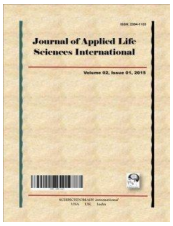

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Cadmium Chloride Reduces Testicular and Epididymal Weights with Degenerative Histoarchitectural Changes in Testis and Pituitary Gland of Wistar Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author MOO carried out the bench work, author ENE wrote and monitored the manuscript, author MOE managed the literature searches, author GTO performed the statistical analysis, author AON designed and supervised the study.

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ABSTRACT

In diagnostic medicine, one of the numerous points for infertility probe is the Hypothalamo-Hypophyseal-Pituitary-Gonadal Axis (HPGA). In males, this neuro-endocrine pathway is a major influence in the biosynthesis and regulation of Testosterone (from the testes), which is responsible for their primary and secondary sexual characteristics. This study sought to investigate the modulatory effect(s) of Cadmium chloride (CC) on the weight and histology of the Testis and anterior pituitary gland; using Wistar rats as an experimental model. Ten (10) male acclimatized rats (between 186 g and 193 g) were grouped (n=5 per group) into two (A=control and B=experimental). While group A received normal rats chow and tap water ad libitum, group B was

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fed normal rat chow and 0.5 mg/kg of CC daily in drinking water for 5 weeks (LD_{50} of CC=88 mg/kg). After a period of experimentation, animals were weighed and sacrificed with testis and pituitary glands harvested, blotted dry and weighed. Tissue sections for microscope studies were prepared. Students' t-test proved a significant reduction in testicular weight, with the insignificant outcome for body and epididymal weights. Histomorphological sections through the testes and pituitary gland showed degenerative changes as well. It is recommended that attention is given to the environmental needs of the oil producing communities, were inhabitants are mostly prone to cadmium chloride (being a traceable component of crude oil), especially in the provision of good health care delivery system.

Keywords: Cadmium chloride; testes, epididymis; pituitary gland; gonad.

1. INTRODUCTION

Though knowledge of the existence of poisonous substances is as old as the history of man, humans increasingly leave in degenerative chemical environment with an estimated 60,000 chemicals added annually to the market as a result of industrialization and creation of large urban centers[1].

Cadmium (Cd) is a naturally occurring metallic element that is used for electroplating and galvanization processes, in the production of pigments, in batteries, as a chemical reagent, and in miscellaneous industrial processes[2]. Its compounds have varying degrees of solubility ranging from very soluble to nearly insoluble. The solubility affects their absorption and toxicity. Exposure to cadmium and cadmium compounds may occur in both occupational and environmental settings, the latter primarily via the diet and drinking water

Cadmium is efficiently absorbed by the lungs (30 to 60%) than the gastrointestinal tract, with the latter being a saturable process [3]. Cadmium is transported in the blood and accumulates primarily in the liver and kidneys [4]. Its burden (especially in the kidneys and liver) can increase in a linear fashion up to about 50 or 60 years of age after which the body burden remains somewhat constant. Metabolic transformations of cadmium are limited to its binding to protein and non-protein sulfhydryl groups, and various macromolecules, such as metallothionein, which is especially important in the kidneys and liver2. Cadmium is excreted primarily in the urine.

Several studies posit that acute oral exposure to 20-30 g of Cadmium can be fatal to humans. Exposure to lower amounts may cause gastrointestinal irritation, vomiting, abdominal pain, and diarrhea2. Though Cadmium's involvement in hypertension is yet to be fully understood4, however, prolonged exposure to it has been reported to affect the kidneys, causing tubular proteinosis. Dietary intake of cadmium has also been implicated in osteomalacia, osteoporosis and spontaneous fractures, conditions collectively termed "itai-itai" (ouch-ouch) disease and originally documented in postmenopausal women in cadmium-contaminated areas of Japan [5]. Exposure to Cadmium has also been implicated in hypertensive disorders, a situation that is currently not thoroughly understood or verified [2].

Inhalation exposure to cadmium and its compounds have been reported to cause several effects including headache, chest pains, muscular weakness, pulmonary edema, and death. Renal toxicity (tubular proteinosis) has also been found to occur from inhalation exposure to cadmium [4].

1.1 Aim of Study

This study aimed at determining the effect of Cadmium ingestion on the weight and histology of the anterior pituitary gland and testes, using wistar rats as an experimental model. Specifically, the study attempted to:

i. Measure the anterior pituitary gland and the testes
ii. Determine the effect of cadmium on body weight, as well as weights of testis and pituitary gland.
iii. Determine the effect of cadmium on the histo-morphology of anterior pituitary gland.

2. MATERIALS AND METHODS

2.1 Study Design

This study investigated the modulatory effect(s) of Cadmium chloride (CC) on the weight and histology of the Testis and anterior pituitary

gland; using wistar rats as an experimental model. Ten (10) male acclimatized rats (between 186 g and 193 g) were grouped (n=5 per group) into two (A=control and B=experimental). While group A received normal rats chow and tap water ad libitum, group B was fed normal rat chow and 0.5 mg/kg of CC daily in drinking water for 5 weeks (LD_{50} of CC=88 mg/kg). After the period of experimentation, animals were weighed and sacrificed with testis and pituitary glands harvested, blotted dry and weighed. Tissue sections for microscope studies were prepared

2.2 Animals

Ten (10) male wistar rats, not more than three months of age (each) where obtained from the College of Medicine, Ambrose Alli University (AAU), Ekpoma, Edo State. The reason for restricting their age to 3 months was because laboratory study of lifespan is currently only feasible for short-lived species, and rats happen to show short life expectancy (about 3 years). This implies that as they age, there is bound to be a decline in their renal clearance of study metal (cadmium chloride). The rats were transported to the animal house of the College of Health Sciences, Delta State University (DELSU), Abraka, Delta State, Nigeria, where they were housed in a wooden cage. They were weighed and confirmed to have between 186 g-193 g. Animals were then grouped into control group A (received normal rats chow and tap water ad libitum) and experimental group B (received normal rat chow and 0.5 mg/kg of Cadmium Chloride daily in drinking water for 5 weeks).

2.3 Cadmium Chloride (CC)

CC administration was analytically graded based on the concentration (in gram/dm3) per unit weight (kg equivalence of between 186-193 g) of each rat. This was done to avoid overdose as CC reportedly has LD_{50} of 88 mg/kg [2]. Issues of drug-drug interactions were also considered.

2.4 Ethical Approval

Ethical approval was obtained from the Research and Ethics committee of the college of Health Sciences, Delta State University, Abraka, Delta State.

2.5 Procedure

Cadmium salt (Obtained from petroleum training institute, Warri, Delta State, Nigeria) was administered for five weeks, following which animals were weighed and sacrificed. Testis and Pituitary glands were harvested and blotted dry, then, weighed. Tissue sections were prepared for microscope study.

2.6 Sacrifice and Tissue Extraction

12 hours following the last administration, the animals (per group) were re-weighed and immediately given a cervical dislocation (after anaesthetizing with chloroform). Thereafter, the Testis and Pituitary gland were carefully removed and fixed in a 10% formal-saline for 48 hours. The reason for using formal-saline was to keep the tissues at constancy with their ex-vivo environment.

2.7 Tissue Processing

With the assistance of a certified anatomist from the Department of Human Anatomy and Cell Biology, Delta State University, harvested organs (Testis and Pituitary gland) were subjected to standard tissue processing techniques that included dehydration, fixation, clearing, impregnation, embedding, sectioning and staining with Haematoxylin and Eosin (H and E) for appropriate microscopy. Fixation was achieved t in six hours using Bowman's fluid, and then, transferring to 50% alcohol to dehydrate harvested tissues. Absolute alcohol and xylem were then used to achieve clearing while embedding tissues in paraffin wax. Serial sections were cut (5microns) thick with the aid of a rotatory microtome. Photomicrographs were then captured with the aid of a 5.0 megapixel microscope of about 500 resolution capacity, having a serial port for connection with a computer's Universal Serial Board (USB).

2.8 Statistical Analysis

Data obtained for the study were expressed as Mean ± SD (standard deviation). Significant differences were tested with the student t-test, with margin of error valued at 0.05, where p-values < .05 were considered statistically significant.

3. RESULTS

See below for result presentation with tables and plates.

Table 1. Shows mean weights of body, testis, epididymis and pituitary gland for control and experimental groups

Group	Body weight (g)	Testis weight (g)	Epididymis (g)	Pituitary gland
A (control)	183±13.26	1.80±0.42	1.13±0.30	0.585±0.01
B	167.4±593	1.00±0.27	0.66±0.11	0.35±0.006
T Critical	2.31	2.31	2.31	2.31
T Calculated	2.12	3.57	2.13	8.7
p-value	p < 0.05	p > 0.05	p < 0.05	p > 0.05
Remark	Insignificant	Significant	Insignificant	Significant

Results are presented as Mean ± Standard deviation (M±SD) of obtained data

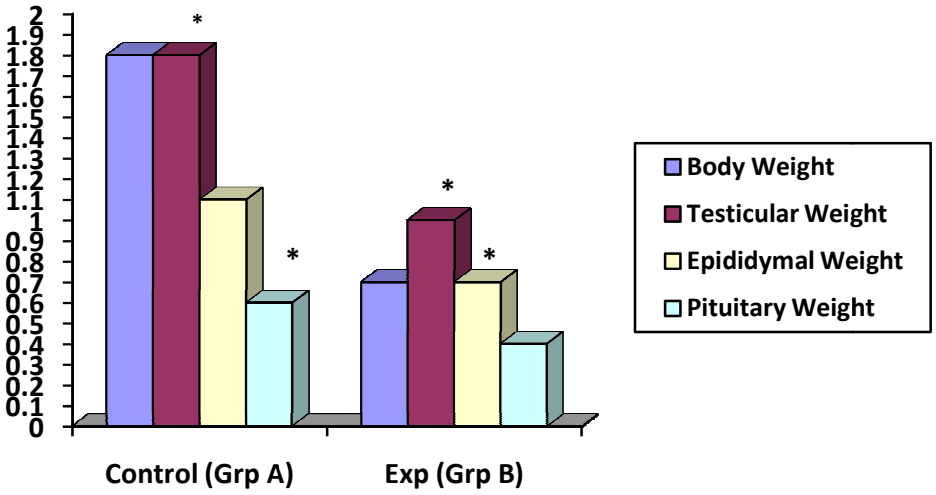

Fig. 1. Relationship between Groups A (control) and B (experimental)
*Keys: *Correlation is significant at the .05 level*

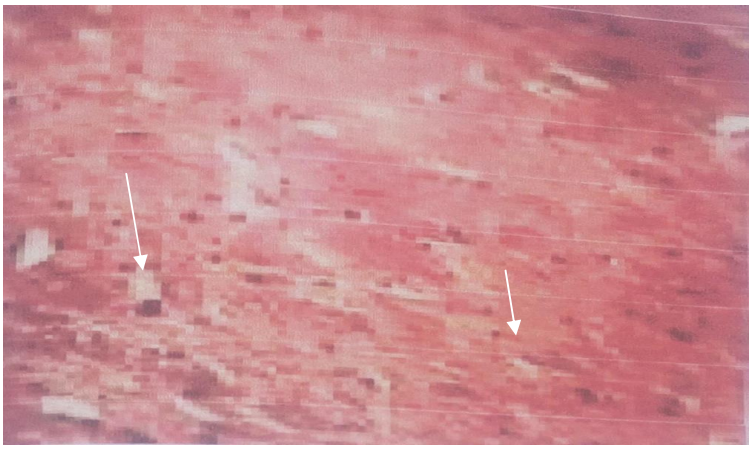

Fig. 2. Showing tissue micrograph of pituitary gland for control group
Control (Pituitary gland) x400. Here, reticulocytes are dispersed in abundant neuro-fibrillatory stroma. Also seen are clusters of chromophobes.

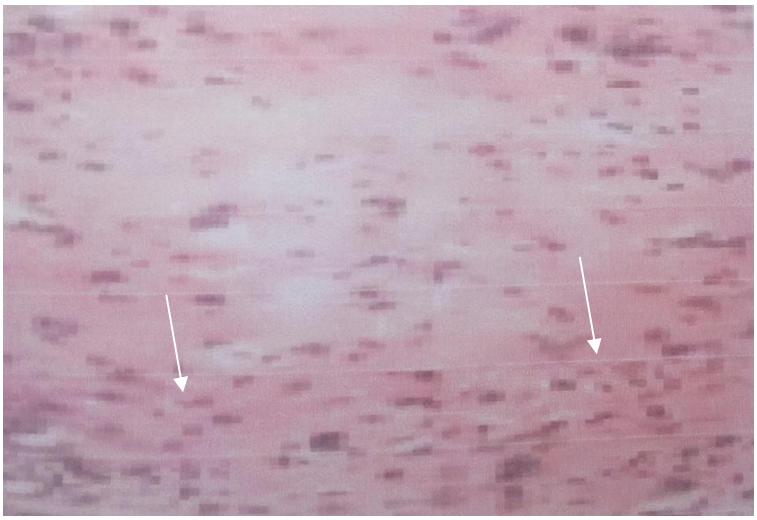

Fig. 3. Showing tissue micrograph of pituitary gland for experimental group

Experimental (Pituitary gland with Cadmium chloride) x400. Notice a few pitusized dispersion in an intermediate fibrillatory stroma, some of which have undergone necrosis and picnosis

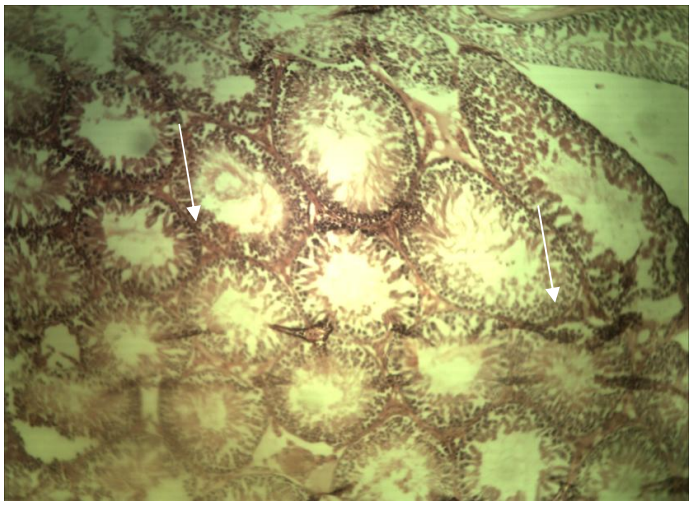

Fig. 4. Showing tissue micrograph of testis for control group

Control (Testes) x100. Visible here are variably sized seminiferous tubules with spermatocytes at different levels of maturation in the lumen. The surrounding interstitial connective tissue is cellular. A few blood vessels are also seen in the interstitium.

4. DISCUSSION

Basically, this study was focused on identifying the effect(s) that Cadmium (Cd) has on the body weights and selected visceral (specifically Testes and the Pituitary gland). To this point, careful observation of results found a partial change in the histological structures of the pituitary gland; the chromophobes, acidophiles and basophiles. Chromophobes, which have affinity for stains had over 60% of its secretary cells affected. Whereas, acidophiles were increased in Cd treated group wherein basophilic cells were not really affected. Edematous changes in stoma leading to increase vacuolization, lymphocyte infiltration, replacement of normal cell by glial cells and increase in chromophobes may be responsible for the alterations in histo-architecture of the testis as observed in the experimental group. We are yet to find reports of such changes in crude oil treated rats or other animals.

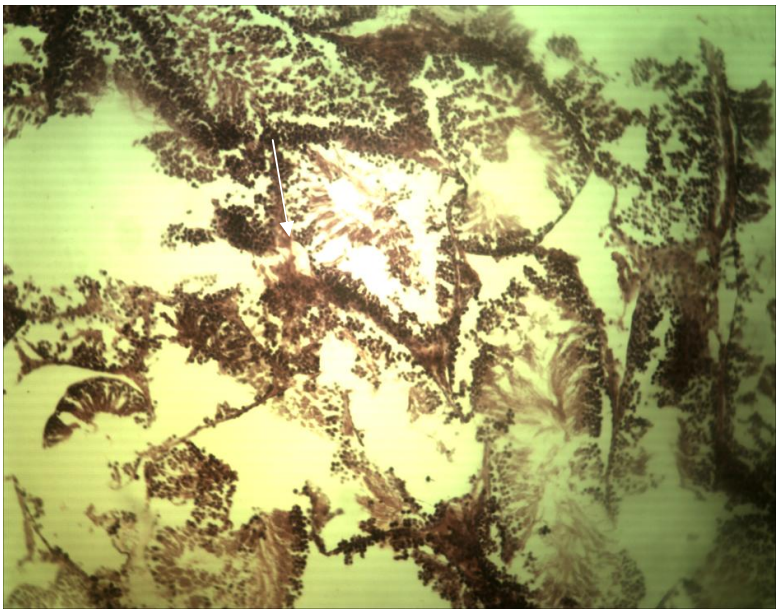

Fig. 5. Showing tissue micrograph of testis for experimental group
Experimental (Testis with cadmium chloride) x100. Section shows destruction of normal histology with loss of seminiferous tubules and interstitial cells.

On the histology of the testes, cadmium chloride at 0.5 mg/kg of body weight overly produced degenerative lesion in in the tests. Whiteman et al (2002) had postulate that high doses of cadmium chloride can cause severe testicular necrosis in rats [6]. This experiment suggests that the cumulative effect of cadmium on the testes is that of near loss of normal architecture, necrosis and loss of seminal epithelium. We observed degenerative changes in testis of cadmium chloride treated rats with disruption of basement membrane, increase in interstitial space with reduced cellularity, sperm maturation arrest were some of the changes observed in testis of treated rats. These findings are in agreement with those of Huang, et al (2008) who observed degenerative changes in rats exposed to motorcycle exhaust, and Ebenezer et al 2009 who reported severe congestion of interstitial vessels, decreased germinal epithelium, and increased number of vacuolization in testes of rats treated with crude oil [7]. These degenerative studies may explain the reduction in fecundity observed in the male treated rats in their research.

Upon comparison, study found experimental group B to have weighed an average of 1.0 g, 0.66 g, and 0.35 g in their Testes, epidermal, and pituitary gland respectively. Whereas, control (group A) had an average of 1.80 g, 1.13 g, and 0.585 g in same organs respectively. Total body weight of animals was also accessed and observed average 183 g and 167 g respectively in control (group A, n=5) and cadmium treated group (B). In the control group, histological microscopy of the testis was similar to group B (Cd treated).

On the pituitary gland, cadmium chloride at 0.5 mg/kg body weight for 5 wks produced necrotic lesions. These changes in the pituitary gland may bear negatively on the reproduction of Wister rats. Therefore, our findings of reduction in fecundity were not surprising. A partial change was also seen in the histology of the pituitary glands of both groups. Here, over 60% of the secretory cells were affected. Acidophil cells (with cytoplasmic granules) increased in cadmium-treated rats without any alterations in the basophils. Upon comparison, there was a noticeable difference between the extents of damage of the chromophobes of rats with those recorded for potoroo over a similar time period (Parizien, 1760).

4.1 Benefits of Study

Data generated from this study will provide objective basis for which governments could development policies for a comprehensive medical care and rehabilitation programmes for

inhabitants of crude oil impacted communities. This is especially so as the outcome of the study shows alterations in testicular histo-architecture and poor reproductive indices in crude petroleum oil impacted community.

5. CONCLUSION

Cadmium chloride (contained in crude oil) has adverse effects on the testis and pituitary gland. This is possible by causing alterations in levels of reproductive hormones which usually function physiologically at small and highly regulated concentrations or by cytotoxic effects on reproductive organs and cells.

6. RECOMMENDATIONS

For further studies, we make the following recommendations:

1. That further studies should be designed to increase sample size.
2. Special stains should be used for advanced histological and histochemical studies.

To government agencies, we make the following recommendations:

1. That attention be given to the environmental needs of the oil producing communities whose residents are prone to the effects seen in this study, have been exposed to some dose (directly or indirectly) of Cadmium chloride overtime.
2. There is need for provision of good health care delivery system for the oil producing communities.
3. Government should consider the possibility of providing free vitamins and other supplements to inhabitants of oil producing communities.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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