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Clinical Aspects and Possibilities of Using Nanoparticles in Modern Dentistry (Literature Review)

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Abstract: ***Dental caries and periodontal diseases are still prevalent among oral diseases due to their polymicrobial and polyetiological nature. The treatment of dental pathologies includes the elimination of microbes. However, their destruction is often impossible due to the resistant strains that were formed by incorrect and long - term use of antibiotics. The rapid development of nanotechnology has led to the use of nano - sized particles for medical and preventive purposes in medicine and dentistry. The nano - particles application is wide in dental practice, restorative dentistry, endodontics, prosthetics and implantation. Research methods: To study the area of application of nanoparticles in dental practice, a systematic search in the following information bases was conducted: Web of Science (ISI), Google, PubMed using the following keywords: "nanoparticles", "dentistry, " "dental practice", Results: This literature review explores the clinical aspects and possibilities of using nanoparticles in modern dentistry. It highlights the effectiveness of silver nanoparticles in in various dental practices, including restorative dentistry, endodontics, prosthetics, and implantation for eliminating bacterial infections and the need for more research on their long - term effects, as well as importance of developing new antibacterial agents to combat resistant strains of bacteria. Conclusion: Nanoparticles favorable properties are indisputable; however, analyses and data on their side effects and harmful properties, as well as long - term effects and results on the body, are scarce and, in some cases, contradictory. Nanoparticles are successfully used in various aspects of medicine and dentistry. However, there are still many unanswered questions and multiple answers thatstill require fundamental study, more experimental and clinical observations.***

Keywords: Nanoparticles, Dentistry, Silver Nanoparticles, Antibacterial Agents, Restorative Dentistry, Endodontics, Prosthetics, Implantation.

1. Introduction

Dental caries and periodontal diseases are still prevalent among oral diseases due to their polymicrobial and polyetiological nature.

The treatment of dental pathologies includes the elimination of microbes. However, their destruction is often impossible due to the resistant strains that were formed by incorrect and long - term use of antibiotics. Therefore, developing new antibacterial agents that will effectively destroy microorganisms and be safe for macroorganisms is essential.

The rapid development of nanotechnology has led to the use of nano - sized particles for medical and preventive purposes in medicine and dentistry.

The nano - particles application is wide in dental practice, restorative dentistry, endodontics, prosthetics and implantation. Studies have confirmed the effectiveness of 100 nm spherical silver nanoparticles in eliminating bacterial infection from periodontal pockets [23].

The bactericidal and bacteriostatic effect of silver nanoparticles is well - known. However, studies and data on their side effects or long - term effects on the body are scarce, and sometimes contradictory. Therefore, more experimental and clinical observations are needed.

Dental caries and periodontal diseases are characterised by the highest prevalence among oral diseases due not only to their infectious - microbial nature but also to the numerous risk factors that influence the development of these diseases.

The treatment of caries does not only involve placing the filling material in the carious cavity. Indeed, it is a very important procedure, the goal of which is to restore the lost functional and aesthetic parameters of the tooth (restoration), which is more effective when the filling material is more similar to the tooth structure in terms of its physical, mechanical properties and chemical composition. Deficiencies in restoration are often associated with post - filling complications such as filling loss, tooth or filling fraction, and secondary (recurrent) caries development. It is the result of iatrogenic factors as well as the less pronounced antibacterial properties of the tooth filling, the penetration of microorganisms and their byproducts (organic acids) and the demineralization of tooth tissue. [1]

Ineffectively treated or untreated caries is often complicated first by pulp inflammation (or necrosis), then by acute or chronic apical periodontitis, and finally, can become the cause of tooth loss.

Many studies have shown that the bacterium is the main etiological agent of pulp infection and periapical disease development [2, 3]. The microbiota of infected root canals is polymicrobial, among which Gram - negative anaerobes predominate [4, 5]. Only carious cavities or improperly treated caries are not the sources of oral infection; the tooth buccal is the product of orderly adsorption and colonization of pathogenic microorganisms on the tooth's surface. The result of this is the main etiological factor of periodontal diseases and oral mucosa pathologies. A lot of researchesare based on the creation of antimicrobial agents. However, the low efficiency and safety of these agents, the high virulence of pathogenic microbes and the ability to form resistant strains often become the reason for the rapid degradation of antimicrobial drugs. Accordingly, nowadays, the spread of bacterial strains resistant to multidrug agents is not alien to modern medicine. [6] And despite the successes in oral health, caries and periodontal diseases are still complex infectious diseases, the fight against which has become a real challenge for modern dentistry [7.8.9.10]. Moreover, in terms of increasing the pathogenicity of oral bacteria, recent scientific studies make the role of dental plaque even more critical. According to Karolina Niska, dental plaque is defined as a multi - cellular microbial structure that represents microorganisms' basic life form [6]. This highly organized three - dimensional structure is characterized by high antibiotic resistance [6].

Microorganisms from the oral cavity, especially the biomembrane, may enter the blood circulation system and spread through the blood flow to various organs and tissues, causing systemic diseases such as diabetes, rheumatoid arthritis, pneumonia, and cardiovascular disease diseases and even premature birth [11.12]. Therefore, maintaining oral cavity health is of great importance for preventing and eliminating both local and general infections. Silver has been used effectively in medicine and dentistry since ancient times to combat aerobic and anaerobic flora and prevent and treat microbial infections. It has often been shown to have excellent results due to its high antibacterial, antiviral and anti - inflammatory effects [13].

In the wake of nanotechnology development, the high interest in nanoparticles led to the formation of our research goal, which is to study the area of their use in different fields of dentistry as well as their clinical aspects, possibilities, effectiveness and results.

Research methods: To study the area of application of nanoparticles in dental practice, we conducted a systematic search in the following information bases: Web of Science (ISI), Google, PubMed using the following keywords: "nanoparticles", "dentistry, " "dental, " "practice".

2. Literature Review

The rapid development of nanotechnology has led to the use of silver nano - sized particles for medical and preventive purposes in medicine and dental practice [14].

A nanoparticle is defined as a particle with a size of 1 to 100 nm, which is characterized by a more pronounced nature than a particular substance as a whole [15]. The antibacterial activity of silver particles grows at the expense of increasing their total surface area and, accordingly, the interaction with the microbe, which is finally manifested in a wide range of nanoparticles with antimicrobial action. Therefore, the size of silver nanoparticles is an important characteristic because while the small particles increase the surface area of contact with the microbe, they reduce the concentration of particles needed to achieve the effectiveness of the action [16.17.18.19]. It is noteworthy that many studies confirm the antibacterial activity of silver nanoparticles, even in the case of antibiotic - resistant microbial strains. [20.21.22].

This characteristic of silver nanoparticles is successfully used in dental practice to prevent bacterial adhesion, growth and biofilm formation in oral surgery, implantology and anti - caries treatment [14]. Moreover, studies have confirmed the effectiveness of 100 nm spherical silver nanoparticles in improving clinical results and eliminating bacterial infection of periodontal pockets [23].

In addition to bactericidal and bacteriostatic effects, silver nanoparticles have many positive aspects - biocompatibility with human cells, a long - lasting antibacterial effect due to the release of ions, and low toxicity [24].

When using nanoparticles, they are in contact with tooth tissue and other tissues and cells of the oral cavity. Therefore, it is appropriate to consider the negative effect on cells (cytotoxicity) and the advantages of silver particles. Also, serious care is needed to ensure compliance of nanoparticle use with safety standards [14, 25]. Therefore, it is natural to ask, are nano - particles non - toxic for human cells with bactericidal concentrations?

Various studies have confirmed that the cytotoxicity of silver nanoparticles depends on the concentration of the particles. The attention of <5 - 40μg/mL (10μg/ml) is safe, and high concentration showed high cytotoxicity, although their bactericidal activity decreases as the concentration decreases [26, 27, 28]. Other studies confirm that the toxicity of nanoparticles is correlated not so much with concentration as with time and many different factors, for example, type of particle [29], size, distribution, duration of action, interaction with other components, etc. [1]. Therefore, in our opinion, there are not enough studies to evaluate the standardization indicators of the toxicity of silver nanoparticles, it is necessary to carry out fundamental studies to study the effect of cytotoxicity on the human body revealed by silver nanoparticles.

In dentistry, silver nanoparticles are used in restorative materials. Their content in various dental materials determines the material's high antibacterial efficiency and biocompatibility [30]. According to multiple studies, resistant bacterial strains do not develop when the nanoparticles are used.

Nanoparticles can penetrate the cell wall of gram - positive and gram - negative bacteria and disrupt cell functioning due to their small size. Consequently, they have advantages in treating and preventing diseases caused by drug - resistant microorganisms [1]. Different mechanisms explain the antibacterial action of nanoparticles. Due to their small size, they easily penetrate the cell membrane at the expense of binding to peptidoglycan and cause cell lysis; they bind to the microbial protein and hurt its synthesis; They act on bacterial DNA and prevent its replication. [31, 32, 33, 34, 35]. Due to the connection with these structures, the chain of respiratory enzymes is broken, ultimately leading to the microbial cell's structural damage.

Nowadays, nanoparticles are successfully used in restorative dentistry during endodontic treatment [36] in prostheses [37] and implants [38].

The content of nanoparticles in composite filling materials is based on the direct effect on the bioavailability of microorganisms. They contain 1% silver nanoparticles (**AgNPs**) or zinc oxide nanoparticles (**ZnO NPs**). Studies have shown that the antibacterial effect of ZnO nanoparticles against **Streptococcus mutans (S. mutans)** is much higher than silver nanoparticles [39, 40].

As mentioned above, the long - term presence of untreated caries and secondary caries developed due to improperly treated cavities may be complicated by pulpitis and periodontitis. Many studies have shown that bacteria is the main etiological agent of pulp infection and the formation of periapical diseases [2, 3]. The microbiota of infected root canals is polymicrobial, which is dominated by gram - negative anaerobes [4, 5].

The microbiota of the inflamed periapical tissues of the tooth includes various microorganisms: Staphylococcus, E. faecalis, Enterobacter, Pseudomonas, P. gingivalis, Stenotrophomonas, Sphingomonas, Bacillus, and Candida species [41]. The treatment of these pathologies involves the elimination of microbes, although their destruction is impossible due to the complex system of root canals and the formation of resistant strains. This is often due to incorrect and long - term use of antibiotics and antimicrobial drugs in dental practice [42]. Therefore, it is important to develop new antibacterial agents that will effectively destroy various microorganisms and be safe for macro - organism.

Enterococcus faecalis (E. faecalis) is often the main etiological factor of reinfection of treated dental canals [43, 44, 45]. A complex canal system makes complete canal irrigation difficult [46, 47]. Nowadays, the most effective way to irrigate the canal system is sodium hypochlorite **5.25% NaOCl**, [48], which has a high antibacterial effect against the polymicrobial flora of the canal system. However, it is highly toxic to the periapical tissues and its transition to the periapical tissue causes necrosis [49].

While the development of nanotechnologies, the possibility of using nanoparticles in endodontic treatment attracted the attention of researchers. Studies have shown that biosynthetic silver nanoparticles had well - defined antimicrobial activity against Enterococcus faecalis [50, 51, 52]. Afkhami et al. revealed a highly effective antimicrobial activity of an irrigation solution containing 100 ppm silver nanoparticles compared to 2.5% sodium hypochlorite (NaOCl) [53].

In the research conducted by Lofti et al., the efficacy of 5.25% Naocl and 0.005% irrigation solutions against entrerococcusfaecalis was the same despite the low percentage of AgNPs solution. Therefore, a solution of 0.005% AgNPs can be used as a new irrigant during endodontic treatment [54, 55], although other studies confirm the greater effectiveness of sodium hypochlorite against Enterococcus faecalis. Moreover, **NaOCl** is considered the most effective irrigant in treating the canal system. [56, 57]

For successful endodontic treatment, it is also essential to use antibacterial canal - filling materials to prevent secondary infection [58, 59, 60]. The study showed that the addition of 0.15% AgNPs silver nanoparticles to the canal filling material (AH Plus) not only harmed the physical properties of the material, but moreover the material with nano - fillers showed significantly higher penetration into dentin tubules, and additional canals and showed antibacterial activity against Enterococcus faecalis. [61]

Nano - silver - gutta - percha [62] was presented by Iranian researchers as a trial and new initiative to improve the antibacterial property of gutta - percha. As a result, a significant effect was demonstrated against Enterococcus faecalis, Staphylococcus aureus, Candida albicans, and Escherichia coli. Furthermore, since gutta - percha is a permanent filling material, the silver nanoparticle added to its composition can have a prolonged effect on the microbiota of the root canal.

As we mentioned, the area of silver nanoparticles in dental practice is quite broad, it is not only about restorative and endodontic treatment, but significant successes are observed in using nanoparticles in prosthetics and implant dentistry.

Prosthodontic dentistry often uses soft tissue conditioners for palliative, curative and diagnostic purposes. These soft and elastic substances are used to treat oral tissue injuries and take available impressions. In addition, their use is often appropriate after placing removable prostheses and implants as a temporary means of tissue regeneration [63].

They have a long - lasting so - called cushion effect and promote the healing and regeneration of traumatized tissues and the retention of intra and extraoral removable prostheses. Unfortunately, these tools often create appropriate conditions and environment for the colonization of microorganisms and the formation of biomembrane, which together with the complications related to the use of the prosthesis (chronic atrophic candidiasis, prosthetic stomatitis) become a source of discomfort and problems for the patient. In addition, deficiency of oral hygiene is often observed in the users of complete non - removable prostheses; the space between the inner surface of the prostheses and the oral mucosa often becomes a place for the accumulation and colonization of mainly the Candida - type fungi microorganisms [64].

Polymethyl methacrylate (PMMA), the material used for the production of self - prostheses, is characterized by inferior antimicrobial properties and is a good surface for the adsorption of microbes [65]

Incorporating antifungal drugs into tissue conditioners is a hypothetical solution to this therapeutic problem, as well as using nano - fillers in prosthetic materials, which increases their antibacterial effectiveness.

The addition of nanoparticles such as silver (Ag) [66, 67, 68, 69], platinum [70], zinc Zn/ZnO [71], and zirconium oxide (ZrO2) [72, 73] dramatically improved the antibacterial activity of prosthodontic materials.

The effectiveness of the nanoparticle is just a little behind in terms of implantation. Nowadays, implantation is considered the best way to restore lost teeth because the implant effectively stops alveolar bone resorbtion and ensures the restoration of aesthetic and functional parameters of the maxillofacial area. Titanium implants are widely used in dental practice due to their strength, durability, and biocompatibility with body tissues [74]. However, in the case of unsuccessful implantation, the risk of infection spread related to the implant and cases in the early stages of its healing over the bone (osteointegration) are frequent: peri - implant mucositis and peri - implantitis, which is a prerequisite for the loss of the implant and is characterized by a high turnover of gram - negative bacteria as in case of periodontitis [74, 75].

Staphylococcus aureus (S. aureus), S. mutans and Escherichia coli, as well as Porphyromonasgingivalis (Pg) Aggregatibacter actinomycetemcomitans and (Aa) Candida albicans (C. albicans) [76, 77, 78, 79] are the main bacterial strains in implant infections. Accordingly, the pronounced antimicrobial effect of implant materials is a severe challenge to modern implants and manufacturers.

The addition of various inorganic nanoparticles to experimental implant models such as Ag [74, 75, 76], copper (Cu) [84], zinc oxide [85, 86], titanium dioxide (TiO_2) [87, 88] and selenium (Se) [89] significantly improved the antibacterial characteristic of implants. Studies have shown their increased effectiveness against gram - positive and gram - negative microbes; however, nanoparticles have shown cytotoxicity to osteoblasts in these studies, consequently limiting their clinical use [90].

As we mentioned, one of the essential steps for developing materials containing silver nanoparticles is to know their properties. [91.92] The dispersion of silver nanoparticles was investigated by transmission electron microscopy. This method allows us to determine the size of AgNPs and observe their distribution in the already tested material [93, 94, 95]. According to Cheng et al. study, 3 nanometer - sized silver nanoparticles were clearly observed and separated throughout the polymer matrix. These results were confirmed in a subsequent study, where the authors reported that the size of the AgNPs ranged from 2 to 5 nanometers. The small size of AgNPs determines its penetration into the tubules of dentin, which can inactivate the bacteria deposited idly on dentin [96]. Furthermore, it revealed that AgNPs were very well dispersed in the material (dentin). [97, 98]

3. Conclusion

Considering everything, we may conclude that silver and other inorganic nanoparticles still require fundamental study. Their favorable properties are indisputable; however, analyses and data on their side effects and harmful properties, as well as long - term effects and results on the body, are scarce and, in some cases, contradictory. There are various studies on the role of silver nanoparticles in the fight against human pathogens and the participation of calcium particles in restoring the bone structure of the jaw. Their osteogenic activity is unquestionable due to their ideal biocompatibility with alveolar bone and tooth structure, although there is a lack of information regarding the effect of different nanoparticles on endo - periodontal pathogens.

Nowadays, nanotechnology is rapidly developing; nanoparticles are successfully used in various aspects of medicine and dentistry. However, there are still many unanswered questions and multiple answers, which are the basis for more experimental and clinical observations.

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