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Salvatore

ARE UNIVERSAL/MULTIMODE ADHESIVE SYSTEMS "OLD WINES IN NEW BOTTLES" OR THEY CAN POTENTIALLY ACHIEVE BETTER CLINICAL LONGEVITY? (Fabrício Mezzomo Collares)

For many years, adhesives systems have been classified into "generations" in order to systematize the different components (e.g. etchant, primer, and adhesive) of all classes of products. However, the use of such a classification, which is based on adhesive generations, cannot be universally accepted. Moreover, since a great number of new materials are created every year, this type of classification has become rather clumsy and confusing. Therefore, nowadays contemporary adhesives are currently classified based on their mode of interaction with dental hard tissues as either etch-and-rinse (ERAs) or self-etch adhesives (SEAs). ERAs require complete removal of smear layer and complete demineralization of superficial dentin by phosphoric acid etching, which is then rinsed, followed by the application of a resin primer, and adhesive (three-step systems) or by a single-bottle self-priming agent (two-step systems). Conversely, self-etching adhesives only partially remove the smear layer and expose a very thin layer of demineralized collagen. This is achieved through the use of acidic methacrylate primers containing phosphate or carboxylic functional monomers, such as glycerophosphate dimethacrylate, 10-methacryloxydecyl-dihydrogen-phosphate or 4-methacryloxyethyl-trimellitic-acid. After allowing the primer to etch for 10–20 s, the primed dentin is not rinsed with water, but the 10-15% water in the primer is evaporated with air, and is then covered with an more hydrophobic adhesive and light-cured (two-step systems). The one-bottle, all-in-one adhesives involve application of 1–3 layers of adhesive that contains acidic-methacrylates, hydrophilic monomers such as HEMA and some cross-linking di-methacrylates such as UDMA, TEGDMA etc. (all-in-one single-step systems). Recently, a "new type" of adhesive known as universal, multipurpose and multimode system has been introduced to be applied using different bonding strategies such as etch-and-rinse, self-etch, or selective enamel-etch. However, such a system is essentially a one-step self-etch adhesive, that may be associated with a phosphoric acid etching step. However, one of

the main apprehensions of previous generation of simplified single bottle self-etch systems may be associated to their bonding performance due to uncontrolled water sorption and degradation over a period relatedly short. As universal adhesives represent one type of one-step self-etch adhesives, the durability and stability of bonded interfaces created by these new adhesives continue to be questionable. However, together with several collaborators, we have been performing different tests on such adhesives and it was observed an overall improvement of their bonding performance over time probably due to their specific formulation. Indeed, our in vitro studies (unpublished results) have demonstrated that when such systems were applied in self-etching or enamel-selective etching mode, the results are comparable to the gold-standard multi-step self-etching adhesive in terms of durability after different ageing periods. Conversely, when such modern universal adhesives are applied in etch-and-rinse mode in dentin, they were still affected by sever degradation over time; in this case multi-steps systems still perform much better and remain the main choice for such a bonding strategy. Thus, to the question "can universal adhesives be considered old wine in a new bottle" my humble opinion is: no, they are not. In my opinion, there is still much more to investigate about this adhesive and about their clinical performance over long periods of time.

WHAT IS THE STATE OF THE ART OF BIOACTIVE RESTORATIVE MATERIALS? HOW LONG WILL WE HAVE TO WAIT FOR A CLINICALLY RELIABLE MATERIAL? (Fabrício Mezzomo Collares)

Unfortunately, current marked restorative materials and adhesives have no therapeutic ability to remineralize poorly resin-infiltrated hybrid layers and caries-affected dentin underneath the hybrid layers. The bonding interfaces in such circumstances are characterized by poor durability/integrity during aging or in vivo performance. However, self-adhesive GIC and RMGIC can bond to dentin both micromechanically and chemically, liberate and recharge fluoride ions and induce mineral precipitation at the bonded interface, in particular when applied after air-abrasion performed with bioactive glasses. Through some similar mechanisms, also Giomers and resin composites containing GIC technology and modified calcium phosphates (e.g. ACTIVA Restorative, Pulpdent, USA) can also induce mineral precipitation at the bonded interface and release/recharge fluoride, at some extent; adhesive systems are however required when using such materials. Conversely, pure calcium silicate cements and hybrid ones (Theracal, BISCO co. USA), which may be used as dentin replacement materials or as pulp-protection systems, can cause a caustic degradation of collagen fibrils due to their high alkaline pH with successive deposition of calcium carbonates or apatite-like crystals when immersed in phosphate-rich solutions (i.e. body fluids such as saliva and blood).

I am not sure how long we have wait to have specific bioactive materials available in the marked. However, I can firmly affirm that it is time for academic dental researchers and dental industry leaders to cooperate more closely in the development of "smart" bioactive materials that can easily be used in dental practice, rather than keep attempting to improve the formulation of "passive" adhesive systems and restorative materials, which can actually be characterized by toxicological effects induced by elution of especially in case of luck of polymerization caused by inappropriate light-curing procedures. Hopefully in the near future, composites and/or adhesive systems will be developed that can backfill any regions of the hybrid layer that do not fill with resin, with apatite crystallites so that resin-dentin bonds will be self-mineralizable under such conditions and last as long as resin-enamel bonds.

DO YOU BELIEVE THAT INNOVATIVE REMINERALIZING ADHESIVE MATERIALS CAN COMPENSATE FOR THE DEMINERALIZATION PROMOTED BY PHOSPHORIC ACID? (Marcelo Giannini)

The use of phosphoric acid in etch-and-rinse bonding procedures, as well as when self-etching adhesives are used, removes smear layers and demineralizes at different extent the underlying dentin. The results is a the exposure and activation of endogenous proteases of dentin matrices metalloproteinases and cathepsins cysteines. However, the 65% of the mineral dissolved by phosphoric acid is replaced by water during rinsing procedures, and resin infiltration does not replace all residual water; that water entrapped within the hybrid layer will fuel degradation within the poorly-infiltrated collagen fibrils. Indeed, resin infiltration of water-saturated dentin matrices is not uniform, especially after selective caries removal, where thick layers of caries-affected dentin are usually left inside the cavity. Some areas of hybrid layers are well infiltrated and exhibit little residual water, while adjacent regions are not properly infiltrated and may contain very little resin, but 30–40% residual water. It is thought that the resin-sparse, water-rich zones in resin- bonded interfaces degrade over 1 to 2 years. Their stiffness is so low that they may undergo excessive cyclic strain under normal function leading to fatigue failure. Clinicians have only one chance for resin infiltration. If the average resin–dentin bond contains 35–55% residual water instead of resin, only one "corrective" strategy can be applied to solve that problem. The residual water must be slowly displaced by filling these water-filled voids with nano-sized crystals of apatite generated by smart ion-releasing materials and/or biomimetic remineralizing bonding approaches. Remineralization is a form of dehydration which removes free water so that activated MMPs cannot function. Such "back-filling" of water-filled voids will not occur in well resin-infiltrated portions of hybrid layers because they contain no residual water, but polymerized resin monomers. The remineralizing back-fill can even

fill water-trees with apatite crystals. Unfortunately, current marked aesthetic composite materials have no ability to remineralize poorly resin-infiltrated hybrid layers and caries-affected dentin underneath the hybrid layers. Such interfaces are characterized by poor durability/integrity during aging or in vivo performance. Reliable remineralization of completely demineralized collagen fibrils should be characterized by intrafibrillar and extrafibrillar mineral deposition with hydroxyapatite crystals orientated in the same direction as those in sound dentin. Innovative bioactive/biomimetic strategies that lead to remineralization of hybrid layers have been demonstrated to be able to restore the modulus of elasticity of mineral-depleted dental collagen structures within bonding interfaces to sound values.

DO YOU THINK NEW "SMART" RESTORATIVE MATERIALS COULD IMPROVE THE CHANCES OF SUCCESS OF THE TREATMENT OF DENTAL CARIES?
(Fabrício Mezzomo Collares)

Composite currently available on the market have minimal, if any beneficial effect on biofilms. This situation does not surprise me as none of the constituents of such resin composites present antibacterial and/or bacteriostatic effects against oral bacteria.

Some restorative materials such as giomers, compomers, GIC and RMGIC have been designed to release fluoride, nevertheless their amount of fluoride released over time has been demonstrated not totally appropriate to inhibit a significant bacterial growth. Moreover, it has been suggested that fluoride antibacterial effect cannot last long and mostly lost after 24 h. However, I am very positive on this aspect. Indeed, innovative "smart" materials should also possess antibacterial properties to combat remaining microorganisms in the bonding substrate, and reduce the risk for secondary caries at the tooth-restoration interface especially upon formation of gaps. Moreover, the use of bioactive materials with antibacterial properties would also provide an additional treatment by suppressing residual infection and increase the survival of the restored tooth especially in minimally invasive approaches. The use of such materials in deep dentin would also lead to the formation of reparative dentin along those walls of the pulp chamber in proximity of the lesion, and to a process of hypermineralisation underneath the front of demineralization of the caries lesion, which may impede the invasion of bacteria and the progression of the lesion toward the pulp.

Several antibacterial agents have been incorporated into restorative materials by researchers to induce antibacterial action. Moreover, there is a particular interest in releasing or slow-releasing low molecular weight antibacterial agents, including ions such zinc, silver or antibiotics, iodine, and chlorhexidine. A further class of agents used in resin-based materials are those with immobilizing properties (quaternary ammonium or phosphonium salts or polyethylenimine nanoparticles) as these have the advantage of long-lasting antibacterial properties, although these may lack of robust and large spectrum antibacterial action. Silver-based compounds are also well known antibacterial agents that can have a large spectrum of action but without developing bacterial resistant strains. However, innovative dental composites incorporating quaternary ammonium dimethacrylate (QADM) and silver nanoparticles have been already tested demonstrating a suitable inhibition of Streptococcus mutans. It is important to say that the ultimate aim is the generation of innovative composite with antibacterial and regenerative properties. Indeed, calcium phosphate nanoparticles have been incorporated into several experimental composites in combination with QADM and silver nanoparticles

(AgNP) in order to achieve materials able to induce a regenerative and antibacterial response. Fluoride-doped bioactive glass, as well as new sol-gel derived Ag-doped bioactive glass have been also formulated to be used as fillers for new restorative materials with enhanced remineralization, regenerative and bactericidal properties.

WHAT ARE THE PERSPECTIVES FOR THE MINIMAL INVASIVE DENTISTRY?

(Fabrício Mezzomo Collares)

Minimal invasive concepts applied to modern restorative dentistry require from dental practitioners, not only scientifically supported rationales for caries removal/excavation to guide the extent of cavity preparation, but also a deep understanding of the clinical situations. This requires biologically active materials to optimize tissue mineral recovery resulting in a biomechanically stable and durable restoration. These clinical situations start with replacing diseased/lost tissue with adhesive materials but also happen at microscopic/ultramicroscopic levels, when, for instance etching procedures are used to catalyze the adhesion mechanisms between the tooth and the dental material. Thus, contemporary intervention approaches should not only focus on the removal of the diseased tissues and replacement by a biocompatible material, but also on the use of "therapeutic" bio-interactive materials, able to reduce the susceptibility of tooth minerals to dissolution and/or able to recover the mechanical properties via remineralization, in case the disease process has progressed.

Caries removal rationale has been recently reviewed and discussed and essentially, dentists are still prompted to excavate lesions when a mechanically resistant tooth restoration complex is needed to restore the patient's function and/or aesthetics. The traditional management approach has been for many years the total removal of the entire carious tissue, in the particular belief that this would stop the caries process, and after that to restore cavity with a conventional restorative dental material. Over the last 30 years though, better understanding of the caries process and clinical trial evidence on carious

tissue removal methods have supported contemporary alternatives of "Prevention of Extension" rather than "Extension for Prevention". For this reason, it is known that after the minimal excavation of caries lesions, just about to achieve good support and bonding substrate, it is likely that the residual dentin will be a combination of sound/sclerotic dentin on the periphery and affected/demineralized dentin at the bottom of the cavity. Although conventional adhesives may achieve lower bond strengths when applied onto such demineralized dentin, the actual values are still quite in the safe standards for dental adhesion. Different caries removal methods result is different dentin substrates and morphology of the residual dentin. In general, chemo-mechanical caries removal reaches a good compromise between soft/infected caries removal and "adhesive friendly" substrate for further restoration. The use of conventional ion-releasing dental materials such as glass ionomer cements (GICs) seems to provide mineral gain in carious dentin, while by using of experimental biomimetic remineralizing adhesive materials it is possible to induce intrafibrillar mineralization of collagen. Therefore, I believe that in the future, innovative materials based on a biomimetic strategy for remineralization will be able to reinstate the mechanical properties of the demineralized dentin, as specific Ca/P compounds such as amorphous calcium phosphate can fill the nanometric size gap regions within the collagen fibrils.

DURING YOUR ACADEMIC AND SCIENTIFIC FORMATION, YOU HAVE WORKED IN DIFFERENT LABORATORIES, SUCH AS IN ITALY, ENGLAND AND THE USA. WHAT IS THE IMPORTANCE OF THESE EXPERIENCES IN YOUR CURRENT PROFESSIONAL PRACTICE? (Marcelo Giannini**)**

Firstly, I would like to say that I will be always extremely grateful to Professor Timothy Watson and Professor Francesco Mannocci (King's College London) and Professor David H. Pashley (Medical College of Georgia) for all they have done for many during my PhD and Post-doc work. It has been such a great pleasure and honor for me to work with extraordinary people like them and it has been a privilege to learn from them

not only about dental research, but in particular about life in and out the laboratory environment. I take this opportunity to show my heartfelt appreciation for their contribution to my life and career. All the time spent in the lab with them and all the things they taught me helped set a clear direction for me to follow in my research and academic activity.

Today, as I looked back at how my dreams have materialized into reality, they stand clearly in my mind. They patiently listened to my challenges, understood them and motivated me to push harder in life. It is because of those times that I have become responsible, professional, committed and successful, in my career. There is nothing I can do to repay them adequately for their contribution to my life. I promise to always cherish their lessons, and hopefully one day be as inspirational others as they were to me.

Based on these amazing opportunities I had my scientific and academic formation, I strongly suggest to all those PhD and post-doc students to take the challenge to work and study in laboratories and schools in different countries available around the world, as it will not make you a better researcher, but more importantly it will open your minds and make you all much better people, in general. Do it as soon as possible, and enjoy such a terrific ride. Good luck and have fun, life is an extraordinary journey!!!

OTHER INTERVIEWERS

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- DDS from the Universidade Federal do Rio Grande do Sul.
- Master and PhD in Dentistry from the Universidade Federal do Rio Grande do Sul.
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