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Hydroxyapatite Toothpaste On Caries Prevention In Children

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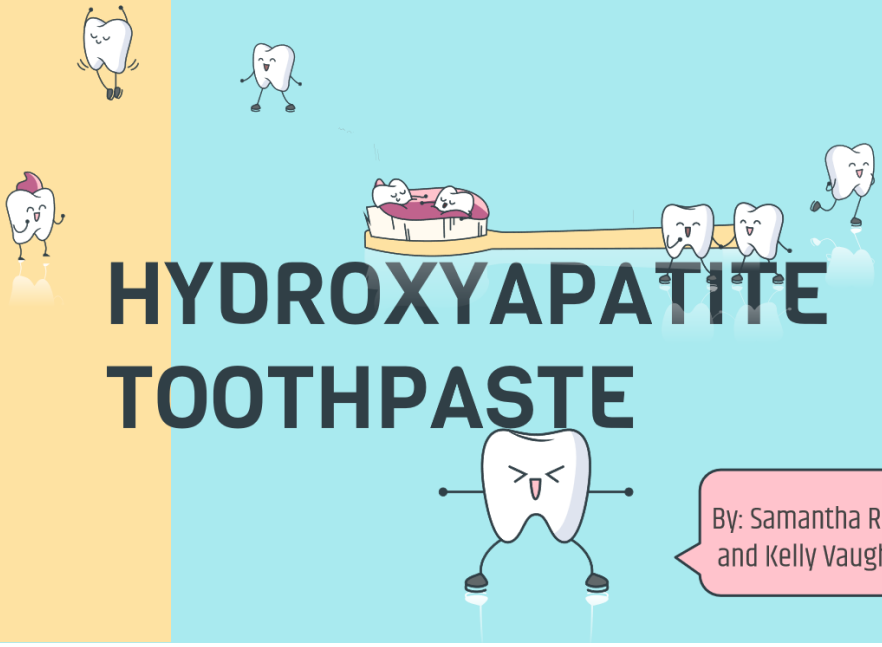


HYDROXYAPATITE TOOTHPASTE

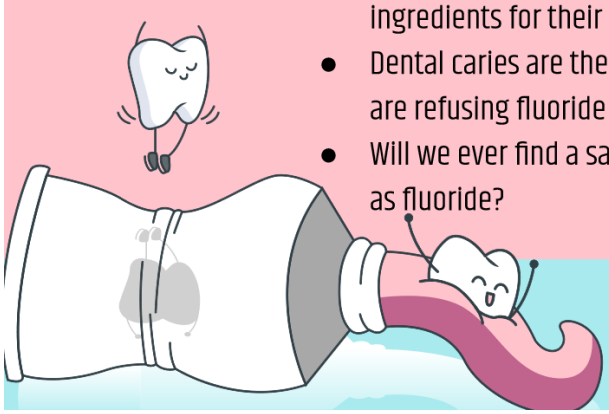
By: Samantha Richardson
and Kelly Vaughan

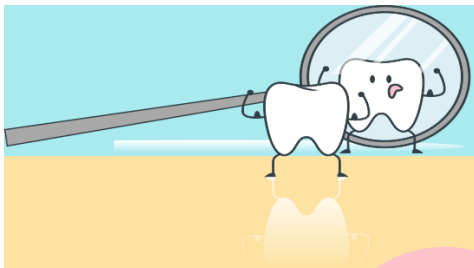
OUR RESEARCH QUESTION

Do hydroxyapatite toothpastes prevent caries equally as well as fluoridated toothpastes in children?

PROBLEM

- Rising trends to become more clean with ingredient lists
- More patients refusing fluoride treatments and fluoridated toothpastes
- Prevalent in our children due to parents only wanting the purest natural ingredients for their children
- Dental caries are the most prevalent diseases in children and now parents are refusing fluoride for their children
- Will we ever find a safe alternative toothpaste that will be just as effective as fluoride?





MILESTONES REACHED

1970

Japan purchased the rights of HAP from NASA

1993

Japan received approval for HAP toothpaste as anti-caries agent

2006-2015

HAP toothpaste became commercially available in Europe & Canada

HAP BACKGROUND

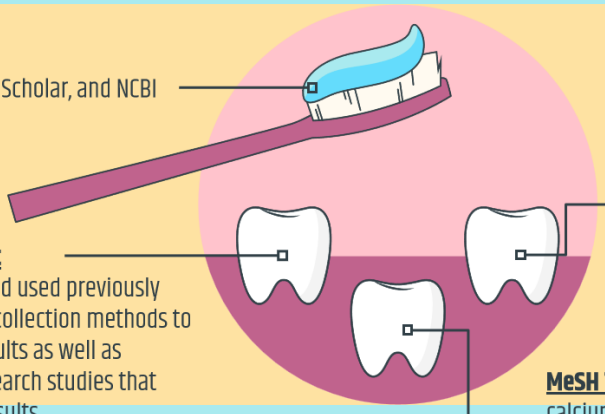
- Nano-HAP remineralizes teeth from inside out for caries prevention
- Replaces lost minerals like calcium and phosphates caused by high levels of acid or bacteria
- HAP is biocompatible because its already present in teeth composition
- When present, HAP helps teeth absorb the properties to rebuild damaged enamel by filling in cracks and bridging fissures

"Based on the recent studies, the use of a HAP toothpaste seems to be an effective alternative for the anti-fluoride patient. "

— Heather Hakes, RDH
Today's RDH Magazine

METHODS & MATERIALS

Databases:
PubMed, Google Scholar, and NCBI



2017 to Present
Studies reviewed used previously validated data collection methods to report their results as well as conducting research studies that yielded valid results

Search Terms:
hydroxyapatite toothpaste, hydroxyapatite, children, fluoride, fluoridated toothpaste, remineralization, children, caries, and demineralization

MeSH Terms:
calcium hydroxyapatite, hydroxyapatite, hydroxyapatite, dentifrices, toothpaste, fluorosis, fluoride, cariostatic agents, and sodium fluoride

2021 Narrative Review

- Goal: Summarize recent findings of the research investigating of the remineralization potential of HAP in vitro, situ and vivo as well as other dentistry applications

- **Tschoppe et al vitro study**: compared remineralizing effects using bovine incisor dentin & enamel lesions brushing 2x daily for 5 seconds for 2 weeks using HAP vs. Fluoride toothpaste
    - Limitations - Exaggerated effects due to higher concentrations of product due to lack of dilutive saliva factors
    - Results - analyzed using Transverse Microradiography (TMR) found all 3 HAP toothpaste produced similar remineralization results and were significantly higher than fluoride group
- **Amaechi et al double-blind randomized crossover in situ/vivo**: participants wore fixed appliance containing demineralized block & sound block of enamel brushing 2x daily with either HAP or FIx for 4 weeks
    - Strengths - Conditions allowed blocks to be exposed to natural oral environments, biofilm, and diet
    - Results - Analyzed lesion rate reduction & mineral content measured by microradiography and found no difference between HAP & FIx demonstrating the non-inferiority of HAP toothpaste under these conditions

7. O'Hagan-Wong K, Enax J, Meyer F, Ganss B. The use of hydroxyapatite toothpaste to prevent dental caries. Odontology. 2021 Nov 22. doi: 10.1007/s10266-021-00675-4. Epub ahead of print. PMID: 34807345.

Randomized Controlled Trial

- 2019 RCT comparing four different toothpastes:
    - Generic brand name toothpaste
    - Toothpaste containing fluoride 500 ppm
    - Toothpaste containing fluoride 1400 ppm
    - Toothpaste containing Hydroxyapatite nanocrystal (Biorepair®)
- UOC of Pediatric dentistry Sapienza University of Rome department of Oral and Maxillo-Facial Sciences
- Control group and patient groups were selected ages 7-10 years old to use one of the four different toothpastes, 3 times a day for 15 days.

- Results:
    - HAP toothpastes leave more particles to remineralize the tooth
    - Toothpaste residue does not have any enamel roughness.
    - Microstructures were covered with a basic matrix from the HAP
    - Does not confirm caries prevention but does promote tooth remineralization

Bossù M, Saccucci M, Salucci A, Di Giorgio G, Bruni E, Uccelletti D, Sarto MS, Familiari G, Relucenti M, Polimeni A. Enamel remineralization and repair results of Biomimetic Hydroxyapatite toothpaste on deciduous teeth: an effective option to fluoride toothpaste. J Nanobiotechnology. 2019 Jan 25;17(1):17. doi: 10.1186/s12951-019-0454-6. PMID: 30683113; PMCID: PMC6346538.

7. O'Hagan-Wong K, Enax J, Meyer F, Ganss B. The use of hydroxyapatite toothpaste to prevent dental caries. Odontology. 2021 Nov 22. doi: 10.1007/s10266-021-00675-4. Epub ahead of print. PMID: 34807345.

DISCUSSION

DESENSITIZING AGENT

Reports of lowered dentinal hypersensitivity in response to air blast after 2-4 weeks of HAP toothpaste use

BIOFILM REDUCTION

HAP had Inhibitory effects of zinc carbonate on biofilm formation by *S. mutans* when compared to Chlorhexidine rinses in reduction of bacterial enamel adhesion

WHITENING AGENT

Color change was observed using spectrophotometry color following use of HAP whitening gel for 9 days

LIMITATIONS

- Enlarging the subject population
- Increasing the studies period of time
- More studies conducted in the U.S.
- Subjects need to be representative of: location, age group, socioeconomic status, oral health status and oral health literacy
- Future studies including adults long term

- Risewell
  - "Safe for developing brains"
- Boka
  - "Unlike fluoride toothpastes, ours is 100% non-toxic, meaning you won't have to worry if your child accidentally swallows some
- Biorepair
- Tom's
  - "Silly enough for kids- good enough for moms and dads!"
- Kid's Crest
  - "Sparkle fun toothpaste"

Hydroxyapatite Toothpaste

Children

Fluoridated Toothpaste

Children

Caries Prevention

Children

CONCLUSION

- HAP's research at preventing and arresting dental caries is equivalent to fluoridated toothpastes
- HAP toothpastes are safe to recommend in children where fluorosis is a concern
- HAP reduces dentin hypersensitivity and reduces biofilm formation making HAP a multifunctional agent
- Still a need to follow these effects long term

CREDITS

- Presentation template by Slidesgo
- Ms. McLee, RDH, MSDH
- Dr. Loughran

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THANKS!

Questions?

Virginia Commonwealth University

Are Hydroxyapatite Toothpastes The Answer To Fluoride Free Patients?

Samantha Richardson and Kelly Vaughan
Research Methods and Study Design DENH 307
Dr. Loughran and Ms. McLee MSDH, RDH
5 March 2022

Are Hydroxyapatite Toothpastes The Answer To Fluoride Free Patients?

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Abstract:

Objectives/Aims: With the rising trend to become more clean with our ingredient lists, we are facing more patients refusing fluoride treatments and fluoridated toothpastes. This trend has been prevalent in our younger generations due to parents only wanting the purest natural ingredients for their children and now declining fluoride application. The goal of this literature is to find a safe alternative toothpaste that will be just as effective as fluoride.

Methods: This review of literature has been developed from searching the PubMed database in order to find relevant research on hydroxyapatite toothpastes. Many of these studies were conducted to compare multiple name brand toothpastes including fluoride and their alternatives like hydroxyapatite toothpastes in order to determine their effects on caries prevention and remineralization.

Results: Toothpastes with hydroxyapatite as an active ingredient were found to not be inferior to fluoridated toothpastes in caries progression in children. Hydroxyapatite has a high safety profile and no risk of dental fluorosis, which is a major point for patients who refuse fluoride use.

Conclusion: Hydroxyapatite has been shown to reduce biofilm formation in children and a preventative measure for further demineralization and caries protection. Although these studies sound promising, there can be improvement by enlarging the subject population, increasing the studies period of time, and the subjects need to be representative of: location, age group, socioeconomic status, oral health status and oral health literacy.

Key Terms: hydroxyapatite toothpaste, hydroxyapatite, children, fluoride, fluoridated toothpaste, remineralization, caries, and demineralization

Introduction:

The enamel layer of the tooth is composed of calcium phosphate, arranged in a crystal structure which is known as hydroxyapatite (HAP). The dentin layer contains 45% hydroxyapatite, 33% organic material, and 22% water [1]. When looking at the composition of primary teeth, the pattern of decay typically spreads from the enamel to dentin layer. Carious lesions typically start by biofilm formation developing on the enamel surface without being removed. Here the biofilm starts to feed off of the nutrients in the children's diet, where the matrix of the biofilm thrives. Demineralization can occur in the enamel layer where the toxic microbes in the mouth wear down, or erode that tooth's enamel. At this stage, the tooth is at a precious time frame to possibly be remineralized. The period for remineralization is typically when a patient would get recommended for a fluoride treatment and serious changes in their oral hygiene habits. A serious and safe recommendation that can be made in a child's oral hygiene routine could involve switching to a hydroxyapatite toothpaste.

The hydroxyapatite (HAP) formula originated from NASA who wanted to create a solution to the lost minerals of astronauts' teeth and bones. NASA proposed a synthetic HAP product as a repairing material for the astronauts' travels. While NASA did not market the product, a Japanese company called Sangi Co Ltd took interest and purchased the rights of the HAP from NASA in 1970. [9] Japan later explored the idea of creating a toothpaste that could repair tooth enamel and launched the first synthetic hydroxyapatite toothpaste. Since its approval as an anti-caries agent in 1993 in Japan, it became available commercially in Europe in 2006 and in Canada in 2015.[7] The effect of a variety of HAP-containing toothpaste formulations has since been tested on enamel remineralization experimentally under laboratory and in situ conditions as

well as clinically. The toothpaste protects teeth with the creation of a new layer of synthetic enamel around the tooth, in comparison to hardening the existing layer from fluoride.

The major clinical benefit of HAP is that it acts as a true remineralization agent where the mechanism of action is to create a new enamel layer to ensure a healed tooth layer. This has been found to have more success in children to improve their pre-carious lesions. [7] Fluoride's mechanism of action asts to harden the already demineralized area in order to prevent any further demineralization from occurring. While the ingredient conscious trend is on the rise in western society today, the oral health professionals need to be aware of the safe alternatives they can offer. A benefit of HAP toothpastes would be the natural ingredient list, while HAP can be naturally extracted from mammalian bones and plants, it is important to note it is the primary component to the enamel layer. [10] 5% HAP toothpaste use was studied in 181 school aged children and there were no adverse effects found over a period of 6 years, says Limeback, et. al. [6] Fluoride does have a risk of overexposure since public fluoridated water is not universally regulated, leading to a risk of dental fluorosis.

The use of fluoride has been a well known source of anti-cavity prevention in children and adults. While fluoride interventions seem to be the most consistent way to cavity prevention, caries still develop in high risk individuals such as children, elderly, low socioeconomic status and minority groups. Fluoride has efficacy limitations depending on the pH level and the bioavailability of calcium and phosphate ions in saliva. Fluoride is less successful below a pH of 4.5 and needs Ca2+ and PO4 ions in saliva to be effective particularly in the outer 30 μm of initial carious lesions.[1] This type of caries prevention ultimately leads to surface-zone remineralization at the expense of the lesion body making remineralization difficult to achieve.[1] Fluoride efficacy is also dose dependent and efficacy increases with higher doses of fluoride. It is

known that infants and toddlers are unable to properly discard toothpaste while brushing and the ingestion of fluoride increases the risk of systemic uptake and fluorosis. While adult toothpaste fluoride levels range between 1000-1500 ppm, children's toothpaste has a threshold of 500-600ppm to decrease the risk of fluorosis. This type of limitation is more pronounced in toothpastes for children under the age of 6 and are suboptimal for effective remineralization of initial lesions.[1] It was reported that dental plaque of caries-free children have higher levels of calcium and phosphorus compared to caries active children. Thus, the use of synthetic calcium phosphates as active ingredients in oral care products, such as hydroxyapatite, seems to be a promising alternative because of its biomikining potential, remineralization features, and caries prevention.[12]

Saliva homeostatic mechanisms, low pH limitations, and the range of fluoride levels justify the need for new age strategies of cavity prevention These strategies need to work equally or better than fluoride, while increasing the dosage of an ingredient without the risk of toxicity or safety concerns for children[1]. Rising trends have encouraged parents to be aware of product ingredients and the side effects which leads to an increased questioning about the use of fluoride in the dental chair. Many parents have taken an interest into hydroxyapatite since the levels can be safely increased to prevent carious lesions and remineralize incipient caries without the risk of fluorosis in children.

Methods and Materials:

This review of literature used the following databases: PubMed, Google Scholar, and NCBI to conduct a relevant search and discover pertinent research articles. MeSH terms included: calcium hydroxyapatite, hydroxyapatite, hydroxyapatite, dentifrices, toothpaste, fluorosis, fluoride, cariostatic agents, and sodium fluoride. The studies reviewed used previously

validated data collection methods to report their results as well as conducting research studies that yielded valid results. Articles included in this review had to be published after 2017 to ensure recent and relevant results.

Results:

A narrative review article was conducted in 2021 to examine the effects of hydroxyapatite toothpaste on enamel remineralization in vitro, vivo, and situ environments as well as additional effects of HAP toothpaste. [7] The Tschoppe et al vitro study compared the remineralizing effects using bovine incisor's dentin, and enamel lesions while brushing twice daily for five seconds for a total of two weeks using either HAP or fluoride toothpaste. Results were analyzed using a transverse microradiography (TMR) and found all three HAP toothpaste formulations produced similar remineralization results in both types of lesions, which was significantly higher than the fluoride toothpaste group.[7]

Amaechi et al conducted a double-blind randomized crossover in a situ and ex vivo environment vs an in vitro to offset the exaggerated and unrealistic effectiveness of the possible higher concentration of the product due to lack of dilutive saliva factors.[7] In this study, participants wore a fixed appliance containing a demineralized block and sound block of enamel positioned on the buccal surface of their lower molars. Participants brushed morning and evening with either the 10% HAP toothpaste or 500ppm fluoridated toothpaste for four weeks. The experimental conditions allowed the enamel blocks to be exposed to the patient's natural oral environments, biofilm, and dietary carbohydrates.The outcomes of this study were lesion rate reduction and mineral content measured by microradiography. The authors found no difference between the HAP and fluoride toothpaste at demineralizing enamel blocks, thus demonstrating the non-inferiority of HAP toothpaste under these study conditions. [7]

This article review also found no reports of adverse dental or systemic effects of HAP toothpastes because of its biocompatibility.[7] When HAP is accidentally ingested the calcium and phosphate particles are dissolved in their ionic forms and have no adverse effects. Eukaryotic cell culture studies have shown that ingested HAP can lead to elevated intracellular levels of calcium ions, but that the cells are quickly able to regulate and return to normal calcium levels. As previously mentioned, calcium phosphate is a naturally occurring mineral in teeth and bones and there are no reported adverse effects on the environment.[7]

A 2021 double blinded randomized control trial was conducted to compare a microcrystalline hydroxyapatite toothpaste is not inferior to fluoride toothpaste in caries prevention in children in Poland. [8] This trial ran for 336 days and used The International Caries Detection and Assessment System (ICDAS) ≥ code 1 on primary teeth. The test group used 10% microcrystalline hydroxyapatite toothpaste and the control group used 500ppm amine fluoride toothpaste three times daily using an electric toothbrush in the morning and night and a manual toothbrush at noon. 214 children, aged 3-7 years, were included in the study, 37 children were released for falling outside of the parameters, and 177 finished using the protocol. [8]

The primary endpoint examined subjects who experienced the development of at least one new enamel caries lesion ≥ ICDAS code 1 or the progression of an existing enamel caries lesion. [8] An increase in development of enamel caries lesions with ICDAS≥ code 1 per tooth was observed in 72.7% of the hydroxyapatite-group (n= 88), compared with 74.2% of the fluoride-group (n= 89).[8] Although this number seems high, it can be explained by the high prevalence of early childhood caries in Poland and the fact ICDAS was used in order to capture any developed lesion as early as possible. A secondary endpoint examined the development of at

least one new enamel caries lesion with ICDAS ≥ code 2 and found it was lower at 56.5% than the proportion of subjects who developed lesions with ICDAS ≥ code 1.[8]

This particular study chose subjects who had active carious lesions because of the very high prevalence of early caries in both developed and developing countries. This RCT showed for the first time that in children, the impact of the daily use of a toothpaste with microcrystalline hydroxyapatite on enamel caries progression in the primary dentition is not inferior to a fluoride control toothpaste. [8]

A systematic review and meta-analysis was conducted in 2021 by Limeback, et al in order to determine hydroxyapatite and its possible effects on caries prevention. The goal of this study was to conduct a systematic review of the clinical evidence of the effects of HAP-based fluoride-free oral care products in caries reduction and conduct a meta-analysis of available randomized clinical trials (RCTs). [6] When the research was being conducted they searched at the following databases: the PRISMA guidelines for literature searches, Ovid MEDLINE (PubMed), EMBASE, Scopus, and Web of Science were chosen as the primary databases. After the search protocol was applied and irrelevant papers were excluded, the authors identified 291 publications relevant to HAP in oral care products in the prevention of dental diseases. Although the authors only determined 22 to be addressed due to meeting their PICO framework of their current study, many mentioned tooth whitening or desensitization rather than specific HAP anticaries mechanisms. A large proportion of the studies were experiments conducted in vitro showing that HAP interacts favorably with tooth surfaces, suggesting HAP could be a useful anticaries agent.[6]

The results of this summary showed multiple randomized clinical caries trials conducted for 6 months to one year with subjects aged 3-35 years old using the new caries measured using ICDAS, digital radiography determination and photographic pixel changes. For the

meta-analysis, caries incidence was used to calculate a weighted odds ratio on the caries preventive effect of the hydroxyapatite group. [6] Among those 22 studies, 5 clinical trials reported the direct measurement of anticaries effects in young adults and children after exposure to HAP toothpaste. It was also found that HAP provides additional calcium and phosphate in saliva and biofilm for improved remineralization of caries in the oral cavity. The odds ratios conducted from these studies included: 1.48 with 50.9% weight, 1.17 with 28.6% weight, and 1.40 with 20.5% weight. These authors calculated the weight by determining how much accuracy and validity the study has into a percentage. In summary, this meta-analysis conducted that the overall odds ratio is to be 1.17 looking at all the sources.

Another experimental study was conducted by Bossù et al in 2019. In this study they compared four different toothpastes: a common toothpaste, commercial toothpaste containing fluoride 500 ppm, commercial toothpaste containing fluoride 1400 ppm, and toothpaste containing Hydroxyapatite nanocrystal. These toothpastes were analyzed by means of HR-SEM microscopy (High Resolution Scanning Electron Microscopy) and VP-SEM (Variable Pressure Scanning Electron Microscopy) analysis on dental samples treated with different toothpastes was also carried out. [3] This study also observed the antimicrobial properties of these toothpastes. The control group was formed using a selection of 30 primary teeth (first deciduous molars in patients aged between 7 and 10 years). The procedures were performed at the UOC of Pediatric dentistry Sapienza University of Rome department of Oral and Maxillo-Facial Sciences. [3] The patient group was selected aged between 7 and 10 years, was advised to use one of the four different toothpastes (ordinary fluoridated toothpaste, Biorepair®, Fluorine 500 ppm, Fluorine 1400 ppm), 3 times a day for 15 days.

The results from this study shows that the microstructures were covered with a basic matrix. In both samples the aggregated particles were visible in the sediment and in the supernatant with the size of those particles ranging from 50 to 100 nm. The size of nanostructured micro-agglomerated is approximately 5 μm and the size of the fine nanostructure characterizing the micro-particles ranges from 50 to 100 nm. [3] Through additional dilution of the sediment obtained in F1, Sample F2 presents micro-agglomerates of approximately 20 micron and the size of the fne nanostructure of the micro-particles ranges from 50 to 100 nm. [3] In order to provide both qualitative and quantitative results, that allowed them to accurately compare different toothpaste effects, for each treatment they analyzed ten micrographs at 500× magnification by means of Image J roughness analysis plug in. It was found that hydroxyapatite toothpastes leave more particles in order to remineralize the tooth and the residue of the toothpaste does not have any enamel roughness.

Discussion:

Additional effects of HAP toothpaste were reviewed and in vitro study findings demonstrate the inhibitory effects of zinc carbonate HAP on biofilm formation by Streptococcus mutans when comparing to chlorhexidine rinses in the reduction of bacterial adhesion to the enamel.[7] Within the context of the study, the HAP rinse formulations did not kill any bacteria present in the biofilm when compared to chlorhexidine, and therefore may have the advantage of preserving naturally occurring oral flora while increasing available mineral content on the tooth surface and preventing pathogenic colonization.[7]

Randomized clinical trials demonstrated the effects of HAP-containing toothpaste as both a descensiting and whitening agent. Participants reported significantly lower levels of dentinal hypersensitivity in response to air blast after two to four weeks of HAP toothpaste compared to

fluoridated toothpaste and has been found to occlude dentinal tubules at the microscopic level.[7] Niwa et al. found that HAP-containing toothpastes produced significant whitening and brightening effects on enamel in dose dependent fashion. Improvement of objective measures of color change was observed using spectrophotometry color following the use of HAP-containing whitening gel used for 9 days.[7]

HAP-containing oral products can be considered as an alternative in young children where fluorosis is a concern. While it may be early to recommend HAP toothpastes over fluoridated to children, it would be beneficial to use HAP products in patients at risk for dental fluorosis. Patients who get over the regulated amount of fluoride can develop dental fluorosis, which is common in areas with no water regulation. In children who may have high public fluoridated water consumption, it would be beneficial to recommend a HAP toothpaste. This way the patient is still able to prevent caries and have remineralization properties without developing the side effects from fluoride.

It would be a great strength to these research studies to enlarge the subject population, increase the studies period of time, and the subjects need to be representative of: location, age group, socioeconomic status, oral health status and oral health literacy. Since this product is newer on the market there is a need to follow the effects on the oral cavity for a longer period of time. These studies were conducted under a shorter timeframe to see if the carious lesions resolved but, there still needs to be studies that are being done after to follow the other long term effects. It would also be beneficial to know the effects of HAP in other oral healthcare products. Would a HAP mouthrinse show the same preventative oral health effects as a fluoridated mouthrinse? While our review looks at the childhood population, we did come across other studies interested in permanent detention and studies that decided to include adults in their

samples. It would be favorable to see the effects HAP toothpastes have on adults' permanent dentition and if it would be appropriate as a fluoride replacement.

Conclusion:

While more research is needed to confirm the clinical effectiveness of HAP at preventing and arresting dental caries, the research suggesting its equivalency to fluoride toothpaste is promising. While there is still a need to follow these effects long term, HAP containing toothpastes can be recommended as an alternative in young children where fluorosis is a concern. In addition to reducing the need for dental restorations from caries, HAP also offers relief from dentin hypersensitivity and reduces biofilm formation making HAP a multifunctional agent in preventative oral health care.

References:

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