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The Use of Innovative Materials in the Organization of Clinical Treatment in Dentistry

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The article examines the features of the use of innovative materials in the organization of clinical treatment in dentistry. In modern conditions, solving the problem of patient safety is one of the main conditions for the functioning of medicine in general and dentistry in particular. For this reason, the search for innovations in the field of antimicrobial protection and, together with it, the functionality of various materials is one of the main tasks of researchers in the field of dentistry. Nanomaterials, which are made on the basis of graphene, are able to demonstrate excellent antimicrobial properties. These materials have the ability to disrupt the integrity of the bacterial cell membrane and produce reactive oxygen species (ROS).

These materials are widely used in the manufacture of dentures, they are incorporated in the composition of composite resins and luting cements in the organization of restorative treatment, are used for the manufacture of adhesive materials. Many experts recognize that these materials are the future of dental practice, since they have the ability to provide a high level of functionality and safety.

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1. INTRODUCTION

Various populations of microorganisms live in the human oral cavity. When dental materials are placed in the oral cavity, the latter are exposed to various types of bacteria and fungi, which form a biofilm in the course of their vital activity. This coating provides microorganisms with survival conditions, causing, at the same time, secondary caries, periodontal infection and other dental diseases.

Most antimicrobial dental materials have been developed to overcome the inefficiency of dental treatment, which was caused by microbial infections. The primary approach is to seal or coat dental materials with antimicrobial agents (e.g. chlorhexidine and quaternary ammonium compounds), as they enhance antimicrobial effects. However, there is often a compromise between the antimicrobial and mechanical properties of these agents. For example, the mechanical characteristics of dental materials decrease with the addition of antimicrobial agents [1].

In the recent period, nanomaterials have been widely used as an alternative in dentistry, which make it possible to improve the mechanical characteristics of dental materials. Compared with other types of biomaterials, nanomaterials have excellent antimicrobial activity, which does not have the mechanical characteristics of dental materials.

In 2004, graphene which is one of the most promising nanomaterials was first discovered in Russia. It is a two-dimensional carbonaceous material and serves as the main structural element of graphite. Graphene includes carbon sp2 with a thickness of one atom, located in a hexagonal honeycomb structure. In addition, graphene has a large surface area, as well as high mechanical, electrical and thermal properties [2].

The appearance of graphene and its derivatives has attracted considerable attention to nanomedicine and tissue engineering. The excellent properties of graphene and its derivatives (e.g. biocompatibility, antimicrobial effect, low toxicity and easy chemical functionalization) contributed to their popularity. It is thanks to these properties that graphene and its derivatives are promising for use as restorative materials in dentistry.

2. MATERIALS AND METHODS

When writing the work, scientific literature sourceswere analyzed, which highlight the features of the use of nanomaterials in dental practice, comparative, comparative and analytical methods were used in the analysis of the literature.

3. RESULTS

Biocomposites can be developed with desired properties due to the ability to function or combine with other biomaterials (e.g. polymer, ceramics and metal). For example, dental materials have been modified with graphene and its derivatives through colloidal dispersion, direct synthesis, sintering and conjugation. However, before the modification process, it is necessary to take into account the current state of the matrix of dental materials to ensure that graphene and its derivatives are well dispersed and functionalized in the selected matrix.

In recent years, several studies have studied the antimicrobial effect of graphene-based nanomaterials on dental pathogens. For example, they have been reported to exhibit strong antimicrobial and anti-adhesive activity against bacteria and fungi. The antimicrobial mechanism of these materials includes physical and chemical effects. The mechanism of activity mainly kills pathogens due to the sharp edges of graphene nanomaterials, wrapping and trapping bacterial membranes with the help of nanosheets and the production of reactive oxygen species [3]. Understanding the basic antimicrobial mechanisms of the materials under consideration can contribute to the development of next-generation dental materials resistant to microbial infections.

Knowledge about the mechanism underlying the antimicrobial activity of graphene nanomaterials is currently limited due to its complexity. The antimicrobial mechanism of graphene and its derivatives may vary depending on their physical and chemical properties. Recent discoveries have shown that the physical and chemical properties of graphene nanomaterials, such as surface functionality, morphology, flake size and concentration, play a vital role in their antimicrobial activity [4].

Zen Graphene Solutions Ltd. (engaged in the use of graphene) proposed a development that uses GO and Ag nanoparticles as an effective viricide that can destroy earlier strains of coronavirus by applying N95 masks and other tissues to advanced workers [5].

The company, known as "G6 Materials", is working on the development of an air filtration system using graphene, which can be used in offices and warehouses to destroy viruses [6]. Another technology using self-sterilizable laser-induced graphene (LIG) has been developed for water filters that eliminate viruses and bacteria in the water, and the same can be used in masks and heating or air conditioning systems to filter the air to reduce the risk of COVID-19 [7].

Another group of authors suggested that graphene nanomaterials could target hepatitis C virus (HCV) RNA to block HCV gene replication. They exhibit antiviral properties due to their distinctive single-layer configuration, sharp edges and negatively charged surfaces, whereas graphite and graphite oxide exhibit negligible antiviral activity. Thus, it can be concluded that the presence of various surface functional groups, the structure of the nanosheet and sharp edges are all important features demonstrating antiviral properties [8]. This is an important area of research and an urgent need for the current scenario of studying and developing effective antiviral coatings in dentistry that can disrupt and hinder the transmission of these infectious viruses [9].

The mechanisms by which graphene nanomaterials cause the inhibition and death of microbes depend not only on their internal and external factors, but also depend on the components and structure of microbial cells and the stage of maturity. There is also a consensus among researchers that the structure of bacteria can affect the activity of antimicrobial agents.

It has also been reported that gram-positive bacteria are more susceptible to graven nanomaterials than gram-negative bacteria. The higher susceptibility of gram-positive bacteria compared to gram-negative ones was strongly influenced by the structure of their cell wall. Bacterial cells consisting of a polymer known as peptidoglycan (PG). Gram-positive bacteria have a thick PG layer, whereas gram-negative bacteria have a thin PG layer. The PG layer protects bacterial cells from changes in osmotic pressure and the effects of small molecules.

In addition, the PG layer serves as a chelating agent due to its adhesive surface proteins (for example, teichoic acids and adhesives). The PG layer of gram-positive bacteria is attached to their surface using tightly functionalized anionic glycopolymers - teichoic acid (WTA) and lipoteichoic acid (LTA). Researchers have suggested that gram-positive bacteria interact with carbon nanomaterials through electrostatic or hydrogen bonds [5].

The reaction of graphene nanomaterials to WTA, lipids and amino acids can cause morphological deformations. These morphological deformations include heterogeneous thickening of the PG cell wall, an increase in cell size, and deficiencies in the location and number of partitions. The change in WTA also causes cell growth retardation and agglomeration of cells in solution.

Unlike gram-positive bacteria, gram-negative bacteria interacted with the nanomaterial only through direct physical contact. Gram-negative bacteria present an outer membrane necessary for their protection in an aggressive environment (for example, in the presence of antibiotics). This outer membrane increases the resistance of bacteria to antibacterial activity. Also, due to this outer membrane, gram-negative bacteria have lower antibacterial activity than gram-positive bacteria.

Most studies of the antimicrobial properties of graphene nanomaterials in relation to a wide range of microbes suggest that the antimicrobial activity of this material can be explained by the following three possible mechanisms:

1) stress of the cell wall (physical cutting, the effect of "NanoKnife " (Irreversible electroporation), the introduction of the membrane, and the extraction of membrane components);
2) environmental isolation (wrapping effect);
3) oxidative stress. These mechanisms coincided in most experimental conditions and caused a deadly effect. Nevertheless, the mechanisms underlying the antimicrobial activity of graphene nanomaterials may differ depending on their application.

Graphene nanomaterials also exhibit broad-spectrum antimicrobial action against phytopathogenic fungi and bacteria. Antifungal research has shown that the sharp edges of the nanomaterials in question can pierce bacterial cells, which leads to stress of the plasma membrane. After processing graphene nanomaterials with nanosheets, the apical cells of conidia swelled and stopped growing, although some of them remained intact. Consequently, nanosheets stopped germination and reduced the viability of conidia. Graphene nanomaterials also disrupted the germination cycle, since spores cannot germinate into mature mycelium to initiate an infection cycle [6].

The wrapping mechanism is the second mechanism that suppresses the activity of bacteria. This mechanism is related to the physical factors of graphene nanomaterials. An antibacterial study of graphene and nanosheets in suspension assays has shown that the packaging mechanism can also cause damage to bacterial cells. Nanosheets of graphene materials wrap bacterial cells and isolate them from the environment, thereby preventing the reproduction of bacteria. This mechanical disturbance can destroy bacterial cells due to electrostatic force, causing a change in membrane potential, depolarization and violation of the integrity of bacterial cell membranes. These cellular changes later lead to osmotic imbalance, disruption of cellular respiration, cell lysis and, as a consequence, cell death.

Oxidative stress is the third mechanism for suppressing bacterial activity. Unlike the wrapping mechanism, oxidative stress is associated with the physicochemical properties of graphene nanomaterials. This mechanism involves the oxidation of fatty acids by lipid peroxides formed by ROS. Lipid peroxides accelerate the chain reaction, cause cell lysis and produce a large number of ROS traces. In bacterial cells, the reduction of molecular oxygen to water occurs through a series of proton-electron transfer reactions, in which adenosine triphosphate (ATP) is subsequently synthesized. However, the presence of superoxide anion and other oxygen-containing radicals, interrupts the formation of water molecules, producing traces of ROS in the mitochondria of the cell. These traces of ROS damage ribonucleic acid (RNA) and DNA.

In addition, traces of ROS disrupt the ability of bacterial cells to maintain their normal physiologically regulated redox function, thereby destroying the integrity of the bacterial cell membrane. Disruption of the bacterial cell membrane through chemical oxidation leads to cell cleavage and the formation of ROS traces, which ultimately cause cell death [7].

4. DISCUSSION

Graphene nanomaterials are successfully used as an alternative material in biomedicine, dentistry and implantology. Basically, these materials are used as an anticorrosive coating and antimicrobial agent. In addition, graphene nanomaterials are used for the delivery of drugs and therapeutic agents.

The use of graphene nanomaterials and composites with nanoparticles as dental restoration materials is being intensively studied at the present time. Studies have shown that some aspects of the physical and mechanical properties of dental ceramics, dental adhesive and dental resin have been significantly improved by graphene nanomaterials. However, less is known about the biological effects (for example, antimicrobial and antibiotic) of graphene nanomaterials on dental restoration materials.

An in vitro study showed that the inclusion of reduced graphene-silver nanoparticles in ordinary glass ionomer cement (GIC) significantly inhibits the growth of *S. mutans*. The antibacterial effectiveness of GIC improves with an increase in the number of graphene-silver nanoparticles, and its addition in an amount of about 2.00 wt.% showed excellent antibacterial activity without compromising their mechanical properties. To preserve the aesthetic quality of GIC, white fluorinated graphene (FG) was synthesized and added to conventional GIC to create a composite with a significant improvement in mechanical, physico-chemical and antibacterial properties. GIC/FG composites showed excellent performance in inhibiting *S. mutans* and *S. aureus* with an efficiency that was almost twice that of pure GIC.

The inclusion of graphene nanomaterials in dental fillings inhibits the growth of antimicrobials and prevents the formation of biofilms. The researchers pointed out that in addition to dental fillings, graphene nanoplates are also used as a filler for conventional polymer dental adhesive. The inclusion of this nanomaterial as a filler in dental adhesives significantly inhibited the adhesion and growth of *S. mutans*, while maintaining the same viscosity as conventional ones [8].

Graphene-based nanocomposites not only act as antimicrobial agents, but can also be used as a therapeutic agent to prevent dentin demineralization by coating its surface. A number of researchers have previously successfully synthesized five types of nanocomposites (for example, GO-Ag, GO-CaF_2, GO-Zn, GO-Ca $_3$ (PO 4)$_2$ and GO-Ag-CaF_2) to evaluate the effectiveness of these nanocomposites with respect to bactericidal properties. and anti-demineralization activities. They found that GO-Ag, GO-Ag-CaF_2 and GO-CaF_2 nanocomposites prevent demineralization without changing the color of teeth. In addition, GO-Ag and GO-Ag-CaF_2 inhibited *S. mutans* growth without poisoning of epithelial cells, except for high concentrations (0.1 wt/ volume).

In addition, graphene nanomaterials can be used to cover dentine surfaces. Immersion of the dentin block in a dilute suspension of these nanomaterials successfully coated the dentin surface with several nanometers of film. The combined effect of the film and irradiation in the near infrared (NIR) significantly showed photothermal and bactericidal effects against *S. mutans*, which allowed bacterial sterilization [9].

A recent study has shown that graphene-based nanomaterials not only improve the mechanical properties of polymethylmethacrylate resin for dentures, but also exhibit antimicrobial properties against dental pathogens. It has been suggested that a possible mechanism of effective antibacterial activity of graphene nanomaterials included in the solid matrix is associated with increased hydrophilicity. In particular, a hydrate layer forms on the surface of the composite and creates a tightly bound water layer. Consequently, it has been suggested that the presence of a hydrate layer or energy barrier on the surface is a key mechanism underlying antimicrobial activity that prevents microbial adhesion.

The use of photodynamic therapy (PDT) is more advantageous than sodium hypochlorite in the treatment of root canals, due to its ability to disinfect the root canal while maintaining the stability of dentin. The principle of PDT is based on the use of a non-toxic photosensitizer (FS), such as indocyanine green (ICG), which forms cytotoxic ROS after photoactivation by specific electromagnetic radiation. The researchers proposed to develop conjugated nanomaterials to increase ROS production during photoactivation. Graphene nanomaterials were chosen as a nanocarrier and included in the ICG because of its large specific surface area, which allows efficient functionalization of photosensitizers using various surface functional groups [10].

Bioactive materials have been actively used in endodontics for regeneration, repair and reconstruction. So, some authors conducted a study in which they studied the potential of graphene nanosheets (GNS) (1357 wt.%) to improve two bioactive cements: Biodentine (BIO) and Endocem Zr (ECZ). The results showed that GNS does not affect the pH release profile. The pH release profile plays a crucial role in the bioactivity and antibacterial properties of bioactive cements.

In addition to bioactive materials, the use of metal nanoparticles or metal oxides in dental materials provides a number of advantages, such as improved physical, mechanical, antimicrobial and antibiotic film properties. However, the aggregation of these nanoparticles remains a serious problem. The use of graphene nanomaterials as a matrix in the GO-silver nanocomposite improved the stability and aggregation of silver nanoparticles, which led to a high binding capacity.

In addition, the synergistic antimicrobial activity of silver and graphene nanomaterials made the GO-silver nanocomposite more profitable. Considering these advantages, the researchers successfully synthesized silver nanoparticles on an aqueous matrix of graphene nanomaterials to study their effectiveness against endodontic biofilms.

An ex vivo study on an infected tooth model showed that Ag-GO nanocomposite successfully kills microbes and disrupts biofilm formation. The use of Ag-GO during ultrasonic activation also selectively improved the efficiency of microbial destruction in the lateral channel.

A recent study modified titanium to seal the pulp with antibacterial and dentin-inductive materials through microarc oxidation (MAO) and self-assembling GO with different contents. The introduction of 1.0 mg / ml of GO with titanium-MAO showed excellent cell adhesion, mineralization and antibacterial properties. Moreover, bacterial colonies were practically absent. The bacterial recovery coefficient was 93.25% ± 2.47%, which can be explained by the highest level of ROS associated with a large number of oxygen-containing functional groups.

The researchers carefully studied the possibilities of using graphene nanomaterials in tissue engineering therapy and created frameworks from composites of these materials. Thus, a GO-frame was manufactured, the implantation of which showed high compatibility with tissues and contributed to the healing of holes after tooth extraction and periodontal defects. In addition, the researchers suggested that zinc oxide/carboxylated graphene nanomaterials nanocomposites induce bone regeneration. Moreover, this type of nanomaterials has attracted a lot of attention due to its potential in the delivery of genes and drugs. The ability of graphene nanomaterials to ionically bind to polyethylenimine (PEI) cationic polymers provides other advantages in gene delivery [11].

Graphene nanomaterials are also used in implantology. Titanium has been recognized as the gold standard in implantology due to its high corrosion resistance, durability and good biocompatibility with excellent osseointegration. Despite these advantages, the growth of microbial biofilms in dental implants is the main cause of implant diseases and their failure. Therefore, the development and modification of a titanium implant with good osteogenic, antibacterial and antibacterial properties is of vital importance. For this reason, over the past few years, several surface treatment methods have been developed to improve the antibacterial activity of titanium implants, including nanotechnology with antimicrobial properties (for example, graphene).

Graphene coating is widely used in dentistry and implantology, because it protects the surface of metal biomaterials from corrosion. The anticorrosive properties of graphene nanomaterials allow them to be used in orthodontics, endodontics and prosthetics. Several methods, such as plasma treatment, electrophoretic deposition, have been used to coat a titanium substrate with a material based on graphene nanomaterials. Effective application of titanium coating on an object without changing the basic properties of graphene gives advantages to implants in terms of their durability, osteogenicity and antimicrobial properties.

Numerous studies have been conducted to evaluate the characteristics of graphene nanomaterials as a coating and anticorrosive material to protect implants from aggressive environments. In addition, the addition of graphene nanomaterials improves the mechanical properties of the coating and promotes cell adhesion and proliferation, which is facilitated by hydrophilic functional groups (for example, carboxyl, carbonyl and hydroxyl).

The excellent characteristics of graphene nanomaterials have inspired researchers to explore the possibility of their use in the treatment of peri-implantitis. A recent study has shown that implants coated with graphene-based nanomaterials have good therapeutic effects.

Another recent study showed that titanium surfaces coated with six different graphene nanoplates exhibit different antimicrobial activity against *S. aureus*. Graphene nanoplates were manufactured using various technologies. Comparison of osteogenic and antibacterial properties of uncoated and graphene-coated titanium implants using the dry transfer technique showed a significant decrease in the formation of *S. mutans* and E. faecalis biofilms on the surface of graphene-coated titanium implants. The study also confirmed that the mechanism of inhibition of bacteria and biofilms is mainly due to the properties of the surface, and not the release of diffusing compounds from the surface (i.e. electron transfer).

5. CONCLUSION

The paper considered the features of the use of graphene nanomaterials in dental practice. Antimicrobial properties and mechanisms of such materials were mainly investigated.

The use of graphene nanomaterials in dentistry improves the antimicrobial properties of dental materials without deterioration of their mechanical properties. The mechanism of antimicrobial action is largely determined by various internal (e.g., size, shape, chemical composition of the surface) and external (e.g., electromagnetic radiation, underlying substrate) parameters.

Although the mechanism of antimicrobial action of graphene nanomaterials is still being discussed, many researchers believe that they can potentially be used in dentistry to improve the antimicrobial activity and mechanical properties of dental materials.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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