(e) ISSN Online: 2321-9599
(p) ISSN Print: 2348-6805

SJIF (Impact factor) 2017= 6.261
Index Copernicus value = 80.90

Review Article

Remineralization - An Evolving Concept: A Review

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ABSTRACT:
Dentin mineral is dissolved by acid produced from the oral bacterial biofilm and the demineralized dentin matrix is further degraded, allowing bacteria to infiltrate the intertubular area. The preservation and stability of dentin collagen may be essential during the remineralization process, because it acts as a scaffold for mineral deposition. It has also been suggested that the presence of an organic matrix may reduce the progression of erosion in dentin. One of the important strategies regarding preventive therapies for root caries is to promote remineralization of demineralised dentin.
Key words: Remineralization, Caries, Hydroxyapatite, Caesin phosphopeptide, Scaffold, Cavitation.

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This article may be cited as: Pannu R, Berwal V. Remineralization - An Evolving Concept: A Review. J Adv Med Dent Scie Res 2017;5(11):60-63.

Access this article online	
Quick Response Code	Website: www.jamdsr.com
	DOI: 10.21276/jamdsr.2017.5.11.15

INTRODUCTION:

Owing to its globally high prevalence, dental caries is a 'pandemic' disease characterized by a high percentage of untreated carious cavities causing pain, discomfort and functional limitations.[1] Dental caries is defined as a microbial disease of the calcified tissue of the teeth, characterized by demineralization of the inorganic portion and destruction of the organic substance of the tooth.[2] Untreated carious cavities, furthermore, has significant impact on the general health of children and on social and economic well-being of communities.[3] Its impact ranges from a minor inconvenience requiring surgical caries removal & restorative treatment to excruciating pain and loss of masticatory function.[4]

The focus on caries has recently shifted to the development of methodologies for the detection of the early stages of caries lesions and the use of non-invasive treatment for these lesions. The non-invasive treatment of early carious lesions by remineralization has the potential to be a major advancement in the clinical management of the disease.

Remineralization is defined as the process whereby calcium and phosphate ions are supplied from a source external to the tooth to promote ion deposition into crystal voids in demineralized enamel to produce net mineral gain.[5]

For remineralization of enamel to occur the following six conditions or events must occur at the same time [6]:

1. Sufficient mineral must be present in the saliva.
2. A molecule of carbonic acid must be produced.
3. The carbonic acid molecule must be produced in proximity to a mineral molecule.
4. This all has to occur in proximity to a demineralized spot in the hydroxyapatite (HAP) latticework.
5. That spot of the tooth has to be clean, so that the mineral deficient spot is accessible.
6. The carbonic acid must convert to carbon dioxide and water before any of the above circumstances change.

Ideal requirements of a remineralization material:-

1. Diffuses into the subsurface or delivers calcium and phosphate into the subsurface.[6]
2. Does not deliver an excess of calcium.[6]
3. Does not favor calculus formation.[7]
4. Works at an acidic pH.[7]
5. Works in xerostomic patients.[6]
6. Boosts the remineralizing properties of saliva.[8]
7. For novel materials, shows a benefit over fluoride.[8]

Indications of a remineralization material:-
1. An adjunct preventive therapy to reduce caries in high‑risk patients.
2. Reduce dental erosion in patients with gastric reflux or other disorders.
3. To reduce decalcification in orthodontic patients.
4. To repair enamel in cases involving white - spot lesions.
5. Orthodontic decalcification or fluorosis or before & after teeth whitening and to desensitize sensitive teeth.[4]

Fluoride
Arnold, in 1957, mentioned the post-eruptive effect of fluoride in the drinking water and the ability of topical fluoride to reduce the incidence of caries.[9]
The mechanism of action of fluorides includes[10]
1. The fluoride ion can exchange with hydroxyl group in the apatite crystal forming fluorapatite which is more stable and less soluble crystal.
2. The fluoride can enter void spaces on the apatite crystal and provide stability by additional bonds.
3. Fluorides can contribute to remineralization of early lesions.
4. Fluorides can act as an antimicrobial agent against bacteria.
5. Inhibits enzymes essential to bacterial metabolism and growth.[11]
Introduced into the oral environment via personal (eg, dentifrices, rinses) or professional applications (eg, varnishes, foams, gels, fluoride releasing restorative materials).
Fluoride levels of about 3 parts per million (ppm) in the enamel are required to shift the balance from net demineralization to net remineralization.[12]
The newly introduced titanium fluoride (TiF) exhibits enhanced uptake of calcium, and TiF-pretreated enamel also shows less loss of calcium during demineralization.[13]

Casein Phosphopeptide - Amorphous Calcium Phosphate (CPP-ACP, GC Tooth Mousse)
Casein phosphopeptides (CPP) contain the cluster sequence of -Ser (P)-Ser (P)-Ser (P)-Glu-Glu from casein.[14]
Casein has the ability to stabilize calcium and phosphate ions by releasing small sequences of peptides (CPPs) through partial enzymic digestion that leads to the development of a remineralization technology based on casein phosphopeptide-stabilized amorphous calcium phosphate complexes (CPP-ACP) and casein phosphopeptide-stabilized amorphous calcium fluoride phosphate complexes (CPP -ACFP).[15]
It is pH responsive, i.e. with increasing pH, the level of bound ACP increases, stabilizing free calcium and phosphate and thus provides an anti-calculus action.
The anti-caries action influences the properties and behaviour of dental plaque through
(1) binding with adhesion molecules in mutans Streptococci, impairing their incorporation into plaque,
(2) elevating plaque calcium ion levels to inhibit plaque fermentation.
(3) providing protein and phosphate buffering of plaque fluid pH to suppress overgrowth of aciduric species when fermentable carbohydrate is in excess.
A dentifrice containing CPP-ACP with fluoride will provide remineralization, which is superior to both CPP-ACP and to conventional and high fluoride dentifrices.[16]

Ozone
Ozone is a chemical compound which is a powerful oxidizing agent. Ozone acts by attacking thiol groups of cysteine amino acid and destroys the cellular membrane of carious bacteria.[17] Ozone can shift microbial flora from acidogenic and aciduric micro-organisms to normal commensals allowing remineralization to occur.[18] Presently HealOzone (KaVo GmbH , Germany) remineralizing solution consisting of xylitol, fluoride, calcium, phosphate and zinc is approved for treatment of caries. It can be used as 2100 ppm of ozone ± 5% at a flow rate of 615 cc/min for 40 seconds.[19]

Xylitol
Xylitol is a naturally occurring pentilol, sugar substitute incorporated in chewing gums.
Manton et al. showed that remineralization can occur with the use of sugar-free gum containing xylitol.[20]
Xylitol acts by
1. Reducing plaque formation
2. Making plaque less adhesive
3. Neutralize plaque acids by decreasing the production of lactic acid
4. Reducing the levels of streptococcus mutans
5. Increasing the salivary flow.
6. Reduce cavities by up to 80%.
7. Assist in the remineralization of tooth enamel.
8. Reduce gum tissue inflammation.
9. Help with dry mouth and bad breath.

Nano-Hydroxyapatite:
10% nano-hydroxyapatite (n HA) is optimal for remineralization of early enamel caries.[21] Effectiveness of synthetically formed hydroxyapatite particles in remineralization of the incipient enamel lesions in comparison with 2% sodium fluoride was checked and it was concluded that the use of biomimetic nano-hydroxyapatite as a remineralizing agent is a potential new synthetic enamel biocompatible material to repair early carious lesions.[22]

Theobromine:
Theobromine (3,7 dimethylxanthine) is a white crystalline powder of methylxanthine family.
Falster et al. 1993 conducted an animal study and it was shown that pure cocoa powder prevents dental caries. An increase in the percentage of cocoa extract in the diet caused

a proportionate reduction in dental caries. It was suggested that cocoa extract has an anti-caries potential.[23]

Self-Assembling Peptide:

Peptide treatment for incipient carious lesion is the most recent area of research. Combination of increased mineral gain and inhibition of mineral loss facilitates peptide treatment. β sheet forming peptides P114 self-assembles themselves to form three-dimensional scaffolds under defined environmental conditions which nucleate the hydroxyapatite de novo and facilitates mineralized tissue regeneration, thus mimicking the action of enamel matrix proteins during tooth development. Single application of P114 is beneficial in the treatment of early caries lesions. The self-assembling peptides are potential materials for mineralized tissue regeneration and repair.[24] P114 is safe, non-invasive and acceptable to patients.

Tri-calcium phosphate [clinprotooth crème]

TCP is a new hybrid material created with a milling technique that fuses beta tricalcium phosphate (ß-TCP) and sodium lauryl sulfate or fumaric acid. This blending results in "functionalized" calcium and a "free" phosphate, designed to increase the efficacy of fluoride remineralization.[25] Products available with TCP include a 5000 ppm sodium fluoride dentifrice and a 5% sodium fluoride varnish. Studies have concluded that TCP provided superior surface and sub-surface remineralization compared with a 5000 ppm fluoride and CPP-ACP.[26]

Bioactive glass

Bioactive glass (Bioglass®) was invented by Dr. Larry Hench in1960s. It acts as a biomimetic mineralizer matching the body's own mineralizing traits and also affecting cell signals thereby benefitting the restoration of tissue structure and function.[27] Novamin®, a trade name for bioactive glass, is manufactured by Novamin Technologies Inc. (Alachua, FL, USA). It has been demonstrated that, fine particulate bioactive glasses (<90 μm) incorporated into an aqueous dentifrice has the ability to clinically reduce the tooth hypersensitivity through the occlusion of dentinal tubules by the formation of the CAP layer.[28]

Challenges

There are several challenges to establishing the clinical effectiveness of remineralization agents:

1. They must demonstrate a benefit over and above an established and highly effective agent, namely, fluoride.
2. They must provide a remineralizing benefit in addition to the natural remineralizing properties of saliva.[4]
3. The organic constituents of saliva can serve as accelerators and inhibitors of the remineralization process. Teeth are covered by the acquired pellicle, which has been shown to retard remineralization.
4. If sugar-free chewing gum is the delivery vehicle, chewing gum has a major remineralizing effect in and of itself, which makes it more challenging to show an additional benefit when using gum as the delivery vehicle.
5. Too much of a good thing could possibly disrupt the mineralization homeostasis of the mouth and favor calculus formation.[4]
6. There may be ingredient compatibility issues. Products are designed to deliver a new agent (i.e., calcium ions) and fluoride simultaneously from single-phase products and may present formulation challenges such as long-term fluoride compatibility.[7]
7. Preclinical models may not necessarily be predictive of clinical performance for these nonfluoride agents and that new agents still require direct clinical validation to ensure efficacy.[7]

CONCLUSION

Evidence suggests that initial noncavitated lesions can be remineralized using appropriate technologies, both fluoride and nonfluoride based. Because of changes in dietary habits, lifestyle, and longer life expectancy, there is an increasing prevalence of enamel and dentin erosion, dental caries and other factors which affect the health of dental tissues. The future of dentistry will rely on regeneration of tooth structure. Understanding the remineralization process allows dentist to treat the lesion before cavitation.

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Source of support: Nil **Conflict of interest:** None declared