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A Brief and Critical Review of Skeletal Fluorosis in Domestic Animals and its Adverse Economic Consequences

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Abstract

When herbivorous domestic animals, such as cattle (*Bos taurus*), water buffaloes (*Bubals bubalis*), sheep (*Ovis aries*), goats (*Capra hircus)*, camels (*Camelus dromedarius*), horses (*Equus caballus*), and donkeys (*E. asinus*) are exposed to fluoride through fluoride- contaminated drinking water and food and air-borne fluoride over a long period of time, then fluorosis is developed in them. The disease generally manifests as dental fluorosis (dental deformities) and skeletal fluorosis (bone deformities). In fact, the latter is more dangerous and is a life-long, extremely painful, and incurable fluoride-induced bone disease and results from excessive accumulation of fluoride in various bones. In skeletal fluorosis, the bones of animals become weak, hard, and less flexible and at an early age of animals the mobility of the joints also decreases. The most common bone changes or pathologies such as periosteal exostosis, osteoporosis, osteoporosis, and osteophytosis are found in severe skeletal fluorosis and are clinically manifested as vague pain in the body and joints. Excessive accumulation of fluoride in muscles also reduces mobility and this condition leads to disability or lameness in animals. Globally, thousands of domestic animals suffer from skeletal fluorosis in fluoride endemic rural areas. However, the severity of bone deformities such as periosteal hyperostosis and osteophytosis increases with increasing bone fluoride levels. Typically, skeletal fluorosis develops or appears above a bone fluoride level of 2,500 ppm. The present communication briefly and critically reviews the various sources of fluoride exposure, the severity of fluoride-induced skeletal fluorosis in domestic animals and its adverse economic consequences, and the methods to prevent this dangerous bone disease. The findings of this review may contribute to the formulation and implementation of health plans for mitigation of skeletal fluorosis in domestic animals and are also useful for livestock farmers.

Keywords: Adverse economic consequences; Bone disease; Bone fluoride level; Domestic animals; Fluoride; Fluoride toxicity; Fluorosis; Lameness; Prevention; Skeletal fluorosis

Introduction

It is well known that fluorosis in animals results from long-term exposure to fluoride through fluoride-contaminated drinking water and food and airborne fluoride (industrial fluoride emissions). However, fluoridated water and industrial fluoride pollution are the main sources of development of fluorosis in animals. Fluorosis developed from these sources is called hydro fluorosis and industrial fluorosis in man and animals, respectively [1-8]. However, former disease is most common in domestic animals while foodborne fluorosis in animals is rare in occurrence. Fluorosis is not only prevalent in domestic [9-40] and wild [41-48] animals but it is also prevalent in human populations when exposed to fluoride for long-time [49-61]. In the world, India, and China, both countries are hyperendemic of fluorosis disease. However, fluorosis in diverse species of domestic animals, such as cattle (*Bos taurus*), water buffaloes (*Bubals bubalis*), sheep (*Ovis aries*), goats (*Capra hircus*), camels (*Camelus dromedarius*), horses (*Equus caballus*), and donkeys (*E. asinus*) has been well studied in relation to various fluoride levels in drinking waters, age, sex, different environments or ecosystems, and species [10, 17,18, 22-24, 26]. In fact, in India, almost all drinking water sources of domestic animals in rural areas are contaminated with fluoride with varying amounts [62-65].

In fluorosis, generally, teeth and bones are greatly affected with varying grades depending upon the concentration of fluoride

and the duration of exposure. However, soft tissues or organs are also affected by fluoride toxicity. When teeth are affected by chronic fluoride toxicity it is known as dental fluorosis while when bones are deformed or affected it is known as skeletal fluorosis. The term non-skeletal fluorosis is also used when soft tissues or organs are affected by fluoride [1,66,67]. Dental and skeletal fluorosis are generally irreversible while non-skeletal fluorosis is reversible [66,67]. The present critical review focuses on how skeletal fluorosis develops and is dangerous to domestic animals and its impact on the economy of livestock keepers and how to prevent this bone disease in domesticated animals. The findings of this review may contribute to the formulation and implementation of health plans for mitigation of skeletal fluorosis in domestic animals and are also useful for livestock farmers.

Sources of Fluoride Exposures for Animals

Fluorine (F-) is the seventeenth most abundant substance in the Earth's crust [1] and is widely distributed in sea water, fresh and ground waters, soil, dust, and mineral deposits. Major sources of fluoride exposure to domestic animals are fluoridated drinking water, vegetation and agricultural crops growing on fluoride contaminated soil and water, fluoridated phosphate feed supplements, mineral admixtures, dust in the air, and some industrial processes such as coal burning power generation stations, and manufacture of steel iron, aluminum, zinc, phosphorus, chemical fertilizers, bricks, glass, plastics, cement, hydrofluoric acid, etc. These industrial processes typically release fluoride into the surrounding environment in both gaseous and particulate/dust forms [1,4]. Eventually, the emitted industrial fluoride gets accumulated in soil and herbs/vegetation and contaminates fresh water sources, such as rivers, lakes, ponds, reservoirs, etc. However, the main source of fluoride exposure in domestic animals is drinking water. In fluorosis endemic India, fluoride levels above 3.0 and 21.0 ppm have been recorded in surface and ground water sources, respectively [6, 10]. In rural areas, fluoride contaminated groundwater is commonly used for irrigation in agriculture. This is why agricultural feed is also found to be contaminated with fluoride. Such feed is also a potential source of fluoride for domestic animals [68, 69].

Absorption, Excretion, and Accumulation of Fluoride

Soluble fluorides are almost completely absorbed from the gastrointestinal tract and are carried to various parts of the body via the blood circulation system [70,71], with maximum plasma levels attained within 20-60 minutes of oral intake [71, 72]. However, fluoride absorption may be reduced by the formation of insoluble complexes or precipitates with food components. Fluoride can cross biological membranes by diffusion as non-ionic hydrogen fluoride (HF) [73]. Fluoride has also been reported to cross the placenta [74,75]. However, the greatest amount of absorbed fluoride is retained or accumulated in the growth or remodeling of calcified organs, such as bone and teeth [76], where approximately 99% of the total fluoride in an organism is found [77]. In contrast, fluoride concentrations may be higher in the kidney than in plasma [78]. Finally, most of the absorbed fluoride is excreted by the kidney, and only a small fraction via the feces [79]. In any case, fluoride concentrations in bones will increase as animals age, even in areas with low environmental fluoride [80]. Fluoride absorption by the skeleton is nearly 100% in growing animals, and the rate slows as bones mature [81].

Skeletal Fluorosis in Domestic Animals

Biological accumulation of fluoride causes diverse toxic effects or pathological changes and interferes with various physiological and metabolic processes. Indeed, fluoride reacts with proteins, especially enzymes, and generally inhibits enzyme activity at concentrations in the millimolar range [70, 82]. However, cell proliferation can be stimulated at concentrations in the micromolar range [82,83]. It is not known whether fluoride has any essential function in cells or organisms. Mechanisms by which fluoride affects cell functions include generation of superoxide anion [84,85]; release of cytochrome c from mitochondria and induction of apoptosis [86,87]; inhibition of the migration of embryonic neurons [88] and sperm [85]; and altered release of the neurotransmitters, such as acetylcholine [89] and gamma-aminobutyric acid [90].

Excessive fluoride intake or bioaccumulation over a long period of time alters the balance between bone formation and resorption. This biological process is accomplished with the involvement of certain regulatory determinants and signaling pathways, leading to various pathological changes in different bones of skeletal known as "skeletal fluorosis". In fact, excessive accumulation of fluoride in the bones of the skeleton and associated muscles and ligaments causes different types of deformities which are more dangerous and highly painful depending upon the concentration of fluoride and the duration of its exposure. This entity of long-term intoxication of fluoride is very painful and more dangerous than other forms of fluorosis, e.g. dental fluorosis and is of extreme importance as it reduces mobility at a very early age of the animals by gradually causing different changes in the bones such as periosteal exostosis, osteosclerosis, osteoporosis, and osteophytosis [91-93]. These changes appear clinically as vague aches and pains in the body and joints associated with stiffness, lameness, small body growth, and recognizable bone lesions. These bone changes are progressive and irreversible and become severe with the aging of the animals and increase in duration or frequency of exposure to fluoride. Intermittent lameness, enlarged joints, debility, disability, hoof deformity, wasting of body muscles, and bone lesions in jaw, ribs, metacarpus, and metatarsus regions are well recognized in animals suffering from severe skeletal fluorosis (Figures 1and 2). Ankylosis deformity is also possible in some fluorosis cases. However, this condition is rare in animals suffering from chronic fluoride poisoning. Excessive accumulation of fluoride in muscles also reduces activities or movements and this condition causes lameness in animals.

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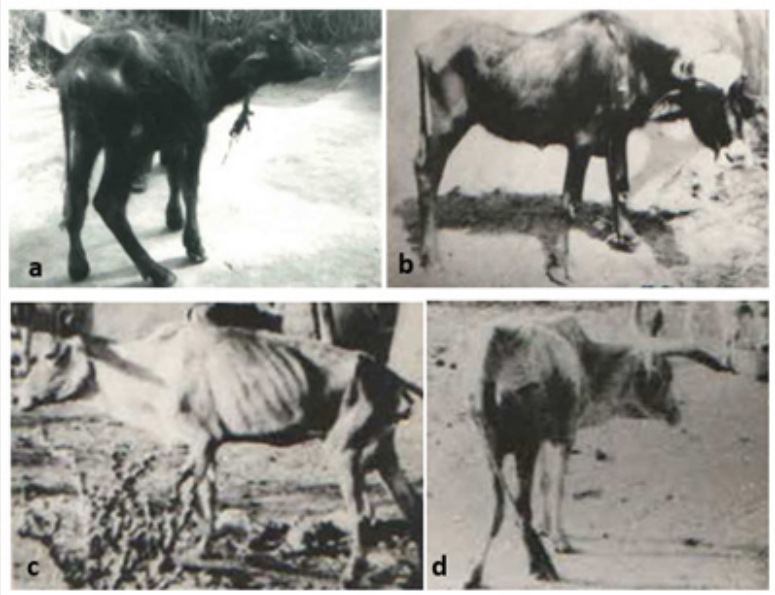

Figure 1: Severe skeletal fluorosis in domesticated calf and juvenile buffaloes (a and b) and old cattle (c and d) showing lameness, enlarged joints, debility, invalidism, hoof deformities, wasting of body muscles and bony lesions in the mandibles, ribs, metacarpus, and metatarsus regions. Ankylosis deformity is also in cattle (a and b).

Figure 2: Moderate (e and g) and severe (f and h) skeletal fluorosis in domesticated bovines and flocks.

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Fluoride-induced bone lesions include mild to marked periosteal hyperostosis that may be localized or generalized and degenerative joint disease (DJD or arthritis), which can cause severe pain and lameness in domestic animals. Ultimately, these fluoride-induced changes impair general health, fitness, body condition, and may reduce reproductive success or performance. Interestingly, in hoofed animals, the lesions are first observed in the metatarsus or metacarpus bones of the limbs as also found in wild animals [94]. Excessive accumulation of fluoride in muscles also reduces/restricts bone movement leading to lameness in animals. Apart from intermittent lameness, joint swelling, loss of body muscle mass, and mortality are also common in animals with skeletal fluorosis.

Interestingly, all bone changes or lesions are visible only when bone fluoride levels exceed a threshold that is variable across animal species. It appears that the rate of fluoride accumulation in bone influences the type of skeletal lesions observed. Periosteal hyperostosis can develop rapidly if bone fluoride levels are sufficiently high in young individuals and generally develops more slowly in response to chronic exposure and bone fluoride levels increase with increasing age of the animal. However, the severity of bone deformities such as periosteal hyperostosis and osteophytosis increases with increasing bone fluoride levels. In general, fluoride levels in the bones of affected animals are shown to be above "normal" (approximately >1000 µg F/g). A threshold level of approximately 4000 µg F/g dry bone, above which obvious lesions become apparent, has been described in various mammalian species [95-97]. However, according to Underwood (1977) no gross or microscopic changes in bones were found in animals exposed to fluoride levels up to 2,500 ppm [98].

Recent studies show that among various species of domestic animals, bovines (cattle and buffaloes) are found to be relatively less tolerant to fluoride toxicity and suffer from more severe skeletal fluorosis than other animal species. Their calves are also found to be relatively more sensitive to fluoride toxicity than immature animals or juveniles of other species [23,24]. However, apart from fluoride concentration and duration and frequency of exposure and the density and rate of bioaccumulation of fluoride in bones, the prevalence and severity of skeletal fluorosis also depends on many factors, such as age, food, nutrients, chemicals in water, environment, individual sensitivity or tolerance and genetics, etc. [99-109].

Adverse Economic Consequences

It is well known that the rural economy of any country depends largely on animal husbandry. Animal husbandry is also the main source of daily income of the villagers. In villages, people keep and raise animals of different species according to their economic condition and convenience. Animal keepers get sufficient income from milk, dung, meat, leather, bones, wool, etc. obtained from different species of domestic animals. When these animals become victims of skeletal fluorosis, there is a huge reduction in these animal products, which also reduces the income of the animal keepers. Because due to this disease, animals become physically weak and lame, due to which such animals get very low prices when sold in the market, due to which the livestock farmers must suffer huge financial losses. Apart from this, skeletal fluorosis reduces fertility in animals, which ultimately affects animal productivity. If the productivity of animals decreases, then it directly affects the economy of the livestock farmers [110]. Whatever chronic fluoride poisoning in domestic animals is responsible for weakening the rural economy in some way or the other. However, it is difficult to tell how much economic loss animal owners suffer due to skeletal fluorosis in animals. Hence, more scientific studies to assess the economic losses caused by endemic skeletal fluorosis in domestic animals are highly recommended. The findings of these studies may be useful in formulating and implementing health and economic policy to prevent such economic losses.

How To Prevent Skeletal Fluorosis in Domestic Animals

Fluoride-induced skeletal fluorosis is usually permanent, irreversible, and incurable in domestic animals. Therefore, prevention is the only way to protect pets or domestic animals from chronic fluoride toxicosis or skeletal fluorosis. This requires that pets are not fed fluoridated water or exposed to any source of fluoride as far as possible. In areas where almost all drinking groundwater sources are contaminated with fluoride, rainwater harvesting is one of the most ideal and effective methods to get regular fluoride-free water for these animals. Unpolluted water from perennial fresh or surface water sources (ponds, reservoirs, lakes, rivers, etc.) is also an alternative drinking water option for domestic animals as water from these sources contains traces of fluoride or having 0.01–0.3 ppm fluoride [1]. Defluorination of fluoridated water is also an option to provide fluoride-free water to these animals. Though there are many defluorination techniques available. However, "Nalgonda defluorination technique" is an ideal technique for defluorination of fluoride containing water [111]. Nevertheless, providing domestic animals with food rich in natural minerals and antioxidants may be the most effective solution. To protect domestic animals from industrial fluoride emissions or pollution, it is necessary to prevent them from moving to areas where there are factories emitting fluoride. Moving animals from fluoride-affected areas to non-fluoride-affected areas is also an effective way to prevent skeletal fluorosis.

Conclusion

Excessive intake/inhalation of fluoride through fluoridated water and industrial fluoride pollution causes a serious disease called fluorosis in domestic animals. Excessive accumulation of fluoride in various bones of the skeleton causes various deformities or changes in the bones. These deformities caused by fluoride are collectively known as skeletal fluorosis which is extremely painful and persists for life in the animal. Thousands of domesticated animals in fluoride affected areas are found to be suffering from this bone disease. The most dangerous aspect of this disease is

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that the animals become lame and there is no cure for this disease in animals yet. This disease in animals can also cause financial loss to livestock owners in diverse ways. Therefore, prevention of this disease in domestic animals is extremely important and this is the only solution. This is possible by providing fluoride free drinking water, nutritious food, and shifting animals from fluoride affected areas to non-fluoride affected areas.

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