Comparative Study of Histo-Pathological Effects of Mercury on Cerebrum, Cerebellum and Hippocampus of Adult Albino Rats

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ABSTRACT

Background: Previously it was thought that mercury sulphide in low dose shows good therapeutic effect without producing toxic effects in the human beings. Symptoms like ataxia, speech impairment, visual field constriction, deafness, tremors, mental retardation, coma and even death has been reported due to chronic use of this heavy metal. The aim of our present study is to compare histopathological changes in different parts of brain, so that clinical symptoms following mercury intoxication can be explained.

Methods: Freshly prepared sterile solution of mercuric chloride in distilled water (0.33 mg/kg body weight) was orally administered daily to total number of 30 adult albino rats (15 males and 15 females) for a month. 3mm thick sections were taken from cerebrum, cerebellum and hippocampus parts. These sections were processed and then stained by haematoxylin & eosin to be observed in light microscope.

Results: Histological pictures of all the three areas were suggestive of multiple foci of necrosis with gliosis. Marked congestion of vessels with perivascular necrosis was also noticed. Increased cellularity of granular layer and molecular layer in cerebellum and hippocampus were seen respectively.

Conclusion: The histopathological examination revealed that normal cytoarchitecture of all the three areas of brain were distorted resulting in various neurological disorders.

Key words: Cerebellum, Cerebrum, Hippocampus, Histopathology, Mercury

INTRODUCTION

Mercury is one of the heavy metal which is considered as the chief ingredient of various medicines. Ayurvedic experts have estimated that approximately 20% of the Ayurvedic formulations contain mercury sulphide as a component. Mercury sulphide in low dose shows good therapeutic effect without producing toxic effects in the human beings. However, safety issues have been raised about mercury content present in allopathic and ayurvedic medicines. Besides the ingestion of medicines and contaminated food, mercury intoxication can also occur through inhalation. Various countries like Japan has drew the attention of the researchers towards the detrimental effects of industrial waste rich in mercury. Symptoms like ataxia, speech impairment, visual field constriction, deafness, tremors, mental retardation, coma and even death has been reported due to mercury toxicity.

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MATERIALS AND METHODS

This study was conducted in the department of Anatomy, Jawaharlal Nehru Medical College (JNMC), Aligarh, India. Total number of 30 adult albino rats (15 males and 15 females) weighing approximately 130gm were used for the study. Out of 15 rats of each sex, 5 were taken as control and 10
were considered in experimental group. The rats were kept in polyacrylic cages (38x23x10cm) with not more than four animals per cage and maintained under standard laboratory circumstances with natural dark and light cycle. Freshly prepared sterile solution of mercuric chloride in distilled water (0.33 mg/kg body weight) was orally administered daily. After the exposure of 30 days, the rats were anaesthetized with ether and perfused with buffered 10% formalin. Brain was dissected out and meninges were removed. 3mm thick sections were taken from cerebrum, cerebellum and hippocampus parts and processed for paraffin embedding. Then 10µm thick sections were obtained by rotary microtome and then stained by haematoxylin & eosin to be observed in light microscope.

**RESULTS**

**Cerebrum**

Cerebrum of control group shows normal distribution of neurons. The outermost cortical layer called as molecular layer is a pale stained zone. Small blood vessels penetrate the cerebral cortex. At higher magnification (40x) pyramidal cells with apical dendrites are visible. These cells are closely associated with round glial cells [Figure 1].

![Figure 1: Photomicrograph of cerebrum of control group (H & E 10x)](image1)

In the experimental group, under light microscope, clustering of neurons was seen. These neurons were pleomorphic in nature and showed marked spongiosis. Histological features were suggestive of multiple foci of necrosis with gliosis. Marked congestion of vessels with perivascular necrosis was also noticed. [Figure 2]

![Figure 2: Photomicrograph of cerebrum of experimental group (H & E 40x)](image2)

**Cerebellum**

The light microscopy of control group shows trilaminar arrangement of neurons. Outer molecular layer, inner granular layer and a row of purkinje cells sandwiched between the two layers. [Figure 3].

![Figure 3: Photomicrograph of cerebellum of control group (H & E 10x)](image3)

The haematoxylin & eosin staining of cerebellum presented marked congestion of vessels. There was marked increase in granular cell numbers with pyknotic nuclei. The 40x view was also suggestive of spongiosis of molecular layer. Few purkinje cells are also visible. [Figure 4].
Hippocampus
In the control group, (10x) neurons were arranged in two layers, molecular and granular. [Figure 5].

In the experimental group, marked increase in the cellularity of molecular layer was visible along with the pyknosis of nuclei. At higher magnification, hyperchromatic nuclei were visible in the molecular layer. [Figure 6].

DISCUSSION
Various studies\[^{13,14}\] have proved neurotoxicity, nephrotoxicity and hepatotoxicity due to mercury exposure. However mercury is still a chief component of different medicines. According to US Environmental Protection Agency (EPA), reference dose (RfD) for methyl mercury is 0.1 µg/kg body weight/day.\[^{15}\]

Earlier studies have revealed behavioral and spatial learning defects in animals due to mercury exposure.\[^{16}\] Baraldi et al\[^{17}\] showed cognitive impairment in rats which were exposed to mercury for chronic period. Cognition functions and motor activities are controlled by acetylcholine, acetyl cholinesterase (AChE) and choline acetyltransferase (ChAT). Numerous studies have proved decreased ChAT and AChE activity after mercury exposure for 24-26 days primarily in hippocampus and frontal cortex of cerebrum. Jadhav et al\[^{18}\] observed dose-dependent vascular, degenerative and necrotic changes in the brain cerebrum and liver of male rats exposed to mercury via drinking water. Histological changes in different areas of brain are suggestive of neurotoxic effect of mercury. Ghusoon et al\[^{19}\] found shrinkage of neurons containing pyknotic nuclei in cerebral cortex. It is documented that heavy metals like mercury can cross blood brain barrier.\[^{20}\] Reports are available, showing degenerating and necrotic changes in purkinje cells of cerebellum secondary to mercury poisoning.\[^{21}\] Recent study has proved increased cellularity and pleomorphism in hippocampus also.\[^{22}\]

CONCLUSION
The findings of the present study suggest that chronic intake of mercury can have adverse effects on
different parts of brain including cerebrum, cerebellum and hippocampus. The histopathological examination also revealed that normal cytoarchitecture of brain was distorted resulting in various neurological disorders. We conclude from our study that the safety regarding the use of mercury in medicines is a controversial issue and requires further research.

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