ORIGINAL ARTICLE

To Study The Deteriorating Effects of Lithium Carbonate on Thyroid Gland a Study in Albino Rats

TAZEEN KOHARI1, ZAFFAR IQBAL MALIK2, AFTAB AHMAD3, RANA M.ASAD KHAN4

¹Associate Professor Anatomy Islam medical and dental college Pasrur Sialkot

²Assistant Professor Anatomy Sahara medical college Narowal

³Associate Professor Anatomy M. Islam Medical and Dental College, Gujranwala

⁴Lecturer Islam medical and dental College, Sialkot

Correspondence to: Tazeen Kohari, Email: tazeenk67@gmail.com, Contact no 0323-29789

ABSTRACT

Background: The human thyroid gland is located in the front of neck. It consists of two lobes. The two lobes are joined with each other by isthmus.

The mood stabilizer Lithium Caronate has deleterious effects on the thyroid gland.

Aim: To observe and report the data of the harmful effect of Lithium on the weight changes of thyroid gland. **METHODS:** Sixteen rats were selected for this experimental study. The rodents were divided into two groups. Group A comprised of eight animals which were given laboratory diet, Group B contained eight albinos who were given Tablet Lithium Carbonate in powder form at a dose of 60 mg/day for four weeks. After completion of the study time animals were sacrificed and thyroid gland weight were recorded and compared in both groups.

Results: The results in both groups were recorded and compared .It was reported that Group B animals had a highly significantly decreased thyroid weight after four weeks Lithium ingestion than Group A control group.

Conclusion: The results of our study concluded that Lithium Carbonate damages thyroid glandular tissue and causes its weight to decline.

Keywords: Thyroid gland, Isthmus, deteriorating

INTRODUCTION

The thyroid gland is an endocrine gland ¹ situated in the anterior lower neck² .It consists of two lobes³ joined by an isthmus⁴.The gland extends from fifth cervical to first thoracic vertebrae⁵ and it is encapsulated and weighs almost 15 -30 grams in an adult human.⁶The weight of thyroid in adult rat is almost 1.5 grams⁷.

Thyroid histology consists of follicular and parafollcular cells. The follicular cells secrete triiodothyronine and tetraiodothyronine which increases basal metabolic rate and somatic growth. The parafollicular cells are present in between the Follicular cells and these cells secrete calcitonin which regulates body calcium concentration.8

The focal antipsychotic drug Lithium Caronate causes adverse effects on brain^{9,} heart¹⁰ and ¹¹Kidneys. It acts as an oxidant agent ¹²and releases Superoxide radical which causes apoptosis and deterioration of the above tissues.

Medicinal literature is deficient of the harmful effects of lithium carbonate on Thyroid gland and for the same reason we carried out this research which enlightens the decrement of the weight of thyroid gland after chronic Lithium intake.

MATERIAL AND METHODS

Our research was carried out at the Animal house of Basic Medical Sciences Institute Jinnah Postgraduate Medical Centre Karachi from fifteen June to fifteen July 2013. For our study sixteen adult albino rats weighing 145-165 grams animals were chosen and were acclimitized for a week. The animals were divided into two groups. Group A which contained eight albinos and Group B which comprised of eight rodents.

Group A animals served as Control Group which were fed Lab diet and Group B animals was the treated group and they were given Lithium carbonate (Adamjee

pharmaceuticals) at a dose of 60 mg /kg in powder form in flour pellets for four weeks. ¹³At completion of four weeks the animals were sacrificed and the thyroid gland was removed and weighed on electronic weighing balance in Group A and in Group B animals.

Statistical Analysis: Statistical Analysis was conducted by using SPSS version -16.Statistical differences between means and experimental data was carried out by student's 't' test. The statistical differences between means and experimental data were carried out. The differences in thyroid gland weights at four weeks was regarded as highly significant if the Pvalue was equal to or less than .001.

RESULTS

Mean values of the weight of thyroid gland in Group A (Control) and Group B (Lithium Carbonate) treated groups are in Table 1.

Table 1: thyroid gland weight in (mg) In different groups of albino

Groups	Treatment	Sub-	4 TH Week	P-value
	Received	Groups		A vs. B
A (n=8)	Control			P<.001
		Α	5.95±0.67	
			mg	
В	Lithium			
(n=8)	Carbonate	В	2.97±0.88mg	

At the end of four weeks values of thyroid gland weight were highly significantly increased (P value, < .001) in Control Group A 5.95 ± 0.67 mg than in Lithium treated Group B.

The values of thyroid gland weight were highly significantly decreased (p < .001) in treated group B 2.97±.88 mg as compared to group A (control) group.

Mean values of thyroid gland weight was highly significantly decreased p< .001 in Group B albinos as compared to Group A

DISCUSSION

The great discovery of classical¹⁴ antipsychotic drug Lithium was almost seventy years ago and it is still used as a single therapeutic drug as well in combination 15 but it causes disintegration of thyroid tissue, these harmful effects of Lithium were reported y Lazarus¹⁶ in 1998.He in his research reported of decreased thyroid hormone secretion and destruction of the microanatomy of thyroid gland. The same damaging effects of Lithium were documented by us. We in our research found that Lithium intake causes decreased weight of the thyroid gland; this may be due to the fact that Lithium therapy causes increased apoptotic cells and vacuolated follicular cell cytoplasm¹⁷resulting in decreased in thyroid weight. The same results of decrement of thyroid weight were found by Dhawan ¹⁸(et al 1988) and our findings are in accordance with their results. The above observations may be due to the fact that lithium causes cell death¹⁹ resulting in decreased organ weight.

CONCLUSION

Our research is a documented proof for psychiatrists to take caution in prescribing Lithium Carbonate to the masses as it has adverse effects on Thyroid gland function.

REFERENCES

- s1. Allen E, Fingeret A. Anatomy, Head and Neck, Thyroid. [Updated 2021 Jul 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-.
- 2 Rodrigo Arrangoiz, Fernando Cordera, David Caba, Manuel Muñoz, EduardoMoreno, Enrique Luque de Le Comprehensive Review of ThyroidEmbryology, Anatomy, Histology, and Physiology for Surgeons International Journal of Otolaryngology and Head & Neck Surgery Volume 7, Issue 4 (July 2018)ISSN Print: 2168-5452 ISSN Online: 2168-5460
- Joshi SD, Joshi SS, Daimi SR, Athavale, A. The thyroid gland and its variations: a cadaveric study. Folia Morphol (Warsz). 2010 Feb; 69(1):47-50. PMID: 2023505
- Hoyes AD, Kershaw DR. Anatomy and development of the thyroid gland. Ear Nose Throat J. 1985 Jul; 64(7):318-33. PMID: 3837720.
- Khan YS, Farhana A. Histology, Thyroid Gland. [Updated 2021 May 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551659/
- Nurunnabi, A., Alim, A., Sabiha, M., Manowara, B., Monira, K., & Shamim, A. (2010). Weight of the Human Thyroid Gland A Postmortem Study. Bangladesh Journal of Medical Science, 9(1), 44–48. https://doi.org/10.3329/bjms.v9i1.5230
- Roe, E, Remington, John W. Remington, Sarah S. Welch .First published: February 1937 https://doi.org/10.1002/ar.1090670308
- Beynon ME, Pinneri K. An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist. Acad Forensic Pathol. 2016 Jun;6(2):217-236. doi: 10.23907/2016.024. Epub 2016 Jun 1. PMID: 31239894; PMCID: PMC6507001.
- Young W. Review of lithium effects on brain and blood. Cell Transplant. 2009;18(9):951-75. doi:

- 10.3727/096368909X471251. Epub 2009 May 13. PMID: 19523343
- Acharya S, Siddiqui A, Anwar S, et al. (March 16, 2020)
 Lithium-induced Cardiotoxicity: A Rare Clinical Entity.
 Cureus 12(3): e7286. doi:10.7759/cureus.7286
- Gupta S, Khastgir U. Drug information update. Lithium and chronic kidney disease: debates and dilemmas. BJPsych Bull. 2017 Aug;41(4):216-220. doi: 10.1192/pb.bp.116.054031. PMID: 28811917; PMCID: PMC5537577.
- Zaki SM, Hussein GHA, Helal GM, Arsanyos SF, Abd Algaleel WA. Green tea extract modulates lithium-induced thyroid follicular cell damage in rats. Folia Morphol (Warsz). 2021 May 21. doi: 10.5603/FM.a2021.0052. Epub ahead of print. PMID: 34018174.
- da Silva Kagy V, Trevisan Bittencourt Muniz L, Michels AC, Luiz ST, Reis Azevedo Alanis L, Brancher JA, et al. (2016) Effect of the Chronic Use of Lithium Carbonate on Induced Tooth Movement in Wistar Rats. PLoS ONE 11(8): e0160400. https://doi.org/10.1371/journal.pone.0160400
- Rufallo M,L. IN Brief report A Brief History of Lithium Treatment in Psychiatry Primary Care Disorders2017;19(5):17br021https://doi.org/10.4088/PCC.17 br02140
- Lee HK, Prabhudesai S, Vadukapuram R, Eskander N, Patel RS. Combination Regimen With Lithium and Antipsychotic in Bipolar Manic Episodes: Impact on Adult Hospitalization Length of Stay. Cureus. 2020 Jun 11;12(6):e8568. doi: 10.7759/cureus.8568. PMID: 32670704; PMCID: PMC7358937.5
- Lazarus JH. The effects of lithium therapy on thyroid and thyrotropin-releasing hormone. Thyroid. 1998 Oct;8(10):909-13. doi: 10.1089/thy.1998.8.909. PMID: 9827658
- Sanaa M. Abd El-Twab, Manal Abdul-Hamid, Curcumin mitigates lithium-induced thyroid dysfunction by modulating antioxidant status, apoptosis and inflammatory cytokines, The Journal of Basic & Applied Zoology, Volume 76,2016, Pages 7-19, ISSN 2090-9896, https://doi.org/10.1016/j.jobaz.2016.10.001.
- D. Dhawan,A,C R. R. Sharma,A R. Sharma A and R. J. DashBEffect of Short-term and Long-term Lithium Treatment on Uptake and Retention of 10dine-131 in Rat Thyroid Aust. J. Bioi. Sci., 1988, 41, 387-9
- 19. Shen, J., Li, X., Shi, X. et al. The toxicity of lithium to human cardiomyocytes. Environ Sci Eur 32, 59 (2020). https://doi.org/10.1186/s12302-020-00333-6
- Thyroid staining Khan YS, Farhana A. Histology, Thyroid Gland. [Updated 2021 May 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551659/
- Discussion Permoda-Osip A, Abramowicz M, Kraszewska A, Suwalska A, Chlopocka-Wozniak M, Rybakowski JK. Kidney, thyroid and other organ functions after 40 years or more of lithium therapy: a case series of five patients. Ther Adv Psychopharmacol. 2016 Aug;6(4):277-82. doi: 10.1177/2045125316643299. Epub 2016 Apr 17. PMID: 27536347; PMCID: PMC4971597cussion
- Lazarus JH. The effects of lithium therapy on thyroid and thyrotropin-releasing hormone. Thyroid. 1998 Oct;8(10):909-13. doi: 10.1089/thy.1998.8.909. PMID: 9827658.
- Lithium and thy wt D. Dhawan, A, C R. R. Sharma, A R. Sharma A and R. J. DashBEffect of Short-term and Long-term Lithium Treatment on Uptake and Retention of 10dine-131 in Rat Thyroid Aust. J. Bioi. Sci., 1988, 41, 387-92
- Sanaa M. Abd El-Twab, Manal Abdul-Hamid, Curcumin mitigates lithium-induced thyroid dysfunction by modulating antioxidant status, apoptosis and inflammatory cytokines, The Journal of Basic & Applied Zoology, Volume 76, 2016, Pages 7-19, ISSN 2090-9896,

- https://doi.org/10.1016/j.jobaz.2016.10.001. (https://www.sciencedirect.com/science/article/pii/S2090989616300224)
- Nasseer Ahmad Shah, Gh. Mohd. Bhat*, Shaheen Shadad, Mohamad Saleem Itoo, Bashir Ahamad Shah, Javaid Ahmad Khan Effects of lithium carbonate on the microanatomy of thyroid gland of albino rats January 2014 International Journal of Research in Medical Sciences 2(1):279 DOI:10.5455/2320-6012.ijrms20140253
- ReferencesNussey S, Whitehead S. Endocrinology: An Integrated Approach. Oxford: BIOS Scientific Publishers; 2001. Chapter 3, The thyroid gland. Available from: https://www.ncbi.nlm.nih.gov/books/NBK28/
- 43 2.Beynon ME, Pinneri K. An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist. Acad Forensic Pathol. 2016 Jun;6(2):217-236. doi: 10.23907/2016.024. Epub 2016 Jun 1. PMID: 31239894; PMCID: PMC6507001.
- Download 3.Goodman H.M, in Basic Medical Endocrinology (Fourth Edition), 2009 https://doi.org/10.1016/B978-1-4377-1604-7.00006-3Get
- Allen E, Fingeret A. Anatomy, Head and Neck, Thyroid. [Updated 2021 Jul 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470452/
- Arrangoiz, R., Cordera, F., Caba, D., Muñoz, M., Moreno, E. and de León, E. (2018) Comprehensive Review of Thyr
- Beynon ME, Pinneri K. An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist. Acad Forensic Pathol. 2016 Jun;6(2):217-236. doi: 10.23907/2016.024. Epub 2016 Jun 1. PMID: 31239894; PMCID: PMC6507001.
- 7.Jin Jianhua, Li Xiaomin, Niu Rong, Fu Songhai, Liu Ye and Li Sijin The influence on rat's thyroid weight and function by applying nicotinamide with 131IJournal of Nuclear Medicine May 2012, 53 (supplement 1) 1212;
- Enemali, F.U. & Hambolu, J.O. & Alawa, Judith & Anosike, I.V. (2016). Gross Anatomical, Histological and Histochemical Studies of Thyroid Glands of African Giant Rat (Cricetomys gambianusWaterhouse, 1840). IOSR Journal of Pharmacy and Biological
- Lithium imtro and use Pérez de Mendiola, X., Hidalgo-Mazzei, D., Vieta, E. et al. Overview of lithium's use: a nationwide survey. Int J Bipolar Disord 9, 10 (2021). https://doi.org/10.1186/s40345-020-00215-z
- Won E, Kim YK. An Oldie but Goodie: Lithium in the Treatment of Bipolar Disorder through Neuroprotective and Neurotrophic Mechanisms. Int J Mol Sci. 2017 Dec 11;18(12):2679. doi: 10.3390/ijms18122679. PMID: 29232923; PMCID: PMC5751281.
- 35. Lithium and thyroid harmoneEtling N, Levy M, Fouque F. Hormones thyroïdiennes des rats recevant des doses croissantes de lithium [Thyroid hormones in rats receiving increasing doses of lithium]. Ann Endocrinol (Paris). 1987;48(6):452-6. French. PMID: 3128158.
- Copy Lithium and thyroid wt The influence on rat's thyroid weight and function by applying nicotinamide with 131I

- Jin Jianhua, Li Xiaomin, Niu Rong, Fu Songhai, Liu Ye, Li Sij in Journal of Nuclear Medicine May 2012, 53 (supplement 1) 121 Material and methods
- Lithium dose da Silva Kagy V, Trevisan Bittencourt Muniz L, Michels AC, Luiz ST, Reis Azevedo Alanis L, Brancher JA, et al. (2016) Effect of the Chronic Use of Lithium Carbonate on Induced Tooth Movement in Wistar Rats. PLoS ONE 11(8):

 60160400.
 https://doi.org/10.1371/journal.pone.0160400
- Thyroid staining Khan YS, Farhana A. Histology, Thyroid Gland. [Updated 2021 May 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-Available from: https://www.ncbi.nlm.nih.gov/books/NBK551659/
- Discussion Permoda-Osip A, Abramowicz M, Kraszewska A, Suwalska A, Chlopocka-Wozniak M, Rybakowski JK. Kidney, thyroid and other organ functions after 40 years or more of lithium therapy: a case series of five patients. Ther Adv Psychopharmacol. 2016 Aug;6(4):277-82. doi: 10.1177/2045125316643299. Epub 2016 Apr 17. PMID: 27536347; PMCID: PMC4971597cussion
- Lazarus JH. The effects of lithium therapy on thyroid and thyrotropin-releasing hormone. Thyroid. 1998 Oct;8(10):909-13. doi: 10.1089/thy.1998.8.909. PMID: 9827658.
- 41. Sanaa M. Abd El-Twab, Manal Abdul-Hamid, Curcumin mitigates lithium-induced thyroid dysfunction by modulating antioxidant status, apoptosis and inflammatory cytokines,
- The Journal of Basic & Applied Zoology, Volume 76, 2016, Pages 7-19, ISSN 2090-9896, https://doi.org/10.1016/j.jobaz.2016.10.001. (https://www.sciencedirect.com/science/article/pii/S2090989 616300224)
- Shah, Nasseer & Bhat, Ghulam & Shadad, Shaheen & Itoo, Mohd & Shah, Bashir & Khan, Javaid. (2014). Effects of lithium carbonate on the microanatomy of thyroid gland of albino rats. International Journal of Research in Medical Sciences. 2. 279. 10.5455/2320-6012.ijrms20140253.
- oid Embryology, Anatomy, Histology, and Physiologyr Surgeons. International Journal of Otolaryngology and Head & Neck Surgery, 7, 160-188. doi: 10.4236/ijohns.2018.74019.
- 6. Beynon ME, Pinneri K. An Overview of the Thyroid Gland and Thyroid-Related Deaths for the Forensic Pathologist. Acad Forensic Pathol. 2016 Jun;6(2):217-236. doi: 10.23907/2016.024. Epub 2016 Jun 1. PMID: 31239894; PMCID: PMC6507001.
- 7.Jin Jianhua, Li Xiaomin, Niu Rong, Fu Songhai, Liu Ye and Li Sijin The influence on rat's thyroid weight and function by applying nicotinamide with 131Journal of Nuclear Medicine May 2012, 53 (supplement 1) 1212;
- 8. Enemali, F.U. & Hambolu, J.O. & Alawa, Judith & Anosike, I.V. (2016). Gross Anatomical, Histological and Histochemical Studies of Thyroid Glands of African Giant Rat (Cricetomys gambianusWaterhouse, 1840). IOSR Journal of Pharmacy and Biological Sciences. 11. 40-43. 10.9790/3008-1104024043. 9.