Lead toxicity

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Abstract. Lead is a heavy metal. It is frequently used in life as a result of its distinct physical and chemical features. It is, nonetheless, a hazardous and widespread heavy metal. Lead is not only a common occupational and environmental toxin, but it also has a significant effect on children's brain development. Additionally, despite the fact that studies on the biochemical and molecular mechanisms underlying lead's harmful effects are still lacking, some research suggests that there may be indirect mechanisms at play. By examining lead's effects on various human body parts and therapeutic strategies for lead poisoning, this essay highlights the pathogenic factors and responses of lead on human tissues. As a result of lead's ability to quickly cross the blood-brain barrier and the growing brain's immature endothelial cells, the data demonstrate that lead is particularly detrimental to the central nervous system. The creation of synaptic connections and neuronal migration are significantly influenced by the normal growth of glial cells. Glial cells may prematurely differentiate as a result of lead exposure, impairing their ability to communicate with neurons. Lead appears to have genotoxic effects not just directly but also indirectly through free radical generation or DNA repair inhibition. The current study provides useful information for future toxicological research on lead poisoning.

Keywords: Lead, chemical properties, lead poison.

1. Introduction

Because of its distinct physical and chemical qualities, lead is a heavy metal that is frequently employed in life. However, lead is also a heavy metal that is widely known to be hazardous. Lead is a common occupational and environmental pollutant that is dispersed all over the world due to its strong persistence in the environment and use in several industrial activities from ancient times. Batteries, cables, bullets, and ammunition are all made with lead, which is also utilized as a raw material and an additive in gasoline. Raw ingredients for pigments, glass, plastics, and rubber include lead compounds. Meanwhile, metallic lead is frequently employed in the production of chemical and metallurgical equipment due to its strong resistance to acid and alkali corrosion. Lead alloys are used for solder, moveable gold, bearings, and other things. Lead has also made a number of new uses possible. For instance, it is employed in the production of high-power battery packs for load balancing in the power industry, stabilizers for asphalt to increase the service life of road surfaces, shields and nuclear waste storage tanks for nuclear power plants, magneto-hydrodynamic devices, etc.

One of the main heavy metal contaminants that poses a substantial threat to human health is lead. Lead enters a person's system mostly through food and tap water use. After entering the body, 90% of the lead is stored in the bones, and the remaining 10% is randomly distributed to all body tissues and organs with blood circulation, affecting red blood cells and the brain, nervous system, and kidney functions. In particular, for infants and young children, more than 30% of the lead absorbed will remain in the body and harm growth and intellectual development. Lead and its inorganic compounds are both categorized by the International Agency for Research on Cancer as likely Group 2B and 2A human carcinogens, respectively. Although lead and its compounds have been studied for their harmful effects on a global scale for many years, the available evidence on their mutagenicity, teratogenicity, and carcinogenicity are still inconclusive.

Lead has been shown to be clearly carcinogenic in animal studies. Rats and mice that are exposed to lead are more likely to develop kidney cancers, particularly renal cortical tubular epithelial carcinoma. Lead and brain tumors are also closely related to one another. In 1987, the World Health Organization's (WHO) International Agency for Research on Cancer (IARC) identified lead as a

substance that may cause cancer in humans. The following factors have been the focus of recent research on the mechanisms of lead-induced tumorigenesis: inhibition of DNA synthesis and repair, disruption of intercellular junctional communication, DNA oxidative damage, alteration of gene expression, and post-transcriptional alteration of the oncogene P53.

The only way to avoid lead poisoning is to avoid it altogether, as there is no especially effective cure for it. However, chelation therapy can still be used to reduce excessive lead levels in the body if a lead contamination event like an industrial accident happens. The word "chelation treatment" refers to a method that people utilize to remove heavy metals from their bodies. Ethylenediaminetetraacetic acid is commonly used as a chelating agent to treat lead poisoning because it securely binds lead elements in the body and allows for their excretion through the kidneys. Although this method appears to be extremely miraculous and efficient, it is often only employed in the most severe situations.

2. Possible impact of lead poison

2.1. General information

Lead's impact on proteins, where it binds to sulfhydryl groups, is thought to be the primary cause of its toxicity. People who are exposed to lead for extended periods of time may exhibit a number of lead poisoning symptoms. In numerous investigations, the effects of lead poisoning have been identified, with symptoms including those related to the cardiovascular system, the immunological system, the skeleton, the reproductive system, the kidneys, and the nervous system. There are now 23 proteins known to play a role in lead poisoning. The neuromuscular syndrome, which includes paralysis of peripheral motor neurons, and anemia brought on by the inhibition of aminolaevulinic acid synthase (ALAS) are the major symptoms of chronic lead poisoning. Aminolaevulinic acid synthase (ALAS), aminolaevulinic acid dehydratase (ALAD), mitochondrial sulfhydrylases, and iron chelatase inhibition all have an impact on the heme biosynthesis process. Renal injury, infertility in both sexes, improper neurological development and function, and abnormal neurological development and function may result from disruption to the heme biosynthesis system. impacted the biosynthesis of heme. The Centers for Disease Control and Prevention presently deems 10 μg/dl of lead to be the maximum acceptable blood level for children. Human neurobehavioral development is harmed when blood lead levels approach 15 μg /dl, and this is probably true even at levels lower than 15 μg/dl

2.2. Effect on the Brain

Many international scholars have experimentally verified that lead poisoning can harm the IQ of children. According to research by Bellinger et al on 74 children at 4-14 years old, IQ is inversely proportional to the amount of lead in the blood, and for every 100μg/L increase in blood lead level, the IQ of a child decreases by about 6 points. Excessive lead levels may even have long-term effects on children's intellectual development, as studies have shown that children's math and reading skills are already affected when lead levels are between 20-50 μg/L [1]. Not only IQ, but also neurological development can be affected, and is particularly toxic to young children, causing potentially permanent neurological and cognitive impairment. To investigate the relationship between lead poisoning and children's intellectual and neurobehavioral abilities, the experimenter randomly selected 100 children from 10 kindergartens with an average age of 2.8 years. After excluding some children born with delivery problems, neonatal problems and acquired disabilities, 96 children were selected to participate in the experiment. In order to prevent lead poisoning from adversely affecting the behavioral and intellectual development of these children, effective preventive measures were prescribed. The results of the examination showed that of the 50 children in the lead poisoning group, 34 had aggressive behavior, 17 had depression, 11 had social withdrawal, 8 had sleep problems, 7 had disruptive behavior, and 6 had atypical body movements, for a behavior abnormality rate of 27.7% [2]. The incidence of depression and aggressive and abnormal behaviors was much higher in the lead poisoning group than in the control group. With the rapid development of industrialization, lead is

commonly found in people's bodies and the level of lead in the bad environment is rapidly increasing. Since children's body functions have not yet reached a fully developed level, it makes them more sensitive to lead poisoning. Especially since their brain barrier is not fully developed, lead can easily penetrate children's brains and cause harm to them. Lead poisoning can cause ongoing damage to children, with the nervous system being the most sensitive to lead poisoning. Studies have shown that the brain barrier of newborn rats has a high lead penetration rate, and the younger the age, the higher the penetration rate. In the same environment, the penetration rate of 16-day-old rats was 2.42 times higher than that of adult rats.

2.3. Potential effect on DNA

Several endpoints have been employed in numerous studies to evaluate the genotoxic effects of lead in various biological systems. The analysis of DNA lesions is the most noteworthy. The effects of lead and other heavy metals on human chromosomes were the subject of tests and research by scientist Gebhart in 1984 [3]. He arrived at this conclusion after studying the mitotic chromosomes in microscopic cultures of peripheral blood cells and noting that smoking also had the same effects as the heavy metals. There was no hard evidence that heavy metals in any way damaged chromosomes. Scientist Chen discovered in 1992 that the frequency of chromosomal aberrations and sister chromatid exchanges dramatically increased with increasing urinary lead concentrations by examining the lead levels in the urine of 84 lead-exposed printers and the frequency of chromosomal aberrations and sister chromatid exchanges in lymphocytes. [4]. Human leukocytes were exposed to lead acetate for 24 hours, and 72 hours later, cultures showed a marked rise in the incidence of non-chromosomal lesions, chromosome breaks, and heterochromosome breaks. The most frequent aberration brought on by lead acetate in human cell cultures was found to be chromosomal fragmentation.

There is a great deal of debate on the effects and capacity of lead exposure to damage individual chromosomes because the majority of the results obtained in CA testing are sampled from employees who have been exposed to lead occupationally. After controlling for potential confounding variables like smoking behavior and exposure to other toxic substances, Maki-Paakkanen et al. examined the frequency of CA in peripheral blood lymphocytes of workers exposed to lead in smelters and discovered no significant difference between them and the unexposed control group [5]. Therefore, lead exposure cannot be completely blamed for the change in CA frequency. However, when viewed under a microscope, the total aberration rate in the 72-hour cultures was consistently higher than in the 52-hour cultures. The abnormalities seen in cultures from lead-exposed individuals may be cultured, and they may be caused by decreased repair function in the presence of lead or by the accumulating levels of other lead-induced metabolites.

In the majority of investigations, researchers found that lead-exposed people had a higher frequency of SCE [6]. However, in certain studies, the rise in SCE frequency was more pronounced in the control groups who did not smoke, not the lead-exposed individuals. This finding would suggest that smoke increases lead toxicity. No notable alterations were observed in two investigations that examined the frequency of SCE in children residing in polluted areas [7].

2.4. Carcinogen

It is well known that lead is harmful to the neurological system, and both animal models and people have provided strong, reliable proof of this. However, lead is comparable to other carcinogenic metals in that it is mostly unknown how it causes cancer. Recent research has demonstrated that lead doses below those that cause cellular damage in target organs can enhance cancer, but this is also incompatible with the existence of some organs. Lead-induced proliferative mitosis does not facilitate carcinogenesis in starting hepatocytes, and no studies have directly linked lead exposure to liver cancer. Lead compounds cause cancers in people and animal models at low doses, although there is no genotoxicity. These arguments make the theory that led promotes carcinogenesis more and more appealing.

The multi-stage process of carcinogenesis involves both genetic and non-genetic material being altered. Lead can have additional carcinogenic effects through non-genetic routes in addition to its direct and combined deleterious effects on genetic material [8]. The primary causes are: (i) Lead may jeopardize genome function due to its impact on nuclear proteins. (ii) The carcinogen benzo(a)pyrene's potential to cause lung tumors can be greatly increased by the effects of lead, and the incidence of kidney tumors can be 100% increased. Lead can encourage cell division and induce an approximately 45-fold increase in the cell division index value. (iv)Lead can impair the body's immune surveillance system and subtly enhance its susceptibility to cancer from lead or other toxins. (v) Lead may have an impact on the toxic metabolic system, which could help carcinogens work more effectively.

2.5. Treatment

The imbalance of oxidants and antioxidant systems, which causes oxidative stress, is a potential molecular cause of lead poisoning. Lead induces OS in two different ways: first, by producing reactive oxygen species (ROS), and second, by depleting antioxidant defenses. Chelating drugs including 2,3-dimercaptopropanol, meso 2,3-dimercaptosuccinic acid (DMSA), and calcium disodium ethylenediamine tetraacetic acid are mostly used to treat lead poisonings (EDTA). Grapes, berries, and other fruits contain significant levels of gallic acid, a naturally occurring hydrolysis product. Gallic acid can be utilized as an adjuvant in the treatment of lead exposure because of its ability to prevent motor and oxidative damage brought on by lead poisoning. Due to its ability to stop lipid peroxidation, GA is frequently employed as an antioxidant. In earlier research, GA had positive results in the management of lead-induced damage. It has been discovered from GA treatment that it significantly reduces lead-induced oxidative damage and can improve the brain's capacity to eliminate lead [9]. This discovery could lessen the incidence and effects of OS while also enhancing treatments for lead exposure. To prove the impact of GA and chelators on lead poisoning, more research is required [10].

3. Conclusions

The toxicology of lead poisoning in humans is the main topic of this article, which also examines its pathogenesis and subsequent therapy. Because the endothelial cells of the developing brain are not fully developed and lead easily passes the blood-brain barrier, lead damage to the central nervous system is devastating. Early in brain development, neuronal precursor cells multiply, divide, and differentiate into neurons in huge numbers. At this stage, lead can have toxic consequences and prevent neurons from proliferating and differentiating. Lead can cause early differentiation of glial cells and abnormal interactions between glial cells and neurons. The blood-brain barrier, which is created by the tight connections of endothelial cells and maintained by the interaction of astrocytes and endothelial cells, can also be impacted by lead.

Numerous studies have been done on the toxicity of lead, however there are still many inconsistencies on its compounds' mutagenicity, teratogenicity, and carcinogenicity. Due to conclusive scientific evidence that led causes cancer in animals, the World Health Organization classed it as a potential carcinogen; however, there are still numerous unanswered questions regarding its effects on humans. The disparities across research may be the result of several experimental factors. In addition to the fact that led exerts its genotoxic effects by inhibiting DNA repair or free radical production as well as other factors that may change the cellular response to lead, examples include smoking habits, exposure time, route, and other factors. Lead also exerts its genotoxic effects indirectly by inhibiting DNA repair or free radical production. There is strong evidence linking lead exposure to a hereditary risk, although the science on lead's genotoxicity is still inconclusive.

The government has implemented certain measures to decrease public exposure to lead in various countries due to the extensive use of lead and sources of environmental contamination, but lead pollution is still at extremely high levels. Lead poisoning must be treated with a novel medication.

GA has fewer negative effects than EDTA, which is a chelating chemical frequently used to treat lead poisoning. GA has a substantial protective impact in treating lead-induced oxidative damage due to its high antioxidant capability, which may improve its ability to remove lead from the brain. These discoveries are primarily intended to lessen OS and its motor repercussions as well as to enhance the therapy strategy employed in lead exposure. GA might be used as an addition to traditional therapies for lead poisoning. The effectiveness of GA and chelators in the treatment of lead poisoning requires further research. There is an increased drive for lead control on a global scale, but it is unclear if these so-called limits would actually protect people's safety and health. As a result, lead and other heavy metals in the environment require more attention.

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