2022, Scienceline Publication
World's Veterinary Journal
World Vet J, 12(3): 311-315, September 25, 2022
ISSN 2322-4568
DOI: https://dx.doi.org/10.54203/scil.2022.wvj39

Effect of the Sublethal Dose of Lead Acetate on Malondialdehyde, Dopamine, and Neuroglobin Concentrations in Rats

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ORIGINAL ARTICLE
pii: S232245682200039-12
Received: 27 July 2022
Accepted: 11 September 2022

ABSTRACT

Lead can have detrimental behavioral, biochemical, and physiological effects on the body. The current experiment was designed to estimate the sublethal dose of lead acetate that induce oxidative stress on the central nervous system (CNS) in adult using the probit analysis. Moreover, the current study examined the dose-response curve by successive doses of lead acetate on some parameters related to oxidative stress for 28 days. A total of 36 adult male rats were randomly selected and divided equally into six experimental groups and treated for 28 days. Rats in the control group received distilled sterile water, and those in G1, G2, G3, G4, and G5 were gavaged with 4, 8, 16, 32, and 64 mg/kg of lead acetate, respectively. The result indicated a positive correlation between the successive doses of lead acetate. Malondialdehyde concentration decreased dopamine and neuroglobin by increasing the dose of lead acetate in experimental groups (G3, G4, and G5), compared to the control group. In conclusion, exposure to the sublethal dose of 16 mg/kg of lead acetate significantly alters the levels of the neurotransmitters and increases the production of oxidative stress in the CNS tissue.

Keywords: Central nervous system, Dopamine and Neuroglobin, Lead acetate, Malondialdehyde, Rat

INTRODUCTION

Lead poisoning is a recognized significant concern to the public's health, particularly in developing nations. Softness, high malleability, ductility, low melting point, and corrosion resistance qualities of lead have make it useful in different fields, including the automotive, paint, ceramic, and plastic sectors. Lead may be found in the water, paints, soil, and brass plumbing fittings (La-Llave-León et al., 2016). Tetraethyl lead and lead acetate are two inorganic and organic forms of the metal lead, respectively, that can be found in nature (Shalan et al., 2005; ATSDR, 2017). Increased production of reactive oxygen species (ROS), which interfere with the antioxidant formation, is the main cause of lead poisoning. Lead produces ROS such as singlet oxygen, hydrogen peroxide, and hydroperoxide (Klimkowicz-Pawlas et al., 2017).

Lead is a pervasive environmental neurotoxin that has harmful effects on the host's behavior and neurochemistry and causes neuronal abnormalities even in trace amounts of exposure. The developing central nervous system (CNS) is vulnerable to Pb neurotoxicity, and any Pb exposure throughout CNS development can have long-lasting negative effects on the CNS's pathway of development as well as neuronal signaling and plasticity, leading to modifications in cognitive and behavioral characteristics that last well into adulthood. The Pb-induced neural signaling disturbance has been linked to a number of molecular processes, including increased oxidative stress, changes in the biochemistry of neurotransmitters, and mitochondrial dysfunction. However, these Pb-mediated changes in synapse growth and function are still poorly understood (Ahmad et al., 2018; Imosemi et al., 2020). The nervous system seems to be the most vulnerable and prime target for Pb-induced poisoning when compared to other organ systems, as it can result in death or lasting CNS damage at higher doses (Imosemi et al., 2020).

Oxidative stress is reportedly one of the mechanisms generating the CNS neurotoxicity caused by Pb exposure (Salim, 2017; Imosemi et al., 2020). Several studies have shown increased lipid peroxidation, reduced glutathione, and superoxide dismutase (SOD) activity in the CNS homogenates of Pb-treated rats (El-Masry et al., 2011; Fu and Xi, 2020). The hippocampus plays a crucial role in animal memory, learning, and spatial cognition (Alexandrov et al., 2013; Wani and Usmani., 2015). The cerebellum also controls muscle tone, saccadic and smooth eye movements, balance, and motor coordination (Pal et al., 2015; Wolf and Lappe, 2021). The architecture, shape, and function of the afflicted portions will be impacted by the Pb poisoning of the affected brain elements. High production of reactive oxygen species (ROS) and disruption of antioxidant production are the main causes of Pb poisoning. In the body, glutathione controls

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ROS. Lead also has an impact on other antioxidant enzymes, including catalase and superoxide dismutase (Navabpour et al., 2021). Lipid peroxidation caused by an increase in oxidative stress damage cell membranes (Al-Okaily and Al-Shammari, 2017; Klimkowicz-Pawlas et al., 2017). Therefore, the current study was designed to evaluate the sublethal dose of Pb acetate that induced oxidative stress in CNS by measuring some criteria related to CNS.

MATERIALS AND METHODS

Study

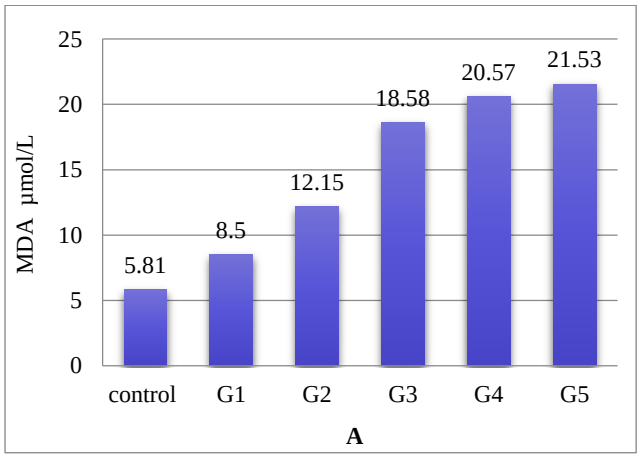
A total of 42 adult male rats weighing between 190 and 220 grams were used in the current study. Animals were housed at 22-25 °C with a 12-hour light/dark cycle. Throughout the testing period, animals had unrestricted access to water and pellets. After acclimatization for 15 days, rats were randomly selected and divided equally into six experimental groups and treated for 28 days. Rats in the control group received sterile distilled water. Those in the experimental groups G1, G2, G3, G4, and G5 received 4, 8, 16, 32, and 64 mg/kg/ orally/ day of lead acetate for 28 days, which is equal to 1/1120,1/560,1/280, 1/140, 1/70 from LD50 of Pb acetate respectively (Ibrahim et al., 2011). Blood samples were taken after the therapy, and the following factors were measured at 28 days of the experiment. Malondialdehyde (MDA) concentration (µmol/l) was determined by a modified procedure as described by Guidet and Shah (1989), and the neuroglobin and dopamine concentrations (pg/mL) were measured using the commercially available ELISA Kit (CEA851Ge, Cloud-Clone Corp Com, USA) according to the manufacturer's instructions.

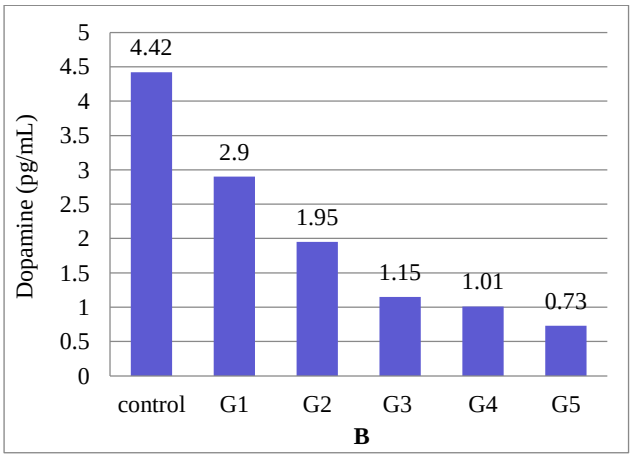
Statistical analysis

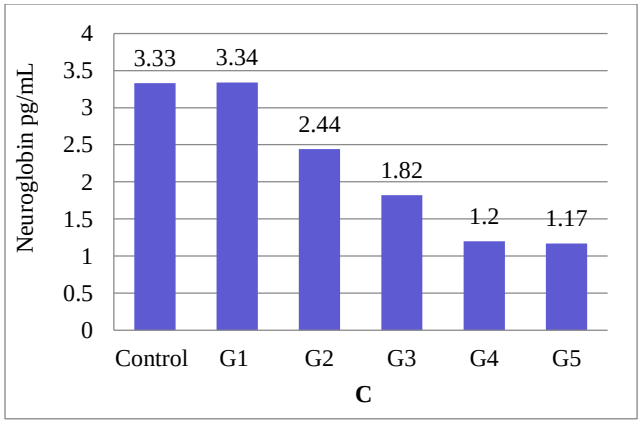
The collected data were analyzed in SPSS (Version 22) by using One-Way Analysis of Variance (ANOVA), LSD test was selected to find the significant level between the different data at the level of $p < 0.05$ (Snedecor and Cochran 1980).

RESULTS AND DISCUSSION

As can be seen in Graph 1, there was a significant ($p<0.05$) elevation in MDA concentration (Graph 1-A) and a significant ($p<0.05$) decline in dopamine (Graph 1-B) and neuroglobin (Graph 1-C) concentration in relation to repeated Pb acetate doses as compared to the control group. Additionally, there was a non-significant ($p>0.05$) difference between the G4 and G5 groups in terms of neuroglobin and MDA concentration (Graph 1-A and Graph 1-C). Additionally, the control, G1, and G2 groups did not differ significantly regarding blood dopamine levels (Graph 1-B, $p>0.05$).







Graph 1. Comparison of administering different doses of lead acetate on serum MDA (**A**), dopamine (**B**), and Neuroglobin concentrations (**C**) after 28 days in male rats (n = 6). Values are expressed as mean ± standard error.

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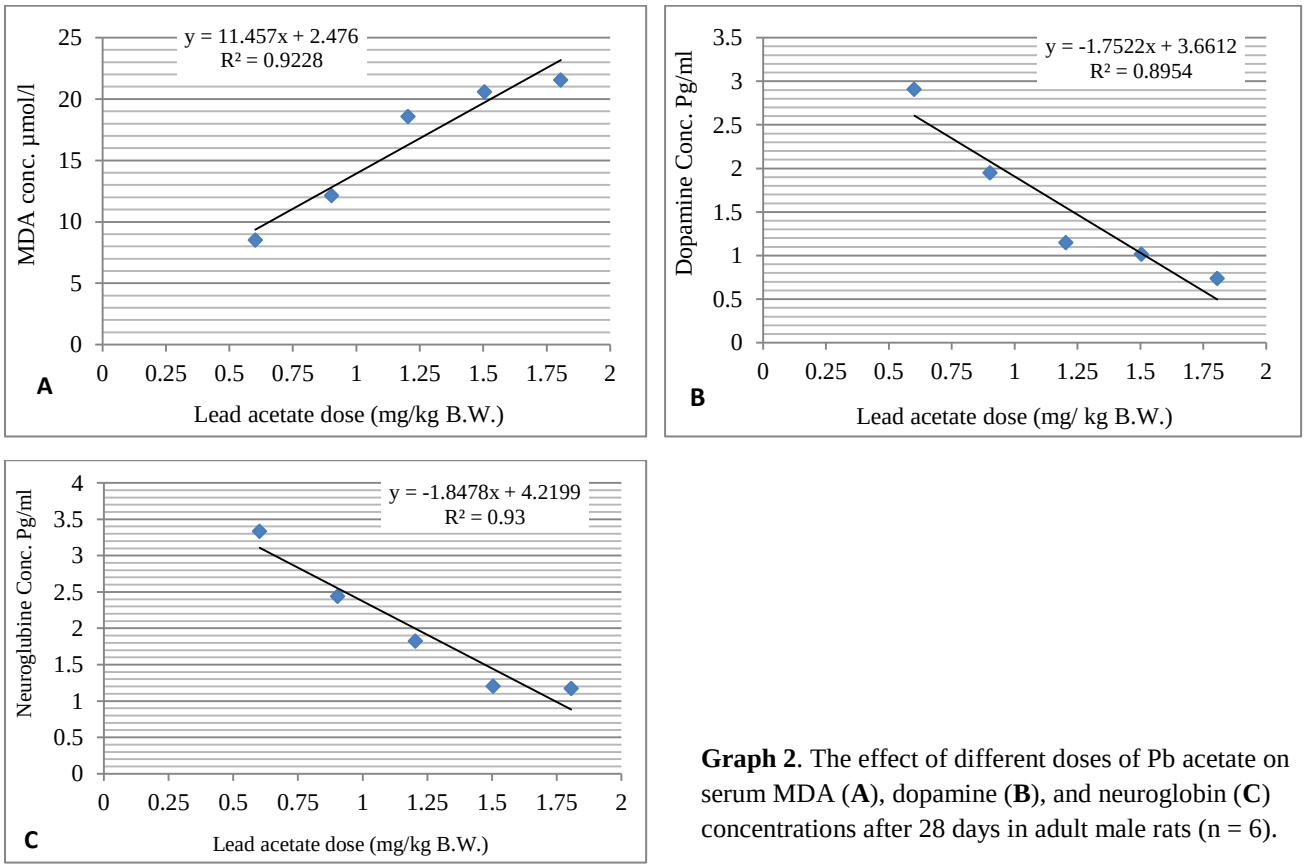
Determination of the sublethal dose of lead acetate

The obtained results of Graph (2-A) explained a highly significant ($p < 0.05$) increase in serum MDA concentration accompanied by a successive increase in the dose of Pb, while a significant negative relationship was observed between serum dopamine (2-B) and neuroglobin (2-C) concentrations ($p < 0.05$). According to probit analysis, the estimated sublethal dose of Pb was equal to 16 mg/Kg BW (1/280 mg/kg BW from LD50 of Pb).



Graph 2. The effect of different doses of Pb acetate on serum MDA (**A**), dopamine (**B**), and neuroglobin (**C**) concentrations after 28 days in adult male rats (n = 6).

DISCUSSION

The dose-response curve was employed using consecutive doses of Pb acetate to estimate the sub-lethal dosage of Pb acetate. The findings revealed a highly significant increase in serum MDA levels together with a drop in dopamine and neuroglobin levels. The current results are in agreement with those reported by Abdel-Wahab and Metwally (2014), Velaga et al. (2014), and Sutaria et al. (2022). Lead-induced neurotoxicity has been linked to oxidative stress, caused by the disruption of the antioxidant balance in cells (Jafarzadeh et al., 2022), dysregulation of cell signaling, and altered neurotransmission (Li et al., 2016).

The findings indicated a significant reduction in dopamine and neuroglobin concentrations with increasing doses of Pb acetate. The Pb exposure to cells or tissues might harm the nervous system through various pathways. It could damage glial cells, mainly in the cerebral cortex, cerebellum, and hippocampus, pass the blood-CNS barrier, and interfere with the structural elements of the CNS (Gandhi and Abramov 2012). As reported, it is preferentially deposited in specific CNS areas and is linked to aberrant behavior, learning disabilities, diminished hearing, neuromuscular weakness, and poor cognitive capabilities in experiment people and animals (Verina et al., 2007). A wide range of neurological illnesses, including mental retardation, behavioral issues, nerve damage, Alzheimer's disease, schizophrenia, and Parkinson's disease, might even be brought on by it, in addition to other biochemical abnormalities (Jaya Prasanthi et al., 2005; Bazrgar et al., 2015).

Lead can prevent the release of neurotransmitters from the preganglionic neurons since Pb is known to play a role in the synthesis and release of neurotransmitters. The Pb neurotoxicity can cause changes in cholinergic and dopaminergic neurotransmission in the CNS, including serotonin, dopamine, norepinephrine, and acetylcholinesterase activity, which are the first behavioral disorders in people and animal models (Flora et al., 2012; Malavika et al., 2021). Lead is thought to have a role in the transmission of processes in dopaminergic, cholinergic, catecholaminergic, and serotonergic neurons. In animal models, it has been shown that Pb interacts with a number of neurotransmitter systems, such as the dopamine, norepinephrine, serotonin, and gamma-aminobutyric acid systems (Mao et al., 2013; Chen et al., 2021). Lead can therefore prevent the utilization of neurotransmitters without selectivity in neuronal conductivity (Ferizi et al., 2020).

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CONCLUSION

The obtained results of the current study reveal that exposure to Pb acetate can significantly affect neurotransmitter levels, increase oxidative stress formation, and harm neurological functions. The sublethal dose of Pb was determined by calculating the concentrations of some indicators (MDA, dopamine, and neuroglobin). Therefore, future studies can be conducted by analyzing factors, such as histological changes or other neurotransmitters and animal behaviors.

DECLARATIONS

Acknowledgments

This study was funded by the physiology laboratory of the University of Baghdad, College of Veterinary Medicine, Baghdad, Iraq.

Authors' contribution

All authors checked and approved the final version of the manuscript.

Competing interests

There is no conflict of interest.

Ethical consideration

All authors have reviewed the manuscripts for ethical concerns, such as plagiarism, permission to publish, misconduct, data fabrication and/or falsification, multiple publishing and/or submission, and redundancy.

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