Original Article

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

Brajesh Ranjan*, S M Dawar Husain**, Kundan Kumar***, Tarun Prakash Maheshwari****

*Senior Resident, Department of Anatomy, JNMCH, AMU, Aligarh.
**Associate Professor, Department of Anatomy, JNMCH, AMU, Aligarh.
***Junior Resident, Department of Anatomy, JNMCH, AMU, Aligarh.
****Demonstrator, Department of Anatomy, SHKM, GMC, Mewat, Haryana.

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.[1] Mercury sulphide in low dose shows good therapeutic effect without producing toxic effects in the human beings.[2] 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.[3]

Name & Address of Corresponding Author
Dr. Brajesh Ranjan
Senior Resident, Department of Anatomy,
Jawaharlal Nehru Medical college,
AMU, Aligarh, Uttar Pradesh, India.
E mail: drbrajeshranjan@gmail.com.

Mercury intoxication is also considered as occupational hazard for dental staff, chloralkali factory workers and goldminers.[4-6] In infants toxicity is found due to lactation from mothers consuming mercury rich diet.[7,8] Various studies[9,10] have reported neurological disorders like disrupted fine motor function, attention deficit, memory loss in children and adults consuming fish as a chief diet.

Few studies[11,12] in the literature have proved histopathological changes in different organs like liver, kidney etc in animals. Since neurological symptoms are commonly seen in subjects exposed to mercury, so it becomes crucial to study its effect on microstructure of brain. 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.

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].

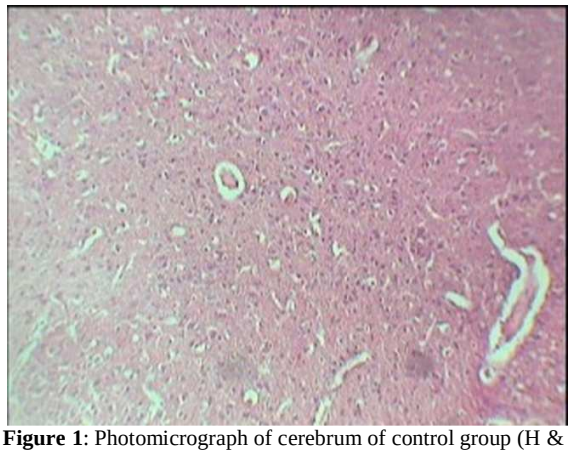

Figure 1: Photomicrograph of cerebrum of control group (H & E 10x)

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]

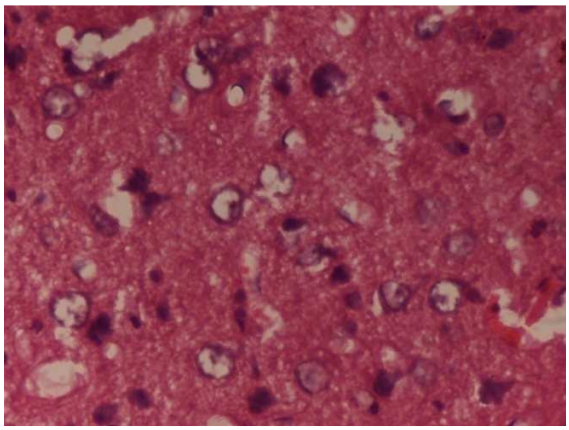

Figure 2: Photomicrograph of cerebrum of experimental group (H & E 40x)

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].

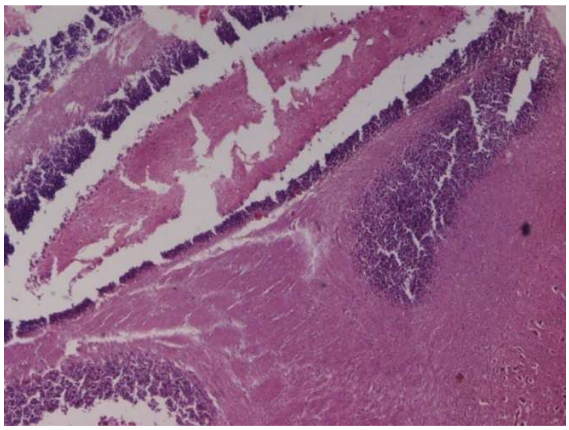

Figure 3: Photomicrograph of cerebellum of control group (H & E 10x)

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].

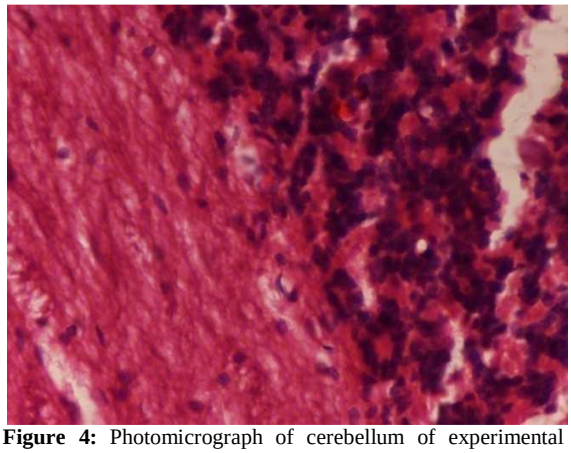

Figure 4: Photomicrograph of cerebellum of experimental group (H & E 40x)

Hippocampus

In the control group, (10x) neurons were arranged in two layers, molecular and granular. [Figure 5].

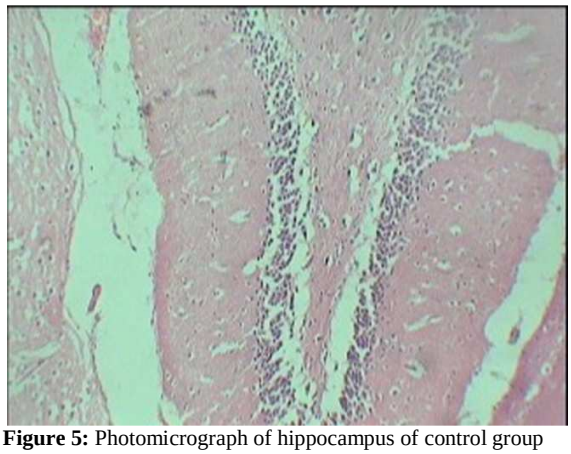

Figure 5: Photomicrograph of hippocampus of control group (H & E 10x)

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].

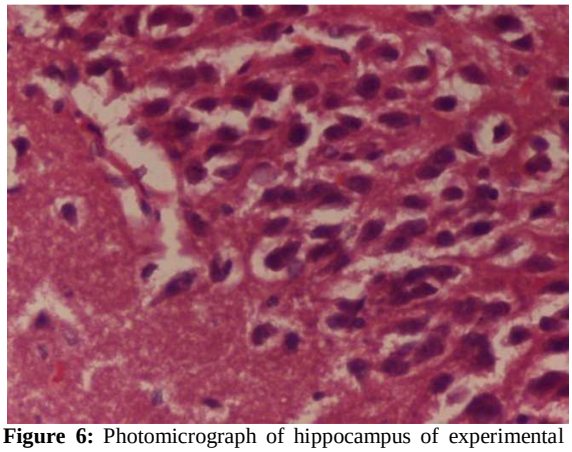

Figure 6: Photomicrograph of hippocampus of experimental group (H & E 40x)

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.

REFERENCES

1. Gogtay NJ, bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug Saf 2002; 25 : 1005-19.
2. Kumar G, Srivastava A, Sharma SK, Gupta YK. Safety evaluation of mercury based Ayurvedic formulation (*Sidh Makardhwaj*) on brain cerebrum, liver & kidney in rats. Indian J Med Res. 2014;139(4):610-8.
3. Bernhoft RA. Mercury toxicity and the treatment: a review of literature. Journal of environmental and public health 2012; 10: 460-508.
4. Rowland AS, Barid DO. The effect of occupational exposure to mercury vapours on the fertility of female dental assistants. Occup Envirom Med 1994; 51(1): 28-34.
5. Berregard L, Hultberg B, Schultz A, Sallsten G. Enzymuria in workers exposed to inorganic mercury. Int Arch Occup Environ Health 1988; 61: 65-69.
6. Grandjean P, White RF, Nielson A, Cleary D, de Oliverira, Santos EC. Methylmercury neurotoxicity in Amazonian children downstream from goldmining. Environ Health Perspect 1999; 107(7): 587-592.
7. Murata K, Wiehe P, Budtz Jorjensen E, Jopergensen PJ, Grandjean P. Delayed brainstem auditory evoked potential latencies in 14 yr children exposed to methylmercury. J. Pediatr 2004; 144(2): 177-183.
8. Grandjean P, Weihe P, White RF. Milestone development in infants to methylmercury from human milk. Neurotoxicology 1995; 16(1): 27-34.
9. Johnson CL. In the environment: sources, toxicities and prevention of exposure. Pediatr Ann 2004; 33(7): 437-442.
10. Yokoo EM, Valente JG, Grattan L, Schmidt SL, Platt I, Silbergeld EK. Low level methylmercury exposure effects neuropsychological function in adults. Environ Health 2003; 2(1): 8-10.
11. Dawar SM, Ranjan B, Yunus SM. Neurohistopathological effects of Mercury on cerebrum of Adult Albino Rat. International journal of scientific research 2014; 3(7): 410-11.
12. Dawar SM, Ranjan B, Yunus SM. Neurohistopathological effects of Mercury on cerebellum of Adult Albino Rat. International journal of scientific research 2014; 3(7): 424-25.
13. Flora SJS, Mittal M & Mehta A. Heavy metal induced oxidative stress & its possible reversal by chelation therapy. Indian J Med Res 2008; 501:501-23.
14. El-Shenawy SM, Hassan NS. Comparative evaluation of the protective effect of selenium and garlic against liver and kidney damage induced by mercury chloride in the rats. Pharmacol Rep 2008; 60: 199-208.
15. United States Environmental Protection Agency (US EPA). Water quality criterion for the protection of human health: Methyl mercury; Human Health Criteria; 2001.Washington, DC, (Available: www.epa.gov/waterscience/criteria/methylmercury).
16. Coluccia A, borracci P, Giustino A, Sakamoto M, Carratu MR. Effects of low dose methylmercury administration during the postnatal brain growth spurt in rats. Neurotoxicol Teratol 2007; 29 : 282-7.
17. Baraldi M, Zanoli P, Tascedda F, blom JM, brunello N. Cognitive deficits and changes in gene expression of NMDA receptors after prenatal methylmercury exposure. Environ Health Perspect 2002; 110 (Suppl 5) : 855-8.
18. Jadhav SH, Sarkar SN, Aggarwal M, Tripathi HC. Induction 33. of oxidative stress in erythrocytes of male rats subchronically exposed to a mixture of eight metals found as groundwater contaminants in different parts of India. Arch Environ Contam Toxicol 2007; 52 : 145-51.
19. Ghusson AK, Neamah AL, Rajiah A, Naimi AL. Assessment of the therapeutic effects of aqueous extracts of cilantro and garlic in mercuric chloride poisoning in rats. The Iraqi J. Vet Med, 2012; 36(2): 231-243.
20. Gallaghar PJ, Lee RL. The role of biotransformation inorganic mercury neurotoxicity. Toxicology, 1980; 15(2): 129-134.
21. Bandy SC, Anderson CL, Harringtan ME, Prasad KN. The effect of organic and inorganic lead and mercury on neurotransmitters high affinity transport and release mechanism. J. Environ. Res, 1979; 19(1): 102-111.
22. Ranjan B, Dawar SM, Yunus SM. Neurohistopathological effects of Mercury on cerebrum of Adult Albino Rat. Global journal for research analysis, 2014; 3(7): 237-238.

How to cite this article: Ranjan B, Husain SMD, Kumar K, Maheshwari TP. Comparative study of Histo-pathological effects of mercury on cerebrum, cerebellum and hippocampus of adult albino rats. Ann. of Int. Med. & Den. Res. 2015;1(1):21-4.

Source of Support: Nil, **Conflict of Interest:** None declared