Prev. Nutr. Food Sci. 2018;23(3):171-180
https://doi.org/10.3746/pnf.2018.23.3.171
pISSN 2287-1098 · eISSN 2287-8602

Review Article

The Fluoride Debate: The Pros and Cons of Fluoridation

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ABSTRACT: Fluoride is one of the most abundant elements found in nature. Water is the major dietary source of fluoride. The only known association with low fluoride intake is the risk of dental caries. Initially, fluoride was considered beneficial when given systemically during tooth development, but later research has shown the importance and the advantages of its topical effects in the prevention or treatment of dental caries and tooth decay. Water fluoridation was once heralded as one of the best public health achievements in the twentieth century. Since this practice is not feasible or cost effective in many regions, especially rural areas, researchers and policy makers have explored other methods of introducing fluoride to the general population such as adding fluoride to milk and table salt. Lately, major concerns about excessive fluoride intake and related toxicity were raised worldwide, leading several countries to ban fluoridation. Health-care professionals and the public need guidance regarding the debate around fluoridation. This paper reviews the different aspects of fluoridation, their effectiveness in dental caries prevention and their risks. It was performed in the PubMed and the Google Scholar databases in January 2018 without limitation as to the publication period.

Keywords: dental caries, fluoridation, prevention, public health, toxicity

INTRODUCTION

Fluoride is the ionic form of fluorine, the thirteenth most abundant element in the earth's crust. It is released into the environment naturally in both water and air. Its concentration in water is variable (1). Water is the major dietary source of fluoride. The variability in water content explains much of the variability in total fluoride intake. Other important sources of fluoride are tea, seafood that contains edible bones or shells, medicinal supplements, and fluoridated toothpastes (2). Fluoride compounds are also produced by some industrial processes that use the mineral apatite, a mixture of calcium phosphate compounds (2). Dietary fluoride is absorbed rapidly in the stomach and small intestine. One-quarter to one-third of the absorbed fluoride is taken up into calcified tissues, whereas the rest is lost in the urine (3-6). In bone and teeth, fluoride can displace hydroxyl ions from hydroxyapatite to produce fluorapatite or fluorohydroxyapatite. About 99% of total body fluoride is contained in bones and teeth (3), and the amount steadily increases during life. The recommended intake for fluoride is expressed as an adequate intake rather than recommended dietary allowance, because of the limited data available to determine the population needs. The adequate intake for fluoride is 0.7 mg daily for toddlers, rising to 3 mg daily for adult women and 4 mg daily for adult men. It remains unclear whether fluoride is truly essential, although fluoride may have some beneficial effects (2). Once taken up into bone, fluoride appears to increase osteoblast activity and bone density, especially in the lumbar spine (7). Fluoride has been suggested as a therapy for osteoporosis since the 1960s, but despite producing denser bone, fracture risk is not reduced. Indeed, there is some evidence that nonvertebral fractures may be increased (8). The only known association with low fluoride intake is the risk of dental caries, acting through both pre-eruptive and post-eruptive mechanisms (5). The American Dental Association strongly supports fluoridation of community drinking water supplies (4); however, strong contradictory opinions also are held (9).

Dental caries is an infectious and multifactorial disease afflicting most people in industrialized and developing countries. Fluoride reduces the incidence of dental caries and slows or reverses the progression of existing lesions (10). Although pit and fissure sealants, meticulous oral hygiene, and appropriate dietary practices contribute to caries prevention and control, the most effective and widely used approaches include fluoride use (11).

The first 'artificial' water fluoridation for caries control

Received 17 April 2018; Accepted 5 July 2018; Published online 30 September 2018
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was introduced in 1945 and 1946 in the United States (US) and Canada, respectively, and it was expected that caries prevalence would be reduced by as much as 50% (12). The success of water fluoridation in preventing and controlling dental caries led to the development of several fluoride-containing products, including toothpaste, mouth rinse, dietary supplements, and professionally applied or prescribed gel, foam, or varnish.

Much of the research on the efficacy and effectiveness of individual fluoride modalities in preventing and controlling dental caries was conducted before 1980, when dental caries were more common and more severe. Several modes of fluoride use have evolved, each with its own recommended concentration, frequency of use, and dosage schedule. Simultaneously, recent resistance has been growing worldwide against fluoridation, emphasizing the possible risk of toxicity. Thus, health-care professionals and the public need guidance regarding the debate around fluoridation. This review examines the different aspects of fluoridation, their effectiveness in dental caries prevention, and their risks.

MODE OF ACTION

Fluoride works to control early dental caries in several ways. Due to its anticariogenic and antimicrobial properties, the fluoride ion (F^-) has been widely used in the treatment of dental caries. The antibacterial action of fluoride is due to the acidification of the bacterial cytoplasm through the formation of hydrogen ion (H^+) and F^- from hydrogen fluoride and the disruption of the bacterial metabolism by inhibiting vital bacterial enzymes such as proton releasing adenosine triphosphatase and enolase.

Moreover, the use of fluoride lowers the pH. Bacteria will thus use more energy to maintain a neutral pH. Therefore, they will have less energy left to grow, reproduce and generate acid and polysaccharides.

The mechanisms of fluoride oral action suggested by Ullah et al. (13) include the following: reduction in demineralization of sound enamel by inhibiting microbial growth and metabolism; enhancement of the remineralization and the recovery of demineralized enamel, and the formation of the fluorapatite mineral phase that provides more resistance to demineralization and acid dissolution following acid production by bacteria; inhibition of enzymes such as reduction of immunoglobulin A protease synthesis; reduction in extracellular polysaccharide production which helps in decreasing bacterial adherence to dental hard tissues. As fluoride concentrates in dental plaque, it inhibits the process by which cariogenic bacteria metabolize carbohydrates to produce acid and adhesive polysaccharides.

The laboratory and epidemiologic research led to a better understanding of the way fluoride prevents dental caries. Its predominant effect is post-eruptive and topical, and depends on the use of fluoride in the right amount, in the right place and at the right time. Fluoride works primarily after teeth have erupted, especially when small amounts of fluoride are maintained constantly in the mouth, and specifically in dental plaque and saliva. Thus, not only children benefit from fluoride as was previously assumed, but also adults since it is more readily taken up by demineralized enamel than by sound enamel (11).

WATER FLUORIDATION

Fluoride is naturally found in fresh water. Its concentration depends on the geographical location and source, and ranges from 0.01 ppm to a maximum of 100 ppm (13). In the 1930s, several studies reported a low prevalence of dental caries among people consuming natural drinking-water with high fluoride (14).

Water fluoridation, in which controlled amount of fluoride is added to the public water supply, was considered one of the greatest successes in public health in the twentieth century (15), and one of the most popular methods of delivering fluoride systemically to a large population with no need for its active participation (13). It is actually practiced in many countries throughout the world. In 1945, public water fluoridation was implemented for the first time in the US, and was recommended by the World Health Organization (WHO) as the main delivery method of fluoride to improve oral health (16). By 2012, more than 435 million people worldwide had access to either naturally fluoridated water (about 57 million) or water with adjusted fluoride concentrations at or near optimal level (about 378 million). Some of these countries include the US, Brazil, Australia, Canada, Spain, Argentina, South Korea, and New Zealand (17).

Over the past 60 years, research studies conducted in several countries were remarkably consistent in demonstrating substantial reductions in caries prevalence as a result of water fluoridation. Prior to 1990, around 113 studies on the effectiveness of artificial water fluoridation were conducted in 23 countries, and recorded a modal percent caries reduction of 40～50% in primary teeth and 50～60% in permanent teeth. More recent systematic reviews summarizing the extensive data have confirmed that water fluoridation substantially reduces the prevalence and incidence of dental caries in primary and permanent teeth (14). Another review of studies conducted between 1990 and 2010 in 10 countries on individuals ranging from 3 to 44 years of age reported average caries reductions of 30～59% and 40～49% in primary and permanent teeth, respectively (14). The fluor-

ide action in the prevention of dental caries was predominantly posteruptive and topical (14).

Large sections of the population in developed countries are suffering from fluorosis as a result of the fluoridation of drinking water and dental products. Between 1999 and 2004, the prevalence of dental fluorosis was 41% in American adolescents aged 12～15 years (13). To minimize fluoride toxicity, the concentration of fluoride in drinking water has been controlled to attain the recommended level of 0.8～1.0 ppm (13).

Although water fluoridation is the most widely used public health measure for caries prevention, less than 10% of the world's population has access to this intervention, as it is not feasible in many areas because of the nature of water supplies (10).

MILK FLUORIDATION

Milk constitutes an essential food in early life and continues to provide benefits from childhood and adolescence up until and through old age. According to O'Mullane et al. (14), the concept of milk as a vehicle for fluoride emerged in the early 1950s and was first investigated almost simultaneously in Switzerland, the US, and Japan (18). Since 1986, programs aiming to validate the feasibility for community use of fluoridated milk for caries prevention were promoted and supported by the WHO International Programme for Milk Fluoridation (14). At present, milk fluoridation programmes, supported by the WHO and Food and Agriculture Organization, are running continuously in about 15 countries and various channels are used to provide fluoridated milk to children attending kindergarten and school.

The bioavailability of fluoride in milk and the biological plausibility of milk fluoridation were demonstrated by a significant amount of non-clinical published research. Four systematic reviews have been published on the clinical effectiveness of milk fluoridation in preventing dental caries. The first three reviews found that all studies reported a reduction in dental decay among those consuming/receiving fluoridated milk (19-21). However, the fourth wider-ranging review, including 18 studies conducted in 12 countries, found that only nine studies demonstrated caries prevention in primary teeth and 12 in the permanent dentition (22). A very recent study, conducted in Bulgaria, also showed that fluoridated milk delivered on a daily basis to children in schools resulted in substantially lowering caries development compared to children receiving milk with no added fluoride (23). In general, milk fluoridation is effective in the prevention of dental caries. In order to protect and reduce caries in primary teeth, it was recommended that fluoridated milk should be consumed by children early on, preferably before the age of 4 years, and at the eruption of their first permanent molars (24). Currently, more than one and a half million children worldwide consume fluoridated milk (24) and considerable knowledge on practical aspects of fluoridation was provided by the experience gained in this international program.

The daily dosage of fluoride per child varies from 0.50 mg to 0.85 mg (14). Children are advised to drink around 200 mL of fluoridated milk per day for about 200 days per year (22). Given that the dose is constant and related to age and background fluoride exposure, the risk of adverse effects is very low (22). However, milk fluoridation is a less efficient method for delivery of fluoride when compared to water fluoridation. The fluoride added to milk forms insoluble complexes that make fluoride absorption difficult (14).

The addition of fluoride to milk is a simple process and the costs of fluoridated and non-fluoridated milk are usually the same. Overall, the annual cost of the programs in Chile, Thailand, and the United Kingdom (UK) is around 2 to 3 US dollars per child (22,25,26).

SALT FLUORIDATION

The fact that the lower social strata consistently show the highest levels of caries in the population has so far remained an unsolved problem (12). The availability of water fluoridation to a large proportion of the world's population is prevented by various political, geographical, financial, and technical reasons such as few central water systems and inappropriate water infrastructure. Based on the successful use of iodized salt in preventing goiter, fluoridated salt was initiated in 1955 in Switzerland to lower the risk of dental caries (17). This practice was facilitated by the following: 1) the successful community trials, 2) WHO and Fédération Dentaire Internationale World Dental Federation recommendations, 3) the approval of the European Union on sodium and potassium fluoride as food additives, and 4) the adaptation to local political, technological, and cultural environments (19). In 1980～82, adding fluoride to table salt was authorized for human consumption (12). Fluoridated salt reaches the consumer through several channels including domestic salt, meals at schools, large kitchens and in bread, and exerts both systemic and topical effects (14).

Effectiveness in caries prevention

Research studies initiated in the early seventies showed that fluoride, when added to salt, inhibits dental caries (12).

The first studies that assessed the effects of fluoride added to ingested salt on the incidence and prevalence of dental caries were carried out from 1965 to 1985 in

Colombia, Hungary, and Switzerland. The results were similar to those observed with fluoridated water (14). The number of teeth affected by caries was reduced by approximately 50 percent. The beneficial effect of fluoridated salt in reducing dental caries was also observed among Hungarian adults in a study (1991) including the following: 1) one group who were lifetime residents in a community with access to 1.1 ppm of natural fluoride in drinking water (N=205; lowest caries experience), 2) another group who had access to fluoridated salt between 1966 and 1985 (N=213; intermediate caries experience), and 3) a third group who had minimal fluoride exposure (N=258; highest caries experience) (17). A further study, conducted by Sagheri et al. (27) in two communities (Dublin and Freiburg) with different oral health prevention strategies (water fluoridation and salt fluoridation), confirmed that both water and salt fluoridation reduced the gap in dental caries experience between middle and lower social classes. Thus, salt fluoridation can be considered a good strategy in preventing or reducing the levels of dental caries, especially where water fluoridation is not feasible. On the contrary, Armfield (9) stated that the effectiveness of fluoridated salt is doubtful since no randomized clinical trials were conducted to prove its efficacy.

Fluoride concentration in salt

Salt fluoridation comprises the addition of a mixture of potassium fluoride and sodium fluoride to domestic or table salt to reach a concentration of 250～300 mg of fluoride/kg salt (15). At this concentration, the level of fluoride in saliva is very similar to that found in the saliva of individuals exposed to water fluoridation at 1 mg/L. In order to achieve a meaningful effect on caries control, the minimal acceptable level of fluoride is 200 mg/kg salt. Moreover, urine is used as a biomarker to monitor salt fluoridation compliance and possible excessive fluoride ingestion by individuals (17).

Domestic salt fluoridation is found to be a suitable automatic method for caries prevention. A regular and continuous consumption of domestic salt containing 250 mg of fluoride/kg significantly reduces caries in both deciduous and permanent teeth. The degree of caries reduction depends on the concentration of fluoride in salt. A domestic salt with 200 mg of fluoride/kg has a lower caries reduction than that with 250 mg of fluoride/kg. The best results are observed when domestic salt contains 350 mg of fluoride/kg. There are no side effects or significantly mottled enamel in any of the three experimental groups using salt with different concentrations: 200, 250, or 350 mg of fluoride/kg, when compared to a control group using no fluoridated salt (10).

Availability

Salt fluoridation is a well-established public means for delivery of fluoride. According to Yeung (19), fluoridated salt is available in several countries including 12 in the American continent and 8 in Europe. It has been used mainly in Europe for decades, and increasingly since the early 1990s in South and Central America. Salt fluoridation has recently been adopted in some Asian countries including Cambodia and Laos, and also implemented in an African country, Madagascar (17). Presently, 300 million people worldwide are using fluoridated salt, including 200 million in Latin America (available in nearly all countries except Brazil, Chile, and Panama) and 70～80 million in Europe (15).

Nowadays, according to Pollick (17), there are national regulations or authorizations for the production and marketing of fluoridated salt in eight European countries: Austria, Czech Republic, France, Germany (67% of domestic salt consumed is fluoridated), Romania, Slovakia, Spain, and Switzerland (85% of domestic salt consumed is fluoridated). In Europe, where there are major discounters, there are safeguards regarding importation of fluoridated salt across borders. There are many variants of the commercial distribution or "channels" that reach the consumer. These channels include domestic salt, meals at schools, large kitchens, and food items such as bread.

The most extensive use of fluoridated salt is in Jamaica, Costa Rica, the canton of Vaud, and Switzerland. In some Swiss cantons, France, and Germany, the domestic salt is the main basis for salt fluoridation programs. Mapping of the natural fluoride content of water is necessary to keep salt fluoridation away from regions where the fluoride content of water is higher than 0.7 ppm (17).

The impact on community coverage and health is affected by many factors such as distribution, marketing, pricing, and implementation methods. For instance, Jamaica prohibited the importation and sale of all non-fluoridated salt for human consumption and achieved reported caries reductions of up to 82% in 12-year-old (14). In Mexico, fluoridated and iodized salt and fluoridated water were used in order to achieve national fluoride coverage for its population of 112 million. In Uruguay, it was legislated that a specific percentage of domestic salt be fluoridated for human consumption. Depending on national implementation methods, part of or entire populations may be covered. The minimum level of implementation is fluoridation of domestic salt only, as practiced in France and Germany. Various levels of implementation concerning multiple products containing fluoride are in place in Costa Rica, Jamaica, and Switzerland. Population coverage is almost complete when salts used in bakeries, institutions, and domestically, are fluoridated. When only a portion of households use fluoridated salt,

consumers retain the capacity to choose between different types of salt, however, the reduction of fluoride intake through salt may impact negatively on communities' dental health (14).

Concerns about salt use

One point of concern is the possibility of contraindication, from the perspective of general public health, when promoting salt fluoridation, because excessive salt consumption is linked to hypertension. Yet the usual behavior leading to benefits does not need to be changed by people, and if a decline in salt consumption is indicated, an increase in fluoride concentration could be considered. Essential hypertension is estimated to be uncommon among communities or groups who usually consume low-salt diets (<5 g NaCl/person/d). Estimates of normal daily salt requirements for adults range up to 15 g/d. The available margin of safety regarding fluoride intake from fluoridated salt is wide. Fluoride intake from fluoridated salt can range from 0.5 to 0.75 mg/d. The upper tolerable limit for fluoride intake is estimated to be 0.12 mg/kg/d, which is equivalent to about 5 mg/d for 9 to 14-year-old children and 7 mg/d for 15-year-old and older people, including pregnant and lactating women. No adverse health effects have been reported when using fluoridated salt, or when combining iodide and fluoride in salt (17). However, combining both salt and water fluoridation is not recommended.

Costs of salt fluoridation

For the initial process of implementation, the equipment costs of salt fluoridation are similar to those for water fluoridation. However, during operation, the estimated cost of salt fluoridation is 10 to 100 times lower than that associated with water fluoridation programs (17). Thus, costs are minimal and coverage can be universal. The collaboration between health authorities, salt processors, distributors, and the community is indispensable for an effective program implementation. Benefits are considerably higher than the investment required for implementing the program as determined by cost-benefit studies comparing anticipated fluoridation costs versus economic resources no longer needed on dental treatment after implementation of salt fluoridation. In different countries, the price of fluoridated salt varies considerably, in comparison with iodized or non-iodized salt, and depends on local policies, regulations, and the fluctuations of the market (14).

Moreover, a recent review shows that, in some circumstances, salt fluoridation is a more cost-effective caries preventive method for children than either water or milk fluoridation or fluoridated mouth rinses (15).

The cost of salt fluoridation is very low, it ranges from 0.02 to 0.05 euros per year per capita. Children and adults from low socio-economic strata tend to have substantially more untreated caries than those from higher strata. Salt fluoridation is by far the cheapest method for improving oral health (12). Table 1 describes several characteristics of the different fluoridation methods.

COMBINATION OF MULTIPLE FLUORIDE SOURCES

Combining several methods of self-administered topical fluoride products with water fluoridation will lead to caries reduction benefits greater than when using only one method. Having a dose-response relationship, the exposure to multiple sources of fluoride, especially in lower concentrations administered daily, increases the caries reduction benefits. Combining topical fluoride products with the consumption of fluoridated water will benefit high-risk patients (28).

As with fluoridated water, there has been some concern about the simultaneous combination of fluoride ingested from both salt and toothpaste. Available data suggest that this combination has not resulted in objectionable enamel fluorosis levels. However, observations of increased mild dental fluorosis were seen in children who consumed fluoride tablets and fluoridated salt (17).

Thus, the statement that combining topical fluorides use and fluoridated water intake will cause fluorosis in the adult patient is uncertain. Fluorosis occurs only when fluoride is ingested in excessive amounts during the late secretion to the early maturation stage of enamel formation in the course of tooth development. Once tooth development is complete, any amount of topical fluoride exposure, whether in combination with fluoridated water or not, is not a risk factor for fluorosis. Children should be supervised when using topical products since swallowing some doses of these products regularly during tooth development has the potential to cause fluorosis (28).

INCREASING OPPOSITION TO FLUORIDATION

More than 80% of fluoride toxicity is seen in children before the age of 6 years, due to ingestion of fluoride-containing toothpaste or mouthwashes (29); it is rare in adults in the developed world. Acute toxicity is characterized by nonspecific gastrointestinal disturbances such as pain, nausea, vomiting, and diarrhea (30,31). In severe cases, this may progress to renal and cardiac dysfunction, coma, and ultimately death (32). In children, as little as 8.4 mg/kg may produce symptoms (30). Chronic fluoride toxicity is usually caused by high fluoride concentrations in drinking water or the use of fluoride supplements.

Table 1. Fluoridation methods

	Water fluoridation	Milk fluoridation	Salt fluoridation
Foundation	First implemented in 1945 in USA (16).	Emerged in the early 1950s and was first investigated in Switzerland, the USA, and Japan (18).	Initiated in Switzerland in 1955 (17).
Supporting bodies	Recommended by the WHO (16).	Supported by the WHO and FAO (14).	Supported by community trials, WHO, FDI World Dental Federation recommendations and others (19).
Accessibility	More than 435 million people worldwide have access to either naturally or artificially fluoridated water (17).	More than one and a half million children worldwide currently consume fluoridated milk (24).	Presently, 300 million people worldwide use fluoridated salt (15).
Benefits	Substantially reduces the prevalence and incidence of dental caries in primary and permanent teeth (14).	Effective in caries prevention in primary and permanent teeth (22,23).	Inhibits dental caries (12); however, the effectiveness of fluoridated salt is uncertain since no randomized clinical trials were conducted to prove its efficacy (9).
Dosage	Fluoride concentration in natural water ranges from 0.01 to 100 ppm (13).	Daily dosage varies from 0.50 mg to 0.85 mg fluoride/child with children drinking around 200 mL of fluoridated milk/d for about 200 days per year (14).	Fluoride concentration ranges from 250~300 mg/kg of table salt (15).
Feasibility	Less than 10% of the world's population is able to have access to fluoridated water (10).	It is a simple process and the cost of fluoridated milk is usually the same as non-fluoridated milk (25).	During operation, the estimated cost is 10 to 100 times lower than that associated with water fluoridation programs (17).
Efficiency	Considered more efficient than milk fluoridation (14).	Fluoride added to milk forms insoluble complexes that make fluoride absorption difficult and less efficient compared with water fluoridation (14).	In some circumstances salt fluoridation was a more cost-effective caries preventive for children than either fluoridated items such as water, milk or mouth rinses (15).
Health Considerations	To minimize fluoride toxicity, the fluoride concentration in drinking water in the US has been controlled with a recommended level of 0.8~1.0 ppm (13).	It is suggested that children begin to drink fluoridated milk preferably before the age of 4 years (24).	In order to achieve a meaningful effect on caries control, the minimal acceptable level of fluoride is attained at a concentration of 200 mg/kg (17). No side effects or significantly mottled enamel were shown in groups using salt containing 200, 250, or 350 mg of fluoride/kg in comparison with groups not consuming fluoridated salt (10). A contraindication of promoting salt fluoridation may be due to the risk of hypertension linked to high salt consumption. The upper tolerable limit for fluoride intake has been estimated to be 0.12 mg/kg/d, which is equivalent to about 5 mg/d for 9 to 14-year-old children and 7 mg/d for 15-year-old and older people, including pregnant and lactating women (17). No adverse impact has been identified when combining iodide and fluoride in salt (17).

WHO, World Health Organization; FAO, Food and Agriculture Organization; FDI, Fédération Dentaire Internationale.

Chronic ingestion of high doses leads to dental fluorosis, a cosmetic disorder where the teeth become mottled (1). In more severe cases, it leads to skeletal fluorosis, in which bone is radiologically dense, but fragile. Fractures can occur, and there may be calcification of ligaments and tendons, leading to reduced joint mobility (1). The syndrome also may include extensive calcification of ligaments and cartilage, as well as the bony outgrowths of osteophytes and exostoses (33).

In Europe, only Ireland, Poland, Serbia, Spain, and the UK fluoridate their water. However, most developed countries, including Japan and 97% of the European population, do not consume fluoridated water (34). In Europe, only four countries have optional salt fluoridation (Germany, France, Switzerland, and Austria), while the majority have neither fluoridated water nor fluoridated salt (34). In the US, about 70% of public water supplies are fluoridated (34). India, China, and parts of Africa have areas with high natural fluoride levels in their water, and are taking measures to remove the fluoride since it may cause health problems (34). Fluoridation has been debated in recent years, and several countries are taking

Table 2. Increasing opposition to fluoridation

Reasons to oppose fluoridation	References
Fluoride intake through fluoridated water is uncontrollable, since people are receiving varying doses regardless of age, health status, and individualized therapy.	35
Water might get contaminated with toxic chemicals while being fluoridated. Not all countries provide certificates of analysis and the amounts of contaminants in chemicals added to water.	37
Excessive fluoride intake may cause dental fluorosis.	50
Studies on animals and humans concerning fluoride intake showed neurotoxic, nephrotoxic, and other adverse effects even when small doses are administered.	39, 40, 43, 48
Fluoride can be received from sources other than fluoridated water, including ingested (mechanically deboned meat, pesticide residue, and tea) and non-ingested products (fluoridated toothpaste).	52, 53, 55
The fluoride benefit is topical rather than systemic, so it is better to be directly delivered to the teeth.	56
In fluoridated low-income countries, tooth decay is widely spread and is mainly caused by the absence of dental care and poor hygiene.	34
The effectiveness of fluoridation was not validated by any randomized controlled trial. The US Food and Drug Administration have classified fluoride as an "unapproved new drug". As of January 2012, over 4,000 professionals have signed a memorandum to end water fluoridation worldwide.	58, 60, 61

measures to reduce fluoride intake because of its toxicity risk and many other concerns (Table 2) mentioned below:

- Once water is fluoridated, it is difficult to control excessive fluoride intake, as people drink different amounts of water. For instance, manual laborers, patients (i.e., diabetics), athletes, and so forth, need and may consume a higher amount of water compared to other people (34). Accordingly, excess in fluoride intake can affect anyone regardless of age, health status, and individualized therapy (35). For example, children are receiving the same amount of fluoride as adults, and some patients (i.e., patients with kidney disease) are receiving the same dose as healthy people. We must also keep in mind that the amount of fluoride added to water (1 ppm) is up to 200 times higher than its amount in breast milk (0.005～0.01 ppm) (36).
- Moreover, while fluoridating water, contamination with toxic chemicals can probably occur (i.e., arsenic). Although all suppliers are required to provide certificates of analysis and the amounts of contaminants in chemicals added to water as in some countries such as New Zealand (37), this is not always the case all over the world.
- In addition, several animal and human studies on fluoride show some neurotoxic (38-42) and nephrotoxic (43) effects. Other negative effects of fluoride, even when administered in small doses (starting 0.3 ppm), occur on the levels of the thyroid function (44), the skeletal system (45,46) and the reproductive system (47-49).
- Another major concern caused by excessive fluoride intake is dental fluorosis, which can range from mild to severe, as proved by the 2010 CDC report on fluorosis among children (50), but the 2009 New Zealand Oral Health Survey found similar cases of fluorosis in both fluoridated and non-fluoridated countries (51). However, this might not be the case everywhere.
- Nowadays, people receive fluoride from many sources other than fluoridated water. These sources include ingested products such as mechanically deboned meat (52), tea (53), pesticide residues on food (54), and non-ingested products like fluoridated dental products (55).
- The fluoride benefit is topical rather than systemic (11,56,57), hence, it is better to deliver fluoride directly to the tooth using the toothpaste instead of ingesting it (34).
- Furthermore, tooth decay is widely spread in fluoridated low-income countries where the absence of dental care and poor hygiene are the main causes of dental decay (34).
- It is important to note that there are no randomized controlled trials to validate the effectiveness of fluoridation (58). In 2000, none of the studies on fluoridation received a Grade A classification by the British Government's "York Review" (59). Correspondingly, fluoride is classified as an "unapproved new drug" by the US Food and Drug Administration (60). As of January 2012, over 4,000 professionals have signed a memorandum to end water fluoridation worldwide (61).

CASE STUDY: SALT FLUORIDATION IN LEBANON

In 1994, a national Oral Health Survey was conducted in Lebanon and showed a high prevalence of dental caries in all age groups (62), which consequently encouraged the Ministry of Health (MOH) to work on the introduction of a massive oral health preventive program, particularly through systemic fluoride supplementation (63). Salt fluoridation was chosen as an alternative to water fluoridation deemed a non-feasible approach in Lebanon. On the third of September 2011, the Lebanese parlia-

ment approved the salt fluoridation law number 178 mandating that all table and kitchen salts in Lebanon be fluoridated by potassium fluoride at a concentration of 250 mg/kg salt. The law was supposed to come into effect on December 2014, but it stirred up controversy among the Lebanese population (64). On the one hand, supporters of the law argued that salt fluoridation can help reduce tooth decay especially since its rate in Lebanese children was among the highest in the world. On the other hand, their opponents claimed that fluoride is toxic and that various adverse effects may be caused by its addition to salt, thus questioning whether the assumed dental benefits outweigh the risks.

In order to reflect on the levels of fluoride exposure and intake in Lebanon, a number of local Lebanese studies, supported by the MOH, have been conducted among Lebanese school children. The results showed that the Lebanese population was not exposed to sufficient fluoride (62). However, the studies had several limitations, including a narrow age range, and 15 of the tested water sources (2 of which fall within an industrial zone) had fluoride concentrations within or above the minimum recommended level of 0.5 mg/L fluoride in water (20,65). Moreover, a significant amount of fluoride surpassing the estimated safe and adequate intake is being consumed by the Lebanese population through non-milk products (especially tea), as shown by Jurdi et al. (66). No data were found regarding local and imported foods which contain high levels of fluoride (67). Furthermore, it was found that a subgroup of the Lebanese population suffers from mild iodine deficiency (68,69) which can be aggravated in the presence of fluoride (64).

Therefore, for all these reasons, the Lebanese law number 178 of salt fluoridation was not clearly applied.

CONCLUSION

Dental treatments are expensive throughout the world. The cost of dentistry has hardly been reduced, even in countries where the decline in caries began 30 years ago. Thus, extension of preventive dentistry is still indispensable for improving oral health (12). The absence of dental care and poor hygiene are still considered the main causes of dental decay (34). Although multifactorial in origin, caries is a preventable disease, with fluoride as a preventive agent used worldwide. Several modes of fluoride use have evolved, each with its own recommended concentration, frequency of use, and dosage schedule. Concurrently, recent opposition has been growing worldwide against fluoridation, emphasizing the potential and serious risk of toxicity. Since the fluoride benefit is mainly topical, perhaps it is better to deliver fluoride directly to the tooth instead of ingesting it (34). Fluoride toothpaste, rinses and varnish applications have proven their effectiveness in some countries, but they are still not universally affordable.

ACKNOWLEDGEMENTS

The authors would like to thank Dr. Charbel El Amm and Mr. Andres Rodrigues for their precious assistance in editing and finalizing the manuscript.

AUTHOR DISCLOSURE STATEMENT

The authors declare no conflict of interest.

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