal treatment:

Hyaluronic acid is present in the periodontal tissues in varying concentrations. In comparison to alveolar bone and cementum, periodontal ligament and gingiva have greater concentrations. Additionally, its large levels in blood serum serve as a marker for overloading of gingival sulcular fluid serum (39). Scaling and roots planning reduces the number of microbes in the periodontal pocket and modifies the microbiota to make it less infectious, which has a good impact on periodontal

parameters (40). Following scaling and roots planning, hyaluronic acid is used as an adjunctive treatment. Prostaglandins, metalloproteinases, and bioactive substances are decreased after hyaluronic acid therapy. This prevents tissue breakdown and aids in the recovery process (41). Use of 0.2 percent hyaluronic acid gel to gingivitis patients locally. According to the findings of this earlier investigation, hyaluronic acid therapy decreased bleeding and fluid flow of gingiva, in addition to enhanced gingival health (41, 42, 43). Additionally, when examining the impact of hyaluronic acid on periodontal parameters in patients had periodontitis. Results from this earlier report showed significantly reduced bleeding upon probing in the hyaluronic acid group compared to the non-hyaluronic acid group, indicating improvement of outcomes (44). Additionally showed reductions in bleeding after receiving hyaluronic acid (45). Outcomes from a prior study comparing the impacts between scaling and root planning with hyaluronic acid and SRP alone in chronic periodontitis patients showed that the SRP with hyaluronic acid group considerably decreased probing pocket depth more than the SRP alone group did (46). The level of clinical attachment, repair, and periodontal indices have all improved as a result of treatment with hyaluronic acid. The effects of hyaluronic acid PLUS SRP and SRP alone in chronic periodontitis PATIENTS were compared in a split-mouth trial. After six and twelve weeks, the test group's gingival indices, clinical attachment level (CAL), and periodontal pocket depth (PPD) all showed a significant improvement (47). Additionally, another comprehensive study showed that hyaluronic acid has positive benefits on CAL gain, bleeding on probing, and pocket depth decrease after surgical and non-surgical periodontal therapy (48). Because hyaluronic acid encourages neovascularization, therapy with injecting hyaluronic acid gel of different concentrations improved regeneration of papilla. hyaluronic acid also enhanced CAL and promoted keratinization. The injections were given up till the gingiva's hue turned white. The interdental region in the maxilla and mandible showed approximately 2/3 coverage continuing after three, twelve, and twenty-four months when compared (49). Hyaluronan functions as an anti-bacterial factor and encourages fibroblast adhesion to the cementum. Additionally, sodium hyaluronate improves cell-to-cell chemical communication. As a consequence, guided tissue regeneration membrane frequently contains sodium hyaluronate (50). The evaluation of esterified hyaluronic acid fibers' clinical efficacy in the therapy of 18 periodontal abnormalities. After a twelve-month follow-up, the average PPD reduced by 5.8 mm, while the CAL increased by 2.8 mm (51). A unique alveolar bone development was noticed in bone lesions during the histological study in laboratory animals (52). A different systematic review further showed that hyaluronic acid produced positive benefits in periodontal regeneration. When hyaluronic acid was utilized alone or in conjunction with bone transplant or other biomaterials, enhancements were seen in regard to radiographic, PPD, CAL, and BOP measures (53).

Conclusion:

Hyaluronic acid is an important biomaterial utilized in periodontal treatment. Patients with gingivitis, periodontitis, implants, and periodontal abnormalities, treated with HA results in clinical benefit. Treatments with hyaluronic acid hasten the reaping of wounds, improving surgical outcomes and increasing patient satisfaction. Hence, more investigation is needed in the therapeutic efficacy of hyaluronic acid in periodontal disorders. It will also help to clarify the precise applications, the best way to provide hyaluronic acid for post-operative management of periodontal diseases, and the potential for complete regeneration of periodontal tissue.

Among the most critical challenges of medicine is developing treatments and gaining effective methods to combat pathologies continuously. Available medications and activated molecules are useful tools for treating different illnesses. However, their efficacy has severe restrictions due to the difficulty in administering them. As a result, huge work has been done to improve so-called 'drug delivery systems, which are instruments that can carry medications and active molecules to therapeutic target site.

Conflict of interest:
Authors declare no conflict present.

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