



The effect of water fluoridation is practically carried away by its topical effect

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Abstract

It is widely acknowledged that one of the main causes of the decline in childhood dental caries in developed nations is the abundant availability of fluoride from various sources. Early fluoridation studies accepted that fluoride act through pre-eruptive incorporation of fluoride into developing enamel through ingestion from different sources, especially through drinking water. But further research could not explain why fluoride levels of surface enamel of those teeth that are exposed to systemic fluoride is not as higher which is required to prevent carious acid attack. Instead, considerable evidence suggests that fluoride acts mainly, if not entirely, through post-eruptive remineralization of demineralized enamel. Maximum benefits from exposing newly erupted teeth to topical fluoride in the oral cavity may have been seriously under-estimated. In this updated review of the pre-eruptive vs post-eruptive benefits of fluoride in prevention of dental caries, a re-examination of the literature, is done to recognize the fact that the topical mechanism as being the primary, if not the only mechanism for the prevention of dental caries.

Keywords: Fluoride, pre-eruptive fluoride, post eruptive fluoride, anti- cariogenic effect

Introduction

Since the late 1960s, WHO has officially endorsed the use of fluoride for population-based prevention of dental caries. Fluoride has been recognized as the main factor responsible for the decrease of caries prevalence in the past decades. Universal access to fluoride for preventing caries was declared to be part of the basic right to human health during the WHO World Health Assembly in 2007.^[1] Improvements to oral health in the post-fluoride era have been dramatic. With the advancement for topical fluoride application the use of systemic or water fluoridation has been reduced worldwide. But still 4 % of worlds population, estimating approximately 350 million people are receiving fluoridated water supply till 2022. In which countries like USA, Australia, New Zealand and few other countries are partly supplying and countries like Singapore and Ireland are fully supplying fluoridated drinking water. Pre-eruptive or post-eruptive mechanism of action of fluoride has been a topic of debate for years. A lot of research work has been done in support of both the hypothesis. The issue is worth exploring further, since better understanding of its mode of action will influence public policy and recommended use of all forms of fluoride. This article reviews the evidence relating to fluoride's pre-eruptive and post-eruptive effects on dental enamel, and suggests hypotheses to explain why frequent fluoride exposure is a primary cause of the continuing decline in caries among children in countries where it is in common use.

Pre-eruptive and post-eruptive mechanism-

Pre- eruptive hypothesis states that when fluoride enters the environment of developing tooth it gets incorporated into the developing enamel to form more acid resistant crystals, which will then be less soluble in presence of acids in dental plaque. Fluoride ingested during tooth development is partly incorporate into tooth enamel, mostly during the pre-

eruptive maturation stage. The amount of fluoride deposited pre-eruptively depends on fluorides concentration in food, water, or supplements ingested, the duration of the ingestion period, and the length of the pre-eruptive maturation stage. The principal benefits of pre-eruptive ingestion are considered to be improved crystallinity and reduced enamel solubility.^[2] Fluoride is acquired in enamel pre-eruptively in 2 developmental phases, firstly, during crown completion (CC) in which the matrix is formed and calcified and secondly just after CC but prior to eruption, known as pre-eruptive maturation. Fluoride found in inner enamel layer is taken up mainly during the secretory or CC phase and the fluoride found in the outer 30–50 µm of enamel layer during the maturation phase.

The post eruptive hypothesis by contrast states that when plaque pH drops, dissolution of the enamel crystals begins. The calcium and phosphate available from dissolution are held in the plaque. As the pH increases those Calcium and Phosphate, along with the fluoride present in the plaque by topical loading, immediately begin to remineralize the lesion. The new enamel thus laid down has more fluoride content than the dissolved original one. Post-eruptive fluoride is also having an antibacterial effect as it can disrupt glycolysis by inhibiting enzymes in the cell, especially enzyme enolase which is essential for bacteria to metabolise carbohydrate to form acids. Remineralization was concluded to be the cause of the arrest, or even the reversal of early carious lesions.

Re-examining literatures

Most of the pre-eruptive F supplement is administered by water fluoridation. The majority of the data supporting the pre-eruptive benefit of fluoride comes from epidemiological data on the incidence of caries in communities that have been fluoridated. Le Geros *et al.* performed a physicochemical investigation of enamel from deciduous

teeth. They found that enamel from children who had been subjected to prenatal fluoridation exhibited more homogeneous and less extensive patterns of acid etching, denser crystal populations in intra-prismatic regions, larger prism dimensions, greater total mineral density, a higher degree of crystallinity, smaller a-axis dimensions, more fluoride and less carbonate contents.^[3] *In vitro* studies revealed that the reduction in enamel solubility by pre-eruptive incorporation of fluoride is less. It is therefore unlikely that the ability of fluoride to produce a decrease in the rate of enamel dissolution when incorporated into the apatite lattice, mainly as fluoridated hydroxyapatite.^[4]

The theoretical concentration of fluoride in pure fluorapatite, which would produce a substantial reduction in acid solubility, is around 38,000 ppm; but recorded values from an enamel depth of two microns are only in the order of 1,700 ppm in non-fluoridated areas, 2,200-3,200 in 1 ppm fluoridated areas, and 4,800 ppm in an area with a water fluoride concentration of 5-7 ppm^[5, 6]. These latter concentrations have also been found in the outermost enamel layers in people from low-fluoride areas^[7]. Renowned scientist JDB Featherstone commented that the 'fluoride incorporated during tooth mineral development at normal levels of 20 to 100 ppm (even in areas that have fluoridated drinking water or with the use of fluoride supplements) does not measurably alter the acid solubility of the mineral. Even when the outer enamel has higher fluoride levels, such as 1,000 ppm, it does not measurably withstand acid-induced dissolution any better than enamel with lower levels of fluoride.'^[8] Therefore, rather than preventing dissolution of enamel crystals triggered by an acid attack, low grade fluoride which present in the enamel surface can be released into the external fluid environment in acid attack, thus having a major effect on stimulating remineralization as soon as the acid environment reduces. This theory currently has greater acceptance than the earlier widely accepted phenomenon of inherently decreased enamel reactivity due to the incorporation of fluoride within the apatite lattice. Shark enamel, which is nearly entirely composed of fluoroapatite and has 30,000 parts per million of fluoride, was shown to be only slightly more resistant to carious attack than human enamel from fluoridated areas, which has 2,000 parts per million of fluoride on its surface. This was revealed by an interesting laboratory investigation. Shark enamel should be nearly completely resistant to caries if the Pre-eruptive hypothesis is true, however this is not the case.^[9] Pre-eruptive hypothesis never able to explain that if the enamel is formed with high F content in a fluoridated area, then why dental caries experience increases when a person leaves the place? The most reasonable explanation is that the longer a tooth is exposed to fluoridated water, the greater its resistance to caries because of the topical effect of F contained water. These observations obviously point to an important post-eruptive mechanism of the preventive effects of fluoridated water^[10, 11, 12].

Lemke *et al.* found that after discontinuation of water fluoridation, the caries incidence of children increased to the level of those in the non-fluoridated area in a period of 4 to 6 years. These types of data provide strong support for a post-eruptive effect^[13]. The pre-eruptive hypothesis has never been able to explain why dental caries experiences rise when an individual leaves a fluoridated area where enamel is formed with a high F content. Fluoridation studies investigating relative pre- and post-eruption water

fluoridation effects did not use a cutoff age (i.e., eruption age) before and after which exposure could be measured as pre- and post-eruption exposure levels, respectively^[14]. Opponents of water fluoridation campaign in Australia have claimed that any small benefit of water fluoride is due to its topical action.^[15]

Also, the mechanism of fluoride placental transfer is controversial. One of the study says, fluoride passes through the placenta freely, after it reaches excessively high levels in the mother's blood, and thus triggers this passage (barrier effect) to protect the fetus from excessive doses. The threshold concentration that pushes the placenta to trigger this function is 0.4 ppm of fluoride in maternal blood.^[16] According to SA Roriz Fonteles' findings in one study, fluoride exposure during pregnancy did not result in any additional, quantifiable fluoride uptake by dental tissues beyond what could be attributed to postnatal fluoride alone^[17].

Long back, Bibby *et al.* conducted preliminary research to support the post-eruptive effect of fluoride. They compared the efficacy of fluoride lozenges and pills in a group of children aged 5 to 14. The coated pills were swallowed while the lozenges were sucked. They were able to show that, in comparison to the group taking the pills, fewer carious lesions developed in the group using the lozenges^[18]. One clinical trial, however, has been reported in which the subjects were instructed to chew tablet containing 1 mg F as slowly as possible, then rinse for 30 seconds and swallow at each day in school. At the end of three years test subjects showed a reduction in mean DMF surfaces of approximately 80 percent compared with controls who used a placebo tablet^[19]. It should be kept in mind that consuming an enteric-coated tablet containing 1 mg of fluoride once a day would only raise salivary fluoride levels in the saliva to 0.05 mg/L for about an hour. Exposure to fluoride containing foods, beverages, and fluoridated water supplies would result in multiple exposures during the day at levels 20 times higher than this, which can create a fluoridated salivary environment that may have a low-grade local effect through remineralization. It shows a significant indirect local effect of frequent fluoride containing food intake. In this angle of view water iluoridaaön is the cheapest mode dental fluoridation, but its effect is almost certainly local. Moreover use of fluoride supplement in first six years of life, especially in first three years significantly increases the risk of fluorosis^[20, 21]

Interestingly, Hargreaves suggested by this "topical route," fluoride that has been incorporated into the deciduous teeth and bone will be released during the resorption of the bone and deciduous roots, before the eruption of permanent dentition. The origin of such "systemic topical Fluoride" (or localized pre-eruptive fluoride) would circumvent the requirement to ingest fluoride, metabolized and transported to the developing teeth by way of the circulation. Further experiments are obviously required to quantify what contribution, if any, for the formation of caries resistant enamel prior to eruption.^[22]

Caries is a transmissible disease, with *Streptococcus mutans* being transmitted to the mouths of infants soon after tooth eruption. Fluoride can interfere with this transmission by reducing *S. mutans* levels in mothers, so that there are fewer bacteria to transmit. Some years of widespread fluoride use in the economically developed world could have induced oral ecological change at a population level, and may be

continuing to do so. The “hostile environment” for cariogenic bacteria created by widespread and long-term use of fluoride may now be the norm in many communities.^[2]

Many of the studies that assert that consuming F daily will alter the morphology of the tooth structure are flawed. Those studies have: i) not use examiner blinding; ii) have too small sample sizes; iii) measure cuspal heights and distances using a crude method, such as calipers on a stone cast; iv) do not measure altered pit and fissure morphology; and v) do not examine plaque retention and caries development in altered fissures^[23, 24, 25]. Furthermore, it is questionable to what extent the small amounts of fluoride in food can alter the morphology of teeth. Rats have shown to experience true morphological changes in their teeth as a result of fluoride exposure, but only after receiving a high level of fluoride in their drinking water. Variables in both animal and human studies need to be controlled when examining the effects of low dose fluoride intake on tooth morphology. According to Smith *et al.*, rats are able to tolerate much higher fluoride levels in their water supply before adverse effects can be documented^[26].

Moreover, use of fluoride supplement in first six years of life; specially in first three years significantly increases the risk of fluorosis. A study in England estimated the prevalence of ‘aesthetically objectionable’ fluorosis to be around 10% in fluoridated cities, compared to 2% in non-fluoridated cities^[19].

In a recent CATFISH STUDY (Cumbria Assessment of Teeth – a Fluoride Intervention Study for Health) examined the effects of a fluoridation scheme in the North West England county of Cumbria. The study looked at two groups: a birth group of children born after fluoridation was introduced, and an older group who were around five years of age at the start of the research project. CATFISH compared dental health across the intervention and control groups over five to six years, monitoring the dental health of a sample of children in West Cumbria where fluoridation was reintroduced in 2013, and a sample of children across the rest of Cumbria which remained non-fluoridated throughout the study period. At the end of the study, 1,444 five-year-olds who were part of the younger cohort and 1,192 eleven-year-olds who were part of the older cohort had taken part. Caries prevention was greater in children who received continuous water fluoridation compared with children who received interrupted water fluoridation.^[27] Other recent Non-UK studies have shown same effects on of the cessation of water fluoridation program^[28, 29, 30].

Keeping in mind that, in 2006, a report by the National Research Council (NRC) acknowledged that fluoride exposure may be associated with adverse cognitive and endocrine outcomes, and recommended further study, especially for vulnerable populations. One NRC panel member, Dr. Isaacson, said the report “should be a wake-up call”^[31]. Khairkar *et al.*, 2021, conducted a case-control study in India, identifying three different areas based on fluoride levels in drinking water. They found a relation between water fluoride levels and the development of psychiatric manifestations such as ADHD, childhood disruptive mood disorder, defiant disorder and arithmetic specific scholastic skill disorder^[32]. 512 mother child pairs enrolled in the MIREC (Maternal Infant Research on Environmental Contaminants) were studied and it was found that higher levels of fluoride in pregnant women and water concentrations were associated with a 3- to 5-point lower IQ

score in their 3- to 4-year-old children^[33]. Though more studies need to be done in this field.

Dr. James summer, Nobel Laureate biochemist at Cornell University explains that fluoride poisons by poisoning enzymes. While poisoning enzymes in oral bacteria might be good, poisoning enzymes elsewhere in the body could lead to a host of undesirable effects.

In 1985 the landmark Tiel-Culemborg longitudinal study in Netherland compared caries experience in fluoridated Tiel with that in non-fluoridated Culemborg over more than 20 years. It was found that when both types of carious lesions, non-cavitated as well as cavitated are compared, there was virtually no difference between the cities. But caries progression beyond the stage of enamel caries was markedly reduced in the fluoridated Tiel. This finding tells us that ingested fluoride does not prevent the initial carious lesion to form but it does prevent many of them to progress beyond enamel lesion. This can only happen through remineralization of the initial carious lesion and the author concluded that the “systemic fluoridation” is not required.^[34]

However, because the systemic fluoridation dogma dominated preventive dentistry at the time, these early studies were disregarded. In 2015 Cochrane Oral Health carried out a systematic review of water fluoridation. It was found that because of the introduction of fluoridation, children suffered 35% fewer decayed, missing and filled primary teeth (dmft) and 26% fewer decayed, missing and filled permanent teeth (DMFT)^[35]. But the included studies were assessed as being at high-risk of bias and most had been carried out prior to the widespread introduction of fluoride toothpastes in the mid-1970s.

Featherstone summarized that localized effect of fluoride at the plaque-enamel interface when the caries process starts is the main preventive action of fluoride. Studies have shown when fluoride toothpastes are used, a high concentration of fluoride is maintained in the mouth (saliva, biofilm fluid) for some minutes. In saliva, fluoride concentration takes 1 or 2 hours to reach the baseline, pre-brushing values. In the biofilm, increased fluoride values are maintained even 10 hours after brushing when fluoride toothpastes are used on a regular basis.^[36] A.Thilstrup, once one of the major contenders of systemic fluoridation, finally surrendered in 1980 and declared “cariostatic effect of fluoride in optimal fluoride areas may well be a result of its topical effect^[37]. If it is so, arguments continue, then why use high concentration topical fluorides? FB Glenn, a practicing dentist from Miami ironically commented, ‘Northern Europe could now take pride in their anti-fluoridation as they had 1,000 to 15,000 ppm topicals while the United States was using a 1 ppm “topical”^[38].

Although we recognise that water fluoridation could make a positive contribution to improvements in oral health, the practicalities of implementing this means we have taken the view that alternative solutions are more achievable^[39]. There is a risk for dental fluorosis in children with systemic fluoride exposure, and a threshold cannot be detected. In children, a very narrow margin exists between achieving the beneficial effects of fluoride in caries prevention and the adverse effects of dental fluorosis. Exposure of environmental organisms to the levels of fluoride used for fluoridation of drinking water is not expected to lead to unacceptable risks to the environment^[40]. In 2014, the Scientific World Journal published a study titled: Water Fluoridation: a Critical Review of the Physiological Effects

of Ingesting Fluoride as a Public Health Intervention. In the conclusions of this study the author's state: the available evidence suggests that fluoride has the potential to cause major adverse human health problems, while having only modest dental caries prevention effect. As part of efforts to reduce hazardous fluoride ingestion, the practice of artificial water fluoridation should be reconsidered globally.... Public health approaches for global dental caries reduction that do not involve systemic ingestion of fluoride are urgently needed.^[41]

Conclusion

Increasing fluoride exposure to public was started with good intentions and based on the best evidence we had. The evidence and science has grown over the last 70+ years, more rapidly over the last 20 and exploded over the last 10 years "There have long been divergent views on whether water fluoridation prevents caries primarily through pre-eruptive systemic uptake by developing enamel, or by post-eruptive remineralization and various antibacterial effects". In the era of evidence-based dentistry suggests that scientific evidences should lead the way when drawing conclusions. It can be assumed that the 'extra' fluoride provides added protection but no study yet has been conducted to prove that fluoride incorporation prior to tooth eruption is somehow superior to that which can be incorporated by means of topical exposure of the teeth during or after tooth eruption. Water fluoridation is considered the simplest strategy to maintain fluoride constantly present in the oral environment, not only by drinking water daily, but also by eating food cooked with fluoridated water. The longer a tooth is exposed to fluoridated water, the greater its resistance to caries because of the topical effect of F contained water. As a result, the post-eruptive hypothesis can be readily adopted as the primary mechanism for fluoride's anti-cariogenic action. Pre-eruptive fluoride may have some anti-cariogenic effects, but when the evidence-based philosophy is applied, the data's inconsistencies make the pre-eruptive hypothesis difficult to believe in. These findings undoubtedly indicate a significant post-eruptive mechanism for the fluoridated water's preventive effects. Dr. Arvid Carlsson, Nobel laureate in medicine for 2000 replied, " Well, in pharmacology, if the effect is local, it's of course absolutely awkward to use it in any other way than as a local treatment. I mean this is obvious. You have the teeth there, they're available for you, why drink the stuff? I see no reason at all for giving it (Fluoride) in any other way than locally — topically, if you wish". The conclusion, based on the arguments presented in this paper, is that near-maximum protection against dental caries can be achieved without swallowing fluoride during the first few years of life. We must re-evaluate policies in the light of new research.

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