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Original Article

PYRAMIDAL LAYER THINNING, SHRUNKEN NEURONS AND DEEP VACUOLATION IN HIPPOCAMPUS DUE TO THE ORGANIC LEAD INDUCED TOXICITY

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ABSTRACT

Lead, a known heavy metal exerts its toxicity on different organ systems of which the neurotoxicity is a considered to a significant consequence. The organic lead exposure on the hippocampus, that plays a significant role in the formation of short and long term memory, navigation and also participates in the limbic system in the brain, was studied. The resulting effects were the thinning of neuron layers, vacuolation and reduction in overall cell population of neurons, thereby showing the primary effect on the pyramidal layers of the hippocampus.

KEYWORDS: Lead acetate, organic lead, neurotoxicity, Charles foster strain, rats, pyramidal layer, hippocampus.

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INTRODUCTION

Heavy metals in different forms in the environment substantiate a major hazard to the different life forms. Among them, the toxicity of lead has been a major cause that has attracted several writings. The clinical effect of lead toxicity called as lumbism, which has been known since ages. Exposure of lead present in the environment can be through ingestion, inhalation or absorption through the skin. The exposure through different routes also has an age related variation, as compared to the human adults were the absorption is 20% in case of ingestion absorption has been found to be 50% in children. The largest proportion of lead absorbed is sequestered by bone followed by liver and kidney.

At cellular level the toxicity is thought to be due to the affinity of lead for cell membrane & mitochondria followed by affecting the mitochondrial oxidative phosphorylation as well as Ca, K & Na ATPases. Further, it also impairs the activity of Ca dependent intracellular messengers and of the brain protein kinase C. additionally, the lead can also alter the gene expression by the translocation in the nucleus by the formation of inclusion bodies.

The most significant result of lead toxicity is its effect on the central nervous system. Several researchers have worked with the effects of lead; the work related to the histological changes is being presented here. In a study by Markov & Dimova (1974) [1] of chronic lead poisoning on Wister rats they observed hypertrophied microglial cells and vascular pericytes in parietal cortex with all other elements appearing intact. Boulding and Krigman (1975) [2] demonstrated the primary toxic effect at neuronal level without

any vascular alteration which was further reconfirmed using tracer probe. In another study Hirano et al. (1975) [3] implanted pellets of organic lead in forebrain of rates and they showed the parenchymal necrosis and reactive changes in the form of edema & macrophage invasion and spongiosis in hypothalamus as a result of swollen axons. Zook et al. (1980) [4] observed degeneration and proliferative changes of small vessels, ring hemorrhages, edema, perivascular hyaline droplets and rosette like deposits of proteinaceous exudates, focal loss of myelin, astrogliosis and necrosis of hippocampal neurons. Brinck, Wechsler (1985) [5] studied incubated slices of hippocampus in media containing lead and found pyramidal neurons of the CA1 region & granule cells of fascia dentate to well preserved whereas neuronal structures towards the outer surface of slices were either vacuolated or hyperchromatic and shrunken, CA4 neurons were mostly lytic.

Investigators working on lead effect on neural tissue in general and hippocampus specifically have presented disparities in the results as a result of toxicity, therefore, this study was taken up to investigate the histological changes in the hippocampus.

MATERIALS AND METHODS

Albino rats of Charles Foster (six) strain weighing 120 gm (+/- 10gm) of either sex were used in the study. Six rats were subjected to the lead acetate exposure in 4% (1/10 of LD50) in drinking water. This was decided after determining the survival period of 18 days. The controlled rats (six) of either sex were administered normal drinking water orally. The rats both experimental and controlled were sacrificed and perfused with 10% formalin.

The cranial vault was removed; the brainstem was lifted from the base of the cranium and observed for any macroscopic changes on the surface. Meningeal coverings were removed and sliced into 3mm coronal sections. These sliced pieces were transferred to specimen tubes containing formalin (10%) for the next 48hrs for additional fixation. The brain was processed with paraffin embedding for block preparation that was refrigerated for further use.

Using rotary microtome, the block was sliced for 6micron thick sections. The sections were flattened on hot water bath and transferred on albumin coated slides for incubation at 48°C. The mounted sections finally were stained with Thionin for Nissl substance and Kluver Barrea (triple staining) technique for light microscopy.

RESULTS

The neurobehavioral effects in higher function were evident from the third day of administration in experimental animals in the first week. Over the second week, the motor activities and response to the sensory stimulus were lowered. The tremors and twitching were apparent at the beginning of the third week there was some variable degree of motor deficit with tremors and twitching to marked paralysis of both the fore and hind limbs.

The gross surface of the dissected brain showed edematous changes with convolutions on the surface becoming less conspicuous compared to that of control animals. The petechial hemorrhage was again an obvious and uniformly distributed feature. The general affect was of disorganization of cytoarchitecture, degeneration of neurons, vacuolation and empty spaces in deeper parts of the brain as well as axonal damage was apparent.

Nissl preparation shows in the experimental group an overall reduction in the thickness of hippocampus affecting all layers of neurons and fibers, however, the affect is markedly evident by thinning out of the pyramidal layer. Neurons in the pyramidal layer are less distinct or can be poorly identified as compared to control. The Kluver Barrera stained section from the experimental group showed highly vacuolated area in the zones of the deep pyramidal layer suggestive of degeneration. There is an overall gross neuronal degeneration of neurons and decrease in the cell population over the entire pyramidal layer of the hippocampus.

DISCUSSION

The observations are in agreement with the known fact that lead affects the brain and is a neurotoxin as was seen on the experimental rats starting in the first week with irritability, agitated and aggressive changes in the behaviour.

HISTOLOGICAL OBSERVATIONS:

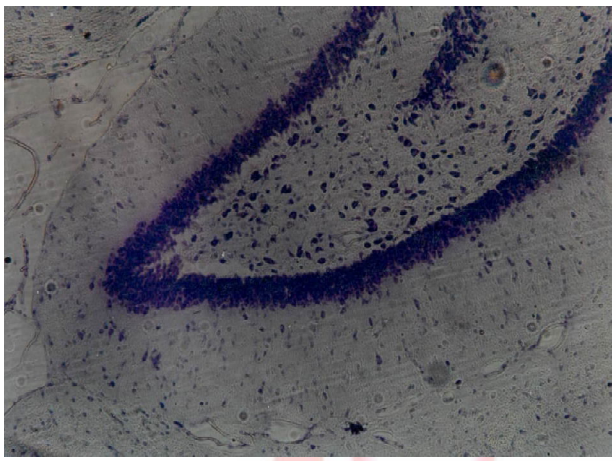

Fig. 1: Low power micrograph of Nissl stained section of the hippocampus from control: Showing well defined neuronal cell layers. Neurons have features of characteristic large multipolar neurons.

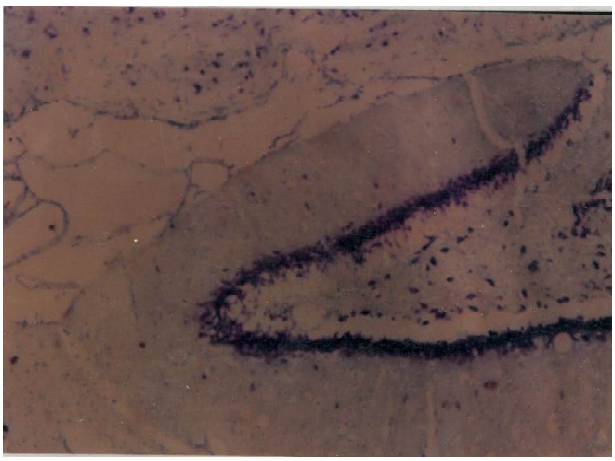

Fig. 2: Low power micrograph of Nissl stained section of the hippocampus from experimental showing shrunken neuron and thinning of all layers with zone of vacuolation deep to the pyramidal layer.

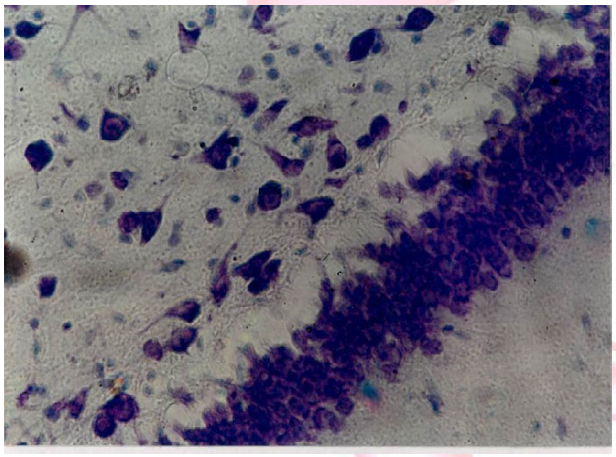

Fig. 3: High power micrograph of Nissl stained section of hippocampus from control: Showing well defined neuronal cell layers. Neurons have features of characteristic large multipolar neurons.

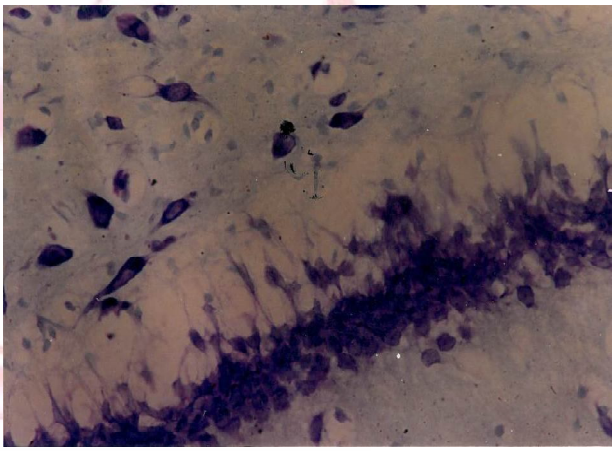

Fig. 4: High power micrograph of Nissl stained section of the hippocampus from experimental showing shrunken neuron and thinning of all layers with zone of vacuolation deep to the pyramidal layer.

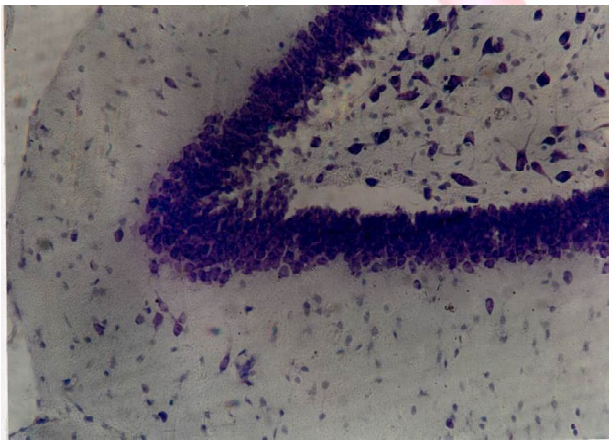

Fig. 5: High power micrograph of Nissl stained section of the hippocampus from control: Showing well defined neurons in various laminae.

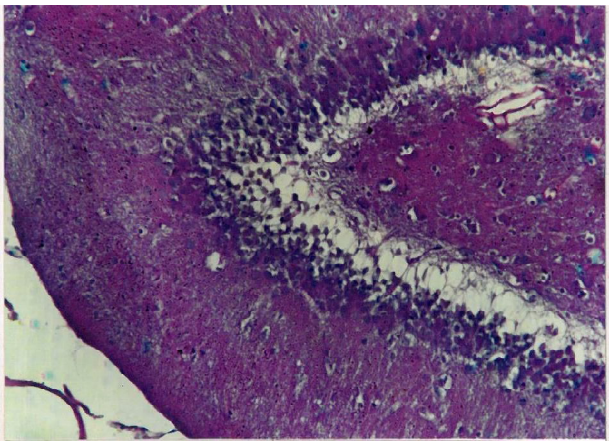

Fig. 6: High power micrograph of Nissl stained (Kluver Barrera technique) section of the hippocampus from experimental showing highly vacuolated region in the zones of the deep pyramidal layer.

Followed by the fall in activity and indifferent behaviour over the next week and finally reflecting with twitching, tremors to the extent of tetraplegia.

An injury to the hippocampus by exposure of neonatal rats through maternal milk as been reported by Kostas et. al (1976) [6]. The hippocampus damage was concluded on the basis of increased activity in the neonatal rats exposed to lead. A similar increase in activity and agitation in the adult rats was found in the present study also. Zook et. al [4] have also reported gliosis and necrosis of hippocampal neurons. These findings were also found in the present study. The findings in the present study are in agreement with those reported by Bansal et al. (1990) [7] who reported a reduction in the width of hippocampus and degeneration of cells in the cerebral cortex. Brinck and Wechler (1985) [5] incubated slices of guinea pig hippocampus in a lead containing medium and reported vacuolation and shrinkage of pyramidal cells in the outer parts of the CA4 neurons. In the present study, however, the effects were more pronounced on the deeper layer of the hippocampus.

CONCLUSION

Based on the finding of the study it can be concluded that lead is toxic to the nervous system of the adult albino rats exposed through oral route with behavioural changes that can be attributed to hippocampus damage and microscopic study revealing the affect with the reduction in overall thickness, degeneration and neuronal loss of pyramidal cells was also evident particularly in the deeper regions were empty spaces and vacuoles were encountered due to neuronal degeneration.

Conflicts of Interests: **None**

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