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The beyond measures: Non flouride preventive measures for dental caries

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Abstract:
While fluoride is an effective anti-caries agent, the search for more effective alternative therapies continues. A wide range of non-fluoride anti-caries agents has been postulated. Although many potential agents have been identified in various models, very few have been taken forward to full anti-caries testing in humans. In the future, non-fluoride agents which modify the production of acid in plaque either anti-microbially, biochemically, or directly and emerge to have the most promise for use in topical products and may prove to be effective anti-caries systems.
Key Words: Non fluoride anti-caries agents, antimicrobial, plaque, dentifrices, Caries Vaccine.

Introduction

As a chemotherapeutic agent to combat dental caries, fluoride occupies a matchless position. It is relatively economical and can be administered through a number of cost-effective routes to large fractions of populations who are at risk of caries, e.g., through water fluoridation as an additive to dentifrices and other oral care products. Fluoride's anti-caries efficacy is well-proven and may arise from multiple modes of action, i.e., inhibition of tooth demineralization, promotion of incipient

lesion remineralisation, and perhaps, antibacterial effects on cariogenic bacteria.[1] The decline in dental caries experienced by most industrialized countries in the latter part of the 20th century can be attributed largely to the widespread use of fluoride.[2] The above notwithstanding, there are a number of reasons to continue to seek alternative and effective anti-caries agents.[1] First, although fluoride has had a profound effect on the level of caries prevalence, it is far from a complete cure. Clinical evidence would suggest that increasing the concentration of fluoride above the conventional level of 1000 or 1500 ppm in dentifrices will give an increased benefit although there would appear to be something of a law of diminishing returns.[3]

It would seem unlikely that there is any concentration of fluoride which will eliminate caries totally. Of course, in most instances, a high-fluoride strategy cannot be followed, since, to avoid the potential for adverse effects (e.g., fluorosis) due to overexposure to fluoride, legislation limits the amount of fluoride that may be used.

Second consideration must be that, although fluoride is highly effective on smooth-surface caries, its effect would seem to be more limited on pit and fissure caries, and these lesions tend to dominate the caries experience of developed countries currently enjoying the benefits of fluoride. Alternative agents which address the pit and fissure caries problem would obviously be of great advantage.[1]

Third, although, when used properly, fluoride presents no problems to the normal individual, but among certain individuals the toxicity of fluoride increases with inadequate nutrition (sub-standard vitamin-mineral intake) or who are immune-compromised (eg., diabetics, renal disease, etc) where it suggests for the limited fluoride exposure.[4] Indeed, in some countries, non-fluoride dentifrices exist to serve the needs of these individuals.[1]

Fourth, the anti-fluoride lobby which is mounting pressure and providing evidence that there are no additional benefits of artificially fluoridated water as compared to non-fluoridated water. Anti-fluoride lobby is claiming that fluoridation causing certain diseases like mental retardation, gastro-intestinal disorders, Down's syndrome, thyroid problems and many more.[5]

Historical considerations:

From the 1930's when the researches came to know the anti-caries effect of the fluoride, many gargantuan water fluoridation program have been implicated, but these programs has shown to be successful only in attaining a 50% caries reduction but none of them was able to contain the caries process.[6]

Since 1970's researches started to search for non-fluoride agents for the prevention of dental caries. Researches also tried to see whether these products can work alone or can be synergistic to the effect of the fluoride in the prevention dental of caries at the community level.[7]

Non-fluoride anti-caries agents:

Phosphate containing agents

These include simple inorganic salts ranging from sodium and potassium to the more complex polyphosphates, such as tri-meta-phosphate and pyrophosphate.[8] Organic phosphates such as glycerophosphate and phytate have also shown cario-static activity in animal studies.[9] The presence of phytate has been proposed as the reason for the cario-static activity of diet additives such as seed husks of oats, rice, etc, in animal studies.[10]

Na salt of caseinate was found to be active in animal caries studies when added in chocolate as part of the diet, but only at quite high concentrations.[11] CaP complex, however,

produced a 55% reduction when applied topically in a 1% solution and was similar in efficacy to 50 ppm fluoride in water.[12]

Possible mechanism of action of phosphate agents is that, the inorganic phosphates could obviously act directly by promoting either remineralisation, mineralization or reducing demineralization.[10] In case of organic phosphates, the phosphate group probably be cleared by hydrolysis to be active. Phosphates in high concentrations have also been shown to decrease acid production by oral streptococci, possibly by preventing the activation of lactate dehydrogenase by fructose diphosphate. However, fructose diphosphate has been shown to be active in its own right. [10]

Another possibility as shown by two clinical trials is that, the plaque calcium and phosphorus levels are increased by phosphates, and this is definitely a property of ca glycerophosphate.[13,14] Further results form longitudinal studies on humans and animals have suggested that plaque is being modified only slowly by the organic phosphates, and that plaque flora may also be changing to one which metabolizes calcium glycerophosphate, although there are no data to support this view.[10]

Calcium containing agents:

Calcium lactate:

Calcium lactate has been demonstrated to be a potential anti-caries agent in at least two animal caries studies using 1.2% and 2.15% levels in diet.[15]

A clue to its possible mode of action can be drawn from the work of Van der Hoeven et al. who found that use of a 1 % calcium lactate mouth-rinse 4 times a day failed to alter gross plaque accumulation, but did double plaque calcium and phosphate levels after only one week's usage.[16]

Calcium carbonate:

Another agent to raise calcium and phosphorous levels in plaque by physically entrapping particles is calcium salts. It was first supported by Duke who compared calcium-carbonate-based toothpastes with alumina based tooth-pastes.[17]

Calcium carbonate is a well-known antacid, but which have limited plaque acid buffering potential. Many clinical trials results support the possible mechanism of action that calcium carbonate particles become physically entrapped in plaque and thereupon are available to buffer plaque acids over several cariogenic dietary challenges.[10]

Anti-microbial:

Many studies have shown that a number of antimicrobials have a positive effect in the reduction of cariogenic bacteria, these antibiotics ranges from such as penicillin to the well-known anti-plaque agents, chlorhexidine and alexidine. In human studies, both chlorhexidine and triclosan have been shown to reduce plaque acid production. For instance, Jackson et al demonstrated a dose-response effect of pre-treatment with chlorhexidine solutions on plaque acid formation 10 min after a 10% sucrose rinse.[18] Data from human trials also support the view that antimicrobials have anti-caries potential.[18] Clinical trials of penicillin toothpastes have produced equivocal results, whereas penicillin employed systemically, and vancomycin and kanamycin applied in trays have all resulted in reduced caries levels.[19] Furthermore, topical chlorhexidine probably has the most human clinical trial support data among all non-fluoride anti-caries agents. In an excellent review of 12 chlorhexidine caries studies, it was reported that 5 showed a significant effect, 4 a positive trend, and 3 no difference. It concluded that chlorhexidine is most useful in caries-prone individuals.[20]

Metals:

A whole range of metals has been investigated in many different types of clinical trials. Different metals investigated were zinc, tin, aluminium, magnesium, copper, iron, strontium,

barium, manganese and molybdenum. It was seen by the clinical trials that aluminum, copper, and iron have the most positive information to support them, although each would probably have organo-leptic problems if used in oral care products as simple salts. Additionally, it must be recognized that toxicity of many of these metals (*e.g.*, aluminum, molybdenum, barium, and copper) would restrict the concentration at which they could be safely used.[21]

Miscellaneous agents:

List of miscellaneous agents like Glyceryl Monolaurate, Monolaurin, Nonanoic Acid, Lysine Phosphate, Propolis, Bacteriocins, Urea Peroxide and Sodium Lauryl Sulphate shown to have anti-caries activity in animal caries studies. Other agent like citrate has shown anti-cariogenic activity in most of the plaque acid clinical trials. Citrate is an interesting agent in that it might be expected to interfere with parts of the enzyme systems which produce acids in plaque, e.g., phosphofructokinase.[22]

In a study of drinks with various citrate levels appears to interfere with plaque acid production with increasing concentration up to approximately 2.0% level, above which acidity increases. This latter effect is ascribed to the citrate solution (pH 5), reaching a level at which it contributes to the pH reading itself to a greater extent than it inhibits plaque acidogenicity.[23]

Dentifrices:

Tooth-pastes are the valuable adjuncts to oral hygiene as they make brushing more pleasant and more effective. Many attempts have been made at various times to add "therapeutic" agents with the object of interfering with oral flora, limiting plaque formation and making teeth more resistant to caries.[7]

Chlorophyll: Chlorophyll was one of the earliest agents added to the paste and is still present in some tooth-pastes. Although in vitro tests showed that chlorophyll- containing tooth pastes limits bacterial growth, but clinical trials have not shown any anti- caries effects.[7]

Ammoniated tooth-paste: This usually contains urea, and developed in an attempt to control the acid production in plaque. A numbers of clinical trials were carried out, but all gave very little positive or inconclusive results. Ammoniated pastes have been superseded by more effective agents, Anti-biotic toothpastes containing penicillin, triclosan or topical anti-biotic such as tyrothricin have also been tried. It was based on the assumption that if acidogenic bacteria are destroyed, caries will be controlled.[7]

Triclosan is another interesting biocide agent which effects many types of oral bacteria, so is given widespread use in dentifrices. Triclosan is a broad-spectrum antimicrobial agent which has been incorporated successfully into dentifrice formulations and shown reduction in supra-gingival plaque and gingivitis. By itself, it has only moderate anti-plaque properties, but its activity may be enhanced when used in conjunction with other compounds.[24]

Greater uptake of Triclosan to saliva-coated hydroxyl-apatite disks in vitro has been observed, without compromising its antimicrobial activity, when combined with polyvinyl methyl ether maleic anhydride copolymer. Triclosan/zinc system has been shown to inhibit acid production from potentially cariogenic plaques.[25] There exists a wealth of in vitro and in vivo data showing Triclosan dentifrices to be effective anti-plaque agents, and suggesting their potential for anti-caries activity.

Although antibiotic containing tooth pastes showed reduction in the caries incidence but they are no longer used because of the fear of hypersensitivity and development of the resistant strains of micro-organisms.[7]

Anti-enzyme paste: These toothpastes were introduced on the basis that they interfere with enzyme systems of the bacteria and thus with their growth and function. Still their effectiveness has not been evaluated by clinical trials.[7]

Oral hygiene:
Oral hygiene is currently the only effective means of preventing and controlling dental caries and periodontal diseases. Studies have shown that by teaching effective methods of tooth brushing, oral hygiene can be improved dramatically both in children and adults.[7]

Nutrition:
Nutrition is, of course, a fundamental importance to the general development, growth, and health of the individual. Inadequate nutrition during childhood interfere with the development of tooth, leading to gross microscopic defects in enamel, either in the form of hypoplasia or hypo-mineralization.[7]
Nutritional influences are greatest during tooth development. Trace elements such as strontium, lithium, boron, molybdenum and selenium are nutritional factors which are directly associated with prevention of dental caries. Protein deficiency causes delay in the tooth eruption and increases the susceptibility to caries and there is evidence that the method of cooking of vegetables has a major effect on the consumption of trace elements. Strontium is the most important of the trace elements and it has been shown that fluoride and strontium has additive effect on the prevention of dental caries.[7]

Diet counseling:
As evident from the literature, type of diet plays a significant role in causation of dental caries; however, modification of the cariogenic diet to a non-cariogenic diet for the individuals identified with high caries activity helps to minimize the burden of dental caries. To accomplish this, it is essential to screen for and correct food related oral disturbances through counseling procedure. Hence, diet counseling involves constant interaction between the counselor and the clients/patients about therapeutic diets to produce a change in food behavior that can help in prevention of dental caries.[26]

Fissure sealants:
Many studies have shown that the sealants were retained for 6 months only, but the advancement of the technologies now it is possible to retain the sealants for up-to 4 years and the reduction of caries incidence up-to 50%. Sealants filled with GIC increases resistance to abrasion and such materials have shown promising results for caries reduction at community level.[7]

Fissure sealants should be applied to newly erupted teeth when whole of the occlusal surface becomes visible or as soon as possible thereafter.[7]

Some effective products have been developed to date, continuing clinical trials will help to prove which among them will be the most effective. Since sealants are applied only to pit and fissures, which are less protected by fluorides than the smooth surfaces, it might be expected that they would be of substantial values in areas where fluoride levels are sub-optimal.[7]

It has also been proved by the studies that the regular examination and replacement of the any lost sealant would probably result in almost 100% caries prevention on treated tooth surfaces.[7]

Caries vaccine:
The prevalence of dental caries has declined to certain extent in developed countries, but in various developing and under-developed countries the incidence of dental caries is on the increase. Despite the wide spread use of fluoride in tooth-pastes and drinking water dental caries still remains most prevalent and costly affair.[27]

Dental caries vaccine has all the potential to decrease the prevalence of dental caries and also it can save billions of dollars that are spent on restorative treatments. Considerable caries reduction could be attained if colonization of *S. mutans* could be prevented or reduced at the time of eruption of teeth.[27]

In third world countries, rapid increase in dental caries have been observed both in children and adolescent, low dentist population ratio, lack of organized dental care services which prevents the delivery and utilization of various modes of oral health care services.[27]
Thus, a successful vaccination directed against *S.mutans* could be a valuable adjunct to other caries preventive measures. Therefore, it was thought that vaccination against dental caries could be of great value as preventive adjunct in some societies and major public health measures in others. Before introduction analysis of need, cost benefit and risk benefits of vaccine against dental caries in various societies and subgroups has to be performed.[27]

If clinical trials prove their efficiency on long term basis without any complications or failure, then dental caries vaccine can be given at the time of regular immunization schedule of a child in order to make it more cost effective and people don't have to come an extra time for vaccination against dental caries.[27]

Dental caries vaccine is not without disparagement, it has been proved that it's just not the S.mutans but there are many organisms which can initiate caries like, *S.sobrenus* and *S.ratus* and *S.downey* and vaccination against all is not possible. It was also suggested that if we contain these organisms, another will become the potential agents for causing caries.[27]

Probiotic approaches:
The term 'probiotics' refers to "live micro-organisms, which, when administered in adequate amounts, confer a health benefit on the host" The concept of 'probiotics' evolved from Elie Metchnikoff's ideas that the bacteria in fermented products could compete with microbes that are injurious to the host and thus are beneficial for health.[28] Classic probiotic strains, such as those that belong to the genera *Lactobacillus* and *Bifidobacterium*, have been tested for their ability to confer probiotic effect in the oral cavity. This also includes the application of *S. mutans* types that cannot produce acids or other bacteria that interfere with the pathogenic effects of *S. mutans*. While these approaches show therapeutic effects against *S. mutans* experimentally, the conversion into commercial products remains a challenge, due to safety and shelf life issues. New high-tech approaches, such as quorum sensing interference of pathogenic bacteria or targeted antimicrobial therapies, offer novel ways to achieve probiotic effects against dental caries.[29]

Conclusions:
We have methods, as currently used, that are partially effective in preventing or, more accurately, in controlling—dental caries; however, we have been extraordinarily slow in applying the fruits of the research to enhance the effectiveness of these agents and in bringing them to developing regions of the world.

Several additional avenues are being explored which will be available in the future; however, the will to apply new knowledge rapidly is critical to the success of any novel procedure.
Moreover dental caries is multi-factorial and all non-fluoride measures should be evaluated properly in human trials so that they can be introduced at the community level for the prevention of dental caries. However, in developing countries like India where prevalence of dental caries is on the rise, it is recommended to use both the fluoride and non-fluoride measures to maximize the benefits over dental caries.

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