Review Article

Role of Flouride on Thyroid Hormone Imbalance –A Mini Review

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Abstract

In India, both Iodine Deficiency Disorders (IDD) and fluorosis (due to consumption of excess fluoride), are the two most prevalent endemic diseases which coexist in certain regions in the country. Fluorosis is associated with delayed tooth eruption, delayed removal of enamel matrix proteins, delayed enamel maturation etc. We conclude this review article by emphasizing that drinking water fluoride is not responsible for elevate the serum fluoride level. It is also likely if someone eats or drinks food high in fluoride such as tea coffee, reconstituted fruit juice, grapes or raisins that have had fluoride insecticide (cryolite), dried eggs, and carbonated drinks.

Key words: Fluorosis, Iodine, Delayed eruption. Iron deficiency.

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Introduction

In India, both Iodine Deficiency Disorders (IDD) and fluorosis (due to consumption of excess fluoride), are the two most prevalent endemic diseases which coexist in certain regions in the country. Though goiter—an enlarged thyroid gland—is commonly recognized as a visible sign of iodine deficiency, the health effects of iodine deficiency reach far beyond those of goiter, and the significant impact of iodine deficiency on brain function in the fetus, as also in the development of the newborn and the child are now well documented. As early as 1928, Stocks observed that children consuming well water in the village of Somerset, England exhibited both goiter and mottled enamel (dental fluorosis). Some years later, Wilson found dental fluorosis associated with goiter and cretinism among children living in areas of Punjab where fluoride was recognized geologically to be significantly high. Besides dental fluorosis and cretinism, children in endemic fluorosis areas of India often have low IQ, deaf mutism, knock-knee and bow-legs. Obviously, these are serious public health problems of great concern. Since fluoride is known to interfere with thyroid gland function and to cause degenerative changes in the central nervous system, impairment of brain function, and abnormal development in children, further investigation is clearly

needed, even where iodine intake is not deficient.[1] In fact, DF is a developmental disorder originating from aberrant thyroid hormone metabolism. Perhaps the most obvious indication that DF is a condition caused by disordered thyroid hormone signaling during the time of enamel development is the long-standing observation of delayed eruption of teeth in fluoridated areas. DF is invariably associated with dental age and eruption of teeth, a process closely controlled by thyroid hormone (TH). TH deficiency leads to delayed tooth eruption, while TH excess leads to the acceleration of tooth eruption. The more fluoride ingested, the longer it takes for the tooth to erupt. The later in life maturation of enamel is completed, the greater is the severity of dental fluorosis. At the same time, other risk factors known to influence DF are identical to those observed in thyroid dysfunction. It is well established that DF can only occur as a result of excessive fluoride exposure during crucial times of development—in utero to approximately 30 months for deciduous teeth and permanent incisors— and is marked by events related of ages. Thus, it is associated with delayed tooth eruption, delayed removal of enamel matrix proteins, delayed enamel maturation etc.[2]

Mechanism of Flouride on Thyroid Hormone Imbalance

Production of thyroid hormones is regulated by a negative feedback mechanism, i.e., when the pituitary gland senses a drop in FT_3 levels in circulation, it releases more TSH to stimulate the thyroid gland which in turn accelerates the production of the thyroid hormone T_4, now considered a "pro-hormone". The major source of circulating T_3 is from peripheral deiodination of T_4 and not from thyroid secretion. The enzymes which catalyze deiodination are called iodothyronine deiodinases, of which three have been identified, namely D1, D2, and D3, of which a brief discussion is relevant to the abnormalities detected. D1 activity is known to be responsible for conversion of T_4 to T_3 in peripheral tissues, particularly in the liver, and is reflected in plasma T_3 levels. D1 has both outer ring deiodination (ORD) as well as inner ring deiodination (IRD) activity. D2 activity reflects conversion of T_4 to T_3 in target tissues (local). This deiodinase has only ORD activity. However, there is recent identification of D2 in human skeletal muscle which supports the view that part of plasma T_3 may be generated from tissues other than liver. D3 activity, on the other hand, converts T_4 into the metabolite reverse T_3 (rT_3) and further, T_3 into 3, 3'-T2. D3 has only an IRD activity and is an inactivating enzyme. Among the three deiodinases, D1 is expressed in thyroid gland besides the liver and kidney. D2 is found in the brain, pituitary gland, and skeletal muscle, and D3 is highly expressed in brain, placenta, and fetal tissues. While our investigations have focused on thyroid hormones and tooth development rather than the deiodinases, fluoride is known to interfere with the activity of the deiodinases. Fluoride and iodine are both halogens. Fluoride, the negative ion of the element fluorine, easily displaces iodine in the body because it is much lighter and therefore more reactive. In fact, the activity of any one of the halogens (Iodine 126.70, Bromine 79.90, Chlorine 35.45, Fluorine 18.99 are the most common) is inversely proportional to its atomic weight. In other words, one halogen can displace another one of a higher atomic weight but cannot displace one of lower weight thereby, results Fluoride-Thyroid-Iodine Antagonism which in turn lead to:

- Interference with iodine uptake
- Fluoride is a Universal G-Protein activator/inhibitor- The stimulation of certain G proteins occurs due to the toxic effect of fluoride (whose function is to govern uptake of substances into each of the cells of the

body), which has the effect of switching off the uptake into the cell of the active thyroid hormone. The thyroid control mechanism is compromised. The thyroid stimulating hormone output from the pituitary gland is inhibited by fluoride, thus reducing thyroid output of thyroid hormones. Fluoride competes for the receptor sites on the thyroid gland which respond to the thyroid stimulating hormone; so that less of this hormone reaches the thyroid gland and so less thyroid hormone is manufactured.[2]

- TSH [thyroid stimulating hormone] analogue- Fluoride is a TSH analogue, and may be active in both the presence and absence of TSH.
- Inhibits thyroid hormone transport
- Mimic the action of TRH i.e. by causing elevated prolactin levels in the pituitary (Yuan et al, 1991).
- Interferes with Deiodinases [enzymes necessary to "deiodinate" or remove iodine from thyroid hormones]

The mechanism of F causing the functional disorder of appendix cerebri-thyroid may be one of competing with iodine and influencing the absorption and condensing of iodine in thyroid, biologic activity of functional enzyme system in thyroid and feedback mechanism of hypothalamus and adenohypophysis of appendix cerebri and control the secretion of thyroid directly (Xiaowei et al., 1994). Chunxiang Wu in (2008) stated that serum thyroid hormone level were significantly affected by excessive F or As, which may be one of the causes that lead to a reduction in the learning and memory of rats. Therefore these damaging effects, all of which occur with small concentrations of fluoride, have obvious and easily identifiable effects on thyroid status.

The running down of thyroid hormone means a slow slide into hypothyroidism. Already the incidence of hypothyroidism is increasing as a result of other environmental toxins and pollutions together with wide spread nutritional deficiencies to which the effect of fluoride also serves as an additive. The excess fluoride ion affects normal deiodination so the children in endemic fluorosis areas are afflicted with physiological derangements. Since deiodinase activities are considered to be under external TSH control, this account for many of the thyroid hormone derangements and could also cause delayed eruption of teeth as observed in the present study. The amount of FT_3 and FT_4 produced by the thyroid gland is controlled by the pituitary gland at the base of the brain. It does this by secreting Thyroid Stimulating Hormone (TSH). When the levels of FT_4 and FT_3 fall, the pituitary secretes more TSH. When FT_4 and FT_3 levels rise, the pituitary secretes less TSH. The fall in the level of FT_3 causes a rise in the TSH level indicating the significant dependence of TSH on FT_3.However, FT_3 is not significantly dependent on TSH, that is, the reverse is not true. FT_3 is a more active molecule and is more sensitive to changes in fluoride levels in the body fluids. Therefore, it shows alterations much more easily than TSH thereby indicating a greater tendency to develop hypothyroidism with in the presence of high fluorine level in body fluids.FT_3 alterations usually result in lower IQ, hearing impairment and other developmental defects in the acoustic organ as studied by various authors. Alteration in the FT_3 levels also leads to TSH level alteration. The combined effect of alteration in FT_3 and TSH may show more drastic consequences on the body in the long run in the children of endemic fluoride areas. The largest US study ever conducted on the effects of maternal iodine deficiency showed that mild sub-clinical hypothyroidism in the mother resulted in lowered IQ in the offspring. Besides low IQ, hearing impairment in children ingesting high fluoride and living in endemic areas of iodine deficiency is also reported. Since the

development of hearing is controlled by thyroid hormone, thyroid dysfunction in late fetal and early postnatal life has severe adverse effects on the development and function of the acoustic organ, as evidenced from the deafness associated with congenital hypothyroidism. Along with the observation of the association of excess fluoride intake and derangements in thyroid hormone status in children with and without dental fluorosis, these factors are also associated with delayed eruption. This relationship is statistically highly significant in the understanding of the health problems of children living in endemic areas. Thyroid hormone deficiency and/or excess arising from fluoride toxicity leading to IDD such as, low IQ, deaf-mutism, and cretinism in children have been reported from elsewhere and need to be taken into consideration so that follow-up studies could be directed in a more meaningful manner. In study conducted by Susheela et al 2005 it was suggested that fluoride is often responsible for thyroid hormone alterations normally ascribed to IDD and delayed eruption of the teeth. Iodine supplementation for control of IDD is widely practiced in Delhi and in other parts of India as well as in certain other countries where fluorosis is endemic. The monitoring of consumption of iodized salt by school children in Delhi was carried out earlier, and the results showed an upward trend in the consumption of iodized salt at the household level from 76.7% in 1994–1995 to 96.4% in 1996 – 1997. A level of 15.0 ppm iodine was tested in the salt consumed and was considered satisfactory. The fluoride in excess may be inducing diseases normally attributed to iodine deficiency. Fluoride itself has been effectively used as an anti-thyroid drug. The history of fluoride/iodine antagonism has been documented by PFPC.

As it is already known that Fluoride is more electronegative than iodine, it easily displaces iodine within the body, thereby affects the functioning of thyroid gland. Fluoride has been known to have shown gross as well as biochemical changes within the body of an individual. Gross changes like lowered IQ levels, hearing impairment and developmental defects in the acoustic organ were seen .Biochemical changes included deranged thyroid hormonal level with in the body.[1]

Conclusion

Keeping in mind the above mentioned only drinking water fluoride is not responsible for elevate the serum fluoride level. It is also likely if someone eats or drinks food high in fluoride such as tea coffee, reconstituted fruit juice, grapes or raisins that have had fluoride insecticide (cryolite), dried eggs, and carbonated drinks. Facts, prevention and control of fluorosis require an integrated approach for diagnosis and patient management, contrary to prevailing practices.

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