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Mini Review

Pathological Impacts of Lead Toxicity

Ahed J Alkhatib[1,2,3]*

[1]*Department of Legal Medicine, Toxicology and Forensic Medicine, Jordan University of Science & Technology, Jordan*

[2]*International Mariinskaya Academy, department of medicine and critical care, department of philosophy, Academician secretary of department of Sociology, Russia*

[3]*Cypress International Institute University, Texas, USA*

***Corresponding author:** Ahed J Alkhatib, Department of Legal Medicine, Toxicology and Forensic Medicine, Jordan University of Science & Technology, Jordan

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Abstract

Lead is widely existing in nature and in wide industrial use. There is no known biological role of lead, and any amount of lead is considered as toxic. Lead can disrupt the physiological pathways in nervous system as a predisposing agent for developing Alzheimer disease and possibly others. It also impacts renal system and participates in disruption of kidney function that may end with renal failure. The control of lead exposure may be a difficult task due to its industrial and environmental existence. Taken together, lead is considered a modern bio-toxin and its monitor among subjects should be seriously taken into consideration.

Keywords: Lead; exposure; toxicity; alzheimer disease; renal function

Introduction

Lead is a common and long-lasting environmental toxin that is extensively utilized in several sectors [1]. Lead is utilized in numerous industries due to its chemical properties, making it the sixth most commonly employed metal globally [2,3]. The primary sources of lead-related dangers encompass the battery sector, vocations associated with radiators, ceramics, plumbing, the paint industry, cable production, as well as exposure to polluted soil, contaminated food, and, in certain regions of the world, opium addiction. Lead can infiltrate the body and induce poisoning through contact, ingestion, or inhalation from any of these sources [4,5]. Epidemiological findings indicate that environmental exposures during perinatal and infant stages contribute to the genesis of various chronic non-communicable diseases, alongside genetic and lifestyle variables [6]. The "Developmental Origins of Adult Disease" (DOAD) concept suggests that gene reprogramming during development contributes to adult disease by triggering latent expression of certain genes [7,8].

Although no epidemiological evidence has been published to link early life Pb exposure to Alzheimer Disease (AD), several longitudinal and cross-sectional studies in the elderly have found a link between Pb exposure and cognitive decline in humans. Mild cognitive impairment may precede AD. Recent research shows that Pb-exposed rats perform badly on cognitive tests as adults [9]. Late Onset Alzheimer Disease (LOAD) accounts for 90% of AD cases. Evidence suggests that amyloidosis and tau damage in AD brains are sporadic. It was previously found that infantile lead (Pb) exposure could alter APP and Ab expression and regulation in old age. It has been found that infantile Pb exposure increased tau mRNA, protein, and its transcriptional regulators, Sp1 and Sp3, in old primates. Furthermore, site-specific tau phosphorylation and cyclin dependent kinase 5 (cdk5) mRNA and protein levels increased alongside these modifications. In old primates exposed to Pb as newborns, the protein ratio of p35/p25 changed with greater Serine/Threonine phosphatase activity. In older primates with prior Pb exposure, these molecular changes favoured extensive tau

phosphorylation and staining in the frontal cortex. These findings support the idea that environmental factors may cause neurological illnesses throughout development [10].

Pb is A Potent Environmental Toxin that Harms Humans

Many countries consider Pb poisoning a public health issue due to its widespread use and the number of persons potentially exposed to it. Pb can be ingested, inhaled, dermally, or transplacentally. The severity of its effects depends on lead speciation, dosages, period, and age of exposure. The consequences of Pb exposure are greatest in early life. Pb poisoning affects the central nervous system, causing cognitive impairment, executive function changes, inappropriate social behavior, and fine motor control problems. This review summarizes the cognitive effects of Pb exposure throughout early life and maturity. Additionally, it covers the neurotoxic pathways of Pb-induced cognitive impairment, including neurochemical, molecular, and morphological alterations that may synergistically affect cognitive performance [11]. Lead (Pb) is a toxic heavy metal found in various sources, such as drinking water, batteries, gasoline, paint, food cans, folk remedies, water pipes, ceramics, cosmetics, jewellery, cigarette smoke, vinyl lunch boxes, toys, and candy [12]. Pb is a global public health issue due to its environmental persistence, transportability, and various sources.

Human Pb poisoning is common in India, Indonesia, the Philippines, Nigeria, China, Pakistan, Brazil, Mexico, Peru, France, and the US [13,14]. Oral Pb intake is the primary route, with 5-15% absorbed by the gastrointestinal tract and the rest eliminated in stool. Ciliary respiratory epithelial cells consume some Pb particles into the gastrointestinal system after inhalation. The body contains diffusible (mobile) and non-diffusible (fixed) Pb [15]. Mobile Pb is biologically active and can be moved around the body, while fixed Pb accumulates in soft tissues and bones [16]. The liver excretes Pb through bile secretion and the kidneys through glomerular filtration and transtubular flow [17]. The bloodstream half-life of Pb is 35 days, but it can be dispersed to soft tissues and stored in bones for 30 years [18]. Highly permeable Pb can pass the placental and Blood–Brain Barrier (BBB) and is found in breast milk. Long-term effects of Pb poisoning have been studied, and the hazardous threshold has decreased from 60 µg/dL in the 1960s to 10 µg/dL in 1991. Although the CDC recommends a blood Pb reference value of ≥5 µg/dL, there are no safe levels of Pb as even low levels can be harmful [19].

Pathological Impacts Lead Exposure on Alzheimer Disease

As mentioned above, the pathology of AD involves the increased expression of tau protein in old primates. As shown in Figure 1A&1B.

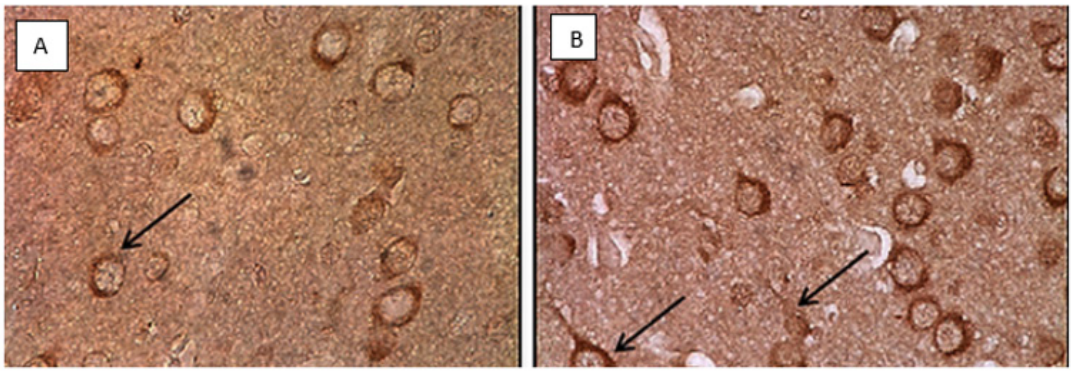

Figure 1: Increased expression of tau protein in old primates, cortex of 23-year-old Cynomolgus monkeys following developmental exposure to Pb [10].

Impacts of Lead (pb) Exposure on Kidneys

Multiple studies have acknowledged and verified a correlation between lead exposure and kidney disorders in the human population [20,21]. Both elemental lead and inorganic lead compounds can be absorbed through food or inhalation, whereas organic lead compounds, such as tetraethyl lead, can also be absorbed through skin contact. Organic lead compounds have the highest level of toxicity [22]. The efficiency of lead absorption from the lungs is notably high, particularly when the particles have a diameter of less than 1 µm. The extent of lead absorption in the gastrointestinal tract is influenced by the age of the individual. In the case of children, around 50% of the ingested lead is absorbed, but adults exhibit a lower absorption rate of just 10-20% of the ingested lead. Chemically, lead exhibits significant similarities to calcium. Consequently, once entering the body, it is processed in a manner akin to that of calcium. Lead does not have any beneficial function in the human body and its presence within the body might result in hazardous effects, irrespective of the route of exposure.

conducted a study in the light of considerations such as that exposure to lead bears the neurotoxicity that may cause AD. The authors aimed to investigate the localization of Pb in the brain through the use of synchrotron micro-x-ray fluorescence technique (µ-XRF). The methodology involved giving mice lead acetate orally at daily basis for 4 weeks, while the mice in control group were

given sodium acetate. The authors found that lead was mainly found in the cortex and hippocampus/corpus callosum regions in the Pb-exposed samples [23]. Lead toxicity has negative impacts on various systems renal [24], cardiovascular [25], and respiratory [26]. In a previous study, [27] using X-ray fluorescence showed that high levels of Pb present in beta amyloid plaques reflecting the impacts on AD.

Conclusion

This review showed that lead toxicity has pathological impacts on various systems in our bodies. These impacts vary according to exposure modes and length. Lead is widely used in industry and widely spread in nature, which in turn, limits its control. Lead toxicity impacts nervous system, renal systems, and others. Monitoring of leads should be seriously taken into account.

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