Fluoride Toxicity

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The practice of community water fluoridation used prophylactically against dental caries increased concern of adverse fluoride effects. Millions of people living in endemic fluorosis areas suffer from various pathological disturbances. Authors assessed the publications on fluoride toxicity until June 2020. Authors present evidence that fluoride is an enzymatic poison, inducing oxidative stress, hormonal disruptions, and neurotoxicity. Fluoride in synergy with aluminum acts as a false signal in G protein cascades of hormonal and neuronal regulations in much lower concentrations than fluoride acting alone. Our review shows the impact of fluoride on human health. We suggest focusing the research on fluoride toxicity to the underlying integrative networks. Ignorance of the pluripotent toxic effects of fluoride might contribute to unexpected epidemics in the future.

Keywords: autism spectrum disorders ; aluminofluoride complexes ; enzymes ; fluoride toxicity ; G proteins ; IQ deficits ; magnesium ; neurotoxicity ; phosphate

1. Introduction

More than 500 million people live in endemic fluorosis areas with an elevated level of fluoride in drinking water and biosphere with public health problems[1][2]. The fluorosis symptoms span from mild effects on teeth enamel, headaches, dizziness, loss of appetite, to severe pathological disturbances. These include dental and skeletal fluorosis, hypothyroidism, sleep disorders, inflammations, IQ deficits, and suspected autism[3][4][5][6].

In 1931, H. Trendley Dean, head of the Dental Hygiene Unit at the National Institute of Health (NIH), began investigating the epidemiology of fluorosis in the USA. Dean and his staff determined the fluoride levels in drinking water causing fluorosis. They discovered that fluoride levels of up to one milligram fluoride per liter of drinking water (one ppm) did not cause dental fluorosis in most people. Dean's reports formed the foundation of the concept that the ingestion of fluoride will augment the teeth enamel and make it less susceptible to dental caries[7]. Dean suggested adding fluoride to water sources deficient in fluoride to bring its concentration up to the optimal value. After trials in the USA, the World Health Organization (WHO) recommended community water fluoridation (CWF), and many countries implemented this program[8][9][10]. The CWF recommendation has been followed for over 70 years in developed countries, such as the USA, Canada, Australia, New Zealand, Ireland, and some parts of the United Kingdom (UK)[9].

CWF started an era of increased income from fluoride as never before in human history. Recently, 370 million people from 27 countries have a supply of fluoridated drinking water[9]. The number of fluoride sources has further expanded since fluoride is used for the improvement of food, beverages, hygiene, and medical products including fluorinated drugs.

The fluorine atom does not exist in nature in a free and unmixed state. The mineral fluorite (CaF_2) is the main source of fluorine for commercial use. Fluorine readily reacts with other elements to form fluoride compounds, within which it always adopts an oxidation state of −1. Inorganic compounds are formed with hydrogen, metals, and non-metals. Therefore, fluoride refers to the negatively charged ion of the fluorine atom. In general, soil fluoride is not available to plants. There are exceptions such as tea plants that are natural accumulators of fluoride from fertilizers[1][2][4]. Fruits such as blueberry and grape concentrate fluoride from soil and it might appear in commercial juices. Fluorine excess had been found to be detrimental also to plants. Injury to plants is common all around industries making aluminum, fertilizers, or glass. Special plants might produce the toxic organofluorine compound fluoroacetate, which is used as a defense against grazing by herbivores.

Conflicting views occur in debates addressing whether fluorine is an essential element for humans. The researchers of the Panel of the European Food Safety Authority (EFSA) state that fluoride has no known essential function in human physiology and development[11]. On the other hand, the WHO and the Centers for Disease Control and Prevention (CDC) consider fluoride to be an important dietary element for humans because of "resistance to dental caries is a physiologically important function"[12].

2. The Implication of Fluoride Toxicity on Human Health

Early reports about fluoride toxicity in humans appeared in the journal Physiological Reviews already in 1933. Aluminum smelter workers and persons living near the factory where fluoride was in high concentration in the atmosphere suffered with psychiatric and neurological disturbances. Endemic fluorosis is caused by persistent fluoride exposure through ingestion or inhalation, and most commonly, as a result of high fluoride levels in drinking water and beverages[13][14]. The WHO's drinking water quality Guideline Value for fluoride is 1.5 mg/L [14].

Dental fluorosis results after excess fluoride ingestion, most commonly in drinking water, during tooth formation. For example, dental fluorosis appears in 43–63% of schoolchildren in endemic areas of China with total fluoride intake 2.7–19.8 mg/day[5]. The rate of dental fluorosis also increases in countries with CWF. In the 2010–2012 survey, dental fluorosis was reported among adolescents aged 12–15 years in the USA with a surprisingly high rate of 65%[15]. Dental fluorosis might be used as a sensitive indicator of excessive fluoride exposure[16].

Skeletal fluorosis impacts millions of people in regions with high natural levels of fluoride, like India, China, Pakistan, Iran, and the Gulf region, to name a few [13]. The U.S. Environmental Protection Agency (USEPA) sets a maximum contaminant level of 4.0 mg/L to protect against skeletal fluorosis. WHO indicates a clear risk of skeletal fluorosis for a total intake of 14 mg fluoride per day. Nevertheless, the recent findings revealed that consumption of fluoride at even 10 times lower concentrations of 1.5 mg/L caused its high incidence in India[17]. The chemical analyses show that 80% of water sources in rural areas exceed the WHO fluoride permissible limits and residents are affected by skeletal fluorosis.

Waldbott et al. examined about 500 people affected by chronic fluoride intake from CWF[18]. These authors observed chronic fatigue, headaches, loss of the ability to concentrate, depression, gastrointestinal symptoms, and deterioration of muscular coordination.

3. The Economic Consequences of Fluoride Toxicity

It is difficult to precisely evaluate the economic consequences of endemic fluorosis. It is now known to be global in scope, occurring on all continents. Except for China, defluorination projects were closed in most countries due to a collapse in their cost.

Conversely, CWF is recognized as one of the most cost-effective, equitable, and safe measures to prevent cavities and improve oral health. Thousands of studies showed that CWF prevents cavities and saves money, both for families and the health care system. An economic review of multiple studies used by CDC found that savings for communities ranged from $1.10 to $135 for every $1 invested. Per capita annual costs of CWF range from $0.11 to $24.38, while per capita annual benefits range from $5.49 to $93.19[19]. Fluoride has modest benefit in terms of reduction of dental caries but also significant costs concerning dental and skeletal fluorosis, hypothyroidism, and mental and cognitive disturbances. Ingestion of fluoride constitutes an unacceptable risk with virtually no proven benefit. The possibility that chronic fluoride intake might evoke chronic diseases with high socioeconomic impact must be involved. Hirzy et al. calculated that the economic impact of IQ loss among USA children is the loss of tens of billions of dollars[4]. The available information supports a reasonable conclusion that economic losses associated with ASD may be also quite large. The annual societal costs for children with ASD were estimated between $11.5–60.9 billion in the USA in 2011. They included a variety of direct and indirect costs, from medical care to special education, and lost parental productivity [20]. Children and adolescents with ASD had average medical expenditures that exceeded those without ASD by $4110–6200 per year. According to estimates of Leigh and Du, annual costs due to ASD in the USA in 2015 were around $268 billion[21]. However, if the rate of increase in the ASD prevalence continues, Cakir et al. estimated in 2020, that costs could reach nearly $15 trillion by 2029 [22].

We suggest that the reduction of fluoride from the daily life of pregnant women as well as of children in infancy could be an efficient way to prevent fluoride developmental neurotoxicity[23].

4. Conclusions

Fluoride toxicity has been demonstrated in many studies. We present evidence that fluoride interferes with enzyme activities, induces oxidative stress, and causes hormonal disturbances, and neurotoxicity. The health impacts of increased fluoride exposition of millions of people in endemic fluorosis areas are of global public concern. At present, there is a divergence between the practice of CWF, which is regarded as valuable and safe for reducing dental caries, and current scientific evidence, which indicates that fluoride is a potent neurotoxin disturbing prenatal as well as postnatal brain development. The dose recommended for dental caries reduction is close to the dose causing pathological effects. Moreover, fluoride in synergy with trace amounts of Al^{3+} has the potential to affect all phosphoryl transfer reactions and most regulations of fundamental biological processes in much lower concentrations than fluoride alone.

The potential neurotoxicity associated with exposure to fluoride has generated controversy about CWF. Given the large number of studies showing cognitive deficits associated with elevated fluoride exposure under different settings, the general tendency of fluoride-associated neurotoxicity seems overwhelming. We concur with the conclusions of many authors over the world that fluoride neurotoxicity is a serious risk associated with elevated fluoride exposure, whether due to CWF, natural fluoride release from soil minerals, food supplements or tea consumption, especially when the exposure occurs during early brain development.

Fluoride is not an essential nutrient. No physiological function can be defined during the development and growth, for which it is required. Fluoride toxicity is a slow, hidden process. Evolving evidence should inspire scientists and health authorities to re-evaluate claims about the safety of fluoride, especially for the fetus and infant for whom it has no benefit at all.

Of all sources of fluoride, artificially fluoridated water is the most available practical source to eliminate fluoride intake to reduce its human hazards. Our review explains that fluoride could evoke unexpected epidemics in the future.

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