

NEUROIMUNOTOXICITY OF ALUMINUM

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Abstract

Aluminium (Al), abundant in Earth's crust, but not found in biochemical systems of plants, animals and humans become increasingly widely used because of its properties. Al accumulates in the body in different ways from various sources such as food, cosmetics, water, vaccines, in the latter being used as an adjuvant. The scientific world brings more and more data about the negative effects on humans and animals, both to the nervous system and to the immune system. Neurotoxic and immunotoxic effects are correlated with genetic susceptibility, thus explaining their relatively low incidence.

Rezumat

Aluminiul, metal abundent în scoarța terestră, dar inexistent în sistemele biochimice ale plantelor, animalelor și oamenilor, a început să devină din ce în ce mai utilizat datorită calităților sale. Studiile efectuate aduc date tot mai multe despre efectele sale nedorite, atât la nivelul sistemului nervos, cât și al celui imunitar. Se acumulează în organism pe diferite căi, din sursele cele mai diverse precum alimente, cosmetice, apă, vaccinuri, în cea din urmă fiind utilizat ca adjuvant. Efectele neurotoxice și imunotoxice ale aluminiului sunt corelate cu susceptibilitatea genetică, astfel explicându-se incidența relativ mică a lor.

Keywords: aluminium, neurotoxicity, immunotoxicity, "ASIA" sy, vaccines

Introduction

Aluminium (Al), atomic number 13 in the Periodic Table of Elements, abundantly distributed in the Earth's crust, seems to play no role in any biological system: plants, animals or humans. So it is perceived as a foreign substance, or antigen, due to its lack of recognition, and as a toxin. Much like mercury, and unlike zinc, iron, copper, manganese, Al is neurotoxic.

Aluminium's chemical properties make it ideal for human using on a daily basis, becoming the second most used metal after steel. Al can be recycled cost effectively, increases the combustible efficiency, is a good conductor of electricity and resistant to corrosion, being used in constructions, transportation, packaging or in household products [1]. It is found in drinking water, cosmetics, antiperspirants, drugs and vaccines. Foods can contain Al as plants and animals bioaccumulate it from their surrounding environment. The absorption of metals by gastrointestinal tract is influenced by various factors like: individual differences, age, pH, stomach content. Some substances increase Al absorption (acidic beverages, phosphates, food acids, carbohydrates). Gastrointestinal Al absorption may be also

increased by deficiency in copper, calcium, magnesium or zinc. It has been reported that silicon might have a protective effect for limiting oral aluminium absorption [2].

Food containing Al toxicity was emphasised one hundred years ago by PhD. William Gies, professor of biological chemistry. Nowadays we have many signals from the scientific world about Al toxicity and a spectrum of neurological diseases like Alzheimer Disease, Amyotrophic Lateral Sclerosis (ALS) and Autism Spectrum Disorders [3, 4, 5].

In 2011 a new syndrome termed "ASIA" Autoimmune/Inflammatory Syndrome Induced by Adjuvants' was defined [17, 18]. It includes some immune-mediated diseases triggered by adjuvants stimulus like aluminum, silicone, mercury, or infectious components. ASIA includes many clinical conditions: siliconosis, Gulf War Syndrome (GWS), Macrophage Myofasciitis Syndrome, Sick Building Syndrome and post-vaccination phenomena. All of this share similar signs or symptoms.

The neurotoxicity of Aluminium

The neurotoxicity of Al depends on the route of administration, the concentration and duration of

exposure, gender and genetic susceptibility. There are a lot of neurotoxic effects exercised by Al, described by Shaw and Tomljenovic [19]: disruption of synaptic activity, disruption of neuronal energy metabolism and brain metal homeostasis, increased permeability of the blood-brain barrier, enhanced amyloidosis, neurofibrillary abnormalities, potentiation of oxidative stress and peroxidation of brain membrane lipids, alterations in chromatin structure and impairment of transcription, upregulation of stress-related pro-inflammatory and pro-apoptotic pathways [6].

Many biochemical changes found in Alzheimer disease (AD) were obtained in animal models of Al toxicity: neurofibrillary degeneration, cholinergic loss, oxidative stress and behavioural alterations [4, 7, 8].

Acute Al neurotoxicity occurs when more than 500 µg/L enters the blood flow, resulting an encephalopathy with *grand mal* seizures, coma and death within days. Intermediate Al levels in blood cause subacute Al neurotoxicity like in dialysis encephalopathy syndrome, in patients with chronic renal failure, due to dialysate composition. The use of Al-based cements in otoneurological surgery has also been implicated in a clinical syndrome indistinguishable from that seen in dialysis encephalopathy [1]. The chronic Al exposure is due by food, cosmetics, vaccines, etc. Long term accumulation of Al in the body might be responsible for AD [9].

Postmortem studies in humans have found elevated Al in the brain and spinal cord of people with ALS. In Guam Island approximately one out of ten people developed ALS with Dementia and Parkinsonism. The causes are toxins of the cycad palm from this island, and abnormally high Al doses in the soil and water. So, we could suppose a potential connection between aluminium and ALS [6, 10].

Gulf War Syndrom is included in the “autoimmune syndrome induced by adjuvants” or ASIA. Loss of strength, weakness, dizziness, imbalance, slurred speech and tremors are commune symptoms with ALS, which might be part of GWS. An explanation for this could be the exposure to: vaccines, bacterial infections, uranium, heavy metals [6].

Systematic researches are directed to assess the neurotoxic effects of Al. Studies on animal models have shown that L-theanine, found in green tea (*Camellia sinensis* L.) and mushroom cultivar extract (*Agaricus bisporous*) are potent antioxidant agents and protect against Al-mediated neurotoxicity [11, 12, 13].

Immunotoxicity of Aluminum

The mechanism of Al immunotoxicity is unclear, but there are studies showing its effects on the

splenic elements, the status of α -naphthyl acetate esterase cells, cytokines, complement, immunoglobulins or macrophages [14].

Due to its strong effects on immune system stimulation, Al as an adjuvant, become a leader for the vaccines market. Nano-crystalline particles composed of Al hydroxide were introduced in vaccines production in 1927. After injection, Al is taken up by monocytes, passes through the draining lymph nodes, then crosses the Blood Brain Barrier and may accumulate in the brain. Here, it can induce some immune-inflammatory undesirable reactions. The principal immunostimulatory pathway for Al as adjuvant is NOD-like receptor family pyrin domain containing 3 (NLPR3). But the same pathway is involved in the occurrence of autoimmune and inflammatory diseases like atherosclerosis, diabetes, demyelinating diseases, colitis [15, 16].

According to Food and Drug Administration (FDA), in the Office of Vaccines, an adjuvant is defined as “an agent that is added to or used in conjunction with a vaccine antigen to augment and potentiate and possibly target the specific immune response to an antigen”. Al adjuvants disturb autoimmune or inflammatory reactions causing the ASIA syndrome described by Shoenfeld and Agmon-Levin [17]. This new concept is supported by animal models experiments for rheumatoid arthritis, myocarditis, systemic lupus erythematosus, autoimmune thyroid, antiphospholipid syndrome [18]. Children up to 6 years old received a huge amount of antigens (90 viral/bacterial antigens, 36 attenuated viruses) in the vaccination schedules from USA. The amount of Al from a single dose of vaccine against hepatitis is 17–30 times greater than the dose approved by the FDA (5 µg Al/kg/day). Experimental evidence also shows that simultaneous administration of two or three antigens can get over genetic resistance to autoimmunity [19]. There is a significant correlation between Al dose and autism spectrum disorder satisfying 8 or 9 Bradford Hill's criteria for causation [20].

Vaccines have not included toxicity studies because have not been viewed as toxic. So nothing is known about the toxicology and pharmacokinetics of Al adjuvants in children. A single hepatitis B vaccine injected to primates within the first 24 h of birth cause neurodevelopmental delays. During the perinatal period, the brain is very vulnerable to neurotoxic injuries. The blood-brain barrier has an incomplete development, being more permeable to toxic substances. This fact is aggravated by developing renal system, ineffective to eliminate the toxic compound [15, 21, 22].

Before six months of age the immune response is weak and short. So, in order to develop an adequate

B-cell immune response, repeatedly strong Al adjuvants are necessary. Vaccines decrease the risk of natural infections in early childhood, but stimulation induced by vaccinations may have greater magnitude than that resulting from natural infections.

Conclusions

In this article, we have summarized the characteristics associated with neurotoxicity and immunotoxicity of Al. There is growing evidence between Al and AD, ALS or ASD as well as Al involvement in ASIA syndrome. Therefore, Al can cause severe health problems in particular populations, including infants, elderly people and patients with impaired renal functions. It is not judicious to assume that the current paediatric vaccination schedules are risk free in the absence of experimental evidence. Scientific efforts should include clarification of the cellular and molecular mechanisms of Al toxicity.

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