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Review

Aluminum Intake and It's Toxic Effects on Health

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ABSTRACT

Aluminum though non-essential to humans, is one of the most common elements on earth; therefore, exposure to it is inevitable for humans. While aluminum is present in insoluble and biologically unavailable form, its ubiquitous use in food, drugs and cosmetics has created a number of pathogenic disorders. It has been implicated in diseases of brain, blood and bones. It accumulates in brain cells causing encephalopathy, dementia and Alzheimer's disease. Aluminum interferes with calbindin synthesis, a carrier protein for calcium, thus reducing normal calcium absorption. It also gets deposited on calcium deposition front and prevents normal calcification causing osteomalacia and osteodystrophy. It is also responsible for the microcytic anaemia as it interferes with iron absorption as well as with the synthesis of erythropoietin. Due to all these complications related with aluminum consumption, there is a need for concern over the ingestion of foods as well as drugs rich in aluminum.

Key Words: Aluminum intake; Toxic effects; Health

Aluminum is nonessential to humans, although it is one of the most common elements in our environment, comprising almost 8% of the earth's crust (Jones & Bennett, 1986). It is abundant in the environment but present in very small amounts in living organisms. Due to its abundance in nature, man has high exposure to aluminum.

Aluminum (Al^{+3}) has a small size and high charge. In nature it exists only in the oxidative state. It is a strong hydrolyzing metal, therefore, it is very reactive and hence found mostly in complex form. In aqueous solutions, it forms hydroxides. Aluminum hydroxides are soluble in more acidic and more alkaline pH, whereas they are insoluble at neutral pH. Due to its characteristics of its insolubility and inertness at neutral pH and despite its ubiquitous presence in nature, plants and animals have low concentrations of aluminum (Ganrot, 1986). Also because of its inertness, aluminum has been used in foods, chemicals and cosmetic industries. Aluminum has a strong affinity to phosphate – the characteristic that is widely used in pharmaceutucal industry (Ganrot, 1986). Drugs such as antacids, buffered aspirin, vaccines and anti-diarrhoeals contain a considerable amount of aluminum.

To foods, aluminum is added during processing, preparation and storage. It acts as an emulsifier in processed cheese, as a preservative in preserves and pickles, as an anti-caking agent in powdered soups, non-dairy creams, dried milk and baby foods etc. It is a component in baking powders and other leavening agents. Man also has exposure to aluminum by using cosmetics. It is added in hand lotions, creams and antiperspirants (Hem & White, 1989).

Aluminum toxicity

In chronic renal failure patients, the failing kidney cannot excrete sufficient phosphate that results in hyperphosphataemia. Phosphate retention brings a cascade of biochemical alterations in the body. It lowers serum calcium levels, and therefore, indirectly stimulates parathyroid hormone secretion causing hyperparathyroidism. Hyperparathyroidism in turn creates extraskeletal calcification in renal patients. To eliminate the adverse effects of phosphate retention, not only reduced dietary phosphate intake is recommended but phosphate absorption is also inhibited. Phosphate binding agents are given to the patients orally; also it is removed from the blood via haemodialysis (Grosso *et al.*, 1996). Aluminum hydroxide and aluminum carbonate have been effectively used as the primary phosphate binders. However, ingestion of large doses of phosphate binding agents containing aluminum for a long time has resulted in aluminum retention and thus toxicity (Alfrey *et al.*, 1976). Its toxicity has been manifested as dialysis encephalopathy or dialysis dementia, dialysis osteodystrophy and anemia (Hewitt *et al.*, 1990).

Dialysis encephalopathy and Alzheimer's disease. Aluminum has been implicated in dialysis encephalopathy or dialysis dementia – a condition resulting in accumulation of aluminum in the brain. It was initially recognized in renal patients, taking oral phosphate binding gels containing aluminum (Alfrey *et*

al., 1976). Aluminum in brain exerts a number of toxic actions, such as it complexes with adenosine triphosphate and is translocated from the cell plasma membrane to the nuclear deposit sites. Aluminum has been found to alter normal process of calcium binding to calmodulin, that increases free calcium ions in the brain (Siegal & Haug, 1982), that are also neurotoxic.

The relationship between aluminum and Alzheimer's disease is controversial. Epidemiological data coming from Guam and other areas where water and garden soil was high in aluminum and low in calcium and magnesium indicated the prevalence of Alzheimer's disease (Perl, 1985). Similar reports in Britain (Martyn *et al.*, 1989) also indicated the risk of developing Alzheimer's disease due to aluminum in drinking water. Whether Alzheimer's disease is related only to aluminum or there are other implicating factors present in those areas, is not known.

The distinction between dialysis encephalopathy and Alzheimer's disease is that in encephalopathy, aluminum appears to accumulate in the cytoplasm, while in Alzheimer's disease it concentrates in the nucleus of cells (McLachlan & Berkcum, 1986). In a healthy brain, there is an aluminum binding ligand in the cell cytoplasm that protects the brain against aluminum toxicity. However, in Alzheirmer's diseased brains, either this cytoplasmic ligand is lost or the blood-brain-barrier is rendered more permeable to aluminum. Therefore, aluminum passes into the nucleus via calcium channels where it penetrates into the DNA containing structures with the nucleus and interferes with normal nuclear functions (McLachlan & Berkcum, 1986).

Evidences suggest that people are relatively well adapted to detoxify low environmental or natural levels of aluminum exposure and hence prevent accumulation of this potentially toxic metal. Many elderly people may be using high levels of aluminum containing pharmaceuticals and are thus at risk for high levels of aluminum intake. In addition, changes in renal function with aging may compromise this important route of aluminum excretion from the body, thus resulting in high accumulation of aluminum in the brain.

Dialysis osteodystrophy or osteomalacia. Aluminum pathogenesis related to bone disorder in renal patients was reported for the first time by Parson *et al.* (1971). Dialysis osteomalacia is vitamin D resistant and is associated with hypercalcaemia (Boyce *et al.*, 1982). The mechanism for the osteomalacia bone disorder is not understood. There is a disturbance in the formation of calcium apetite crystals (Hewitt *et al.*, 1990). Aluminum and iron have been found at the calcification front (Bushinsky *et al.*, 1995). Aluminum initiates the precipitation of calcium-apetite by forming an insoluble aluminum-phosphate complex. In chronic renal patients, aluminum acts as a crystal poison by depositing at the interface between the osteoid and the calcified matrix, the place where bone-mineral deposition normally occurs, thus preventing bone mineralization (Hewitt *et al.*, 1990). Aluminum has also been found to interfere with calcium absorption by depressing the synthesis of calbindin both in chicks (Dunn *et al.*, 1993) and rat models (Zafar *et al.*, 1997).

Dialysis anaemia. Anaemia in renal patients occurs due to a number of factors including decreased synthesis of erythropoietin (necessary for haemoglobin synthesis). It is produced in the normal kidney and goes to the bone marrow for haemoglobin production. Anaemia in renal patients may also occur due to the process of haemodialysis *per se*, which does not involve aluminum. Aluminum, however, causes disturbance in the iron status possibly through displacement of iron from transferrin or erythropoietin synthesis impairment, which increases the risk of anaemia (Wills & Savory, 1983). Aluminum induced anaemia is microcytic and hypochromic, but it is not due to iron deficiency (Hewitt *et al.*, 1990).

Sources of aluminum

Aluminum is naturally present in trace amounts in water and most foods. However, depending on the geographical location, aluminum concentration of water varies from place to place. Due to adverse effects of acid rain in the modern era of industrialization, soil aluminum has become more soluble and therefore, has leached out in the water (Jones & Bennett, 1986).

Besides the natural occurrence in water, aluminum sulfate is added as a flocculent to drinking water for the purpose of purifying it (Nutrition Recommendations, 1990), resulting in aluminum residue in the water. Water aluminum concentration was found to be higher than 14 (g/L in 186 water utilities randomly selected in the United States (Miller *et al.*, 1984). The aluminum concentration of drinking water may vary from 0.001-1.6 mg/L depending on the geographical conditions and water purification methods (Lione, 1983). Some foods such as tea-leaves and coffee beans naturally accumulate more aluminum. Aluminum content of other foods varies depending on the amount present in the soil. Higher amounts of aluminum are present in plant foods (<0.1-2.0 mg/kg) and in some fish (0.7-4 mg/kg) (Sorenson *et al.*, 1974). Mackerel and tuna contain 1-178 mg/kg and shell fish, i.e. crab and cray, contain 35-

45 mg/kg (McLachlan & Berkcum, 1986). Meats and dairy products are comparatively low in aluminum content.

Processed foods in which aluminum is added as an additive are especially high in aluminum. Processed cheese contains 50 mg/serving. It is added to soup powders, non-dairy creamers and baby formulas as an anticaking agent @ 2% by weight (Lione, 1983). In infant formulae, it ranges from 351 (g/L to 124 mg/L (Hawkins *et al.,* 1994). In pickles and preserves as well as in baked products, aluminum concentration range from 5-15 mg per serving. Small amount of aluminum may be contributed from cooking utensils, especially through cooking of acidic foods in aluminum saucepans (Lione, 1983). These sources are insignificant, however, in comparison with the contribution from medications and drugs.

A number of non-prescription drugs such as antacids, antidiarrhoeals and buffered aspirin contain a considerable amount of aluminum. It is reported that a nonabusive use of antacids or aspirin may contribute 500 mg and 730 mg, respectively (Nutrition Recommendations, 1990). The aluminum from drugs ranges from 1-5 g daily (Lione, 1983).

Other sources of aluminum exposure include occupational exposure. Aluminum exposure from respiratory particles was reported as 1- 190 (g/m^3 in 279 workers from 15 plants throughout the United States. These workers were exposed to aluminum for 2-9 years (Gitelman, 1995). Most cosmetics, i.e. hand lotions and deodorants, all contain aluminum.

Aluminum toxicity levels

A large amount of evidence suggests that aluminum in large doses is potentially toxic. However, humans are relatively well adapted to detoxify low levels of aluminum. Total body aluminum content has been estimated as 30 mg in a healthy adult man (Alfrey *et al.,* 1980). Despite high exposure to aluminum, this low body burden suggests its low absorption and efficient excretion from the body under normal conditions of health. Several studies, both animals (Meirave *et al.,* 1991; Zafar *et al.,* 1997) and human (Day *et al.,* 1991) suggest only 1% absorption from a low physiological level of intake. On the other hand, its excretion from the body is also efficient (Meirave *et al.,* 1991; Priest *et al.,* 1995). However, high doses of aluminum result in increased blood level and high urinary excretion (Gitelman, 1995).

Intake of aluminum could be more, depending on food choices, cooking and food storage practices of individuals. Also an individual's vulnerability to low level aluminum accumulation over time is not known. Low intake of aluminum from drinking water and aluminum cooking utensils have been associated with dementia type disorders (Martyn *et al.,* 1989; Forbes *et al.,* 1995), and osteoporotic fractures (Cumming & Klineberg, 1994) in epidemiological studies. A recent study in France with 3777 subjects aged 65 and older showed a positive association between cognitive impairment and aluminum in the drinking water, especially when the pH and silicon concentration was low. The threshold for an aluminum effect was found as low as 3.5 (g/L (Jaegmingadda *et al.,* 1996).

In contrast to food and water, use of aluminum containing drugs contribute a significant amount of aluminum to the habitual users. Together with aging, the renal function of aluminum excretion in elderly people is impaired which results in higher aluminum retention in the body.

CONCLUSION

In the best interest of public health, it is recommended that intake of aluminum from food, water, drugs and cosmetics be reduced. Furthermore, it is suggested that a better substitute be found for the phosphate binder for dialysis patients.

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