Antibacterial and bioactive dental restorative materials: Do they really work?

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ABSTRACT: Purpose: This proceedings reviews current antibacterial and bioactive dental materials and new agents in development. Methods: Experts from academia, industry and clinical practice were invited to present, discuss, and work together to develop solutions to the challenge of formulating and applying antibacterial dental materials in a symposium in Seoul, Korea in June, 2016. (Am J Dent 2018;31:3B-5B).

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Introduction

The publication of the symposium proceedings is very timely. The National Institute of Health reports that bacteria growing as a biofilm cause 80% of infections in the body. Biofilms at the margin of an existing restoration give rise to secondary caries (NIH). One approach for overcoming the development of dental biofilms and secondary caries is to develop antibacterial and bioactive dental restorative materials. This proceedings reviewed current dental materials and new agents in development. We invited experts from across academia, industry and clinical practice working together to develop solutions to this challenge.

Bioactive or antibacterial?

The first paper (Chen et al) sets the tone of the proceedings. This current manuscript and others by the same group looked at both bioactive and antibacterial materials. The terms bioactivity and bioactive material both have recently emerged in the dental literature. On the surface, bioactive is defined as having a biological effect. As such, all dental materials fit into that category. The term bioactive material appears to have originated with Dr. Larry Hench, the developer of the calcium silicophosphate glass. Drury et al (in this Special Issue) did touch on the calcium-mediated mineralization or re-mineralization and the fact that particulate MST-Ca(II) complexes exhibit sustained release of calcium, and that release might be customized by conditions of pH and ionic strength. Regrettably, bioactive glass is a topic we hardly explored in this symposium.

On the other hand, an antibacterial is an agent that kills bacteria or stops their growth. The determination of the antibacterial activity is described in international norms. Not all dental materials can be antibacterial.

In the oral cavity, mixed microbial biofilms can accumulate on hard and soft tissue, and are involved in the pathogenesis of caries and periodontitis. A biofilm is an accumulation of bacteria, fungi, or protozoa on solid surfaces. Two popular approaches in dentistry to prevent biofilm formation are: (A) to design a biomaterial that slowly releases an agent that is lethal to approaching bacterial cells; and (B) to develop a non-adhesive surface by modifying the surface chemistry of restoration materials. Various chemical agents can affect bacterial adhesion indirectly by disrupting bacterial cell metabolism. Numerous materials have been impregnated with various antibiotics only to have most of the agent released over a very short time, thus providing no long-term effect. Recent studies have shown that sub-lethal doses of antibiotics can induce bacterial resistance and counteractively actually enhance biofilm formation. The potential negative consequences of bacterial resistance to antibiotics are dire because they put all of society at risk.

The question of whether it is more advantageous to be bioactive or antibacterial probably will never be settled. Usually dental bioactive materials can improve mechanical integrity and offer protective bioactivity e.g. in the form of fluoride release. One must remember that not all bacteria are bad, and to be antibacterial indiscriminately may cause more harm than good.

Bioactive and antibacterial strategies - Metal or non-metal based?

Two papers (in this Special Issue) dealt with development and synthesis of new antibacterial monomers. Both new agents are organic in nature and can be classified as non-metal. MDPD is commercially available and much has been published on MDPD. Fujimura gave us a historical perspective and serves as an excellent blueprint for translation of basic science from laboratory to clinical use.

Wang et al presented a small library of antibacterial dental monomers based on quaternary ammonium salts. Quaternary ammonium polyethyleneimine (QAS-PEI) nanoparticles (NPs) have been incorporated into restorative materials to improve antibacterial activity and further reduce adverse effects on mechanical properties. Incorporation of QAS-PEI NPs into dental resin composites at 1 wt% concentration has been effective against Streptococcus mutans (SM) as well as against biofilm formation in vivo.

However, given the increasing resistance of bacteria to organic antibacterials, metal-based antibacterials are a promising alternative. Our group here at University of Washington took a different approach. We looked at metal-based antibacterials since metal-based antibacterials such as silver and zinc are an attractive alternative to antibiotics. Metal ions have chemical properties that inhibit bacterial growth. The unique binding, coordination, and redox properties make development of bacterial resistance less likely, and predict effectiveness across a broad bacterial spectrum. Unfortunately, development of new metal-based antibacterials has been severely impeded due to previous controversies and fears. If systemic toxicity could be limited and therapeutic indices were optimized, metal ions and their associated compounds could emerge as a new powerful class of antibacterial agents.
The most recent addition to the growing list of metal-based antibacterials are our gold-titanate nanoparticles. Our team has developed micro-particulate metal-titanate complexes as a new class of antibacterial agents. The micro-particulate gold (III)-loaded titanate complexes inhibit growth of oral bacteria at low molar concentrations. We have shown that nano-particulate metal-titanate complexes are even more effective than micro-particulate complexes at inhibiting oral bacteria growth as these nano-particulate complexes have a significantly greater surface-to-volume ratio, resulting in more effective ion-exchange characteristics.

Our current approach is to incorporate the gold-titanate nanoparticles in adhesive systems because of manufacturing availability issues, but in the long term, gold-titanate nanoparticles may also be incorporated into restorative materials as fillers, or as coating on implant systems. Additionally, because these complexes are not organic, degradation is not an issue and thus they can have long-term effectiveness, and also may be less likely than organic antibacterial agents to contribute to bacterial resistance.

Wang et al. and Giannini & Andre (both in this Special Issue) evaluated a few species of bacteria. It will be ideal to analyze a standard microbial mixed culture such as the one developed by Guggenheimg and is considered by the research community as a “model” of dental caries microbial flora.

Applications of antibacterial and bioactive dental restorative materials

Regardless of the types of materials, clinicians would eventually hope to apply the science and technology in real life situations. Based on the discussions in this Issue’s articles, most of the applications seem to be focused on usage as restorative materials, cements, and adhesives (Fig. 1a-d). We will attempt to expand the discussions to root canal sealers and bioactive denture resins. Another important area not to be forgotten is implant coating, especially when usage of implants is on the rise and peri-implantitis is getting more common.

Root canal sealers

Successful endodontic treatment depends on the effectiveness of the cleaning and shaping of the root canal system. Any remaining tissue, bacteria, or debris can contribute to endodontic failure. Elimination of bacteria from the root canal system can be done via chemomechanical debridement and also placement of intracanal medicament for reduction and elimination of any residual bacteria remaining post-instrumentation.

Calcium hydroxide is routinely placed as an inter-appointment intracanal medicament for non-surgical endodontic procedures. Despite efficacy of calcium hydroxide, this medicament has some limitations in its antimicrobial efficacy and due to the fact that certain bacteria can withstand a high pH environment.

Other alternatives to calcium hydroxide have been investigated and used. Examples of historic medicaments are phenolic compounds, essential oils, aldehydes, halogens, and quarternary ammonium compounds. The use of these materials has been discontinued due to their cytotoxicity and limited antimicrobial efficacy. Antibiotics have been and may be used as intracanal medicaments, however they may produce resistant microbes and cause host sensitization. Therefore, their routine use is not recommended. Steroids that have been used as intracanal medicaments can prevent the inflammatory response and subsequent pain. However they have limited antimicrobial efficacy. Due to these reasons, antibiotics and steroids are not routinely placed.

The antimicrobial activity of gold nanoparticles (AuNPs) has been studied in both Gram-positive and Gram-negative bacteria such as Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa. Based on the bacterial protein assay, nano-sized mono-sodium titinate (nanomonosodium titinate) nMST-Au(III) showed the best effectiveness among titanates and gold-titanates to decrease bacterial protein concentrations. A Universit of Washington Master’s thesis study examined the efficacy of gold-titanates on E. faecalis when used in intracanal medicament separately or in addition to calcium hydroxide and compared it with calcium hydroxide alone. Unfortunately, it cannot yet be concluded that gold-titanate nanoparticles have antimicrobial efficacy against Gram-negative E. faecalis, most likely due to insensitivity of culturing technique. The study did find that gold-titanate nanoparticles mixed with sterile water or added to calcium hydroxide leave residual crystals in the canal system, which may occlude the dentin tubules and bacteria (Fig. 2).

Bioactive fillers in denture resin

Much attention has been paid to the development of direct dental materials that are antibacterial. Surface pre-reacted glass-ionomer fillers (S-PRG) are a newly introduced bioactive material and is of high potential interest to address the problem of caries in denture-wearing populations. S-PRG fillers are a novel class of particle that can be incorporated into resinous...
implantitis, which is caused by the same bacterial biofilm formation that also causes caries and periodontal disease. Newer studies are looking at affecting bacterial adherence to implants by modification of the surface topography. Silver nanoparticles have been used on surfaces modified to create a combination of silver, titanium dioxide and hydroxyapatite (HA) nanocoatings. Coated implants were found to have both antibacterial properties and HA biocompatibility and did not seem to be compromised (Fig. 1e). We found this to be very exciting since metal coating for direct restorative material has an inherent problem of discoloration (Fig. 3). Implant as well as root canal sealer applications seem to be more appropriate.

Conclusion

Given the limits of time and resources, we have of necessity left out many topics and experts, and many questions remain unanswered. Our ultimate goal was to initiate a fruitful and rewarding exchange with this proceedings and to motivate ongoing discussion and research.

Disclosure statement: The authors declared no conflict of interest.

Dr. Chan is Professor and Chair, and Dr. Chung is Professor, Department of Restorative Dentistry; Dr. Paranjpe is Associate Professor, Department of Endodontics, University of Washington School of Dentistry, Seattle, Washington, USA.

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Peri-implantitis

The prevalence of peri-implant diseases has been reported in the literature. Peri-implantitis, as defined by Albrektsson & Isidor, was reported from a low of 6.47% to a high frequency of 43% of individual implants. Many factors, such as the lack of standardized criteria for diagnosing peri-implant mucositis and peri-implantitis, the different implant systems used, or the differences in the observation periods may be the causes for the discrepancy in the results.

One of the most common causes of implant failure is peri-implantitis, which is caused by the same bacterial biofilm formation that also causes caries and periodontal disease. Newer studies are looking at affecting bacterial adherence to implants by modification of the surface topography. Silver nanoparticles have been used on surfaces modified to create a combination of silver, titanium dioxide and hydroxyapatite (HA) nanocoatings. Coated implants were found to have both antibacterial properties and HA biocompatibility and did not seem to be compromised (Fig. 1e). We found this to be very exciting since metal coating for direct restorative material has an inherent problem of discoloration (Fig. 3). Implant as well as root canal sealer applications seem to be more appropriate.

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