

Macroscopic, Microscopic and Histological Evaluation of Lead Induced Encephalopathy in Swiss Albino Mice Pups.

Sachdev Yadav¹, Dr. Veena Sharma²

Assistant Professor, Department of Pharmacy, Banasthali University, Rajasthan – 304022
Associate Professor, Department of Biosciences and Biotechnology, Banasthali University, Rajasthan – 304022

Summary

It has been known since ancient times that lead is virtually toxic to every organ of body including central nervous system where it may manifest as encephalopathy. The present study was aimed to evaluate the macroscopic, microscopic and histological alterations in the brain of pups induced by oral administration of a lead compound in gestational period of adult albino mice. A total number of 30 adult albino mice of either sex were included in the present study consisting of equal numbers in both control and experimental groups. Experimental groups received 4.5% lead nitrate and lead acetate trihydrate in gestational period. Animals of groups were euthanized with overdose of general anaesthesia and were dissected out and observed for macroscopic, microscopic and histological alteration in brain. On gross examination brains from the experimental group revealed; cerebellum grossly hemorrhagic and petechial hemorrhages are distributed throughout the cerebral cortex and brainstem, large fluid-filled cavities, cerebellar cortex neutrophil contains extravasated red blood cells (RBC) and an enlarged extracellular space. It was concluded that lead has toxic effects on the central nervous system including brain. This may explain the clinical manifestations of lead toxicity. Key words: Albino mice pups, cerebellum, lead nitrate and lead acetate trihydrate, neurotoxicity, edema.

Introduction

It has been known since ancient times that lead may cause poisoning in man (1). In the modern era, thousands of hazardous chemicals and heavy metals are being produced and used in a wide variety of work places all over the world. Heavy metals are trace metals that are at least five times denser than water and are taken into body via inhalation, ingestion and skin absorption. It should be noted that most of the pathological conditions in body arise as a result of the exposure to these injurious substances. Lead and other heavy metals create reactive radicals which damage cell structure including DNA and cell membrane (2). Lead poisoning can cause a variety of symptoms and signs which vary depending on the individual and the duration of lead exposure (3,4). Gestational lead exposure has many adverse effects on development; a few of them may be most pronounced during the first trimester (5). The amount of lead in blood and tissues, as well as the time course of exposure, determines the level of toxicity (6). Blood often shows pathological changes before the external signs of poisoning become apparent.

The absorbed lead enters the blood stream where over 90 percent of it is bound to the red cells with a biological half life of 25-28 days (7). Toxicological effects of lead have their origin in perturbation in cell function of various organ systems. The major biochemical effect of lead is its interference with heme synthesis which leads to hematological damage (8). Despite several published accounts on pathophysiological alterations of lead toxicity and the cure of lead poisoning by sequestering agents (9), the approaches are limited in scope. Therefore the present investigation was focused to evaluate the changes macroscopic, microscopic and histological alteration in pups of albino mice.

Materials and methods

Random breed Swiss albino mice were used for the present study. Sexually mature male and females weighing 25-30 gm were put in breeding cages in the ratio of 1:1 (3 female: 3 male) and provided standard diet and water ad libitum. The cages were checked every day in the morning and females showing vaginal plug were isolated. The pregnant female was housed in an individual cage and was started on diet containing 4.5% lead nitrate and lead acetate trihydrate respectively along water ad libitum. Comparable litters that received normal standard diet and water ad libitum were studied concurrently as controls. The day, on which the pups would be first found will be designated as day zero, their real age may have been 0 to 12 hours more and was studied for alterations in macroscopic, microscopic and histological alteration in brain. All the experimental work was approved by the institutional animal ethics committee (Ref. No.IAEC/257).

Observations

Lead-poisoned mice pups gain weight and behave as control mice pups during the first 4 days; thereafter, their weight gain was less and their behavior was altered. From postnatal Day 5 to Day 8, symptoms of lead poisoning are evident. Experimental animals show periodic tremors and seizures. This shaking usually involves the whole body and lasts 3 to 5 seconds. At about 8 days, the lead poisoned mice become very lethargic and slow even to right themselves when placed on their backs. The period from 9 to 13 days is marked by the appearance of paraplegia. (10) The mice usually die within 24 hours of the onset of paralysis. Very few animals (<5%) survive longer than 15 days. (10)

Macroscopic examination of the brains of 5-day-old lead poisoned mice shows hemorrhagic lesions throughout the brain. The cerebral cortex and brain stem contain only petechial hemorrhages while the cerebellum is very hemorrhagic. (Figure 1) In addition to varying degrees of hemorrhage, 10-day-old mice show signs of brain edema including the accumulation of fluid in cavities (Figure 2).

Histologic and electron microscopic examination of the cerebellum of paraplegic mice shows lesions typical of lead encephalopathy including fluid-filled cavities deep in the internal granular layer and fiber tracts, extravascular red blood cells, and an enlarged extracellular space (Figure3). In both human lead encephalopathy and experimental lead encephalopathy, there is a susceptible period after which encephalopathy can not be produced. Children may develop lead encephalopathy during the first 3 or 4 years of life, (11) while lead encephalopathy can be produced in mice during the first 20 days of life.

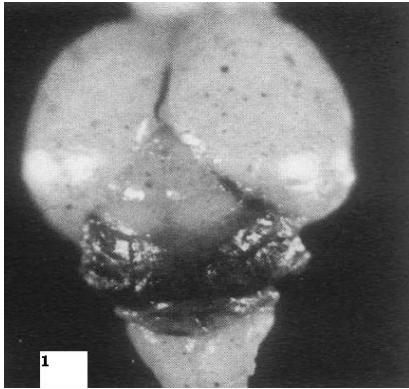


Figure 1 Photomicrograph of 5-day-old lead-poisoned Swiss albino mice pup brain. The cerebellum is grossly hemorrhagic, and petechial hemorrhages are distributed throughout the cerebral cortex and brainstem. (x 2.7)

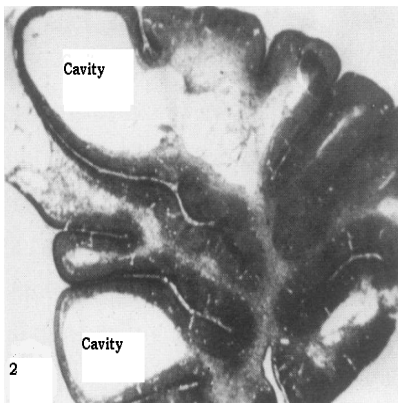


Figure 2 Photomicrograph of a cerebellar sagittal section from 10-day-old lead-poisoned Swiss albino mice pup. Large fluid-filled cavities are demonstrated. (x 14.5)

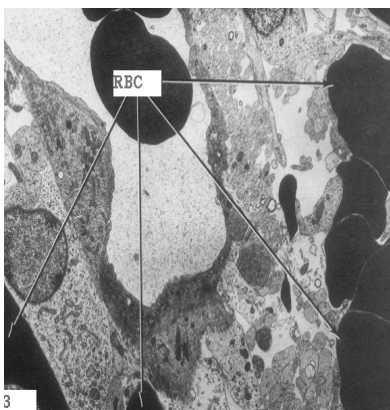


Figure 3 Electron micrograph of lead-poisoned Swiss albino mice pup cerebellar cortex. The neutrophil contains extravasated red blood cells (RBC) and an enlarged extracellular space. (X 4400)

Conclusion

From the above study it was concluded that brain is vulnerable to toxicity of lead. Introducing lead nitrate and lead acetate trihydrate to female Swiss albino mice during gestation period produced encephalopathy which is characterized by an exudative extracellular edema common in both human and experimental lead encephalopathy.

Acknowledgements

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