REVIEW ARTICLE

Is fluoride still a pivot of preventive dentistry?

Poonam Mahajan, K. L. Veersha[1], Ajay Mahajan[2]

Departments of Community Dentistry, HPGDC, Shimla, Himachal Pradesh, [1]Dental College, Mullana, Ambala, [2]Periodontics, HPGDC, Shimla, Himachal Pradesh, India

Address for correspondence:
Dr. Poonam Mahajan,
Department of Community Dentistry,
HPGDC, Snowdown, Shimla - 171 001,
Himachal Pradesh, India.
E-mail: poonammahajan81@gmail.com

ABSTRACT

Fluoride is considered the corner stone of the preventive dentistry. Fluoride has both beneficial and detrimental effects on human health. In terms of dental health, the prevalence of dental caries is inversely related to the concentration of fluoride in drinking water; while there is a dose-response relationship between the concentration of fluoride in drinking water and the prevalence of dental fluorosis. Fluoride has a statistically significant association with a wide range of adverse effects like increased risk of bone fractures, decreased thyroid function, and lowered intelligent quotient, arthritic-like condition, early puberty and possibly, osteosarcoma. The aim of the present review is to discuss the current status of fluorides in dentistry in view of its benefits and adverse effects.

Key words
Adverse effects, caries, dentistry, fluorides

INTRODUCTION

Fluorine is the 17th most abundant element in the nature. It is most electronegative and reactive of all elements, it reacts its surrounding and rarely found free or in elemental state Fluoride ion is present in all water sources, including the ocean.[1] The word fluoride is derived from Russian word 'FLOR' which comes from FLORIS which means destruction in Greek and from Latin word 'FLUOR' means 'to flow' since it was used was used as flux. History of fluoride in dentistry is more than hundred years old. It begins with the arrival of Dr. Fredrick MacKay in Colorado springs in U.S.A, where he discovered some permanent stains on teeth of his patients which were referred as Colorado stains. MC Kay termed it as mottled enamel later Dr. Trendly H. Dean made a thorough documentation of the degree of mottled enamel. Afterwards a chemist Churchill identified the anonymous element responsible for mottling is fluoride. The term mottled enamel gave way to more exact term 'dental-fluorosis'.[2]

Whilst almost all foodstuffs contain at least traces of fluoride, water and non-dairy beverages are the main sources of ingested fluoride. Other significant sources of ingested fluoride are toothpaste in very young children (who tend to swallow most of their toothpaste), tea in tea-drinking communities, and inhaled fluoride in some communities in China where coal containing very high levels fluoride is burned indoors.[3]

There are two delivery systems of fluoride for prevention of dental caries:

- Systemic - E.g., fluoride in water, milk, salt etc.
- Topical - Topical fluoride can be delivered in two ways: Self applied topical fluoride (e.g., fluoride tooth paste, fluoride mouth rinse. Fluoride mouth rinse etc) and professionally applied topical fluoride (e.g., sodium fluoride, acidulated phosphate fluoride).

METHODOLOGY

Search of the literature

1. Online search was done using the key words: Fluoride, dentistry, side effects, current status, adverse effects, systemic, complications, fractures, fluorosis, water-fluoridation, cancer, and caries. Search process included review of data bases: PubMed, the Cochrane Central Register of Controlled Trials, OVID Evidence-based Reviews, EMBASE, Allied and Complementary Medicine Database (AMED), (WHO Library Database (WHOLIS), Current Contents Search (Science Citation Index and Social Science Citation Index, SCOPUS and SOCOLAR. Each database was searched from its starting date to January 2010
2. World Wide Web was searched via Google Scholar

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search engine and yahoo search directory
3. Relevant articles published in various journals and chapters from relevant text books were also considered for review[1,3-5]
4. Perusal of the references of all relevant papers found (and sometime the references of the references).

The Review was conducted from February 2012 to July 2012.

Eligibility criteria and assessment of study quality

Enclusion and exclusion criteria

All the studies published in the mentioned time frame which discussed the role of fluoride in dentistry or which mentioned the side effects of using fluoride in dentistry were included in the study. Studies which lacked well explained materials and methods, which did not discuss the previous literature on fluoride and its side effects sufficiently or which were sponsored by some pharmaceutical company were excluded. Studies published in language other than English and unpublished studies were also excluded [Figure 1].

Assesment of study quality

Three reviewers assessed the inclusion criteria and study quality. Initially, we evaluated all identified citations on the basis of titles and/or abstracts against the eligibility criteria. Those deemed to be irrelevant were excluded and reasons for exclusion noted. When the information provided by titles/abstracts was insufficient to decide on inclusion/exclusion, or the titles/abstracts were relevant to the project, we retrieved and evaluated the full-text.

The reviewers were blind to the authors, their institution, results, and conclusions of primary studies. Evidence with high risk of bias was not considered.

Data extraction

On the basis of previously established check list (http://www.york.ac.uk/inst/crd/pdf/crdreport4_app3.pdf) a list of relevant items extracted from the included studies by two reviewers and checked by a third reviewer. Each reviewer independently examined the articles. The information regarding authors, their institution of primary studies was removed before data extraction.

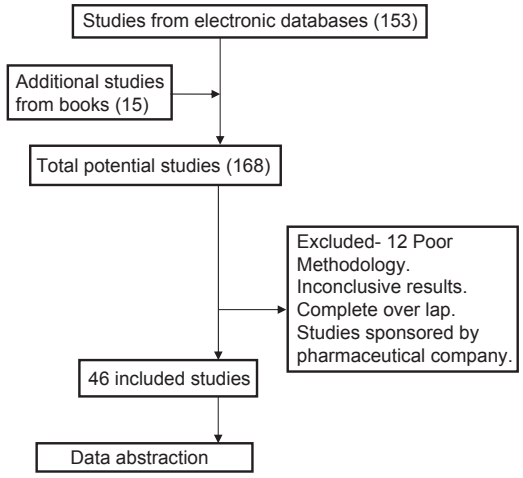

Figure 1: The output of search strategy

Statistical methods

The inter-observer agreement beyond chance was calculated using the Cohen's Kappa statistics using Statistical Product and Service Solutions (SPSS) statistical software and found to be 0.60 (95% CI 0.52 to 0.69). This value corresponds to moderate to substantial agreement between the reviewers. Once data extraction was completed, data were reviewed to identify duplicate data, for example the same results published in more than one journal or published papers whose unpublished drafts had been identified previously.

Literature review

Fluoride role in preventive dentistry

Fluoride is considered the corner stone of the preventive dentistry. It continues to be regarded as the pivot of the preventive dentistry because of its cariostatic efficacy. There is abundance of literature on its role in general and dental health. Fluoride has both beneficial and detrimental effects on human health. In terms of dental health, the prevalence of dental caries is inversely related to the concentration of fluoride in drinking water; while there is a dose-response relationship between the concentration of fluoride in drinking water and the prevalence of dental fluorosis.[6]

The dental effects of fluoride naturally present in public drinking water were established during the 1930s and 40s by Trendley Dean and his colleagues at the US Public Health Service. In a series of epidemiological studies across the United States they demonstrated that as the concentration of fluoride naturally present in drinking water increased, the prevalence and severity of dental fluorosis increased and the prevalence and severity of dental caries (decay) decreased[5] Fluoridation was first introduced as a public health measure in the USA in the 1950s, after cross-sectional studies of naturally fluoridated regions of that country suggested that levels of tooth decay declined as the fluoride concentration in drinking water increased. Several 'controlled fluoridation trials' were conducted in the USA and Canada. Then, in Australia, the National Health and Medical Research Council, Australian Dental Association and Australian Medical Association all endorsed fluoridation in the 1950s, despite considerable opposition from doctors in the letters columns of the Medical Journal of Australia. At that time there was almost no knowledge of the mechanisms of action of fluoride in the human body.[7]

Fluoride the other side

Despite the presence of enormous data on the beneficial

effects of fluorides in prevention of dental caries the fact that fluoride has serious adverse effects can not be ignored. The most common side effect noticed is dental fluorosis which occurs as a result of fluoride overdose and results in tooth discoloration a condition called "mottled enamel". In artificially fluoridated regions, dental fluorosis is now much more prevalent and severe than the initial proponents of fluoridation predicted. The University of York's Fluoridation Review,[8] estimates that up to 48% of children in fluoridated areas have some form of dental fluorosis.

In addition to dental fluorosis there is also a large and growing body of research on a fluoride-induced bone disease called skeletal fluorosis. This disease is observed on X-rays as increased bone density, structural damage to bones, and calcification of joints and ligaments. In severe cases, some patients cannot even straighten their arms or even walk upright.

The health effects of fluoride were reviewed by Moulton in 1942,[9] prior to the Grand Rapids intervention and regularly ever since by numerous organizations and individuals. More recently International Programme on Chemical Safety (IPCS),[3] have carried out a detailed review of fluoride and the potential for impacts on health. Studies and reviews have concentrated not only non bone fractures, skeletal fluorosis, cancers and birth defects but also cover many other disorders claimed to be caused, or aggravated, by fluoridation.[5,10-15] There is clear evidence from India and China that skeletal fluorosis and an increased risk of bone fractures occur as a result of long-term excessive exposure to fluoride (total intakes of 14 mg fluoride per day), and evidence suggestive of an increased risk of bone effects at total intakes above about 6 mg fluoride per day.[3] Most people assume that these severe manifestations of skeletal fluorosis occur at much higher fluoride levels than the 1 ppm. To the contrary, clinically significant cases of skeletal fluorosis have been reported in at least 9 papers from 5 countries when natural fluoride concentrations are below 4 ppm and are mostly below 2.5 ppm.[16] A few cases are even reported in India and China at fluoride concentrations slightly below 1 ppm. In India and China naturally occurring fluoride is regarded as a chronic poison and the main issue is how to remove it from drinking water as effectively and cheaply as possible. In particular, a recent epidemiological study, which examined the aged in six naturally fluoridated Chinese villages, hip fracture rates doubled at 1.5 ppm, and tripled at 4.3 ppm, when compared to the fracture rates at 1 ppm fluoride.[17] In Mexico, a linear correlation between the severity of dental fluorosis and the incidence of bone fractures in children has been observed.[18] Guifan Sun (School of Public Health, China Medical University, Shenyang) in his inaugural address stressed on active research of fluoride and improvement of the health condition of people all over the world because fluoride has a statistically significant association with a wide range of adverse effects. These include not only dental and skeletal and dental fluorosis bit also increased risk of bone fractures, decreased thyroid function, lowered IQ, arthritic-like condition, and possibly, osteosarcoma. On 9 August 2007, the Fluoride Action Network (FAN) statement signed by over 600 professionals, stated that it is time for advanced nations and fluoridating countries to recognize that fluoridation is outdated and has serious risks that far outweigh any minor benefits, violates sound medical ethics and denies freedom of choice.[19]

Some worrying results have also been published on the biological effects of fluorides, based on laboratory and animal experiments. It is well known to biochemists that, contrary to one of the pro fluoridation myths, fluoride is highly active biologically, forming a strong hydrogen bond with the groups found in proteins and nucleic acids.[20] *In vitro* experiments demonstrated that fluoride inhibits enzymes, and induces chromosome aberrations,[21] and genetic mutations.[22] Professor Anna Strunecka of Charles University in the Czech Republic has shown in laboratory experiments that fluoride in the presence of aluminum disrupts G-proteins.[23] G-proteins take part in a wide variety of biological signaling systems, helping to control almost all important life processes. Furthermore, pharmacologists estimate that up to 60% of all medicines used today exert their effects through a G-protein signaling pathway. Animal experiments reveal that fluoride increases the uptake of aluminum into the brain at 1 ppm in the drinking water. It has been suggested that aluminum fluoride (AlF_3) complexes might induce alterations in homeostasis, metabolism, growth and differentiation in living organisms. Thus, the malfunctioning of G-proteins could be a causal factor in many human diseases, including Alzheimer's disease, asthma, memory disturbance, migraine and mental disorders.[24] Dr. Z. Machoy, from the Pomeranian Academy of Medicine, Poland, points out that AlF_3 activates several guanine nucleotides, mimicking the actions of some neurotransmitters and hormones. His group has performed computer modeling of how AlF_3 attacks the biologically important GDP nucleotide.[25]

Dr. NJ Chinoy from Gujarat University, India, has found that higher doses of fluoride cause reproductive problems.[26] Research on aged human cadavers by Dr. Jennifer Luke at University of Surrey has shown that fluoride concentrates in the pineal gland.[27] Furthermore, in animal studies, it has been shown that this concentration is associated with the earlier onset of puberty. As a mechanism hypothesis has been made that the increased fluoride concentration leads to the reduced production of melatonin (because fluoride is known to inhibit the enzymes needed to produce it) and that this in turn leads to an accelerated sexual maturation. This work dovetails with studies which have shown that girls in the US-one of the world's most heavily fluoridated countries

are reaching puberty earlier and earlier.[7] According to Dr. John R. Marier, of the Division of Biological Sciences at the Canadian National Research Council, Ottawa, Fluoride (in vitamins or water) interferes with magnesium metabolism in the body. This is significant because fluoride toxicity is increased when magnesium levels are low. Magnesium deficiency is widespread in the U.S., especially among children and teenagers, reaching the 99th percentile among young women.[28]

Benefits of fluoridation a fallacy

A major cross sectional survey of eighty four cities in the USA by JA Brunelle and JP Carlos at the National Institute of Dental Research found that children aged 5-17, who had lived their whole lives in fluoridated cities, had on average only 0.6 fewer decayed, missing and filled tooth surfaces (DMFS) per child than those in un-fluoridated cities.[29] In Australia a survey by Professor John Spencer from University of Adelaide (1996) found an average reduction of only 0.12 to 0.3 DMFS per child.[30] Since the total number of permanent tooth surfaces in a child's mouth is one hundred twenty eight, the US and Australian reductions are less than one half and one quarter of one percent of tooth surfaces, respectively.

Fluoride is also not approved by the U.S. Food and Drug Administration (FDA).California is 28% fluoridated; Hawaii is 9% fluoridated. These states are tied for the lowest rate of tooth loss in the USA. On the other hand, Kentucky is 100% fluoridated and has the highest toothless population of older adults.[28]

Also the role of vested interests in promoting the use of fluoride in dentistry cannot be under estimated. Several fluoride researchers have published accounts of attempts by dental, medical and public health authorities to intimidate them and to suppress their work.[7] Behind the dental and medical associations, who promote fluoridation, are powerful corporate GFFGG interests like-the sugary food industry (e.g., sugar, soft drinks, processed breakfast cereals and sweets) that benefits from the notion that there is a magic bullet that stops tooth decay, whatever junk food our children eat; the phosphate fertilizer industry that sells its waste silico-fluoride to be put in drinking water instead of paying for its safe disposal; and the aluminum industry, which had an image problem with the atmospheric fluoride pollution it produces, and funded some of the early research in naturally fluoridated regions of the USA that appeared to show that fluoride was good for teeth.

Some governments support fluoridation because they consider it to be a cheaper way of addressing tooth decay than running effective dental services for school children and older people, and politically safer than tackling the promotion of sugary foods that are the main cause of tooth decay.

Fluoride alternatives

A lot of research is going on towards efforts to develop new methods to prevent caries for e.g., caries vaccine, laser, probiotics, benign microorganism replacement therapy, Self assembling polypeptides (SAP), caries preventive chewing gums, microdentistry, teledentistry etc. The evidence of a specific bacterial cause of dental caries and of the function of the salivary glands as an effectors site of the mucosal immune system has provided a scientific basis for the development of a vaccine against this highly prevalent and costly oral disease. Research efforts towards developing an effective and safe caries vaccine have been facilitated by progress in molecular biology, with the cloning and functional characterization of virulence factors from mutans streptococci, the principal causative agent of dental caries.[2] The application of health-promoting bacteria for therapeutic purposes is one of the strongest emerging fields in this regard. Although the use of such probiotics specifically to improve oral health is still in its infancy. The widespread oral intake of probiotics as preventive and therapeutic products for gastrointestinal health makes it of considerable interest for oral healthcare workers. These products usually contain *streptococci, lactobacilli* or *bifidobacteria*.[31] Reports have been suggested the use of self assembling polypeptides for augmentation host resistance. They may be useful in enamel re-minerlization.

Genetic engineering is also providing better alternatives by mutating a gene which controls the acid production in *S. mutans*. Lasers-CO_2 laser can be used to alter the tooth surface of enamel and make it less prone to caries. Pits and fissures and root surfaces may be the area targeted by the laser. An novel technique involves the use of chewing gum after meals in order to counter the pH drop that occurs with the intake of sugar. Various sugar free gums have been tried out, with additions such as xylitol, lactitol.[1]

CONCLUSION

Fluoride because of its anti-caries action was considered pivot of preventive dentistry. It was considered as double edge sword as the excess amount was responsible for dental as well as skeletal fluorosis, which is incurable. But its benefits as anti-caries element were so much endorsed that it over shadowed its serious side effects. But with changing scenario attention is now being drawn on potentially permanent damaging effect of fluoride. This review of literature on fluoride research reveals a situation where people in fluoridated communities are required to ingest a harmful and ineffective medication with uncontrolled dose. The medication actually doesn't need to be swallowed, since it acts directly on tooth surfaces. The benefit of fluoridation is at best a reduction in tooth decay in only a fraction of one tooth surface per child. It is time for advanced nations and fluoridating countries to recognize that fluoridation is outdated and

has serious risks that far outweigh any minor benefits, violates sound medical ethics and denies freedom of choice. With the advancement of recent methods for caries prevention role of fluoride in preventive dentistry needs to be readdressed.

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