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Nano-hydroxyapatite Use in Oral Medicine: A Review

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Abstract: Nano-hydroxyapatite (nHA) are fine particles, and its crystal structure is similar to the inorganic composition of natural bone, similar to ordinary hydroxyapatite, nHA has higher solubility biocompatibility and excellent osteogenicity, especially in repair of bone defects. In recent years, nHA as a new oral material is widely used in various fields of stomatology. The application of nano-hydroxyapatite in dental pulp, Periodontal field, maxillofacial surgery and oral health care is discussed in this paper. We describe by this article that nHA as root canal paste filling is anti-inflammatory and promote the closure of apical foramen. nHA can promote regeneration of alveolar bone cementum and periodontal membrane to form healthy periodontal tissue. nHA can also be widely used in the repair of oral bone tissue defects such as periodontal bone defect, alveolar bone reconstruction and jaw cyst. Besides, in the field of surgery, nHA can be used in defected bone area caused by surgery, it can promote bone union. In the field of oral health care, nHA can inhibit the formation of dental plaque, promote enamel remineralization, whiten teeth and relieve dentin sensitivity when applied to toothpaste, mouthwash and oral spray. The aim of this study is to provide a broad understanding of nHA and promote the use of nHA materials in the treatment of oral disease.

Keywords: Nano, Hydroxyapatite, Oral Materials, Re-mineralization, Bone Repair

1. Introduction

Hydroxyapatite is the main inorganic component of human and animal bones and teeth. It can be closely combined with human soft and hard tissues in a short time after implantation and stimulate bone hyperplasia to promote bone tissue repair. At present, nano materials have been widely used in clinic. Nano-hydroxyapatite (nHA) composited by nano materials and hydroxyapatite has fine particles. Its crystal structure is similar to the inorganic composition of natural bone. It combines with polysaccharides and proteins on the surface of human cell membrane by hydrogen bonds, and has no cytotoxicity. Compared with ordinary hydroxyapatite, it has higher solubility, biocompatibility and excellent osteogenic activity, which is very effective in repairing bone defects. However, the application of nano-hydroxyapatite in dentistry is limited due to its non-antibacterial property, and its compressive and flexural strength is not suitable for dental restoration. In recent years, with the deepening of the properties and preparation methods of nano-hydroxyapatite, nano-hydroxyapatite and its composites as new oral materials are widely used in various fields of oral cavity and have achieved good results. Based on the latest research status at home and abroad, this paper reviews the application of nano-hydroxyapatite and its composites in stomatology in recent years.

2. Application of Nano-hydroxyapatite in Stomatology

The application of nano-hydroxyapatite in oral medicine is mainly reflected in root canal therapy. In the application of root canal therapy, the filler should have two characteristics: on the one hand, it should have the dead cavity formed by eliminating the primary site of inflammation; on the other hand, the material should have a certain recovery effect on the lesion, can promote apical foramen calcification closure. Hydroxyapatite can be used as root canal paste filling, which basically has these two characteristics. In the filling experiment of human in vitro teeth with hydroxyapatite paste combined with gutta Percha tip and Grossman paste combined with gutta Percha tip, it was found that hydroxyapatite paste had good sealing performance under electron microscope scanning, and its physical and chemical properties were similar to those of natural bone [1]. Hydroxyapatite as an inorganic filler material itself does not have osteogenic properties, but it can be used as a good physiological matrix for new bone deposition to provide good conditions to guide the regeneration of surrounding bone tissue, can also guide new bone deposition to close the apical foramen effect. In addition, hydroxyapatite materials can absorb root exudates and keep the root tissue relatively dry, which is conducive to the growth of granulation tissue.

Hydroxyapatite has the advantages of non-toxic, inert, non-stimulation to tissues, good biocompatibility, biodegradability and bone conductivity, but it has the disadvantages of high brittleness and micro leakage [2-3]. Nano-composite hydroxyapatite has similar physical and chemical properties to human bone. It has good compatibility with the original dentin, which can reduce micro leakage and is more conducive to root canal closure. It can also carry organic bone inducers to achieve organic polymerization with bone cells and strengthen the bone induction performance of materials [4].

3. Application in Periodontal Field

Periodontal disease is the most important factor of adult tooth loss. Periodontal disease mainly occurs in gingival tissue and periodontal supporting tissue. The fundamental method for the treatment of periodontal disease is to form new physiological periodontal tissues on the diseased root surface, namely the formation of alveolar bone, cementum and periodontal ligament.

3.1. Regeneration of Alveolar Bone

de Vasconcellos et al. used nano-hydroxyapatite / graphene nano-ribbon composites to induce osteogenesis in vitro [5]. It is suggested that nHA has a good ability to guide the growth of bone tissue, and the combination with graphene nano-belts is helpful for the regeneration of alveolar bone.

3.2. Formation of Dentin

Jain et al. used nHA to repair dentin and reduce periodontal pocket and attachment lost [6]. de Vasconcellos et al. used nano-hydroxyapatite / graphene nano-ribbon composites to induce bone formation in vitro [5]. De tullio et al. evaluated and compared the therapeutic effects of calcium sulfate and nano-hydroxyapatite on alveolar bone after tooth extraction to determine the biological materials used as bone substitutes for bone augmentation surgery, and both had good results [7].

3.3. Periodontal Membrane Formation

Periodontal cells are the main cell source for the formation of new attachment. However, near the damaged periodontal tissue, periodontal membrane cells are very limited, which makes it difficult to effectively reconstruct periodontal tissue. Some scholars have studied the effect of hydroxyapatite nanoparticles (HAPNPs) on human periodontal ligament cells, and observed that HAPNPs can promote cell proliferation and periodontal tissue regeneration to some extent [8].

4. Application in Oral and Maxillofacial Surgery

Bone defects and maxillofacial fractures caused by inflammation, trauma, tumor, congenital malformation and periodontitis are common diseases in oral surgery. Bone grafting or increasing bone mass are the main methods of repairing oral bone defects. The good biocompatibility and Osteoinductivity of nHA play a key role in the repair of bone defects and the rapid formation of bone bonding between implants and surrounding bone. Its application in oral surgery is mainly reflected in the expansion of alveolar ridge and the repair of jaw defects.

4.1. Alveolar Ridge Amplification

The height and width of alveolar bone will be greatly reduced after tooth extraction. In order to ensure sufficient bone mass for later repair treatment, site preservation after tooth extraction has become an important method to reduce bone resorption. The ideal atrophied alveolar bone augmentation and widening material should be able to guide bone formation and absorption in vivo and in vitro. After the implantation of nano-hydroxyapatite material, it is beneficial to guide the crawling of new bone, and can be gradually degraded and absorbed. Wang et al. implanted nHA into the extraction socket of adult dog after the second premolar was extracted, and found obvious bone regeneration [9]. The hydrogel / hydroxyapatite hybrid scaffold (GH) formed by mixing hydrogel with hydroxyapatite was applied to the study of bone tissue regeneration, and the experimental results showed that the composite scaffold had excellent bone regeneration potential, and its good mechanical strength could support the alveolar fossa at the early stage and prevent the alveolar bone from absorbing and collapsing inward [10, 11].

4.2. Repair of Jaw Defects

Hydroxyapatite particles artificial bone repair of bone

defects caused by oral diseases, is a new effective treatment of bone defects in this year. While filling, the infection problem is solved, and the effect on bone induction is obvious. The operation is simple and easy, so it is widely used in oral and maxillofacial surgery. Du et al. pre-vascularized the nano-hydroxyapatite / coral block (nHA / coral block) with vascular endothelial growth factor (VEGF), and then implanted it into the mandible of dogs with severe defects. The results showed that nHA / coral block allowed the growth of cells and collagen due to its suitable pore size and pore connectivity. The local delivery of VEGF could significantly improve the angiogenesis and mineralization of newly formed bone at the early stage of bone healing, indicating that nHA / coral block may be applied in bone tissue engineering, and vascularized pretreatment with VEGF can achieve excellent results [12]. Fukui et al. implanted nHA into the rabbit mandibular defect model, and observed early bone tissue reactions, indicating new bone formation [13].

4.3. Inhibition of Oral Cancer Cells

Foreign scholars have found that nHA also has a broad-spectrum anticancer effect [14]. But the effect on common oral tumors has not been reported. Zhang et al. observed the effect of nHA on the growth of human tongue cancer cell, the results showed that nHA could effectively inhibit the proliferation of cancer cells and promote the apoptosis of cancer cells [15]. Domestic scholars have detected the application of intelligent response fluorescent nano hydroxyapatite drug delivery system in the diagnosis and treatment of oral squamous cell carcinoma, and found that the prepared FYH-PDA-DOX has good targeted killing effect on Cal-27 cells, It can realize the early diagnosis, accurate positioning, high-efficiency and low-toxicity targeted diagnosis and treatment of oral squamous cell carcinoma [16]. Nano-hydroxyapatite does not have the problem of rejection when applied in human tissues, and it has a specific role in inducing tumor apoptosis, so it has broad application prospects as a drug carrier.

5. Application in Oral Health Care

In recent years, nano-hydroxyapatite has attracted more and more attention in the field of oral health care. It has been reported to be used in toothpaste, mouthwash, mouth spray, denture cleaner and other products, it has the functions of inhibiting plaque breeding, promoting enamel remineralization, whitening teeth and relieving dentin sensitivity.

5.1. Inhibition of Dental Plaque Formation

nano-hydroxyapatite can adsorb pathogenic bacteria in the mouth, proteins and dextran in saliva, which is helpful to prevent the formation of dental plaque. Teng et al. studied the anti-adhesion effect of nano-hydroxyapatite on Streptococcus Mutans. The results showed that nHA had an inhibitory effect on the adhesion of Streptococcus Mutans and had a de-adhesion effect on the attached Streptococcus Mutans [17]. The above experimental results show that nano-hydroxyapatite has good anti-streptococcus Mutans adhesion, can prevent streptococcus Mutans adsorbed on the acquired membrane and destroy the formation of dental plaque.

5.2. Promoting Enamel Re-mineralization

In the mouth, tooth demineralization and re-mineralization are a dynamic equilibrium process. If re-mineralization is stronger than demineralization then caries may be healed. Nano-hydroxyapatite has excellent re-mineralization effect on tooth tissue, which comes from the synthesis of apatite with similar physical and chemical properties to natural tooth hydroxyapatite. TSCHOPPE P et al. used bovine incisors to make demineralization model, and studied the effect of HAPNPs toothpaste on re-mineralization in vitro, the results showed that the re-mineralization effect of toothpaste containing nano-hydroxyapatite was stronger than that of toothpaste containing fluoroamine on dentin and enamel [18]. DAAS et al. found that nHA has nano-size effect, and its high surface energy and high biological activity make it easier to combine with dentin and deposit on the surface of de-mineralized dentin than ordinary HA, thus having better ability to block dentin tubules and re-mineralization [19-20].

5.3. Whitening Teeth

NIWA et al. studied the whitening effect of toothpaste containing hydroxyapatite. The experiment showed that the addition of hydroxyapatite in toothpaste could significantly increase the whitening effect of toothpaste, and the whitening effect increased with the increase of hydroxyapatite content [21]. NIWA believed that the whitening performance of hydroxyapatite toothpaste was not caused by its friction performance on the tooth surface, but the mineralization of hydroxyapatite on the tooth surface increased the density of the tooth surface, thereby improving the gloss of the tooth.

5.4. Relieving Dentin Sensitivity

Experiment of Dentinal tubule occlusion in vitro has become the gold standard for the study of anti-dentin allergy materials [20, 22]. The reason of dentin sensitivity is that the integrity of enamel is damaged or gingival atrophy leads to exposure of dentin tubules. According to the theory of fluid dynamics, the basic way to treat dentin hypersensitivity is to close the opening of dentin tubules and reduce the diameter of dentin tubules in order to avoid and reduce fluid flow in dentin. At present, most studies in domestic and overseas on the anti-sensitization effect of nHA are to add it as an active component to oral care products such as toothpaste and mouthwash to study its desensitization effect. Studies have shown that nHA alone or in combination with other components can block or even wedge into Dentinal tubules, and nHA has better anti-sensitivity than fluoride or arginine because it can form biomimetic apatite and surface mineralization on the surface of dental hard tissue [20].

BROWING WD et al. studied the effect of HAPNPs on the sensitivity of bleached teeth, and concluded that the toothpaste containing HAPNPs could reduce the sensitivity of bleached teeth without any Desensitizer [23].

6. Conclusion

In summary, nano-hydroxyapatite is extremely similar to hydroxyapatite in enamel in structure and composition, and has better solubility, biocompatibility and excellent osteogenic activity compared with the latter. Therefore, it has been widely used in biomedical fields in recent years, such as root canal therapy, alveolar bone amplification, tooth sensitivity relief, and anti-tumor. Although the research and application of nHA and its composites have made rapid development in recent years, their strength and toughness still cannot fully meet the clinical requirements. It is believed that in the near future, people can further explore hydroxyapatite and find new materials that are more suitable for stomatology, which will bring greater contributions to the development of stomatology.

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