Ee-JRIF

Ethiopian e-Journal
for Research and Innovation Foresight

Vol 2, No 1 (2010) - Health Issue pp (59 - 84)

HEALTH HAZARDS OF FLUORIDE AS RELATED TO ETHIOPIA: A REVIEW OF SOME RELEVANT ISSUES FOR PREVENTIVE APPROACHES

Worku Abebe, PhD*

Abstract

Ethiopia is one of the 23 countries in the world with excessive fluoride concentration in drinking ground waters in many rural communities. While the majority of these communities are located in the rift valley, some of them are found dispersed in the surrounding highlands. Consistent with the presence of high-fluoride in drinking water, clinical findings have provided evidence for increased incidences of dental and skeletal fluorosis. However, despite observations of many other health effects of fluoride elsewhere, no attempts have been made to describe/assess these effects in the context of the Ethiopian situation. In addition, there are no comprehensive accounts on fluoride that have broad implications for a multidimensional approach for prevention and/or treatment of its toxicities in Ethiopia. The present paper reviews the biological mechanisms responsible for the action of fluoride with regard to dental and skeletal fluorosis, the factors that may be involved in the body's handling of fluoride, other chronic health effects of fluoride, and preventive measures that can be taken to mitigate the adverse effects of fluoride resulting from consumption of contaminated drinking water. While some attempts have been made in Ethiopia to tackle some of the problems of fluoride with the provision of low-fluoride drinking water, no significant sustainable success has been achieved. A better understanding and appreciation of the complex nature of the problem of fluoride by all stakeholders, coupled with a more comprehensive and feasible approach of prevention are vital for achieving desirable results. Aspects believe to be crucial for these considerations are particularly highlighted in the current review.

Keywords: Ethiopia, fluorosis, fluoride in drinking water, defluoridation, adverse effects, prevention, alternative water sources, water purification, nutritional supplementation

Department of Oral Biology/Pharmacology, School of Dentistry, Medical College of Georgia, Augusta, Georgia, USA

Corresponding address:

Worku Abebe, PhD
Department of Oral Biology/Pharmacology
School of Dentistry (CL2140)
1459 Laney Walker Boulevard
Medical College of Georgia
Augusta, Georgia 30912-1128, USA
Phone 706-721-3181/3197
FAX: 706-721-6252
E-mail: wabebe@mail.mcg.edu

1. Introduction

Fluoride is the ionic form of fluorine, the most electronegative element in the periodic table. It exists in different chemical and physical forms in combination with other elements; it is distributed widely in nature, both in inanimate and living things (1, 2).

Fluoride is widely recognized for its beneficial health effects as well as toxicity (2, 3). At a relatively optimum low dose range (eg., 0.7-1.5 ppm or mg/l, as specified by the WHO) fluoride has been demonstrated to reduce tooth demineralization (cavities) and stimulate bone formation. However, at higher doses, it displays acute or chronic toxic properties, depending upon the amount ingested and the duration of ingestion.

Ethiopia is one of the 23 countries in the world where a significant number of its population suffers from the toxic effects of high levels of fluoride in drinking water (2, 4, 5). In 2008, this number was estimated to be nearly 14 million (6). The toxicity of fluoride in Ethiopia was realized more alarmingly with the detection of high prevalence rates of dental and skeletal fluorosis in several towns/sugar estates in the Rift Valley in the early 1970s (4, 7-9). Out of the region's 10 million inhabitants, 8.5 million were reported to have been exposed to high fluoride contamination in 2005 (10). Since the initial observation of fluorosis, many public and private organizations and individual investigators have carried out follow up studies largely geared towards determination of the distribution of fluoride in water sources and the clinical and epidemiological manifestations of dental and skeletal fluorosis in a number of places (11-21). The general consensus is that while most places in the Ethiopian Rift Valley have much higher fluoride levels in drinking water compared to the level recommended by the WHO, the majority of these sites lie within the central portion of the Valley. This observation is attributed to the dynamic geochemical characteristics of the Rift Valley (22). In line with the fluoride contents of drinking water, the prevalence of dental and skeletal fluorosis has also been found to be high, with the demonstration of direct correlations between the severity of toxicity and degree of exposure to fluoride. Along with the advancement of skeletal fluorosis, crippling osteofluorosis and neurological complications, as manifested by different versions of myelopathy, have been reported (19). Fluoride assays performed on water sources outside the Rift Valley have also indicated the associated health problems of the ion being extended beyond the region into some highland communities, although the extent of the problem is generally much less (4). More recently, it has been shown that foods prepared using high-fluoride water contribute to the total intake of fluoride, suggesting the significance of considering this aspect too when assessing total fluoride consumption and its potential health consequences (18).

It is surprising that in spite of excessive fluoride in drinking-water sources in a large area of Ethiopia and the high prevalence rate of fluorosis among the population, so far no significant preventive measures have been taken in any part of the country to alleviate the problem. Various reason have been forwarded by concerned authorities for this failure, including limitation of financial resources, lack of adequate technical expertise, cultural barriers on the part of the consuming population and limited priority assignment to the problems of fluoride (4, 9). As there seem to be some inconsistencies to justify this failure, these reasons need to be verified more objectively.

The present review is not intended to provide detailed accounts of what have already been reported by previous researchers regarding the distribution fluoride in Ethiopia and its dental and skeletal effects in relation to fluorosis. Besides the availability of the original research articles, this information has also been compiled as reviews by several authors (2, 4, 9). Interested readers may refer to these sources for further information.

While studying the distribution of fluoride in drinking water sources in Ethiopia and observing the clinical manifestations of the toxic effects of the ion on teeth and bone, no mechanistic approaches have been considered for a better understanding of the health effects observed. In addition, given the documented multiple actions of fluoride in humans, no efforts have been made to describe or assess its potential other chronic toxicities in the context of the Ethiopian situation. The current review is an attempt to briefly address these and related issues on fluoride. Accordingly, the author reviews the (1) nature of occurrence of fluoride in the body after ingestion and the manner it is eliminated, (2) biological mechanisms of dental and skeletal fluorosis, (3) other documented chronic adverse effects of fluoride and (4) preventive approaches to mitigate fluoride's undesirable health effects. It is hoped that the information contained in this review will help further understand and appreciate the health problems associated with the consumption of excess fluoride in drinking water in Ethiopia and will ultimately lead to the implementation of appropriate mitigating measures.

The review was made possible by searching bibliographic database, including MEDLINE/PubMed, bibliographic lists from collected references and other Internet sources.

2. Occurrence of Fluoride in the Body and its Elimination

2.1. Fluoride absorption

Ingestion by mouth is the primary route of administration of fluoride present in drinking water. Fluoride compounds that occur naturally in drinking water (as is the case for fluoride-rich ground waters in Ethiopia) yield fluoride ions which are almost completely absorbed from the gastrointestinal tract (GIT) (1-3). This makes the bioavailability of fluoride from drinking water relatively high. In other words, fluoride compounds with high absorption characteristics have high water solubility and vise versa. Examples of such compounds include sodium fluoride, hydrogen fluoride, fluorosilicic acid and sodium monofluorophosphate. Thus, following ingestion of water with dissolved fluoride, there is a rapid rise in the plasma fluoride concentration, with the peak usually occurring within 30 min (1-3). The magnitude of the peak is proportional to the amount of fluoride ingested.

The absorption of fluoride from the GIT takes place by passive diffusion, which depends on concentration gradient (movement from high to low concentration) (1-3). By this process, fluoride is absorbed mainly from both the stomach and the small intestine. Gastric acidity plays a significant role in the stomach absorption of fluoride. When the ion enters the acidic environment of the stomach, it is largely converted into hydrofluoric acid, which can readily be absorbed and enter the systemic circulation. Most of the remaining (unabsorbed) fluoride in the stomach will move to the small intestine and be rapidly absorbed from there.

The intake of fluoride with food has been found to retard its absorption from the GIT, thus decreasing its bioavailability. The intensity of this effect depends upon the type of food ingestion (1-3). For instance, it has been shown that when fluoride is ingested as sodium fluoride on an empty stomach, the bioavailability of fluoride is almost 100%. When the compound is taken concomitantly with a glass of milk or with a calcium-rich breakfast its bioavailability decreases to 70% and 60%, respectively (1-3). The reduction in the absorption of fluoride in the presence of milk or food is due to its binding to certain food components, including calcium and other divalent and trivalent cations. When binding occurs, the fecal excretion of fluoride is enhanced due to formation of insoluble complex. This situation can be exploited to reduce the amount of fluoride in the circulation and consequently its adverse effects in the body. Furthermore, the timing of fluoride administration in relation to food intake is significant for fluoride bioavailability. Consistent with this, the plasma peak time for fluoride has been found to increase from 30 minutes to 60 minutes when a dental preparation containing fluoride was ingested 15 minutes after meal (1-3). It is likely that the same basic principle applies when fluoride is ingested with drinking water, with or without food.

2.2. Fluoride distribution and retention

Once absorbed from the GIT, fluoride enters the circulation to mix with the blood. The ion is not bound to plasma proteins present in the blood. Given all things equal, under steady state, the concentration of fluoride in the plasma (blood) is directly related to the amount in drinking water. However, the plasma fluoride concentrations tend to increase slowly with age until the 6^{th} or 7^{th} decade of life when they tend to spike rapidly, probably in response to declining renal function or resorption of bone (1-3).

Fluoride is readily distributed from the blood throughout the body. The rate of delivery is determined by blood flow to the tissue under consideration, well perfused tissues such as the heart, lungs and liver being supplied more rapidly. Fluoride is found at a higher concentration within the kidney tubules relative to the concentration in the plasma. Fluoride concentrations in other specialized body fluids such as gingival cevicular fluid, ductal saliva, breast milk, cerebrospinal fluid and bile are low, but are related to the concentration in the plasma at a steady-state condition. Although it is not entirely clear, the mechanism underlying the transmembrane migration of fluoride seems to be the diffusion equilibrium of hydrogen fluoride. Factors that alter the magnitude of transmembrane pH are thus expected to affect the tissue distribution of fluoride. Generally, cell membranes of most tissues appear to be impermeable to fluoride ion per se due to its charge and large hydrated radius (1-3).

More than 90% of the total body burden of fluoride is retained in calcium-rich areas such as teeth and bones (1-3). Most of the remaining portion is distributed in highly vascularized soft tissues and the blood. However, the level of fluoride in bone can vary with age, sex, and the type or part of the bone. During growth, a relatively higher portion of the ingested fluoride is incorporated into the skeleton.

Fluoride may not necessarily be bound to bone irreversibly, especially at an early stage of toxicity in younger individuals (1-3). This has been demonstrated in persons with chronic occupational exposure as well as in those chronically exposed to high fluoride drinking water after moving to low fluoride environments (2). The plasma fluoride concentrations of these individuals were observed to reflect their bone fluoride levels for long periods of time in their new conditions. Mobilization of fluoride from hydration shells and bone crystallite surfaces by ionic exchange and normal bone remodeling processes are hypothesized to play a role in the reversal process. With the application of appropriate techniques, these mechanisms have the potential to be utilized for reversal of skeletal fluorosis under certain conditions.

Overall, the plasma levels and the urinary excretion of fluoride reflects a physiological balance that is determined by previous fluoride exposure, the degree of its accumulation in bone, the mobilization rate from bone and the efficiency of the kidney in excreting the ion (1-3). Factors that can alter this balance, such as impaired kidney function due to disease conditions, can affect the plasma concentration of fluoride and by extension its toxicities.

Fluoride crosses the placenta barrier reaching the fetus; there is a direct relationship between the mother's serum fluoride concentration and that of the fetus. From the blood of the fetus, fluoride is taken up by calcifying fetal bones and teeth (1-3).

While the concentrations of fluoride in other tissues, organs and body fluids (such as breast milk) are generally low, in most cases these concentrations seem to vary from each other (1-3).

2.3. Fluoride elimination

The major route for the elimination of absorbed fluoride from the body is via the kidneys (1-3). Fluoride is freely filtered through the glomerular capillaries and then undergoes tubular reabsorption. The renal clearance of fluoride is directly related to urinary pH, and perhaps to also urinary flow rate. It has been shown that fluoride reabsorption is greatest from distal nephron, the site where the tubular fluid is acidified. As with gastric absorption and transmembrane migration (ie., the tubular reabsoprtion) of fluoride appears to be the diffusion of the ion in the form of hydrogen fluoride. Therefore, factors that affect urinary pH such as diet, drugs, metabolic or respiratory disorders and altitude of residence can influence the extent to which absorbed fluoride is retained (or excreted) in the body. This phenomenon can be manipulated to facilitate the excretion of fluoride from the body.

There is limited information about the renal handling of fluoride by different groups of people such as infants, young children, and the elderly. However, in patients with compromised renal function where the glomerular filtration rate falls to less than 30% of normal (chronically), fluoride excretion declines sufficiently to result in increased soft-and hard-tissue fluoride contents (1-3). Accordingly, conditions that impair the function of the kidneys can affect the renal excretion of fluoride and hence the body's load of the ion.

Studies have revealed that about 10% of the fluoride ingested daily is not absorbed and remains to be excreted in feces (1-3). This amount can be increased if the fluoride is made insoluble in the GIT, for example, by forming calcium fluoride, with the concurrent intake of calcium-rich food (or any multivalent cation for that matter).

Other means of fluoride excretion from the body (eg., via saliva, breast milk, sweat) generally play minor roles (1-3).

3. Biological Mechanisms of Dental and Skeletal Fluorosis

3.1. Mechanisms related to dental fluorosis

Fluoride ingestion of an optimum dose (0.7-1.5 ppm) during tooth formation at young age (up to 8 years) results in dental enamel which is resistant to caries (3, 23). However, with increasing levels of fluoride, the enamel changes in structure and composition, resulting in a condition known as enamel/dental fluorosis (3, 23, 24). In severe condition, this problem is manifested by porous, pitted and discolored (brownish) enamel, which is more prone to fracture and wear. The concentration of fluoride to which the developing enamel is exposed is related to the serum fluoride concentration. The mechanisms involved in dental fluorosis are briefly described.

Dental matrix consists of amelogenin, proteins synthesized by secretary ameloblasts that have functional role in establishing and maintaining the spacing between enamel hydroxyapatite crystallites (3, 23, 24). Complete mineralization of enamel occurs when amelogenin fragments are removed from the extracellular space. However, inhibition of matrix proteinases (which are responsible for removing amelogenin) by fluoride causes improper mineralization with enamel fluorosis. Delay in removal impairs crystal growth, making the enamel porous. It has been shown that fluoride interferes with protease activities by lowering the concentration of free ionized calcium in the mineralized milieu. In connection to this, fluoride has been demonstrated to alter intracellular transport in ameloblasts through various processes that involve G proteins (3, 23-25). The manipulation of the mechanisms involved in the action of fluoride in relation to dental fluorosis could be a potential target for mitigating this problem.

3.2. Mechanisms related to skeletal fluorosis

The effect of fluoride on bone and the development of skeletal fluorosis are complex. Thus, the mechanism of skeletal fluorosis is not well understood, and below is given only a brief description of what is widely known.

Osteoblast is a key cell responsible for bone formation (3, 23). Fluoride stimulates the proliferation (mitogenic effect) of osteoblasts. This in turn results in stimulation of bone formation. This action of fluoride takes place in the presence of relatively low doses of the ion and with limited exposure. It has been documented that osteoblast stimulation and proliferation involve activation of different signal transduction systems, including tyrosine kinases, MAP kinases, G proteins, protein kinase C and/or calcium mobilization (3, 23, 25).

With greater exposure to fluoride (ie., increased dose and duration), a reduction in calcium concentration leads to secondary hyperparathyroidism (23, 25, 26). The increased parathyroid hormone causes enhanced activity of osteoclasts in bone. As opposed to osteoblasts, osteoclasts are cells responsible for bone resorption. Activation of osteoclasts in bone, via a number of cellular processes, causes lysis of different types of lysosomes. The availability of active lysosomal enzymes catalyses reactions that favor the depolymerization of glycoprotein in bone and cartilage. The resulting breakdown of hydroxyprolin causes desegregation of collagen polymers, reducing the mineral binding capacity of the bone metrix and thereby releasing calcium. As a consequence, the solubility of hydroxyappetite crystals increases, facilitating its breakdown along with a reduction in the laying down of collagen by inhibiting hydroxylation of proline and lysine. The net result of degradation of ground substance in bone and other surrounding calcified tissues leads to the symptoms of skeletal fluorosis (23, 25, 26).

4. Other Chronic Adverse Effects of Fluoride

In addition to the well known effects of fluoride on teeth and bone, more recently many other effects of the ion have been recognized. Some of these effects are significant enough to warrant further precautionary measures with the consumption of fluoride. This problem has become the concerns of many researchers and clinicians dealing with fluoride, particularly with regard to its effects on susceptible individuals and on those who take considerably high amounts of fluoride for a prolonged time. Among the different effects fluoride can produce in different organ systems of the body, only those that are widely recognized are briefly reviewed. As the mechanisms for most of these effects are not yet clear, no details are attempted to be given in this regard. The understanding of this additional problem of fluoride can further alert to be more vigilant and to consider preventive measures more seriously in areas of endemic fluorosis.

4.1. Endocrine effects

The main endocrine effects of exposure to fluoride in both animals and humans include reduced thyroid function, enhanced clacitonin activity, increased parathyroid hormone activity, secondary hyperparathyroiodism, impaired glucose tolerance, and possible effects on timing of sexual maturity (23, 26, 27). Some of these effects are associated with fluoride concentrations in drinking water of even ≤4 ppm, especially for young children or for individuals with high water intake.

4.2. Reproductive and developmental effects

A number of animal studies indicate that adverse reproductive and developmental outcomes occur at relatively high concentrations of fluorides that are likely to be encountered by Ethiopians in areas of endemic fluorosis (23, 27). Studies carried out on humans further suggest that high concentrations of fluoride exposure might be associated with alterations in reproductive hormones, fertility, and developmental outcomes.

4.3. Neurotoxicity and behavioral effects

Both animal and human studies have shown significant adverse cognitive and behavioral effects of fluoride (23). Epidemiological studies of Chinese populations have also reported IQ deficits in children exposed to fluoride at 2.5 to 4 ppm in drinking water (23, 28). Other studies using rodents have also shown alterations in the behavior of rodents after treatment with fluoride. Even more compelling were findings of molecular, cellular, and anatomical changes in the nervous system observed after fluoride exposure, suggesting that functional changes associated with these factors could occur.

4.4. Genotoxicity and carcinogenicity

Bone is the most plausible site for cancer associated with fluoride due to its deposition into bone and its mitogenic effects on bone cells (23, 27). Also, incidence of osteosarcoma in male rats exposed to different amounts of fluoride in drinking water has shown a positive dose-response trend. Several epidemiological studies of the relation between fluoride and cancer have demonstrated a positive correlation, although there are some studies with no association.

4.5. Miscellaneous effects on organ systems

Human case reports, animal studies and in vitro experiments indicate that exposure to fluoride at concentrations greater than 4 ppm can be irritating to the GIT, affect renal tissue functions, and alter hepatic and immunologic functional indices (23, 27). Potentially susceptible individuals with renal impairments who can retain more fluoride are more prone to be at a risk.

5. Preventive Approaches for Mitigating the Adverse Effects of Fluoride

The chronic adverse effects of fluoride are difficult to be treated or reversed, once established. Therefore, prevention is a method of choice to combat this serious health problem caused by fluoride. The occurrence of fluoride at excessive levels in drinking water is the primary reason for the fluoride-inflicted health hazards in Ethiopia. The ultimate goal of prevention is to limit the burden of fluoride in the body to less than what is believed to be toxic, by reducing exposure to the ion. It is noteworthy that according to the WHO guideline the consumption of water containing more than 1.5 ppm (1.5 mg/l) is considered to be undesirable (2).

5.1. Prevention through defluoridation of drinking water

For prevention of fluorosis, various approaches have been used in different parts of the world to reduce fluoride consumption through the management of drinking water. This is not, however, an easy task as it requires a number of favorable conditions that combine knowledge, motivation, prioritization, discipline, and technical and organization support (2). However, defluoridation of water is considered as an option only when low fluoride water is not available from alternative sources. Although several different defluoridation methods are known to exist, what may work in one community may not work in another. Also, what may be appropriate at certain time and stage of development may not be at another. It is thus important to select an appropriate defluoridation method carefully if a sustainable solution to a fluorosis problem is to be achieved using this approach. Desirable characteristics of defluoridation processes include cost-effectiveness, easiness to be operated (by local population), independent of influences of such factors as fluoride concentration, pH (acidity/alkalinity) and temperature, no effect on taste of water, and not requiring the inclusion of other undesirable substances (e.g.. aluminum) for treatment of water (2, 29).

Keeping in mind the cost that may be involved in defluoridation, it is desirable that the application of the technology be restricted to water used for drinking and food preparation only (2). In this case, the most suitable economical and practical choice is domestic water defluoridation.

Although many kinds of water defluoridation methods are now available, in this review paper, only the methods that are believed to be more relevant for domestic application in developing countries like Ethiopia are discussed in brief. Excluded are ”advanced” treatment technologies plus methods exclusively based on patented media. These technologies include electrodialysis, reverse osmosis and distillation, which require special equipment, significant power energy and especially trained persons to operate, among others. Also, operation and maintenance of these units is usually very expensive, further becoming prohibitive. For the interested reader, details of the currently available defluoridation methods can be found in a number of sources (2, 29).

Following is a brief summary of selected techniques recommended by the WHO, that have been utilized for domestic water defluoridation in many third world communities (2). It is hoped that with appropriate modifications, these techniques would be suitable for application in all such places suffering from excess fluoride in drinking water. Along with this information, water defluoridation techniques that have been tried so far in Ethiopia and the possibility of developing plant-based defluoridation methods are mentioned.

5.1.1. Nalgonda: This method is based on the adsorption of fluoride on flocs of aluminum hydroxide as they are formed in solution from aluminum and calcium salts. In this process, the two chemicals, alum and lime, are rapidly mixed with the fluoride-containing water. Facilitated by gentle stirring, "cotton wool"-like aluminum hydroxide micro-flocs develop, which carry most of the dissolved fluoride (as a negatively charges species) and are removed after being allowed to settle. The Nalgobda technique was initially developed in India for both community and household use. Since then it has been introduced to many other countries, including Kenya, Tanzania and Senegal (2).

Based on the above basic principle, simple, inexpensive protocols suitable for most developing country households have been developed with some improvements. However, for many households, this technique is still considered cumbersome and difficult for use by uneducated rural population who needs the service most. In addition, it is difficult to adjust the amount of alum because it is different for each source of water. It has been reported that the Nalgonda process can be more effectively used for water having a fluoride content of less than 10 ppm. If the alum amount is not properly controlled, it may result in high residual aluminum content in the output drinking water. There is a maximum limit (0.2 ppm) set for aluminum in drinking water. Excessive alum has been found to render metallic taste to the water as well as produce significant health adverse effects. Further, the residual sludge from Nalgonda process is also thought of as a serious environmental health problem since it contains toxic level of fluoride in a concentrated form. This problem can be taken care of following the required precautionary measures (2).

5.1.2. Activated alumina: This technique utilizes aluminum oxide grains prepared to have a sorptive surface. That means, as water passes through columns of the activated alumina, pollutants like fluoride become adsorbed onto the surface of the grains. The alumina column can be saturated, eventually, but this should be avoided from happening in order to obtain desirable results regarding the purity of the outcome water. At optimum pH, the efficacy of this method for removing fluoride has been found to be more than 90%. Activated alumina can be regenerated by flushing with appropriate concentration of sodium hydroxide solution, which displaces fluoride from the alumina surface. This process is followed by acid flashing to re-establish a positive charge on the surface of the alumina (2).

The activated alumina technique is relatively expensive, although under certain conditions it can be affordable for low income communities. Also, the reactivation process is cumbersome occasionally requiring the help of trained persons. The process also results in high residual aluminum in output water (2).

5.1.3. **Bone charcoal:** This is a blackish, porous, granular material composed of calcium phosphate, calcium carbonate and activated carbon. In contact with water, the material is able to adsorb a wide range of pollutants such as color, taste and other components. Of particular interest here is that bone charcoal also has the ability to take up fluoride from water (2).

The preparation of bone charcoal is crucial to optimize its properties as a defluordation agent and as a water purifier. Unless performed properly, the bone charring process may result in a product of low defluoridation capacity and/or deterioration in water quality which may be aesthetically (smellwise/tastewise) unacceptable. Another limitation is problem of supply of bone charcoal to local users. This problem can, however, be overcome by carefully preparing the material locally (2).

Three types of bone charcoal filters (drum, double bucket and column) are widely available for domestic use, with their own unique advantages and disadvantages. All three filters can be made locally using cheap, robust and corrosion-resistant materials. At household level, bone charcoal defluoridation has been found to work well in Thailand and Africa, but so far there is no experience of wide scale implementation. Relatively expensive filters, which are based on packages of medium and a modification of the candle-type stainless steel domestic filters, are commercially available (2).

One of the constraints of the bone charcoal defluoridation technique is related to religious or cultural beliefs in some communities where use of any or certain types of animal bones is unacceptable. Although resistance to the use of animal parts is not expected to be common in Ethiopia, this aspect should be given due consideration before attempting to implement this technology for water defluoridation in every community (2).

5.1.4. Contact precipitation: This is a process by which fluoride is removed from water through addition of calcium and phosphate compounds and then bringing the water in contact with an already saturated bone charcoal medium (2). Precipitation of calcium fluoride and fluorapatite is easily catalysed in contact bed that acts as a filter for the precipitate.

The construction of contact precipitation plant is simple, although the theory behind it is more complex. The defluoridation set-up comprises a column containing a relatively small, saturated bone charcoal contact bed. Gravel, or course grained bone charcoal is used as a supporting medium. A relatively large space above the bed is used for mixing the chemical with the raw water. From the bed the defluoridated water flows by gravity to a clean water tank. Clean water taps are fitted at the bottom. In this process, it is important to allow for appropriate contact time in the bed (usually 20 to 30 minutes) (2).

This technique seems to be promising for several reasons, including relatively less daily work, high efficiency and reliability, low operation cost and low health risk in case of misuse. Contact precipitation technique has been implemented at village levels in Tanzania and Kenya (2). It is also believed to be suitable for use in other places too and at any required level.

5.1.5. Clay: This is a sedimentary material from earth comprising mainly fine particles of hydrous aluminum silicates and other minerals and impurities. Its physical appearance and utility depend on the way it is treated. Both clay powder and fired clay are capable of sorption of multiple pollutants from water, including fluoride. To take up fluoride effectively, clay may be used as a flocculent powder in a batch system. Domestic clay column filters are usually packed using clay chips found as waste from the manufacture of bricks, pottery or tiles (2).

Different studies have reached to different conclusions about the capacity and usability of clay technique for removing fluoride from water. Therefore, for design purposes the operational capacity has to be settled first. Another consideration is that toxic heavy metals and a wide range of other pollutants may be retained in the clay strata (from soil contaminants) that should be taken care of (2).

It has been reported that nearly 80% of clay column defluoridatiors installed in households in Sri Lanka were in operating conditions for more than two years (2). Motivation of users through information and campaigns are believed to have played a big role for this success.

5.1.6. Water defluoridation experience in Ethiopia.

It has been documented that, following the realization of the negative medical and economic consequences of skeletal fluorosis in Wonji sugar factory in the early 1970s, a plant for water defluoridation was installed for the supply of low-fluoride water to factory workers (4, 5, 9). This plant did not, however, seem to operate as expected. The reason for this failure is unclear and it may be relevant to know why in order to draw a lesson from the experience encountered. There is also a report that, at the end of 1990, a drinking water treatment project was initiated by government support around the Nazret area, but this project did not also accomplish what was anticipated (4, 5, 9). It should be noted that the above reports have not specified the type(s) of defluoridation methods used in both projects. Subsequent water defluoridation pilot studies carried out by research institutions using bone-meal and bone-char have also failed to deliver expected results on the basis of technical difficulties and cultural/religious rejections (4, 5, 9). A more recent report has described other studies on the use of the Nalgonda and activated alumina techniques for small and large-scale schemes in Ethiopia. From preliminary observations, it seems that the costs and technical expertise required for running these programs do not match what could be made available. In brief, the water defluoridation experience so far encountered in Ethiopia is largely negative. Compared to most other developing countries, one may then wonder if this is unique to Ethiopia, and if so, what can be done to improve this deterring situation.

5.1.7. Summary of evaluation and selection among available defluoridation methods.

From the above discussion, it is clear that as such there is no a universal defluoridation method which is appropriate under all social/political, financial/economic, environmental and technical conditions (2). None of the methods has been implemented successfully at large scale in many parts of the world. This may be largely due to certain inherent disadvantages associated with each of the defluoridation methods. As noted earlier, these disadvantages may include high cost, limited efficiency and capacity, shortage of operating technology, maintenance limitations, deteriorated water quality and taboo limitations, among several others.

On the other hand, each method described does have its own advantages too and is capable of effectively removing fluoride under specified suitable conditions (2). Four points are worthy of stressing again as essential criteria for the success of fluorosis prevention through defluoridation of drinking water: selection of the right method, appropriate understanding of the design and processes involved, availability of necessary materials, and the provision of training and motivation to users and other decision-makers (2).

5.1.8. Plant-based water defluoridation

Records show that water defluoridation techniques of various types (mostly chemical-based) have been around for more than half a century. However, as pointed out above, the primary objective of developing these techniques has not yet been fully realized where they have been tried, although there are significant tangible progresses in some sectors (2, 4). Therefore, the search for alternative or additional ways of defluoridating drinking water naturally continues. A relatively less known approach of potential utility, particularly in third world rural communities, that has attracted the attention of researchers in recent years is plant-based (natural) defluoridation technique (4, 5, 9, 30-32). This approach has already been tested in some counties and preliminary results have suggested that it has the potential to be a useful alternative to the currently available chemical and animal-based methods. There are many advantages to water defluoridation using plants in these countries, including Ethiopia. The plants can be grown locally as needed and the costs for production and transportation can be relatively low. The use of plants for defluoridation might also achieve widespread acceptance and application by local communities more easily. Below is a list of popular water purifying plants locally used in different parts of the world, with the potential to be developed as means for drinking water defluoridation in Ethiopia and other developing countries.

***Moringa oleifera*:** This plant is commonly known as drumstick tree. It is popular in rural India and Aftrica (32). In Ethiopia, *Moringa oleifera* has been reported to grow in Harergae Administrative Region (32). Crushed seeds of *Moringa oleifera* have long been a traditional method for purification of turbid water elsewhere, particularly in India. This has been verified to work in laboratory experiments by expert scientists. Studies conducted in India, have further demonstrated *Moringa oleifera* seeds to have remarkable defluoridation efficiency, even better than that of activated alumina (32-34). The seeds contain cationic polyelectrolytes (eg., calcium and magnesium) that also bind to fluoride and prevent its GIT absorption by forming insoluble fluocculents. More research work is needed to further establish these findings and determine the application of Moringa seeds for defluoridating drinking water at household and community levels.

Moringa stenopetala**:** This plant is widely found in southwestern part of Ethiopia (32). It is known by different vernacular names: shiferaw (Amarigna), aleko, halako (both Gidoligna), shalchada and shelaga (both Konsogna). *Moringa stenopetala* is considered native to Ethiopia, and except in Kenya, it is not known if it grows elsewhere outside Ethiopia.

Traditionally, *Moringa stenopetala* seeds are used for purifying turbid river water, in addition to the multipurpose use of the entire plant (32). The process of water purification involves formation of flocculent masses in the turbid water. Research has shown that the seeds of this plant contain an effective water purifying chemical ingredient, the properties of which need to be determined. Within the Moringa family, *M. senopetala* is considered to be the most effective and perhaps the least toxic water-clarifier (32). However, its effectiveness for water defluoridation remains to be tested.

Maerua subcordata**:** This plant is widespread over the plain of the Omo basin and the adjacent areas in southwestern Ethiopia (32). It is known by the vernacular names wuha mataria (Amarigna), kuluf (Geleb), guluf (Karo) and kamogi (Murasi). The water purifying property of *Maerua subcordata* is well known among the locals in the Omo River area. Research performed in the Sudan has provided evidence that special polysaccharides present in the roots of this plant cause flocculation of colloidal particles in turbid water (32). These macromolecular particles possess a sorptive property. Although the roots of *Maerua subcordata* have been proved to be effective in clarifying turbid water, their ability to defluoridated drinking water is yet to be determined.

Tamarindus indica**:** *Tamarindus indica* is commonly known as tramarind. It is indigenous to tropical Africa, and today the plant is found widely distributed throughout the tropical belt all over the world (32-34). *Tamarindus indica* is used for a multitude of purposes in many of the countries it is found, but its application for water purification or removal of fluoride is not as much widely recognized.

Recent studies carried out India, however, have demonstrated that constituents of fruit pulps of *Tamarindus indica* have adsorptive property for removal of fluoride from water (33, 43). These constituents bind fluoride through bonding with tartaric acid. In addition, earlier animal studies were able to shown that extracts of *Tamarindus indica* fruit pulps enhance the urinary excretion of fluoride. The binding of components of tamarind to fluoride suggests the possibility for reducing the absorption of the ion from the gut, using this plant. These observations are further supported by the protective action of tramarind against fluoride toxicity.

Currently, preparation (gel) made from the tamarind plant is used in Kenya for drinking water defluoridation (35, 36).This gel product has been shown to decrease fluoride concentration by at least 50%.

Other plants: Other plants with the potential to be developed as drinking water defluoridating agents include *Vetiveria zizanoides*, *Emblica officinalis*, *Cyanodon tactylon* and pickly pear. Preliminary observations made on these plants in different places outside Ethiopia provide support for this undertaking (30-32).

5.2. Exploring alternative sources of drinking water

In any attempt to mitigate the effects of fluoride from excessively contaminated drinking water, the provision of safe, low fluoride water from alternative sources should be a priority, if possible. Alternative drinking water should aim to provide low fluoride water not only to humans but also animals which are also venerable to the hazards of high fluoride (35). Defloridation of drinking water for animals would even be too costly and less practical, making the harvesting of low fluoride water sources highly desirable. In other words, defluoridation of contaminated water remains as an option for fluorosis prevention only when the possibility of an alternative water source is non-existent.

In high-fluoride regions of Ethiopia where there is rain, rainwater storage can be considered an alternative source of drinking water with no fear of fluoride contamination. With the sensitivity and willingness to care for the victims of fluoride toxicity, this is possible to be achieved relatively easily because similar attempts have been seen working in other developing countries with scanty rainfall.

A more attractive and sustainable alternative source of drinking water for both humans and animals is the provision of ground waters with an acceptable level of fluoride (2). In Ethiopia, the distribution of fluoride even in endemic problem areas is not uniform (4, 5, 17). Accordingly, wells and springs that are only a short distance apart may have radically different concentrations of fluoride. This variation in fluoride concentrations is believed to be due to the geology of the regions, in which case fluoride may dissolve in selected types of rocks underneath or preferably be associated with geothermal waters (17). It is thus plausible to locate springs and wells (new and old) at sites that have low fluoride concentrations midst a dense zone of high fluoride. In order to do this, fluoride distributions should be mapped in all existing sources to sort out their fluoride status and discover new water sources based on scientifically grounded information. With this determination, specific recommendations can be made on the selective use of ground water sources by avoiding those with high fluoride concentrations. As fluoride levels in shallow seasonal springs and shallow wells are likely to be low, these sources of water are recommended to be included in the survey.

5.3. Dietary considerations and avoiding fluoride-rich items

The consumption of defluoridated drinking water alone, if at all possible, may not necessarily bring the body's fluoride level to a safe limit in endemic areas, as there are other ways of ingesting fluoride and adding to the burden it causes (35). In addition, the provision of low-fluoride alternative sources of water may not be feasible in all affected areas. Therefore, additional means of mitigating the health effects of excess fluoride should be sought. An important aspect of consideration in this regard is to avoid the consumption of items rich in fluoride as much as possible. Of particular interest are foods prepared form materials obtained from local sources, such as injera from locally-grown teff or fish from local lakes which are likely to contain high levels of fluoride (18). There are also certain agricultural items that inherently have high contents of fluoride, no matter where they are grown or obtained from. The best example for this is tea which contains as much as 70 ppm (35). Furthermore, the use of manufactured products that contain significant levels fluoride, such as fluoridated toothpastes, cosmetics and fertilizers should be avoided, particularly in young children. It is noteworthy that neighboring Kenya is the first country in the world to ban fluoridated toothpaste (36). However, meanwhile, it should be noted that fluoride intake through drinking water results in the highest toxicity compared to other natural means of exposure.

In addition to attempting to minimize exposure, efforts should also be made to counteract the effects of the remaining fluoride ingested from the surrounding environment. Researches have demonstrated that fluoride or its adverse effects can be reduced by certain types of food components (35, 37). Accordingly, the use of food substances rich on these ingredients is highly promoted. Among others nutrients, calcium and magnesium are well known to reduce the blood levels of fluoride and thus its biological effects. These divalent ions have the ability to interact with fluoride (a negative charge) in the GIT to form insoluble salts which are not readily absorbed, but rather be excreted through the feces (1-3). The use of these nutrients is also recommended as a replacement therapy to compensate for their diminished levels in the body caused by fluoride. Moreover, additional calcium may be needed to help build or protect bone affected by skeletal fluorosis (37). Among the commonly available food items, milk and milk-products have relatively high calcium contents while magnesium is present in significant amounts in different types of cabbages. Milk in its natural state is generally low in fluoride and thus is considered safe. Simultaneous exposure to vitamin D (vitamin D_3) is usually recommended since it enhances calcium absorption among other advantages. Vitamin D also inhibits excessive release of parathyroid hormone, which in turn prevents activation of osteoclasts, thus diminishing hyperosteoidosis and osteopenia (35, 37). Vitamin C (ascorbic acid) is advocated to be taken for fluorosis because of its antioxidant activity and the ability to control collagen synthesis in bone formation (35, 37). The development of oxidative stress and impairment of collage synthesis are two of the consequences of high fluoride intake. Vitamin C can be obtained from different plant sources such as citrus fruits, papaya, mangoes, strawberries, tomatoes and broccoli. Added to the antioxidant arsenal is vitamin E which can be obtained from such sources as whole wheat, millet, cornmeal, sunflower seeds, flax seeds, herring, salmon, eggs, liver and sweet potatoes. The ingestion of adequate protein is vital for bone and muscle formation particularly in cases of skeletal fluorosis (35, 37).

The importance of nutrition in mitigating the effects of fluoride is getting more acceptance from time to time. Many scientists and practitioners now comment that fluorosis is more prevalent in the economically backward countries, and, even within a given society, it is more common among those who are uneducated and unaware of the importance of good nutrition and balanced diet (35, 37). Although such a generalization awaits further verification, nutrition, no doubt, has a role to play. Under current circumstances it may be difficult for the fluorosis victims of Ethiopia to fulfill their nutritional requirements. However, every effort should be made to make the best out of what is and can be available, and education and material supports are two important ingredients that should be incorporated as parts of these efforts. In summary, along with the minimization of fluoride intake, it is generally beneficial to provide supplementation of a diet rich in essential nutrients and antioxidants to counteract, at least in part, the chronic adverse effects of high doses of fluoride. This measure is likely to be more effective if its implementation is carried out prior to developing any condition or at an early stage of the condition, particularly in young children.

5.4. Health Education

Creating awareness about fluorosis is vital to combat the condition. The awareness should not be limited to the people affected but should also be extended to all those related to them and others who have something to do with fluoride, including professionals and policy makers.

Depending upon the availability of resources, the level of understanding and the acceptability of the methods employed, the awareness can be effected in a variety of ways (21, 35). Teaching children at an early stage in schools about fluoride and fluorosis is considered by many as one of the effective ways of creating awareness about the fluoride controversy (21). Delivering health education to the larger community through such professionals as community health workers and agricultural extension agents is also a consideration of prime importance (4). The education delivered should incorporate information about the overall health consequences of excessive fluoride intake and sources of fluoride, along with preventive methods that need to be taken.

Creating awareness about the toxicity of fluoride can be done, among others, in the form of graphic presentation of the final consequences of the condition to the extent possible (35). At times, live presentation of patients who are suffering from the severe form of the disorder, in areas where the gravity of problem has not yet reached to that extent could be a powerful approach to motivate the community for engagement in preventive measures. Creating awareness about the sources of fluoride can help make informed choices regarding water and other items of consumption, enabling potential victims to be engaged in need-based preventive measures in the affected areas (4, 35).

6. Summary and Conclusion

Ethiopia is one of the 23 countries in the world where excessive amount of fluoride is commonly found in drinking ground waters, particularly in the rift valley region. This has been observed to be associated with increased dental and skeletal fluorosis. Following ingestion, fluoride enters the circulation and is distributed rapidly throughout the body. While most of the fluoride in the body is excreted via the kidney, more than 90% of that retained is deposited in bone and teeth. The dental and skeletal effects of excess fluoride involve the disruption of a number of cellular and molecular mechanisms that are commonly linked to the lowering of ionized calcium. Experimental and human studies have also shown that excess fluoride intake causes many other adverse effects involving different organ systems and cell types. Although a number of preventive approaches are known to exist for mitigating the health problems of fluoride, the approaches so far considered in this regard in Ethiopia have largely been ineffective. It appears that the problem of fluoride in Ethiopia has not been well appreciated and researched in the context of the country's particular situation. The unsuccessful attempts that have been made so far to counter the effects of fluoride are based on the replication of the methods implemented elsewhere without appropriate modifications to suite local demands and capability. In this review, besides describing the sources and pathophysiology of fluoride, approaches that can be taken for prevention of its toxicities resulting from consumption of contaminated drinking water are highlighted. These approaches include selection of appropriate water defluoridation techniques, harvesting alternative low-fluoride drinking water sources, developing more accessible plant-based (natural) water purifying methods, consideration of appropriate dietary supplementations, avoiding fluoride-rich consumable items and the provision of effective health education. It is recommended that these factors should be given due considerations in efforts made to mitigate the adverse effects of exposure to excessive fluoride in drinking water. Existing realities appear to demand that a combination of different scientifically sound approaches adapted to local conditions is the right way to go.

Acknowlegement

The author thanks Dr. Gary Whitford of the Medical College of Georgia School of Dentistry for providing invaluable information materials from his library collections, which otherwise are not readily accessible.

Special announcement for research collaboration

The author of this paper and his colleagues at the Medical College of Georgia School Dentistry are interested in quantifying the levels of fluoride in different potentially contaminated sources (eg., water, foods, body fluids, etc.) that can be obtained from Ethiopia. Interested individuals or institutions are encouraged to contact this author via wabebe@mail.mcg.edu for further information.

References

1. Whitford, G, M. The physiological and toxicological characteristics of fluoride. J Dent Res. 1990; 69(5390):556-7.

2. Hardman, J.A., Limbird, L.E., Gilman, A.G, (eds.), Goodman and Gilman's The Pharmacological Basis of Therapeutics, 11th ed., Mcgraw Hill, New York, 2005, pp. 1735-39.

3. Fawell, J., Balley, K., Chilton, J. et al. (eds.), WHO, Fluoride in Drinking-Water by Publisher IWA publishing, London, UK, 2006.

4. Kloos, H., Haimanot, R.T. Distribution of fluoride and fluorosis in Ethiopia and prospects for control. Trop Med Int Health. 1999; 4(5):355-64.

5. Walther, I. Fluoride contamination in the main Ethiopian Rift valley. http://www.goek.tu-freiberg.de/oberseminar/OS_04_05/ines_walther.pdf. Accessed August 16, 2010.

6. Ethiopia: over 14 million at risk of fluorosis-Ministry. http://www2.fluoridealert.org/Alert/International/Ethiopia-Over-14-Million-At-Risk-of-Fluorosis-Ministry. Accessed August 16, 2010.

7. Olsson. B. Dental caries and fluorosis in Arussi province, Ethiopia. Community Dent Oral Epidemiol. 1978; 6(6):338-43.

8. Fekadu, A. Annual report of the medical services of the Wonji Sugar Estate. Prepared for the Wonji Farm office, Addis Abeba, 1977.

9. Kloss, H., Haimanot, R.T. Fluorosis. In: Kloss, H. and Zein, Z.A. (eds.). The Ecology of Health and Disease in Ethiopia. Westview Press. Colorado, USA, 1993, pp. 455-61.

10. Fluoride contamination and treatment in the Ethiopian rift Valley. http://www.cepis.ops-oms.org/bvsacg/e/foro4/19%20marzo/Strategies/Fluoride.pdf. Accessed August 16, 2010.

11. Haimanot, R.T., Fekadu. A., Bushra, B. Endemic fluorosis in the Ethiopian Rift Valley. Trop Geogr Med. 1987; 39(3):209-17.

12. Wondwossen, F., Astrøm, A.N., Bårdsen, A. et al. Preception of dental fluorosis amongst Ethiopian children and their mothers. Acta Odontol Scand. 2003; 61(2):81-6.

13. Chernet, T. Hydrology of Lake Region of Ethiopia, Addis Abeba: Ethiopian Institute of Geological Surveys, 1982.

14. Solonso, F., Final report on water defluoridation in the Rift Valley, Addis Abeba: UNICEF/WHO, 1985.

15. Water supply and Sewerage Authority (WSSA). 34 towns water feasibility study. Report prepared by German Water Engineering for WSSA, Addis Abeba, 1983.

16. Wondwossen, F., Astrøm, A.N., Bjorvatn, K. et al. The relationship between dental caries and dental fluorosis in areas with moderate- and high-fluoride drinking water in Ethiopia. A. Community Dent Oral Epidemiol. 2004; 32(5):337-44.

17. Reimann, C., Bjorvatn, K., Frengstad, B. et al. Drinking water water quality in the Ethiopian section of the East African Rift Valley I--data and health aspects. Sci Total Environ. 2003; 311(1-3):65-80.

18. Malde, M.K., Zerihun, L., Julshamn, K. et al. Fluoride, calcium and magnesium intake in children living in a high-fluoride area in Ethiopia. Intake through food. Int J Paediatr Dent. 2004; 14(3):167-74.

19. Haimanot, R.T. Neurological complications of endemic skeletal fluorosis, with special emphasis on radiculo-myelopathy. Paraplegia. 1990; 28(4):244-51.

20. Melaku, Z., Ismail, S. perception on fluoride related health problems in an area of endemic fluorosis in thiopia: an exploratory qualitative study. Ethiop J Health Dev. 2002; 16:85-93.

21. Berhanu, Y., Demissie, B., Mekonnen, E. et al. Preventing dental fluorosis. Ethiop J health Dev. 2002; 16(2):225-226.

22. D'Alessandro, W. Human fluorosis and volcanic activity. http://www.earth-prints.org/bitstream/2122/2590/1/D'Alessandro_EnvTox06.pdf. Accessed August 16, 2010.

23. National Research Council. Fluoride in Drinking water: A Scientific Review of EPA'S Standards, Washington, DC, 2006.

24. DenBesten, P.K, Thariani, H. Biological mechanisms of fluorosis, and level and timing of systemic exposure to fluoride with respect to fluorosis. J Dent Res. 1992; 71(5):1238-43.

25. Li, L. The biochemistry and physiology of metallic fluoride: action, mechanism, and implications. Crit Rev Oral Biol Med. 2003; 14(2):100-14.

26. Pathophysiology of fluorosis. http://www.krassindia.org/fluoride_pat.htm. Accessed August 16, 2010.

27. Dhar, V., Bhatnagar, M. Physiology and toxicity of fluoride. Indian J Dent Res. 2009; 20(3):350-5.

28. Tang, Q.Q., Du, J., Ma, H.H. et al. Fluoride and children's intelligence: a meta-analysis. Biol Trace Elem Res. 2008; 126(1-3):115-20.

29. Mohapatra, M., Anand, S., Mishra, B.K. et al. Review of fluoride removal from drinking water. J Environ Manage. 2009; 91(1):67-77.

30. Campbell, C. Poor missing out on montinga seed's water-purifying power. Current Protocols in Microbiology. 2010; http://www.scidev.net/en/news/poor-missing-out-on-moringa-seeds-water-purifying-powers.html. Accessed August 16, 2010.

31. Friedman, L.M. Cactus purifies water on the cheap, finds study. 2010, http://www.scidev.net/en/news/cactus-purifies-water-on-the-cheap-finds-study-1.html. Accessed August 16. 2010.

32. Gottsch, E. Purification of turbid surface water by plants in Ethiopia. Walia; 1992; 14: 23-28.

33. Ranjan, R., Swarup, D., Patra, R.C. et al. Tamarindus indica L. and Moringa oleifera M. extract administration ameliorates fluoride toxicity in rabbits. Indian J Exp Biol. 2009; 47(11):900-5.

34. Subramanian, E. and Ramalakshmi, S. Prestine, purified and ployaniline-coated tamarind seed (Tamarindus indica). J. Sci. Ind Res. 210; 69:612-628.

35. Fluoride and fluorosis. http://www.krassindia.org/downloads/ebook1.pdf. Accessed August 16, 2010.

36. Fluorosis-fear and remedy. http://www.ieiknowledgepark.com/TechPaper%5CFlourosis08.pdf. Accessed: August 16, 2010.

37. Susheela, A.K., Bhatnagar, M. Reversal of fluoride induced cell injury through elimination of fluoride and consumption of diet rich in essential nutrients and antioxidants. Mol Cell. Bochem. 2002; 234-235(1-2):335-40.