Original Article

Lithium Induced Male Reproductive Organ Injury in Albino Rats

Tazeen Kohari[1], Meshaal Azhar[2], Faryal Azhar[2] and Usama Faruqui[3]

ABSTRACT

Objective: Metal ingestion causes degenerative injury to seminiferous tubules and antipsychotics drugs like Lithium brings deleterious changes to seminiferous tubules in this study the diameter of seminiferous tubules was measured and documented.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Anatomy department and Animal house of Basic Medical Sciences Institute from May, 2013 to June, 2013 for a period of 02 months.

Materials and Methods: Three months of age weighing 270 -290 grams were chosen for this study and distributed into two equal groups A and B. Group A served as control, received only laboratory diet group B received Table Lithium Carbonate 20 mg/kg body weight for four weeks. At end of the study period the dissection of lower abdomen was carried out and testis were removed and the diameter of seminiferous tubules in both groups were measured and documented.

Results: The total number of albino rats selected for this study was twenty. The results showed a highly significantly increased diameter of seminiferous tubules P value <.001 in Group A animals as compared to group B animals and a highly significantly decreased P value < .001 diameter of seminiferous tubules in Group B Animals as compared to Group A rodents.

Conclusion: Lithium carbonate causes highly significant decreased thickness of seminiferous tubules.

Key Words: Antipsychotic drugs, seminiferous tubules, deleterious effects

Citation of article: Kohari T, Azhar M, Azhar F, Faruqui U. Lithium Induced Male Reproductive Organ Injury in Albino Rats. Med Forum 2021;32(12):107-109.

INTRODUCTION

Male reproductive organs being the testis are two in number [1] one on each side. Each testis is present in the scrotal sac. Each testis has coiled seminiferous tubules[2] which are responsible for the production of sperms.[3]

It has been documented that seminiferous tubular, diameter [4,5] ranges between 200-300 µm. Toxins, [6] Heavy soft metals like lead [7] and lightweight alkali metals like Lithium[8] decreases spermatocytes and diameter of testicular tubules. Many deleterious effects of lithium are documented on various organs like Central nervous system, Kidneys, Thyroid, and Parathyroid also, the damaging effects of Lithium on testis have been documented by Saad et al[9] 2017 they in their research found that Lithium causes, decreased diameter of seminiferous tubules.

1. Department of Anatomy, Islam Medical and Dental College, Pasrur, Sialkot.
2. Department of Medicine, Ghurki Trust Hospital / LMDC, Lahore.
3. Department of Radiology, Shaukat Khanum Memorial Hospital, Lahore.

Correspondence: Dr. Tazeen Kohari, Department of Anatomy, Islam Medical and Dental College, Sialkot
Contact No: 0323-2967849
Email: tazeenk67@gmail.com

Received: August, 2021
Accepted: October, 2021
Printed: December, 2021

Still there is decrement of literature on the damaging effects of lithium on testis and seminiferous tubules; we conducted this study so as to bring to light the damaging effects of the drug on seminiferous tubules.

MATERIALS AND METHODS

Our experimental study was designed and conducted at Anatomy department Basic Medical Sciences Institute Jinnah Post graduate Medical Centre Karachi from fifth May to 5th June 2013. Total twenty Albino rats of three months of age and weight ranging between 270 -290 Grams were taken from the Animal House of Basic Medical Science Institute, Jinnah Postgraduate Medical Centre, and Karachi. They were kept under observation for seven days prior to the commencement of the study.

The animals were divided into two groups A, B each comprising 10 rats:

Group A: served as control

Group B: received. Lithium Carbonate of 20 mg[10] /g /day

November--2016-1.qx

The albino rats were kept under laboratory favourable environment, at animal house, water and food supplied ad libitum. At the end of the period of treatment, rats were sacrificed under light Ether[11] anesthesia. A midline abdominal incision [12] extending up to the skin of scrotum, all coverings of scrotum were dissected and both testes were identified and removed.

Testis after cutting them longitudinally were fixed in Bouins fluid for 24 hours[13]. After fixation of the tissue it was passed in ascending grades of alcohol and placed in paraffin blocks. Almost five micron thick sections of testis were taken in both groups. The level of significance (P) was calculated by the help of student's t-distribution table. The highly significance level was considered as p<.001 All the calculations were done utilizing, SPSS version 2007.

RESULTS

The total number of albino rats selected for this study was twenty.

The results showed a highly significantly increased diameter of seminiferous tubules P value <.001 in Group A animals as compared to group B animals and a highly significantly decreased P value < .001 diameter of seminiferous tubules in Group B Animals as compared to Group A rodents.

Group A contained ten rodents and Group B comprised of ten rats. Five micron thick Haematoxylin and Eosin stained sections of Testis were visualized which showed seminiferous tubules. They are lined by a complex seminiferous epithelium. The section on microscopy of Group A (Control group) Showed Modified Stratified Columnar epithelium present on a continuous basal lamina. The Germinal epithelium was showed several types of germ cells. There was a highly significantly increase mean thickness of seminiferous tubule of control group A at four weeks which was 276.02±05µm. There was no pyknosis of nuclei, also Apoptosis of germinal cells was absent

Group B five micron thick Haematoxylin and sections Eosin stained sections of seminiferous tubules showed Damaged and apoptotic germinal cells and a highly significantly decreased diameter of seminiferous tubule which was 167.05±.55µm. There was marked vacoulation with in seminiferous tubules. The seminiferous tubules had a distorted appearance and were empty spaces due to germinal cell death within the seminiferous tubules.

Table No.1: Mean Diameter in µM of the Thickness of Seminiferous Tubules JN Different Groups of Albino Rats

Groups	Treatment Received	Sub-Groups	4th Weeks	P-Value A vs. B
A (n=10)	Control	A	276.020±. 5 µm	P<.001
B (n=10)	Lithium Carbonate	B	167.05±0. 55 µm	

DISCUSSION

Lithium the Typical Antipsychotic[14] and atypical antipsychotics like olanzapine[15] causes germinal cell death due to oxidative stress. It is observed that medicinal literature is deficient on the adverse effects of Antipsychotics like Lithium carbonate on diameter.

For the above same reason, we concluded our study and documented the decrement of seminiferous tubular diameter after ingestion of Lithium Carbonate.

This study documented changes of distortion and degeneration of the diameter of seminiferous tubules due to harmful effects

Heavy Metals like Cadmium[16], Mercury. Arsenic, Lead causes sperm cell death due to release of reactive oxygen species. The ROS causes increased oxidative stress, lipid peroxidation and DNA damage resulting in cell death and due to germinal cell loss, there was decline in the diameter of the seminiferous tubules. The same results of depletion of germinal epithelium and diminished seminiferous tubular diameter was documented in this research and this may be due to the reason that the drug Lithium carbonate caused release of Reactive oxygen species which resulted in sperm cell.

The above results of oxidative stress causing damage to seminiferous tubules were also found by Ghazal, Nabiuni and Elaheh[17].They reported a highly significant reduction in seminiferous tubular diameter. Our results in accordance with them this may be due to the fact that Lithium causes release of Reactive oxygen species which results in DNA damage causing cell death and apoptosis which is visualized as increased space between the germinal cells.

CONCLUSION

This is study concluded that Lithium carbonate reduces the diameter of seminiferous tubule. It is suggested that, the results should be considered when prescribing lithium to male patients who may lead to infertility.

Author's Contribution:

Concept & Design of Study:	Tazeen Kohari
Drafting:	Tazeen Kohari, Meshaal Azhar
Data Analysis:	Faryal Azhar, Usama Faruqui
Revisiting Critically:	Tazeen Kohari
Final Approval of version:	Tazeen Kohari

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Tiwana MS, Leslie SW. Anatomy, Abdomen and Pelvis, Testicle. [Updated 2021 Jul 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470201/
2. Garcia RA, Sajjad H. Anatomy, Abdomen and Pelvis, Scrotum. [Updated 2021 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL):

StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549893/

3. Kesselring T, Viquerat S, IJsseldijk LL, Langeheine M, Wohlsein P, Gröne A, Bergmann M, Siebert U, Brehm R. Testicular morphology and spermatogenesis in harbour porpoises (Phocoena phocoena). Theriogenol 2019;126:177-186.
4. Kumar A, Nagar M. Histomorphometric study of testis in deltamethrin treated albino rats. Toxicol Rep 2014;1:401-410.
5. Kumar H; Inayatullah, Qamar A. Preventive role of magnesium sulphate on dexamethasone induced testicular injury in albino rats. J Pak Med Assoc 2016;66(11):1407-1411.
6. Hasanin NA, Sayed NM, Ghoneim FM, Al-Sherief SA. Histological and Ultrastructure Study of the Testes of Acrylamide Exposed Adult Male Albino Rat and Evaluation of the Possible Protective Effect of Vitamin E Intake. J Microsc Ultrastruct 2018;6(1):23-34.
7. EKEH, Felicia Nkechi IKELE, Chika Bright and Obiezue, IN The Effect of Lead Acetate on the Testes of Male Albino Rats in Life Science and Technology www.iiste.org ISSN 2224-7181 (Paper) ISSN 2225-062X (Online) Vol.38, 2015.
8. Iqbal T, Cao M, Zhao Z, Zhao Y, Chen L, Chen T, et al. Damage to the Testicular Structure of Rats by Acute Oral Exposure of Cadmium. Int J Environ Res Public Health 2021;18(11). Spermatogenic Parameter in the adults Male Wistar Rats. Life Sci J 2012;9(4):4360-4367]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 655
9. Saad AB, Rjeibi I, Alimi H, Ncib S, Smida A, Zouari N, Zourgui L. Lithium induced, oxidative stress and related damages in testes and heart in male rats: The protective effects of Malva sylvestris extract. Biomed Pharmacother 2017; 86:127-135.
10. Kolachi GM, Sheikh B, Quddos I. The comparison of the body and renal weight in lithium carbonate and L-Arginine treated albino rats. Medical Channel 2011;17 (3):9-12**.**
11. Okonkwo CO, Ohaeri OC, Atangwho IJ. Haematological changes in rats exposed to insecticidal oils from the leaves of Cassia occidentalis and Euphorbia milii. Heliyon 2019; 5(5):e01746.
12. Rahmanifar F, Tamadon A, Meharabani D, Zare S, Abasi S, Keshavarz S, et al. Histomorphometric evaluation of treatment of rat azoosper-mic seminiferous tubules by allotransplantation of bone marrow-derived mesenchymals stem cells. Iran J Basic Med Sci 2016;19(6):653-61.
13. Niedenberger BA, Geyer CB. Advanced immunostaining approaches to study early males. germ cell development, Stem Cell Research 2018;27:162-168.
14. Nardi AE, da Silva AG, Gentil Filho V. Where are lithium carbonate, typical antipsychotics, imipramine, and some other efficacious medications? Braz J Psychiatr 2021;43(1):2-3.
15. Chokhawala K, Stevens L. Antipsychotic Medications. [Updated 2021 Oct 2]. In: StatPearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2021 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519503/ 01552
16. Mood-Balati M, Naseri K, Tahergorabi Z, Khazdar MR, Sadeghi M. Toxic mechanisms of five heavy metals, Mercury, Lead, Chromium, Cadmium and ArsenicFront. Pharmacol 1s 3 April 2021 | https://doi.org/10.3389/fphar.2021.643972
17. Ghajari G, Nabiuni M, Amini E. The association between testicular toxicity induced by Li2Co3 and protective effect of Ganoderma lucidum: Alteration of Bax & c-Kit genes expression, Tissue and Cell 2021;72.