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Oral homeostasis, kill the microbiome or not?

Abstract

The objective is to short review the current state of the art of dental antimicrobial agents in term of minimal invasive restorative dentistry. An outline of the most important aspects of dental antimicrobial agents was created, and a subsequent literature search for articles related was conducted. The current state of the art of antimicrobial agents includes a variety of species with broad ranges of properties. There is no agreement as to the choice of substances and concentration, however, there is a growing consensus regarding the need to use antimicrobial agents as additions into dental restorative materials' compound in patients with high intensity of active caries disease.

Keywords: glass ionomer, antimicrobial

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Tomasz 'Tomi' Kupka
Unit of Dental Materials Science, Medical University of Silesia in Katowice, Poland

Correspondence: Tomasz 'Tomi' Kupka, Unit of Dental Materials Science of Department of Prosthodontics and Dental Materials Science, School of Dental Medicine, Medical University of Silesia in Katowice. Pl. Akademicki 17. 41-902 Bytom, Poland, Tel +48 32 2827917, Email tkupka@sum.edu.pl

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Objective

The objective is to short review the current state of the art of dental antimicrobial agents in term of minimal invasive restorative dentistry. An outline of the most important aspects of dental antimicrobial agents was created, and a subsequent literature search for articles related was conducted.

Background

Various studies have shown that glass ionomer cements (GICs)[1,2] have potential bioactivity, adhesion to hard tissues and also reduce the formation of plaque by *Streptococcus mutans* strains. [3–12] The antibacterial activity of glass ionomer cements (GIC) is mostly attributed to their fluoride and other ions release for secondary caries inhibiting effect, which has been already confirmed *in vitro* with lower demineralization depths of the glass ionomer groups adjacent to the dental hard tissue.[13–19] Thus, these cements are expected to actively control microbial biofilm formation, while biofilms modulate the release of fluoride from GICs.[20,21] On the other hand, studies have shown that fluoride-releasing activity of GICs is insufficient for effective protection. Moreover, more viscous GICs release substantially less cumulative fluoride ions than less viscous ones, resulting in no microbial balancing attribute *in vivo*.[22–28]

The oldest documented medical use of an antimicrobial agent concerned copper mentioned in the Smith Papyrus; this Egyptian medical text, written between 2600 and 2200 B.C., describes the application of copper to sterilize chest wounds and drinking water. Ancient Egyptians and Greeks also used specific molds and plant extracts to treat infections. Earlier, since the time of the Persian kings, vessels made of Cu and Ag had been intentionally used for water disinfection and food preservation.[29–31]

The first contemporary antimicrobial agent in the world was salvarsan, a remedy for syphilis that was synthesized by Ehrlich in 1910. In 1935, sulfonamides were developed by Domagk and other researchers. In 1928, Fleming discovered penicillin.[32] The idea of using antiseptics to control dental decay was originally suggested by Miller in 1890. In 1893 Naegli observed lethal action of heavy metal ions upon microorganisms and called this phenomenon oligodynamic.[33]

Contemporary concepts

Among contemporary antimicrobials modifying glass ionomers' composition, non-organic, organic – synthetic, with antibiotics and natural, or hybrid agents can be distinguished.

Non-organic antimicrobials

Plenty of non-organic species have been tested, and among them zinc sulphate ($ZnSO_4$), strontium dioxide (SrO_2), barium sulphate ($BaSO_4$), ytterbium fluoride (YbF_3), copper, gold, palladium, platinum, strontium, zinc or silver nanoparticle (nCu, nAu, nPa, nPt, nSr, nZn, nAg), calcium-zinc-silicate, amorphous calcium phosphate nanoparticles (nACP), zinc oxide (ZnO), copper oxide (CuO), sodium hypochlorite (NaClO), copper iodide (CuI), fluoroapatite (FAp), borate glass, hydroxyapatite (HAp), porous nHAp, nanocrystalline calcium deficient hydroxyapatite (nCDHA), titanium dioxide nanoparticles ($nTiO_2$), zirconia dioxide ($nZrO_2$), monosodium gold(III)-titanate nanoparticles (nMST-Au(III)), magnesium carbonate apatite, forsterite nanoparticles (nMg_2SiO_4), amorphous peroxo-titanate (APT), tri-sodium citrate (TSC), sodium hypochlorite (SHC), boric acid (BA), niobium silicate, silver phosphoric zirconium (SPZ), tetrapod-like zinc oxide whisker (T-ZnOw), bioactive glass (BGN), fluorinated graphene (FG) have been intensively evaluated.[34–78]

Organic antimicrobials

Synthetic

On the other hand, lately popular participation of synthetic organic substances like chlorhexidine digluconate, diacetate, dihydrochloride (CHG, CHA, CHHCl), alexidine (ALX), alexidine combined with N-acetylcysteine (NACALX), monomers 12-methacryloyloxydodecylpyridinium bromide (MDPB), quaternary ammonium dimethacrylate (QADM), furanone chloride and bromide (GLC), thymol, chloroxylenol, polyquaternary ammonium salt (PQAS), cetrimide (CT), polyethyleneimine nanoparticles (nPEI), cetylpyridinium chloride (CPC), glutaraldehyde (GA), benzalkonium chloride (BACH), sodium fusidate (SF), triclosane (TRC) and triclosane with zinc citrate complex (TRC-ZnC), furanone (FN), Poly(Acrylic Acid-Co-DCAGAGM) GM-tethered 6-arm star-shaped poly(acrylic acid), 2,2'-bipyridine, 2-dimethylaminoethanol (DMAE-CB), anthocyanin, quaternary ammonium monomer dimethylaminododecyl methacrylate (DMADDM), 2-methacryloxylethyl dodecyl methyl ammonium bromide (MDMAB), dimethyl ammonium chloride (DMAC), octenidine dihydrochloride (OIDC), theobromine (THEO) is observed in many researches.[78–119]

Antibiotics

Also antibiotics have been tested as potential additives to GICs compound, namely metronidazole, ciprofloxacin, cefaclor, minocycline or doxycycline.[120–124]

Natural

Due to the widespread antibiotics resistance in the last decades, natural organic compounds, such as miswak extract (ME), grape seed extract (GSE), ethanolic extract of propolis (EEP), epigallocatechin-3-gallate (EGCG), morphogenetic proteins, cinnamon bark oil (CBO), chitosane (CHT), seashell powder, coumarin (CO) derivatives, collagen, cellulose microfibers and nanocrystals, *azadirachta indica* (neem) or turmeric extracts have been previously tested as possible antimicrobial agents.[125–147]

Some attention was given to the hybrid version of antimicrobial agents, i.e. casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), chlorhexidine–hexametaphosphate nanoparticles (nCHX–HMP), chlorhexidine-bioactive glass, chitosan/chlorhexidine-cetrimide, chitosane-titanium dioxide nanoparticles CHT-nTiO_2, chlorhexidine-encapsulated mesoporous silica nanoparticles, 12-methacryloyloxydodecylpyridinium bromide (MDPB)-nAg.[148–163] Cariostatic effect of GIC is still questionable, and it is also claimed that the low pH of GICs during setting reaction may contribute more than the fluoride leached to their antibacterial properties and that no antibacterial activity is exhibited after setting,[164–167] thus, the ability of GICs to ions exchange might lead to the hypothesis that GICs could potentially be used as carrier systems/delivery matrix for other active components, e.g. antimicrobial agents[168, 169] in term of caries balancing, microbiome colonization inhibition.

The prevalence of caries and the increase in drug resistance in the pathogenic microbiome at an alarming rate is a matter of serious concern. Therefore, there is a pressing demand to discover novel holistic strategies and identify new solutions, taking into account dental restorative materials. Changes in oral ecosystem may induce shifts of biofilm microflora towards pathologies of teeth hard tissues, gingiva and bone. The caries disease still remains a major systemic health problem in humans.

The caries cavity is an adverse effect of homeostasis confusion towards demineralization and proteolysis; remineralization through restoration may level this pathology with GICs – biomimetic materials of the first choice in an active form. Possibly the modification of GIC – a 'Grandbiomaterial Inactivating Caries' with microbial inhibiting agents[170–172] would help to solve the holistic problem in high intensity active caries disease patients and be a step ahead in minimal invasive dentistry, taking into consideration equivalent dietary, behavioral, hygiene and prophylaxis aspects.

Conclusion

There is no agreement as to the choice of substances and concentration, however, there is a growing consensus regarding the need to use antimicrobial agents as additions into dental restorative materials' compound in patients with high intensity of active caries disease.

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None

Conflicts of interest

The author declares there are no conflicts of interest.

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