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Review Article

A brief review of fluoride-induced bone disease skeletal fluorosis in humans and its prevention

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Abstract

Fluorosis disease is common in areas where people drink water containing fluoride (>1.0 ppm or 1.5 ppm) and/or are exposed to airborne fluoride or other sources of fluoride over a long period of time. In this disease, primarily the teeth and bones are affected to varying degrees depending on the level of fluoride and the duration and frequency of exposure. In general, fluorosis appears mainly in two forms, dental and skeletal fluorosis. The latter is extremely painful and irreversible. Actually, skeletal fluorosis is a bone disease caused by excessive accumulation of fluoride which weakens the bones. In advanced state, skeletal fluorosis causes varying degree of damage to the bones and joints depending on the fluoride concentration and its duration of exposure. In fact, in this disease the bones become harder and less flexible, resulting in increased frequency of fractures. Thickening of the bone structure and accumulation of bone tissue, both of which contribute to decreased joint mobility. Ligaments and cartilage can also be ossified in this disease. Skeletal fluorosis is extremely important as it reduces mobility at a very young age due to progressive changes in bones such as periosteal exostosis, osteosclerosis, osteoporosis and osteophytosis. These changes manifest clinically as vague pains in the body and joints. Excessive accumulation of fluoride in muscles also reduces mobility and this condition leads to disability or disfigurement. In severe cases, neurological complications (paraplegia and quadriplegia) and deformities of the limbs, such as bowing of legs at the knee outward (genu-varum) and inward (genu-valgum), also occur. Once skeletal fluorosis develops in humans it persists for life. In the present brief review, the focus is on the origin of skeletal fluorosis and ways to prevent it in humans. The aim of this review is to create awareness about this disease among people living in fluoride-affected areas.

Key words: airborne fluoride; bio-accumulation; bone deformities; dental fluorosis; drinking water; fluoride; industrial fluoride pollution, fluorosis; skeletal fluorosis; prevention

Introduction

It is well known that fluoride is universally present in water, soil, air, and food at varying levels. This may be due to geological processes and/or anthropogenic or industrial activities. Fluoride intake has both beneficial and negative effects on humans depending on the concentration of fluoride. Intake of fluoridated water in the range of 0.5 to 1.0 ppm is beneficial and reduces the incidence and possibility of dental caries [1,2], but excessive intake through drinking water containing fluoride beyond the recommended or standard value of 1.0 ppm or 1.5 ppm leads to the dangerous and extremely painful fluorosis disease [3-5]. Globally, water-borne fluorosis also known as “hydrofluorosis” is the most common and widespread disease in humans [3]. But “industrial fluorosis” is limited to specific areas or regions due to exposure to fluoride emitted from various industrial activities, such as such as power generating stations and the manufacturing of steel, iron, aluminum, zinc, phosphorus, chemical fertilizers, bricks, cement, hydrofluoric acid, etc. These are generally discharging fluoride into their surrounding areas which create industrial fluoride pollution [6,7]. An industrially emitted fluoride not only contaminates the surrounding environment including soil, air, and fresh water reservoirs, but also contaminates vegetation, agricultural crops and many other biological communities on which man and animals generally survive. Fluoride-induced fluorosis disease occurs not only in humans [8–22] but also in herbivorous wild [23–29] and domestic animals [30–56] if they are exposed regularly to fluoride for long periods of time.

Once fluoride enters the body it is absorbed by the digestive and/or respiratory tract and then eventually reaches all parts of the body through

the blood. More than 50% of the absorbed fluoride is excreted through feces, urine, and sweat, while the rest is retained in the body where it is deposited in various organs. However, its maximum accumulation is occurred in calcified organs, bones and teeth compared to non-calcified organs. This bio-accumulation of fluoride causes diverse toxic effects or pathological changes in all kinds of hard and soft tissues and also interference with various physiological and metabolic processes and ultimately triggers the occurrence of adverse reversible and non-reversible health effects in people of all age groups. These fluoride-induced pathological or health changes are collectively called fluorosis [3-5] Various fluoride- induced anomalies or deformities in teeth and bones are permanent, irreversible, and not curable and can be easily observed. However, other fluoride-induced changes in soft tissues or organs are mostly reversible and disappear when the source of fluoride exposure is removed.

Chronic fluoride exposure through ingestion of drinking water containing high fluoride levels (>1.0 or 1.5 ppm) can lead to three forms of fluorosis namely dental fluorosis (dental mottling), skeletal fluorosis (bone deformities), and non-skeletal fluorosis [57,58]. But it is not necessary that all these three forms exist in the same person. However, among the various forms of fluorosis, skeletal fluorosis is a relatively more dangerous and highly painful bone disease in both man and animals [57,58].

Skeletal fluorosis

Excessive fluoride intake or fluoride bio-accumulation alters the balance between bone formation and resorption. This physiological process is accomplished with the participation of certain regulatory determinants and signaling pathways, leading to various bone malformations (lesions) known as skeletal fluorosis. This disease is also known as fluoride-induced bone disease in both humans and animals. The severity of skeletal fluorosis and the different clinical stages depend on the amount of fluoride accumulation in bones (mg F/kg). At bone ash fluoride concentrations of 500 to 1,000 mg F/kg, there will be no bone changes. The different clinical stages of skeletal fluorosis and the development of various symptoms and signs in different ranges of bone ash fluoride concentrations are shown in Table [59].

Table 1. Various clinical phases and symptoms and signs of skeletal fluorosis at different range of bone ash fluoride concentration. Source: [59]

Osteosclerotic phase	Bone ash fluoride concentration (mgF/kg)	Symptoms and signs
Normal Bone	500 to 1,000	Normal
Preclinical Phase	3,500 to 5,500	Asymptomatic; slight radiographically-detectable increases in bone mass
Clinical Phase I	6,000 to 7,000	Sporadic pain; stiffness of joints; osteosclerosis of pelvis and vertebral column
Clinical Phase Il	7,500 to 9,000	Chronic joint pain; arthritic symptoms; slight calcification of ligaments; increased osteosclerosis and cancellous bones; with/without osteoporosis of long bones
Clinical Phase Ill	8,400	Limitation of joint movement; calcification of ligaments of neck vertebral column; crippling deformities of the spine and major joints; muscle wasting; neurological defects/compression of spinal cord

[59]. This entity of chronic fluoride intoxication or skeletal fluorosis is very painful and more dangerous than other forms of fluorosis (dental and non-skeletal fluorosis) and is extremely important as it reduces mobility at a very young age. The most common fluoride-induced changes that develop slowly in bones are periosteal exostosis, osteoporosis, osteoporosis and osteophytosis. These bony changes can be seen in radiographs of various bones (Figure 1)

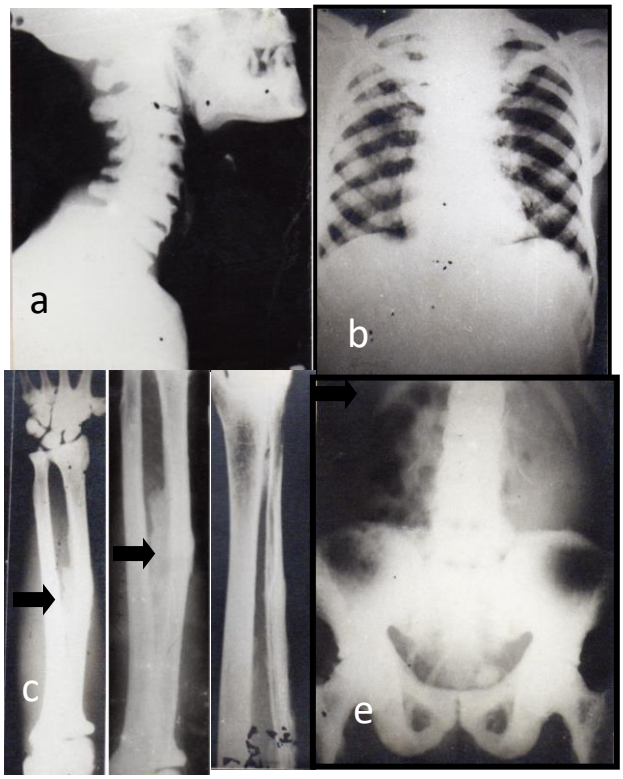

Figure 1. Radiographs of different bones of subjects, afflicted with skeletal fluorosis. Cervical and dorsal spines showing extreme osteosclerosis, lipping and osteophytosis (a, e); osteosclerosis of the pelvis with calcification of ligaments (e); contrast of the osteosclerosis in bony cage with radiolucent lungs and clavicular involvement (b); calcification of interosseous membrane (arrow) between radius and ulna bones of forearm (c); bony exostosis in tibia (d). The calcification of interosseous membrane (arrow) is the most ideal and confirmative indication of skeletal fluorosis.

[60-62]. Skeletal fluorosis can be diagnosed and confirmed based on radiographs. The severity of skeletal fluorosis can also be interpreted or determined based on radiological findings. These bone changes manifest clinically as vague pain in the body and joints. Excessive accumulation of fluoride in muscles also reduces mobility and this condition causes disability or disfigurement (Figure 2).

Figure 2. Subjects afflicted with severe skeletal fluorosis characterised with invalidism, kyphosis, genu-varum (a, b, d, e) and genu-valgum (c)syndromes, crippling with paraplegia and quadriplegia (a, d), and crossing or scissor-shaped legs (e).

In its advanced stages, neurological complications like paraplegia and quadriplegia and genu-varum (outward bending of legs at the knee) and genu-valgum (inward bending of legs at the knee) syndromes also result from long term fluoride exposure and is the worst form of skeletal fluorosis.

These bone changes or skeletal fluorosis caused by fluoride can occur in people of any age. However, children are more susceptible to the changes in various bones of the skeleton. Interestingly, all these bone deformities or changes in humans persist throughout their lifetime and cannot be cured by any treatment. The most negative aspect of skeletal fluorosis is that many people suffering from skeletal fluorosis in rural areas are unable to perform daily tasks and have a high rate of bone fractures. Women may also face problems in delivery due to skeletal fluorosis. However, the severity of skeletal fluorosis depends not only on the fluoride concentration and the duration and frequency of exposure but also on age, sex, food, nutrients, chemicals in water, physical function, individual fluoride sensitivity or tolerance and genetics, environmental factors, etc. [63-73].

How to prevent skeletal fluorosis

It is well documented that all types of fluoride-induced bone deformities, such as disability, neurological complications (paraplegia and

quadriplegia), limb deformities (genu-varum and genu-valgum syndromes), etc. are irreversible and cannot be cured. But their further progression or severity in people can be prevented or controlled by adopting and implementing the following potentially effective and feasible methods: (a) regular supply or provision of fluoride-free treated drinking water, (b) control of fluoride entry into the body from various potential sources such as fluoridated water, air-borne fluoride (industrial fluoride emission), and various food items such as alcohol, tea, rock salt, tobacco, and betel nut which naturally contain high amount of fluoride, (c) provide nutritious foods containing adequate amount of calcium, vitamin C, vitamin E nutrients and antioxidants, and (d) disseminate current knowledge about various causes and severity of the dreaded skeletal fluorosis disease and create general awareness among people living in fluoride endemic areas regarding preventive measures of fluoride poisoning with the help of well-trained volunteers, students, and teachers [3].

It is well known fact that expectant and lactating mothers are most vulnerable groups for chronic fluoride poisoning. Therefore, these mothers should only consume fluoride- free water. It is well known that fluoride is also potential to cross the placenta barrier and enter in foetus where it can affect the developing foetus. To avoid fluorosis, as far as possible, only fluoride-free water should be used for drinking and cooking. If this is not possible, then water from such a source should be used in which the fluoride content is less than 1.0 ppm or 1.5 ppm. But the water in which the fluoride content is more than 1.0 ppm or 1.5 ppm should neither be used for drinking nor for cooking. Otherwise, there is a high possibility of getting fluorosis. For regular supply of fluoride- free drinking water in the community or population inhabiting fluoride endemic areas defluoridation technology can be used or adopted. However, several defluoridation techniques have been developed that are readily available [74,75]. Nevertheless, among these techniques, "Nalgonda Defluoridation Technique" is an ideal technique as it is simple, effective, and low cost which can be used at both household and community levels [76,77].

In fluoride-affected India, where hydrofluorosis is most common and hyperendemic in almost all rural areas, this Nalgonda technique is the most successful and potential in the prevention and control of chronic fluoride poisoning or hydrofluorosis. Although this technique is inexpensive and gives good results but its success rate at the community level is poor due to lack of public participation, lack of responsibility for its supervision and lack of proper monitoring and maintenance [77]. Instead of adopting any defluoridation technique, harvesting and conservation of rainwater is a better option to get low fluoride or fluoride free water on regular basis. Perennial freshwater sources like ponds, rivers, lakes, dams, reservoirs etc. also allow regular supply of fluoride free water to the community as their water contains only small amount of fluoride [3]. But use of groundwater for drinking and cooking in India should be avoided as it is most likely to contain fluoride [44]. However, controlling skeletal fluorosis requires a holistic approach, collective efforts and people's participation; while monitoring and evaluation of fluorosis control projects also need to be done with sincerity.

Conclusion

Long-term exposure to fluoride or excessive intake of fluoride through drinking water and industrial fluoride emissions causes severe fluorosis disease which can develop in all age groups, children, adolescents, adults and the elderly. Even low levels of fluoride can develop fluorosis in humans. The disease is endemic in many countries, especially in their rural areas. Among the various forms of fluorosis, skeletal fluorosis is the most dangerous and highly painful. Excessive bio-accumulation of fluoride in various bones of the skeleton leads to the development of various deformities or changes in the bone, such as disability, neurological complications, and lower and upper limbs deformities, and these persist for a lifetime and are irreversible or even incurable. This condition is the worst form of skeletal fluorosis. Therefore, the only cure or solution to this dreaded disease in human population is prevention which is possible by regular supply or availability of fluoride-free drinking water, checking the entry of fluoride into the body, providing nutritious food and spreading current knowledge about fluorosis and creating awareness among people about preventive measures. However, controlling fluorosis requires a holistic approach, collective efforts and people's participation.

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Conflict of interest

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