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Remineralizing Agents: Minimal Invasive Therapy A Review

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Abstract: *The aim of modern dentistry is to manage the non-carious lesion non –invasively through remineralizationia an attempt to prevent disease progression & improve form, function, strength & esthetics of teeth. Remineralizing agents treat the demineralization by minimal invasive Technique. Demineralization of enamel occurs due to various causes. Various remineralizing agents are available to reverse the tooth demineralization into demineralization.The aim of this paper is to review the contemporary remineralizing agents available for remineralization & their implementation in clinical practice. Discussed about Indication of reminerlizing agents, Ideal requirement of remineralizing agents & various remineralizing agents i.e. CPP-ACPF, NovaMin & ß-tricalcium phosphate.*

Key Words*: Demineralization, Remineralization, CPP-ACPF, NovaMin & ß-tricalcium phosphate.*

I. Introduction

Critical pH

Under normal physiological conditions (pH 7), saliva is supersaturated with calcium and phosphate ions, making caries progress slow. However, as the bacteria in the biofilm continue to produce acid with sugar consumption, plaque pH falls to 4.5-5.5. This shifts the driving force within the tooth to mineral dissolution. As the pH is lowered, the saturation point of the minerals in the surrounding fluid is changed. The lower the pH, the higher the concentrations of calcium and phosphate required to reach saturation with respect to hydroxyapatite. This is called the "critical pH", the point where equilibrium exists. The critical pH of hydroxyapatite is around 5.5 below critical pH, demineralization occurs while above critical pH, remineralization occurs.(6)

Demineralization

Oral bacteria excrete acid after consuming sugar, leading to demineralization. Upon this acid challenge, the hydroxyapatite crystals are dissolved from the subsurface.(6)

Remineralization

Remineralization is the natural repair process for non-cavitated lesions. It relies on calcium and phosphate ions, assisted by fluoride, to rebuild a new surface on the existing crystal remnants in the subsurface. The remineralized crystals are less acid soluble than the original ones.(6)

The requirements of an ideal remineralization material are as follows (6)

• Must diffuse into the subsurface or deliver calcium and phosphate into the subsurface
• Does not deliver an excess of calcium
• Does not favor calculus formation
• Works at an acidic pH
• Works in xerostomic patients
• Boosts the remineralizing properties of saliva
• Shows a benefit over fluoride

Various remineralizing Agents (22,6)

- Fluoride
- CPP-ACP
- Xylitol
- Bioactive Glass
- Tricalcium phosphate
- Ozone
- Recaldent **(**CPP-ACP**)**
- NovaMin
- Tri-Calcium Phosphate **(**TCP**)**

- Chewing gums [1]

Indication

- Caries –high risk pt
- Dental erosion- gastric reflex or other disorder- 50% increase in consumption of soft drink[15,19]
- Orthodontic pt
- WSL[17]
- Bleaching—(60 % sensitivity due to peroxide ,demineralization due to 10% carbamide peroxide)[16,23]
- Dentin hypersensitivity -1-74% population affected[17,20,21]
- Micro abrasion
- 1st **ICNARA conference** (International conference On Novel Anticaries & Remineralizing Agents) was held in Chile in Jan 2008.[5]

Objectives

- 1) summarize current state of research on antibacterial & remineralizing agents
- 2) Assess presentation & data included therein
- 3) Document a research agenda for future based upon discussions & presentation of meetings.

Topics Covered in ICNARA-I

- 1) Biofilm
- 2) CPP/ACP
- 3) Xylitol
- 4) Ca/Na/ Phosphosilicate
- 5) Probiotics
- 6) Antimicrobial peptides
- 7) Naturally occuring Antibacterials
- 8) Implementation of new Remineralizing technologies
- 9) Dental erosion.
- In Jan 2012 2nd conference (ICNARA-2) provided an update on science[5]

Objectives

- 1a) To explore further state of knowledge on caries antibacterials (anticaries) & remineralizing agents.
- 1b) provide a forced for discussion of new & underutilized technologies & data
- 1c) provide a shared multidisciplinary research agenda for next decade topics presented.
- 1d) Biofilm management
- 2) New remineralizing agents
- 3) CPP/ACP
- 4) Slow release technologies
- 5) Nanotechnology
- 6) Probiotics
- 7) Targeted Antibacterials
- 8) Oral microbials
- 9) Lasers & Antibacterial action
- 10) Computational biology
- 11) Xylitol
- 12) polylos
- 13) Genomic analyses

CPP-ACP & CPP-ACPF

Casein phosphopeptides (CPPs) are phosphorylated casein-derived peptides produced by proteolytic digestion of as1-, as2-, and ß-casein in vitro or in the digestive tract. CPPs, containing the sequence Ser(P)-Ser(P)-Ser- (P)-Glu-Glu, stabilize nanoclusters of amorphous calcium phosphate (ACP) in metastable solution.Casein Phosphopeptide–Amorphous Calcium Phosphate (CPP–ACP), (Tooth Mousse, GC India) was introduced as a RML agent in the year 1998. It contains nanocomplexes of milk protein CPP with ACP.[8] CPP–ACP is available as a professional dental product (GC Tooth Mousse; GC Corporation, Tokyo, Japan). GC Tooth Mousse containing 0.09% fluoride is available as a CPP–ACPF paste (GC Tooth Mousse Plus; GC Corporation, Tokyo, Japan). CPP–ACPF has been reported to have a greater potential for remineralization than CPP–ACP.[31] In liquid milk the majority of the casein and calcium and phosphate ions are bound in micelles and then upon consumption would not necessarily be available to promote enamel remineralisation. Milk could not be used as a natural product against dental caries, because it needs the addition of 2.0–5.0 g CPP-ACP to substantially increases its ability to remineralise enamel subsurface lesions, a commercial paste containing CPP-ACP showing a remineralization effect on early enamel lesions is investigated.[3,4] CPP-ACPF due to its added fluoride content has shown improved ability to remineralize initial caries.[14] Recent laboratory studies have

shown that calcium-containing compounds can prevent dental erosion. CPP-ACP complex provides optimal concentrations of calcium and phosphate ions for enhancement of enamel remineralization. Tooth mousse (™) is a water-based sugar-free cream that contains CPP-ACP. *In vitro* studies have demonstrated that CPP-ACP can be absorbed by the salivary pellicle and dental plaque. Thus, a calcium-rich reservoir is formed that can facilitate remineralization.[15] When placed on the surface of tooth CPP-ACP interact with hydrogen ions and form calcium hydrogen phosphate which releases calcium and phosphate ions, thus aid in remineralization.[44]

Novamin

Another group of mineralizing materials are bioactive glasses, though to date they have been mainly used in bone mineralization. These materials are capable of bonding chemically to bone and their components are oxides of calcium, sodium, phosphorus and silica in ratios that impart bioactivity. *In vivo*, these glasses are able to form a layer of hydroxyapatite on their surface as a first step in becoming fully incorporated into the human body. One commercial bioactive glass that has been used in the treatment of the dentinal hypersensitivity is NovaMin™, a material which was originally developed as a bone regeneration material. NovaMin™ is a ceramic material consisting of amorphous sodium- calcium-phosphosilicate which is highly reactive in water, and as a fine particle size(<20 micron) powder can physically occlude dentinal tubules. In the aqueous environment of the tooth, sodium ions from the NovaMin™ particles rapidly exchange with hydrogen cations (in the form of H3O+). This leads to release of calcium and phosphate (PO43–) ions from the material. A localized, transient increase in pH occurs during the initial exposure of the material due to the release of sodium. This increase in pH helps to precipitate the extra calcium and phosphate ions provided by the NovaMin™ particles to form a precipitated calcium phosphate layer. As these reactions continue, this layer crystallizes into hydroxycarbonate apatite which is chemically and structurally equivalent to naturally occurring biological apatite. The combination of the residual NovaMin™ particles and the newly formed hydroxycarbonate apatite layer physically occludes the dentinal tubules.[2] As the particles' reaction continues and deposition of calcium phosphate complex takes place, this layer crystalizes into a calcium hydroxyl apatite, also known as hydroxyl carbonate apatite. Likowski et al. indicated that 2.5% and 7.0% w/w bioglass® containing dentifrices could significantly reduce the patient's pain and sensitivity against stimuli through their daily use. Antibacterial effect of NovaMin tooth paste has been documented against several periodontal pathogens. Sodium Ion is released for several days providing a long term re-mineralization potential. Sodium Ion is released for several days providing a long term re-mineralization potential.[7]

Recently, a new prophylaxis paste (Nupro_Sensodyne_, DENTSPLY Professional) has been brought to the market that contains 15% of a calcium sodium phosphosilicate (CSPS). CSPS is an inorganic amorphous material that was designed based on a class of materials known as bioactive glasses and marketed under the trade name NovaMin® (Glaxo Smith Kline, London, UK). NovaMin® was originally developed as a bone regenerative material and recently has been engineered for oral care applications. The material has shown in vitro (Parkinson & Earl 2009) and in situ (West et al. 2011) to occlude dentine tubules, and is hypothesized to form a mechanically strong hydroxyapatite-like layer on the dentine surface, which can resist degradation by repeated acid challenges (Burwell et al. 2011, Earl et al. 2011).[8,11] Recently, a bioactive glass (NovaMin®, developed by NovaMin™ Technology Inc, Alachua, FL, USA) based on the original 45S5 Bioglass® (US Biomaterials Corp., Jacksonville, FL, USA) composition has been incorporated as a remineralising ingredient in dentifrice formulations for treating dentinal hyprsensitivity.[17] The combination of the residual calcium sodium phosphosilicate particles and the HCA layer results in the physical occlusion of dentinal tubules, which will relieve hypersensitivity.[20]

45s5 Bioglass

45S5 bioglass (BG), originally developed by Hench et al. consists of 45% SiO2, 24.5% Na2O, 24.5% CaO and 6% P2O5 in weight. It is a highly biocompatible material possessing remarkable osteoconductivity, osteoinductivity and controllable biodegradability. In aqueous media, this material is capable of forming hydroxycarbonate apatite that resembles biological mineral, and thus was widely used in bone regeneration and tissue engineering.18 Specializing for dental application, the commercial products derived from 45S5 bioglass include PerioGlas (NovaBone Osteobiologics, Jacksonville, FL, USA) and NovaMin (NovaMin Technology, Alachua, FL, USA). Previous studies suggested that BG can occlude dentine tubules, inhibit dentine demineralization and promote dentine remineralization via interfacial apatite precipitation.19–20 This apatite layer was reported tightly adherent to dentine tubules and resistant to acid and brushing abrasion wear challenge.21 Furthermore, BG has also been shown capable of inhibiting and reversing initial caries progression in enamel.

ß-tricalcium fosphate/ CLINPRO

Clinpro tooth crème (3M ESPE) is a 0.21% w/w sodium fluoride (NaF) anti caries dentifrice that contains 950 ppm fluoride and a functionalized tricalcium phosphate (f-TCP) ingredient. One major advantage of this calcium phosphate system is that it is stable in aqueous environment and also does not affect the fluoride activity added in the dentifrices. Furthermore, it has been suggested that fluoride combination with f-TCP not only provides greater RML in terms of microhardness and fluoride uptake, but also decreases the dose of fluoride required to achieve the same degree of RML[(8)]

Researchers at 3M ESPE, working with leading scientists, developed Clinpro 5000, a 1.1% sodium fluoride anticavity toothpaste coupled with a proprietary formulation of tri-calcium phosphate (TCP). This prescription-strength dentifrice works to optimize the remineralization process, which has been shown to slow and even reverse the progression of pre-carious white lesions[(9)] produced by the solid-state ball milling of beta-tricalcium phosphate and sodium lauryl sulfate. f TCP can prevent calcium from prematurely interacting with ionic fluoride and forming calcium fluoride, thus delivering more fluoride and calcium ions to the enamel surface.6–7 f TCP has been shown to have remineralizing effects in both in vitro and in situ studies.8–10 f TCP has been commercially developed, and is now available as a 950 ppm fluoride toothpaste (Clinpro Tooth Crème; 3M ESPE, Saint Paul, MN, USA)[(10)]. In particular, 3 M ESPE's Clinpro® Tooth Crème (0.21% NaF) and Clinpro® 5000 (1.1% NaF), which contain the TCP ingredient, are two of the newest professional-grade toothpastes commercially available. Inclusion of the functionalized TCP ingredient in NaF formulations has been shown to produce stronger, more acid-resistant mineral relative to fluoride alone in laboratory and clinical evaluations (Karlinsey et al., 2010a, b, c, 2009a, b, 2011a; Amaechi et al., 2012.[(13)] fTCP is produced by milling TCP with sodium lauryl sulfate.Therefore, it could prevent and resolve enamel demineralization during orthodontic treatment.[(18)]

II. Conclusion

Remineralizing agents is one of the treatment modality parts of minimal invasive dentistry. We can treat demineralizad tooth by using various remineralizing agent none surgically & none invasively. Need more research work to fulfill best result? CPP-ACPF, Bioactive glass, NovaMin & Clinpro among this CPP-ACPF is best remineralizing material because it incorporated 900ppm fluoride & stabilize ACP, which is very unstable when used alone. Hence, it helpful for further remineralization in demineralized condition of enamel.

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