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Research article

Pathological effects of mercury chloride on reproductive system in white rats

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Abstract

The present study was undertaken to know the reproductive toxicity of mercury chloride in male and females of white rats. This study was used twelve (6 male and 6 females) white rats of approximately of the same body weight (200-220 g) divided equally in to 3 groups; the first group (T1) was received mercury chloride (1mg/kg B.W intraperitoneally once daily for 30 days). While the second group (T2) was received, mercury chloride (1.5mg/kg B.W intraperitoneally once daily for 30 days). Third group was received only 0.2ml of Distilled water considered as control group. At the end of experiment, the animals were sacrificed and small pieces of (2cm³) were taken from ovary, uterus and testis of all animals to histopathology. Histopathological sections of these organs of (T2) group was showed severe pathological changes characterized by vaculation in epithelial cells of uterus, cystic dilatation of uterine glands with degeneration of epithelial lining of its ,hemorrhage and decrease in number of growing follicles in ovary also there were sever pathological changes in the testes. While (T1) group was showed less pathological changes characterized by hyperplasia of epithelial lining with few and small uterine gland in uterus, presence of large secondary follicles in ovary and there were less pathological changes in testes.

Keyword: Mercury Chloride, Pathological effects, White rats.

Introduction

Mercury is one of the most dangerous environmental pollutants to living organisms and it is considered as one of the heavy metal, which is the chief component of various medicines (1). Its discharge can occur through natural sources such as volcanoes or anthropogenic activities such as industrialized processes, agriculture and metallization (2) The release of mercury can cause increase in the amount of atmosphere mercury, which enters to the soil-water distribution cycles where it can remain in circulation for many years. Mercury poisoning is occur due to exposure to mercury or mercury compounds lead to various toxic effects depending on route of

exposure and chemical form of its (3). Animals and humans reacts with their environment daily and are exposed to a lot of chemicals and heavy metals present in the environment by food, air and water(4). It causes a variety of health effects including respiratory, neurological, reproductive, renal, immune and dermatological effects (5). Mercury is an element found in the environment causing oxidative stress in the exposed living organisms leading to tissue damage (6). Its toxicity is linked to its high affinity for sulfhydryl groups (-SH), forming stable complexes causing several changes, like structural changes of sulfhydryl enzymes and inactivation of their active sites (7).

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Mercury influences antioxidant mechanisms in the cell lead to cell degeneration, lack of membrane safety and then cellular necrosis (8). Most of the studies with experimental animals are undertaking on male adult rats or pups exposed for short periods to mercury (9), (10) and (11). However, few studies using acute treatments on female's reproductive system have been carried out. So my presence study is make to investigate the pathological changes induced by difference dosage of mercury chloride on male and female reproductive system of white rats for 30 days.

Materials and Methods

Ethical approval

The Animal Ethical Committee of Veterinary Medicine College, University of Al-Qadisiyah, Iraq, has approved the present study under permission No: 416

Experimental animals: The present study was conducted on (12)white rats (6 male and 6 female) of approximately the same age and body weight(200-220gm).The animals were housed in plastic cages in an air conditioned room with temperature maintained at 25 ± 2 C in animals house of Veterinary. Medicine Collage/ University of Al-Qadisiyah under 12 hours light/12hours dark. Rats were given food pellets and water ad libitum and divided

Results

Histopathological section from uterus, ovary and testis from treated rats were examined under light microscope. Uterus: Uterus of second group (high dose group) show vaculation of endometrium cells, cystic dilatation of endometrium gland with degeneration of epithelium which lining these glands Figures (1, 2). while the first group(low dose group) show less pathological changes characterized by hyperplasia of endometrium with infiltration of inflammatory cells also there were few and small of uterine glands Figures (3, 4).

into three groups 4 rats each (2 male and 2 females) and this study continued for 30 days.

Chemicals: Mercury chloride is a heavy metal obtained from central laboratory in University of Al-Qadisiyah. Mercury chloride (BDH chemical Ltd (England)). The rats administered 1.5mg/kg B.W and 1.0 mg/kg B.W (12) as chronic doses.

Experimental design: Twelve white rats, both sexes were divided into 3 groups (4 rats each)

and were treated as following:

1st group was injected with (1mg/kg B.W) intraperitoneally .

2nd group was injected with (1.5mg/kg B.W) intraperitoneally.

3rd group was injected with (0.2ml) distal water as control group.

Tissue samples:

The rats were sacrificed and the ovary, uterus and testis were dislocated by sterile scissor. Then 10% formalin fixed, small pieces (2cm³) were taken from these organs of all groups for histopathology. Processed routinely in histokinette, cut at 5 Mm thickness by microtome (Jony 4291, West Germany) and stained with Haematoxylin &Eosin stain then examined under light microscope (13).

Ovary. The present study revealed that the severity of pathological changes on the ovary was increased with increased of doses, in second group (high dose group). We showed decreased number of growing follicles, also we showed small ovarian follicles at different stages of maturation including primary and secondary follicles also there were hemorrhage in stroma of ovary Figure (5). While in first group (low dose group) these changes is less compared with high dose group and can we showed ovarian follicles at different stages of maturation including

primary, growing and mature follicles. The mature follicle appeared nearer to the surface of the ovary and has the ova Figure (6). Testis: Histopathological examination of testis in second group (high dose group) showing extensive degeneration in some tubules characterized by vaculation of

Spermatogonia, severe suppression of spermatogenesis Figure (7) and There are few Leydig cells Figure (8). The severity is depending on the dose whereas these changes is mild in first group (low dose group) which characterized by slight degenerations in spermatids and spermatozoa Figure (9).

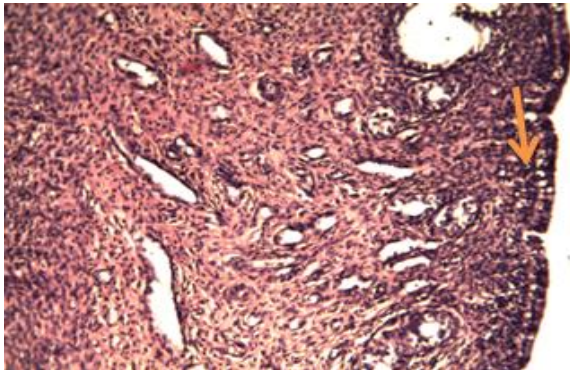


Figure (1): Histological section of uterus in rats treated with mercury chloride (1.5mg/kgB.W) show of endometrium cells vaculation. 10XH&E.

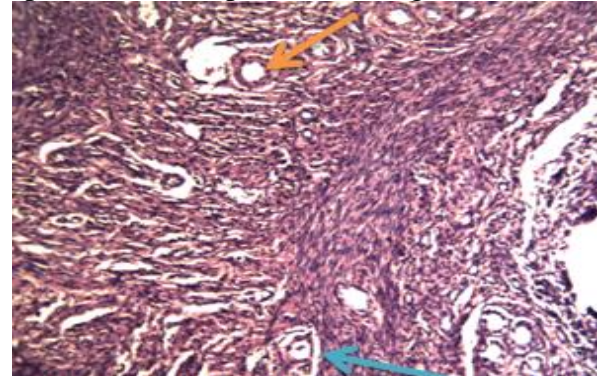


Figure (2): Histological section of uterus in rats treated with mercury chloride (1.5mg/kgB.W) show cystic dilatation of endometrium gland (red arrow) with degeneration of epithelium which lining these glands (blue arrow).10XH&E.

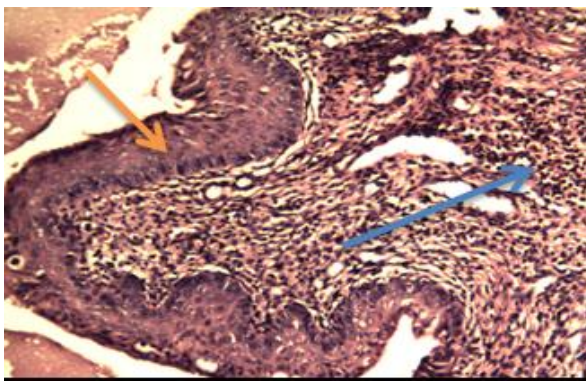


Figure (3): Histological section of uterus in rats treated with mercury chloride (1mg/kgB.W) show hyperplasia of endometrium (red arrow) with infiltration of inflammatory cells (blue arrow). 10XH&E.

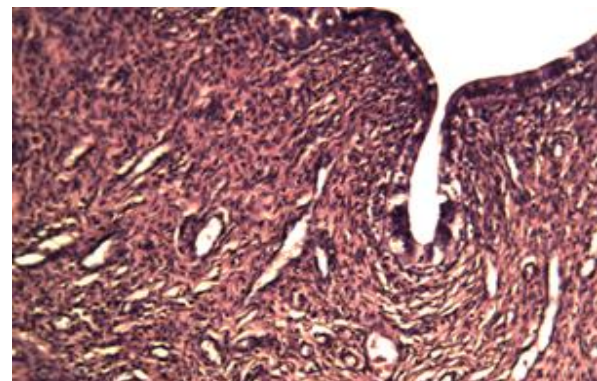


Figure (4): Histological section of uterus in rats treated with mercury chloride (1mg/kgB.W) show few and small of uterine glands. 10XH&E.

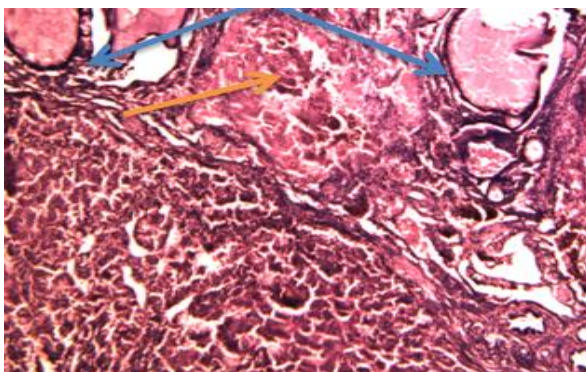


Figure (5): Histological section of ovary in rats treated with mercury chloride (1.5mg/kgB.W) show small and decreased number of growing follicles (blue arrow) and haemorrhage (red arrow).10XH&E.

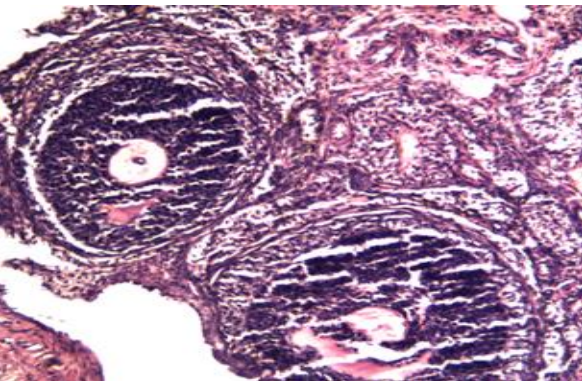


Figure (6): Histological section of ovary in rats treated with mercury chloride (1mg/kgB.W) show normal section of ovary of characterized by present of mature follicle.10XH&E.

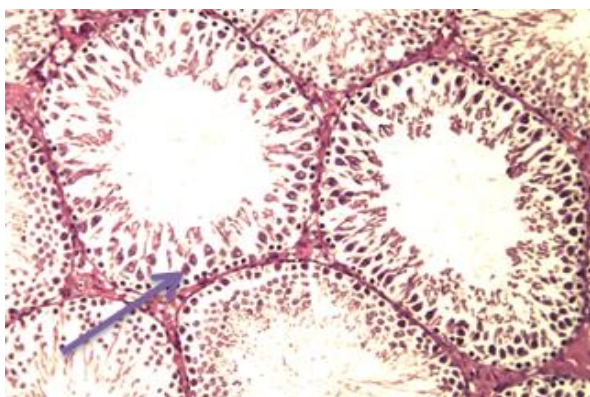


Figure (7): Histological section of testis in rats treated with mercury chloride (1.5mg/kgB.W) show vacuolation of spermatogonia.10XH&E

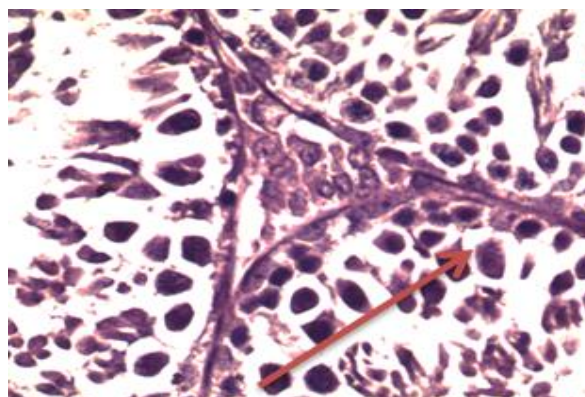


Figure (8): Histological section of testis in rats treated with mercury chloride (1.5mg/kgB.W) show vacuolation of Spermatogonia (red arrow) and There are few Leydig cells (blue arrow).40XH&E



Figure (9): Histological section of testis in rats treated with mercury chloride (1mg/kgB.W) show slight degenerations in spermatids and spermatozoa.10XH&E.

Discussion

Reproductive problem like abortion, congenital malformation, infertility and decrease in ovulation are the most signs conducted with mercury toxicity (14). The present study demonstrated that mercury chloride has toxic effects on reproductive system of rats in high doses due to histopathological changes, which showed in these organs. The changes in uterus of second group (high dose group) show vacuolation of endometrium cells, cystic dilatation of endometrium gland with degeneration of epithelium which lining these glands. while the first group (low dose group) show less pathological changes characterized by hyperplasia of endometrium with infiltration of inflammatory cells also there were few and small of uterine glands

.These changes occur may be due to altering of levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen and progesterone (14, 15) and the results agreed with (16, 17) who recorded that high dose of mercury has been shown to inhibit the release of FSH and LH from the anterior pituitary which in turn can effect estrogen and progesterone levels leading influential on endometrium. The present study revealed that pathological changes on the ovary in second group (high dose group) showed decreased in number of growing follicles also we showed small ovarian follicles at different stages of maturation including primary and secondary follicles also there were hemorrhage in stroma of ovary. While in first group (low dose group) these changes is less

compared with high dose group and can we showed ovarian follicles at different stages of maturation including primary, growing and mature follicles. The mature follicle appeared nearer to the surface of the ovary and has the ova. These changes are agreed with (18). Who were revealed that chronic nonlethal levels of mercury induced histopathological changes in the ovary of rats interfering with their breeding. In accordance (19) revealed that oral given of mercuric chloride in a dosage of 1.5 mg/kg BW using in vivo and in vitro fertilization of mouse could damage the ovary function and reduce the number of ovulation oocytes. These pathological changes in the present study may be explained by the direct toxic effect of mercury on the ovarian tissues by its high affinity for sulfhydryl groups (-SH), forming stable complexes also its reacts with phosphoryl, carboxyl, and amide groups resulting in many dysfunction of enzymes and structural proteins(20). However, it is possible that mercury chloride accumulating in the ovaries and having little effect on ovulation (21). or indirectly via the hypothalamus– pituitary– ovarian axis (22). While the changes is less and may be near to normal is may be due to the less effect of mercury in ovary and ovulation in low dose (23). Histopathological

examination of testis in second group (high dose group) showing extensive degeneration in some tubules characterized by vacuolation of Spermatogonia, severe suppression of spermatogenesis and There are few Leydig cells. The severity is depending on the dose whereas these changes is mild in first group (low dose group) which characterized by slight degenerations in spermatids and spermatozoa. The result of our study is in agreement with the results obtained from previous study (24) and (25) They mention HgCl₂-induced testicular damage in animals is commonly associated with Spermatogonia damage, spermatid degeneration, Leydig cell dysfunction, testicular disorder and giant cell formation. Various mechanisms have been suggested to explain Hg induced cellular toxicity. Among these mechanisms, lipid peroxidation has been considered a primary initiating mechanism during Hg injuries (26). Many studied recorded that an increase in free radical formation relative to loss of antioxidant defense system (27). Also (27) suggested that HgCl₂ generates free radicals by interacting with DNA that interferes with antioxidant defense system and results in the tissue injury, testis and epididymis are more susceptible to oxidative damage leading to their functional inactivation (28).

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-Li P, Feng XB, Qiu GL, Shang LH, Li ZG. Mercury pollution in Asia: a review of the contaminated sites. *J Hazard Mater.* (2009); 168:591-601.
- 3-Kevin M Rice, Ernest M Walker, Jr, Miaozong Wu, Chris Gillette, Eric R. Blough. Environmental Mercury and Its Toxic Effects. *J Prev Med Public Health.* (2014) Mar; 47(2): 74–83.
- 4-Burger J, Jettner C, Gochfeld M. Locational differences in mercury and selenium levels in 19 species of saltwater fish from New Jersey. *Journal of Toxicology and Environmental Health A*, (2011); vol. 74, n. 13, p. 863-874.
- 5-Nabi SA, Bushra R AL-Othman, ZH Inanuddin, Naushad MU. Synthesis characterization and analysis applications of a new composite cation exchange material acetone nitrile stannic (IV) selenite: Adsorption behavior of toxic metal ions in non-ionic surfactant medium, *separation Sci: Technol., Inpress*; (2011).
- 6-Ekstrand J, Bjorkman L, Edlund C, Sandborgh E. Toxicological aspects on the release and systemic uptake of mercury from dental amalgam. *Euro J Oral Sci.* (1998); 106: 678–686.
- 7-Rooney JP. The role of thiols, dithiols, nutritional factors and interacting ligands in the toxicology of mercury. *Toxicology.* (2007); 234:145–156.
- 8-Agarwal R, Goel SK, Chandra R, Behari JR. Role of vitamin E in preventing acute mercury toxicity in rat. *Environ Toxicol Pharmacol.* (2010); 29:70–78.
- 9-Favero AM, Oliveira CS, Franciscato C, Oliveira VA, Pereira JSF, Bertoni CM, et al. Lactating

- and non-lactating rats differ to renal toxicity induced by mercuric chloride: the preventive effect of zinc chloride. *Cell Biochem Funct.* (2014); 32:420–428.
- 10-Moraes-Silva L, Bueno TM, Franciscato C, Oliveira CS, Peixoto NC, Pereira ME. Mercury chloride increases hepatic alanine aminotransferase and glucose 6-phosphatase activities in newborn rats in vivo. *Cell Biol Int.* (2012); 36:561–566.
- 11-Oliveira CS, Favero AM, Franciscato C, Luz SCA, Pereira ME. Distinct response of lactating and nonlactating rats exposed to inorganic mercury on hepatic δ -aminolevulinic acid dehydratase activity. *Biol Trace Elem Res.* 2014; 158:230–237.
- 12-Akhlas Abdul-Hamza Al-Alwany, Kareem H Rasheed. Toxic effect of mercury chloride and Selenium treatment in blood value in male rate. *Scientific Journal of Karbelaa University* (2013); Vol.(11)No.(2)
- 13-Luna LG. Manual of histologic staining methods of the armed force institute of pathology. 3rd ed., McGraw Hill Book Company, Toronto. London, Sydney. (1968); p.p.12-31.
- 14-Davis BJ, Price HC, O'Connor RW, Fernando R, Rowland AS, Morgan DL. Mercury vapor and female reproductive toxicity. *Toxicol Sci.* (2001); 59(2):291–296.
- 15-Schrag SD, Dixon RL. Occupational exposures associated with male reproductive dysfunction. *Annu Rev Pharmacol Toxicol.* (1985); 25:567–592.
- 16-Chen YW, Huang CF, Tsai KS, Yang RS, Yen CC, Yang CY. Methylmercury induces pancreatic beta-cell apoptosis and dysfunction. *Chem Res Toxicol.* (2006); 19(8):1080–1085.
- 17-Andrei N. Tchernitchin, Leonardo Gaete, Rodrigo Bustamante, and Aracelly Báez. Effect of Prenatal Exposure to Lead on Estrogen Action in the Prepubertal Rat. (2011); 329692, 8
- 18-Dey S, Bhattacharya S. Ovarian damage to *Channa punctatus* after chronic exposure to low concentrations of Elsan, mercury, and ammonia. *Ecotoxicol. Environ. Safe.* (1989); 17:247–257.
- 19-Shen W, Chen Y, Li C, Q Ji. Effect of mercury chloride on the reproductive function and visceral organ of female mouse. *Wei Sheng Yen Chiu J. Hyg. Res.* (2000); 29, 75–77.
- 20-Merfat Oreby, Reda ElBakary, Tarek Al-nimer. Mercury level and histopathological effects of one Egyptian skin lightening cream on the ovary of adult albino rats. *Departments of Forensic Medicine and Clinical Toxicology* (2010).
- 21-Al-Saleh I, Shinwari N and Al-Amodi M. Accumulation of Mercury in Ovaries of Mice After the Application of Skin-lightening Creams. *Biol Trace Elem Res.* (2009); 131:43–54.
- 22-Hoyer PB. Damage to ovarian development and function. *Cell Tissue Res.* 2005; 322 (1):99–106.
- 23-JC Heath Y Abdelmageed, TD Braden, AC Nichols, DA. Steffy The effects of chronic mercuric chloride ingestion in female Sprague–Dawley rats on fertility and reproduction, *Food Chem Toxicol.* (2009); July; 47(7): 1600.
- 24-Rajiha A. Al.Naimi, Eman HY Al-tae Layth AM Alsoufi, Ghussan AK Al-Neamah. The therapeutic effect of combined aqueous extract of coriander sativum l. and allium sativum l. on the mercuric chloride induced reproductive toxicity in adult male rats *Bas.j.vet.Res.* (2013); Vol.12, No.2, 581.
- 25-Muthu K, Krishnamoorthy P. Effect of Vitamin C and Vitamin E on Mercuric Chloride -Induced Reproductive Toxicity in Male Rats. *Biochem Pharmacol.* (2012); 1:102.
- 26-Samir Haouem, Karima Dardouri and Abdelhamid El Hani. Simultaneous Effect of Cadmium and Mercury on Some Biochemical Parameters of Testis Function In Male Rats *J. Curr. Chem. Pharm. Sc.:* 5(1), (2015); 1-6 ISSN 2277-2871
- 27-Heath JC, Banna KM, Reed MN, Pesek EF, Cole N, et al. Dietary selenium protects against selected signs of aging and methylmercury exposure. *Neurotoxicology*, 2010; 31: 169-179.
- 28-Wang CJ, Wang JM, Lin WL, Chu CY, Chou FP. Protective effect of Hibiscus anthocyanins against tert-butyl hydroperoxide-induced hepatic toxicity in rats. *Food Chem Toxicol.* (2012); 38: 411-416.