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Neurotoxicty of Mercury Chloride Administration On the Cerebellar Cortex of Adult Wistar Rats.

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ABSTRACT

This study was carried out to investigate the effect of mercury II chlorideoin the cerebellar cortex of adult wistar rats, average weight of 220g were divided into groups of 5 rats per group. Group 1- served as control group and was administered distilled water orally for two weeks. Groups 2, 3, 4 and 5 were administered orally with 6.5mg, 13mg, 26mg and 52mg per kg Body weight of mercury II chloride respectively for two weeks. All the groups were given standard feed and water *ad libitum* and were housed in plastic cages. After oral administration, the animals were sacrificed and the cerebellum was fixed in Bouin's fluid and the tissue was processed histologically and stained with H & E stains. Photomicrographs were taken and the slides were examined under the low power microscope. The result shows that there was decrease in physical activities in the treated groups and degeneration of the cells of the molecular and purkinje layers of the cerebellum. Our study showed that mercury II chloride could cause cerebellar neuronal degeneration.

Key words: Mercury II Chloride, Cerebellare cortex, degeneration.

Man in his environment has been exposed to many potential of heavy metals through bioaccumulation and biomagnifications which has been transferred to man via food chain as a result of anthropogenic activities. Mercury is a heavy metal that is toxic and has led to many health problems the world. (Nduka and Orisakwe 1991)

Mercury poisoning known as hydrargria mercurialism is a disease caused by exposure to mercury or its compounds. Toxicity due to mercury has been known to cause dilapidating effects on the kidney, lungs, liver etc. resulting in some diseases namely Hunter-Russel syndrome (concentric constriction of the visual field, ataxia, dysarthria, etc.), acrodyria (pink disease) and minimata disease; this was seen in four workers exposed to methylmercury fungicide. The type and degree of symptoms exhibited depends on dose, method and duration of exposure. Toxicity has been compared in many countries e.g. Japan has ban mercury altogether despite its being an important element found in large deposit all over the world (Goyer 1991, WHO 1991). Mercury II chloride is not a salt but a linear triatomic molecule, hence it has tendency to sublime. In crystal. Each mercury atom is bounded to two close chloride ligands with Hg...CI at a distance of 2.38 A° (WHO 1991, Well 1984). Mercury (II) chloride was used as a photographic intensifier to produce pictures in the colloidal process. It is also used in preservation of anthropological and biological specimens, (Goldberg 1996). Syphilis was frequently treated with mercury chloride before the advent of antibiotics; it was inhaled, ingested and applied tropically. (Pimple *et al* 2002). The consumption of fish is by far the significant sources of ingestion related mercury exposure in human. Although plants and livestock also contain mercury due to bioaccumulation of mercury from soil;, water and atmosphere and also due to biomodificantion of ingesting other mercury organism (Ingri1999). Exposure to mercury can also occur from breathing contaminated air or from improper disposal of mercury and its compounds e.g. after spill of elemented mercury or improper disposal of florescent light bulb. Two third of human-generated mercury comes from stationary combustion mostly from coal, gold production, crematories, caustic soda, dental clinics, batteries, cosmetic industries etc. Mercury and its compounds are not dest5royed by metabolism but rather converted to different forms and states. Their metabolism appears to be similar for animal and human
(ATSDR 1978).

In this study we investigated the effect of mercury chloride on the histology of the cerebellum of adult wistar rats. The cerebellum plays an essential role in the control of movement. It is responsible for ensuring that movement takes place smoothly, in the right direction and to the right extent. The cerebellum is also important for learning of movement (e.g., in learning to write) (Singh, 2006).

MATERIALS AND METHOD

Chemicals: Mercury II chloride manufactured by May and Baker Limited Dagenham, England was purchased from a reputable scientific chemical store in zaria. It was authenticated in the Department of Chemistry, Faculty of science, Ahmadu Bello University, Zaria, Nigeria. All other chemicals used were of analytical reagent grade. The chemical was dissolved in distilled water to prepare the following concentrations, 6.5mg/kg, 13mg/kg, 26mg/kg, and 52mg/kg Body weight of mercury II chloride solution.

Animals: Adult wistar rats of either sex of average weight of 200g obtained from our own breeding colony bred in the animal house of the Department of Human Anatomy, Faculty of Medicine, Ahumadu Bello University, Zaria, Nigeria, were used in this study. They were fed with standard rat food and water *ad libitum* and maintained under laboratory conditions, (temperature 26 ± 2°C, and 12h natural light/dark cycle). They were grouped into five (5) groups of 5 animals per group. The experiments were conducted in accordance with the Guiding Principles in the Use of Animals in Toxicology, adopted by the Society of Toxicology in July 1989.

Animal Treatment: Based on the oral LD_{50} of mercury II chloride for rats which was reported to be 210mg/kg (Baker 1999), the following administration was done daily for 14 days:

Group 1 = control group administered distilled water
Group 2 = 6.5mg/kg Body weight
Group 3 = 13mg/kg Body weight
Group 4 = 26mg/kg Body weight
Group 5 = 52mg/kg Body weight

Tissue Processing: After the period of administration of the mercury (II) chloride solution, the animals were sacrificed by chloroform inhalation. The skull was opened neatly and the cerebellum was removed and fixed in Bouin's fluid and the tissue was processed using the Automatic Tissue Processor (Histokinett bench Model). It was stained in H & E stains.

RESULTS

Physical Observation

Physical observation of all animals in the group showed that the control group showed no changes in physical appearance throughout the duration of experiment. However the treated groups shows gnawing and less active than the control group. These observations were highest in the highest dose treated animals.

Histopatheological Studies

Group 1 (control): showed no significant histopathological change. All the layers of the cerebellar cortex (granular, purkinje, molecular) were intact as seen in figure 1. In Group 2 (6.5mg/kg), there was slight degeneration of the molecular layer. However the granular and purkinje layer of the cerebellar cortex were intact as seen in Figure 2.In Group 3 (13mg/kg), there was moderate degeneration of the molecular and purkinje layers of the cerebellar cortex as seen in figure 3.

Group 4 (26mg/kg) and Group 5 (52mg/kg) showed serious degeneration of the molecular, purkinje layers. There were focal areas of satellitosis and gliosis as shown in figures 4 and 5 bellow.

DISCUSSION

The central nervous system is probably the most sensitive target organ for mercury exposure. Nervous system disorders following exposure to mercury are both consistent and pronounced. Acute-, intermediate-, and chronic-duration exposures elicit similar neurological effects. Symptoms intensify and may become irreversible as exposure duration and/or concentration increases. Most occupational studies discuss chronic-duration exposure to a time-weighted average (TWA) concentration or to a concentration range, thereby preventing the assessment of dose response relationships within the populations studied. However, the average exposure levels for affected groups are similar in many of these studies. There were also neruopathological effects, first detected after two weeks, namely peripheral vacuolization of cells in the dorsal root ganglia, followed by the development of multiple small lesions in the ganglia (Chang *et al* 1972).

The essence of this is to investigate the effect of mercury II chloride solution on the cytoarchitecture of the cerebellum of adult wistar rats. This is very important because the effect on the cerebellum layers of wistar rats may be synonymous to the effect it will have humans.

This study shows that there was degeneration in the cytoarchitecture of the cerebellum of the wistar rats in the treatment group

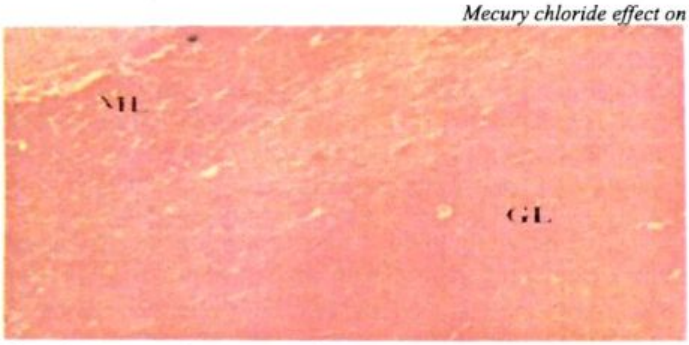

Plate 1: Photomicrograph of group 1 (control) administered distilled water showing the Molecular layer (ML) and the Granular layer (GL) of the Cerebellar Cortex. H&E x 250.

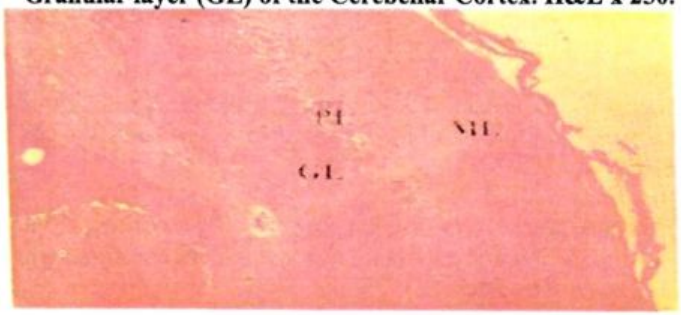

Plate 2: Photomicrograph of group 2 (6mg/kg BW)) showing the Molecular layer (M.L, Granular layer (GL), and the Purkinje layer (PL) of the Cerebellar Cortex. H&E x 250

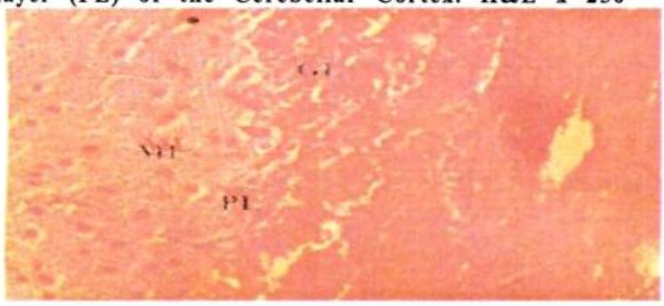

Plate 3: Photomicrograph of group 3 (13mg/kg BW) showing the Molecular layer (M.L), and the Pukinje layer (PL), Granular layer (GL) of the Cerebellar Cortex. H&E x 250

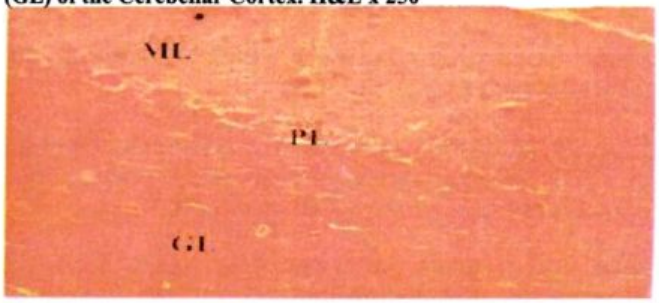

Plate 4 Photomicrograph of group 4 (26mg/kgBW) showing the Molecular later (ML), Purkinje layer (PL) and the Granular layer (GL) of the Cerebellar Cortex. H&E x 250

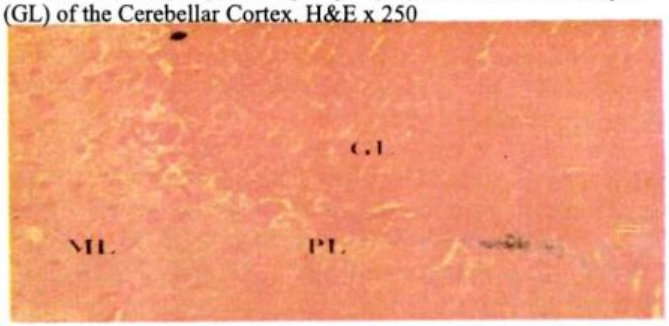

Plate 5 Photomicrograph of group 5 (52mg/kgBW) showing the Molecular later (ML), Purkinje layer (PL) and the Granular layer (GL) of the Cerebellar Cortex. H&E x 250

when compared with the control group. It has been shown from the above observation, that there is a direct relationship between the dose administered and the level of neurological degeneration in the cerebellum. This can be traced to the fact that low level of mercury in the blood can easily be excreted, however, as the dose increases there is redistribution of the mercury from blood to peripheral tissues especially nervous tissues as reported by ASTDR (1989) and Goyer (1991).

The severe degeneration seen in then high dosage groups could possibly be as a result of occlusion of blood brain barrier. This is because nutrients, metabolites and gases diffuse into and out of the brain across the blood-brain barrier and mercury is suspected to cause the occlusion (Doul and Amdur 1988). This finding agreed with previous findings that reported neuropathological effects, after two weeks of mercury exposure, namely peripheral vacuolization of cells in the dorsal root ganglia. Followed by the development of multiple small lesions in the ganglia (Chang *et al* 1972),the brain cells are known for their high demand of nutrients and gases reaching the cerebellum. Furthermore, deficiency in nutrients gaseous exchange will inevitably lead to hypoxia, cell shrinkage, necrosis and cell death of the cerebellar necrosis, which are said to have 50% of brain cell density. This finding agrees with the observation made by doull and Amdur (1988) and Reynolds *et al* (1987).

The decrease in physical activities, observed in the high dosage group can be related to the fact that mercury cause blockage of neurotransmitters secretion and also blocks catecholamine degradation pathways (Doull and Amdur 1988, Albaus 1972). The satellitosis and gliosis seen in the high dosage groups results from proliferation of neuroglia or macrophages in the cerebellum surrounding the degenerating neurons, and when they die, they engulf them. A spontaneous gliosis is an indication of degeneration change in nervous tissue (Chaurasia 2004, Musa *et al* 2009). This findings also agreed with other works that report mercury neurotoxic effects (accumulates in the brian, damages brian cells and nerve cells, and inhibits production of neurotransmitters by inhibiting dihydroteridine reeducate and effect on phenylalanine, tyrosine and tryptophan transport to neurons) (Matt 1988, D Gonzal-Rairez 1995, Weiner 1995). By implication cerebellar

degeneration could lead to lesion of the cerebellum giving rise to signs and symptoms, namely shook, cardiovascular collapse, acute renal failure, and severe gastrointestinal damage. Acute oral poisoning results primarily in hemorrhagic gastritis and colitis; the ultimate damage is to the kidney. Clinical symptoms of acute intoxication include pharynigitis, dysphagia, abdominal pain, nausea and vomiting, bloody diarrhea, and shock. Later, swelling of the salivary glands, stomatitis, loosening of the teeth, nephritis, anuria, and hepatitis occur (Stockinger 1981, Marls et al 1981).

Considering all these findings, it could be concluded that oral administration of mercury II chloride for two weeks causes degeneration of he neurons of the cerebellum especially at high doses of 23mg/kg and 52mg/kg. In addition it can bring about a decrease in physical activities, mucus secretion from the nostril of adult wistar rats.

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