Fluoride Toxicity and Human Health: A Review

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Abstract- ***Industrialization and change in life style have incorporated lot of unwanted chemicals, which shows toxicity and annihilate the normal functioning of biological molecules. Fluoride is one of them naturally occurring element and its contamination in ground water is the biggest problem for the world. The fluoride contaminated ground water is very harmful and shows adverse effects on not only the calcarious tissue (skeletal and dental fluorisis) but also on almost all soft tissue including liver, brain, kidney, reproductive organs, endocrine glands etc. Thus, it also causes fluorios's fatigue, problem of back bone, neck and limbs, which leads to frangibility and deformity. Day by day increasing level of this chemical in the food chain has increased the need to realize its noxious effects.***

Indexed Terms- Fluoride, Dental fluorosis, Skeletal fluorosis, human health.

I. INTRODUCTION

Water pollution is one of the most serious problems for all the living organisms on earth. Water is an extremely essential element for life on the earth. There would have been no life without water. About 79% of the total water available on earth is found in oceans, which is too salty for drinking purpose and the remaining 3% in freshwater. Out of the total easily available volume of water, ground water is the main source used for drinking purpose in our country with 85% of population dependent on it. So there is huge problem of pure drinking water, because of increasing level of Urbanization, industrialization and population growth. Therefore, due to industrial waste, agricultural uses and domestic sewage, climatic conditions are becoming worst day by day.

Fluorine is an element of the halogen family and its inorganic and organic compounds called fluorides. Fluoride (F^-) the anion with oxidation state-1 is a reduced form of fluorine, a gas that never occurs in Free State. Fluoride is mainly found in the form of hydrogen fluoride (HF), sodium fluoride (NaF), calcium fluoride (CaF_2), sulfur hexafluoride (SF_6) and fluorosilicic acid or hexaflurosilic acid (H_2SiF_6). Ground water containing fluoride dissolved ions beyond the permissible limit is harmful and not suitable for drinking and domestic use. Fluoride concentration in ground water varies with the ground water level fluctuation. Weathering of rocks and leaching of fluoride bearing minerals are the major resource, which contribute to elevated concentration of fluoride in ground water. Human activities also releasing fluorides into the environment mainly the mining and processing of phosphate rock and its use as agricultural fertilizer, as well as manufacturing processes (aluminium, steel, copper, nickel, brick, ceramic, glues, adhesive and fluoride containing pesticides). To an estimate, 20% of pharmaceutical and nearly 30-40% agrochemicals are used organo fluorines. Fluorosilicic acid, sodium hexafluorosilicate and sodium fluoride are used in municipal waste fluoridation schemes. The other important natural phenomenon that contributes to high fluoride is evaporation.

Small amount of fluoride (<1ppm) in diet helps preventing dental caries and strengthening of bones but at higher levels i.e. above permissible limit (1.5ppm, by WHO), shows cumulative toxic effects. Prolonged ingestion of fluoridated water or consuming high fluoride (i.e. in excess of 10 mg/L) leads to dental fluorosis, skeletal fluorosis and non-skeletal fluorosis. The dental fluorosis is characterized by dental mottling and loss of coloration of teeth, while skeletal deformation and rigidity in joints was observed in case of skeletal fluorosis. Fluoride also affects cells of soft tissues including renal, endolithial, gonadal and neural cells.

II. SOURCE AND FATE OF FLUORIDE

Fluoride is an important element of public health concern. It is naturally present in almost every water bodies but higher concentrations are found in ground

water, rocks, earth, crust etc. Drinking water is the main source of fluoride exposure in humans. It is also present in most of everyday essential needs like cosmetics, drugs, chewing gums, tooth pastes and mouth wastes, but it is found in permissible limits. It is experimentally proved that a small amount of it is experimentally proved that a small amount of it is beneficial for human health but is very harmful when present in excess of 1.0ppm but day by day the concentration of fluoride is increasing in our food chain. WHO recommended that the fluoride content in drinking water should be in the range of 1.0 to 1.5 ppm.

Virtually all foodstuffs contain at least trace amounts of fluoride. Elevated levels are present in fish and in tea leaves, which are particularly rich in fluoride. The level of fluoride in food is significantly affected by the fluoride content of water used in food preparation or processing, particularly in beverages and dry foodstuffs to which water is added prior to consumption. The dietary fluoride in alimentary canal, due to its electronegative nature receives a negative charge and converts into ionic form. Such ingested fluoride is converted to hydrofluoride acid (HF) due to acidic conditions in stomach. As HF is easily absorbed this leads to GI irritation or corrosive effect on intestinal wall. The penetration of HF is much faster than dissociated fluoride ions. When the concentration of fluoride increases in the gastrointestinal tract, it is passed over to the blood stream where it's level increases quickly within 20-60 minutes. After absorption, blood fluoride gets distributed throughout the body, with maximum absorption by calcarious tissues such as bones and teeth.

The unabsorbed Fluoride is pass out from body via faeces. Fluoride is concentrated at high levels within kidney tubules, so kidney has higher concentration of fluoride than plasma. Fluoride is freely filtered through the glomeruluar capillaries and re-absorption takes place due to diffusion of HF. Among all the halogens, the renal clearance of fluoride is usually high. Though the rate of renal clearance is low in children than adult (Jaiswal *et al*., 2012).

III. IMPACT OF FLUORIDE ON HUMAN HEALTH

Fluoride in very limited quantity is desirable for healthy growth of teeth and bones in human beings and prevents dental caries (Prakash, 2010). But intake of more fluoride, results in multidimensional health manifestations, the most common being dental and skeletal fluorosis. This is caused chiefly through consumption of water, having excess fluoride content. Higher concentration of fluoride also causes General paralysis, respiratory failure and low blood pressure, loss of weight, anemia, anorexia, cochexia are among the common remits in chronic fluoride poisoning. Fluoride ions inhibit a variety of enzymes, often by forming complexes with magnesium ions and other metal ions. Continuous ingestion of fluoride causes inhibition of growth.

IV. INTAKE, METABOLISM, AND DISPOSITION OF FLUORIDE

Approximately 75-90% of the fluoride ingested each day is absorbed from the alimentary tract. In the acidic medium of the stomach, fluoride and hydrogen ions can combine to form hydrogen fluoride, which at sufficiently high concentrations, can be irritating to the mucpoc membranes of the stomach lining. Because of its affinity for calcium compounds, about half of that fluoride becomes associated with teeth and bones within 24 hours of ingestion. Ingestion of fluoride causes decrease in ionized calcium. This hypocalcamia (lowering of calcium level in Plasma) causes hyperparathyroidism that activate cyclic AMP and ultimately osteoclast cativity increases that rises the level of citric acid and lactic acid which ultimately increase the hydrogen ion concentration and lysis of lysosomes. Lysosomal lysis release hydrolase enzymes, causing depolymerisation of glycoprotein of bone and cartilages. Hydroxiproline is responsible for stabilizations of collagen triple helix. Depolymerisation of glycoprotein collapse this collagen triple helix. As the protein polymer disintegrate and dissolves, the mineral binding capacity is also reduced and calcium is liberated. The net result of this degradation of ground substance in bones and other calcified tissues leads to symptoms of non-skeletal fluorosis.

V. DENTAL FLUOROSIS

Fluoride prevents tooth decay by enhancing the remineralization of enamel that is under attack, as well as inhibiting the production of acid by decay-causing bacteria in dental plaque. Ingestion of too much fluoride in early childhood damages the enamel covering of the teeth and fails to crystallize properly is dental fluorosis. It is a dose response conditions: the greater the fluoride intake during tooth development, the more severe the dental fluorosis. In adult, long term exposure to fluoride causes mottling of teeth and presence of white chalky patches on teeth. In case of mild fluorosis teeth becomes yellow, brown or sometimes black. Excessive withholding of this enamel protein leads to porosity in teeth. Fluoride concentration above 2mg/l in drinking water causes dental fluorosis in 60% of the affected population, whereas concentration above 6mg/l affects 100% of the population (Jaiswal *et al*., 2012).

VI. SKELETAL FLUOROSIS

Bones can negatively affect by fluoride. Causes of skeletal fluorosis are associated with high level of fluoride in drinking water or in ambient air at work place or at home. Although several other factors, including nutritional factor can play a significant role in skeletal fluorosis. During high intake of fluoride, it bounds with the calcarious tissue and replaces hydroxyl and bicarbonate ions and accumulates there causing crippling of bones. Fluoride increases bone density and appears to exacerbate the growth of osteophytes present in the bone and joints, resulting in joint stiffness and pain. Early signs of skeletal fluorosis are pain in joints and bones, ultimately leading to increased bone density (osteosclerosis) and rigidity of joints (Edmunds and Smedley, 2005).

VII. EFFECT OF FLUORIDES ON SOFT TISSUES

Number of studies shows that fluoride also affects the soft tissues including liver, kidney, brain and reproductive organs of the exposed animals.

Fluoride toxicity causes dysphasia i.e. alteration in shape and size of the erythrocytes. This effect gets more pronounced with the increase in dose concentration as well as after prolonged duration of exposure (Ruhela *et al*., 2011). Several alterations were observed in the liver, including degeneration of hepatocytes, nuclear pyknosis, cellular swelling and congestion of blood vessels (Ruhela *et al*., 2012).

High concentration of fluoride exposure causes changes in reproductive hormones such as testosterones and follicle stimulating hormones that effects on fertility by alliterating the mobility and morphology of sperms, causing decreased birth rates and in the development of embryo. In pregnant woman, fluoride easily passes through placenta and causes incomplete closing of embryonic neural tube.

Renal excretion is the major route of elimination for inorganic fluoride from the body as a result it shows its adverse effect on renal cells at high concentration, making the kidney a potential site for acute fluoride toxicity. Very high concentration of fluoride causes necrosis of renal tubules, interstitial nephritis and dilation of renal tubules (Ruhela *et al*., 2011 & Srivastava *et al*., 2011). Studies conducted in regions where fluoride concentration was high showed increased rate of occurance of urolithiasis (Kidney stones).

Continuous intake of drinking water having the fluoride concentration about 4mg/l especially by young children alters the hormone level in blood. It includes decreased the activity of thyroid hormone, increased the activity of calcitonin and parathyroid hormone, secondary hyperparathyroidism, impaired glucose tolerance, and possible effects on timing of sexual maturity.

Due to high electronegative nature, fluoride forms strong hydrogen bonds with –OH and –NH moieties causing oxidative stress that results in neurodegeneration (Bhatnagar *et al.,* 2002). Synergistic effects of fluoride with other metal toxic compounds such as aluminum, affect G-protein couple receptors and disturb second messenger system in brain. Studies revealed reduced learning and memory, reduced motor co-ordination, lower IQ levels and short-term memory loss including behavioural symptoms like nervousness, depression, tingling sensations in fingers and toes, frequent urination, excessive thirst in the subjects suffering from fluorosis

(Bhatnagar *et al.*, 2011). Long term exposure of high fluoride disturbs metabolic functions of brain, brain cell architecture, level of neurotransmitters, growth factors, enzymes and to a great extent affect the endogenous antioxidant level of brain causing oxidative stress (Bhatnagar *et al*., 2006).

VIII. GENOTOXICITY AND CARCINOGENICITY

Prolonged exposure of fluoride causes mutation and chromosomal damage in mammalian cells. Sodium fluoride inhibits the protein and DNA synthesis and causes chromosomal aberrations in human cells. High fluoride is also responsible for causing cancer conditions rooting different types of cancer most, important being blood and bone cancer (Jaiswal *et al.*, 2012).

CONCLUSION

On the basis of this review on the toxicity of fluoride it can says that:

- All organisms are exposed to fluoride released from natural sources and/ or by human activities.
- Fluoride can help prevent cavities, but at high intakes it can harm teeth development (dental fluorosis) and at higher intakes still, weaken and deform bones (skeletal fluorosis). There is a narrow range between intakes which are beneficial and those which begin to be detrimental.
- Effects on the bone, such as skeletal fluorosis and fracture, are considered to be the most relevant outcomes in assessing the adverse effects of long-term exposure of humans to fluoride.
- High concentration of fluoride also hazardous for the soft tissues including liver, stomach, kidney, brain and reproductive organs and even to the developing embryo of exposed animal and human.
- There is a need to improve the knowledge available on the accumulation of fluoride in organisms and how this can be monitored and controlled.

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