Check for updates

OPEN ACCESS

DOI: 10.46903/gjms/23.1.Special.1623

ORIGINAL ARTICLE

LITHIUM INFLUENCE ON INORGANIC COMPONENT OF DEVELOPING DENTAL TISSUES IN PREGNANCY

Shakila Nazir, Arsalan Mirza

Department of Oral Biology, Baqai Dental College, Baqai Medical University, Karachi, Pakistan

ABSTRACT

Background: Teratogenicity of human dentition may cause aesthetic complications. Deformed enamel of teeth is generally vulnerable to carious lesions and sensitivity of dentition. The contemporary study was initiated to consider the effect on inorganic component in the developing teeth of newborn babies when Lithium was ingested during pregnancy.

Materials & Methods: In this study, female rabbits were taken as mammalian model treated with lithium, their off springs were used to evaluate the teratogenicity of teeth. Quantitative analysis of inorganic component was done in three types of teeth. The experimentation was piloted by means of scanning electron microscope and energy dispersive X-ray spectroscopy (SEM-EDX).

Results: Ample disparities were perceived between the samples of control and the treatment group, though conferring the consequences that incisors and the molars seemed appealingly and operationally affected teeth.

Conclusion: Significant results could not be achieved; however, it is mandatory that the medication should hence be taken by doctor's advice, especially in the course of pregnancy, avoiding the unfortunate effects on the newborn's teeth.

KEY WORDS: Defects; Dentition; Developmental; Female; Lithium; Rabbits.

Cite as: UNazir S, Mirza A. Lithium influence on inorganic component of developing dental tissues in pregnancy. Gomal J Med Sci 2025 Jan-Mar;23(1)Special:101-5. https://doi.org/1046903/gjms/23.1.Special.1623

INTRODUCTION

The drugs easily pass through the placenta and equilibrate between maternal and fetal circulation. First trimester of the pregnancy is critical to the usual growth of the fetus. During that phase when all main body organs are developing, the fetus is predisposed to disfigurement and being the possibility of teratogenicity. Lithium is considered to be a drug of choice for the treatment of mood disorders, the consumption of lithium during gestation period is said to be related with a 2-3-fold high risk of preterm birth.[1] Evidence for adverse effects of Lithium may be apprehensive. Its systematic severity might be well-thought-out before it is used during pregnancy.[2]

Corresponding Author:

Dr. Shakila Nazir
Professor of Oral Biology
Baqai Dental College, Baqai Medical University
Karachi, Pakistan

E-mail: shakila.nazir@gmail.com

Date Submitted: 15-04-2024
Date Revised: 18-02-2024
Date Accepted: 04-03-2025

lithium carbonate (LC) is a drug commonly used in the treatment of bipolar disorders for the patients going through dental treatment procedures.[3] The results of a prior study suggested that an endogenous cell homing approach, which stimulated a self-healing mechanism using cells already present in the tissues, has the potential to provide novel therapeutic options for dentin regeneration. Concerning the efficient dentin regenerations, LiCl has great potential as a bioactive mediating organ-specific trans differentiation.[4] It was reported that Li_2CO_3 medication might change periapical lesions' inflammatory states to healing states at early stages of inflammation. Furthermore, regulatory T cells induced by Li_2CO_3 supported alveolar bone healing through osteoblast differentiation and reduced the volume of periapical lesions. Li_2CO_3 could be a bioactive medicament in root canal treatments.[5] Regarding a restorative material the physical properties of lithium. disilicate glass-ceramics depend on the microstructure, having an important role in defining their flexural strength, toughness, elastic modulus, and optical properties. Features important for instance chemical composition, nucleating agent, additives, and process control the microstructure.[6]

Results of a prior study showed that the systemic

LiCl improved in repairing of the socket after tooth extraction, stimulated an overall increase in bone creation markers, and controlled the levels of tartrate-resistant acid phosphatase (TRAP) in rats.[7] There is another information confirming the similar results in which Lithium chloride ingestion boosted the bone healing and stirred an overall expression of bone markers in healing the alveolar sockets after extraction of tooth in rats having estrogen insufficiency, mostly in the early healing stages. Such primary outcomes advocated that lithium chloride administration might characterize a favorable scheme for cultivating alveolar socket healing in osteopenic/osteoporotic individuals.[8] The former study documents Lithium also decreased bone density in bipolar patients on long term Lithium treatment, results possibly support that lithium caused a significant decrease in bone density.[9]

One of the experimental studies in animals, revealed that lithium decreased the rate of orthodontic tooth movement (OTM) through the active treatment stage by growing bone density and volume also dropping the root resorption. Lithium enhanced the alveolar bone development through orthodontic maintenance, which showed that it clinically, might impact the orthodontic treatment duration in patients receiving lithium.[10] Lithium disilicate glass ceramic was used in clinical practice and proved to be a prevalent choice owing to extraordinary flexural strength, decent biocompatibility, exceptional esthetic properties, and the prospective to bond adhesively on enamel and dentin.[11]

Contrary to these reports it was also testified that actual dental decay and alterations in tooth structure have been reported in relationship with the use of lithium, but the effects of the drug on inorganic composition of teeth sustain to be unknown.[12]

Effect of lithium on inorganic composition of teeth has not been reported in prior studies. The contemporary study was designed to explore the inorganic component of the dental tissue effected by this drug used by the mother during pregnancy.

MATERIAL AND METHODS

The study was conducted using rabbits as an experimental model. Female bunnies were pregnant having 1.5 71 to 2.0 kg weight and declared healthy subjects by the veterinary surgeon were designated to initiate the study. Distributing them into two groups. Categorized as an experimental and a control group. Each set having (n=7) subjects. Lithium Carbonate was used which was available with the commercial name (Neurolith SR. 400 mg).

Medicine was prepared considering the Clark's rule in view of body weight of the subject.[13]

One tablet of Neurolith SR. 400 mg. was liquefied in 10 ml of the distilled water to formulate the medicine. The preparation of 3 ml (80 mg/kg) was given by oral rout, two times a week, to the selected animal for the investigational purpose up till the birth of their off springs. These off springs were sacrificed after reaching the age of three months to acquire their maxillary and mandibular jaws. Teeth were then extracted from both the jaws of the rabbit. Twelve teeth of three categories were taken from each subject, the total range being 168 samples. Three types of teeth were analyzed including incisors, first premolars and first molars from both the jaws. Investigation was done by means of Scanning electron microscope and energy dispersive X-ray spectroscopy (SEM-EDX). The research methodology was piloted according to the same procedure enumerated in one of our published articles.[14]

RESULTS

Quantifiable analysis of inorganic component of teeth e.g. Calcium, Phosphorous, and Magnesium were scrutinized by means of scanning electron microscope and energy dispersive X-ray spectroscopy (SEM-EDX) expressed in mass % age.

Since considering the Mean ± Standard Deviation the P-Value showed a noteworthy effect on the Magnesium in maxillary incisors (Table 1) Whereas in Mandibular incisors the effect of the drug influencing the Calcium of incisors, premolars and molars, while Magnesium exhibited a substantial effect on molars (Table 2).

Mean mass % age of minerals in the maxillary and mandibular teeth between control and treated animals are represented in (Figure 1,2) respectively.

The intrauterine effect of Lithium on the developing teeth is lacking in the published literature.

The present study has provided the results regarding the effect of lithium on the inorganic component of teeth i.e. calcium, phosphorous and magnesium. Lithium effect on the Calcium and Phosphorous of maxillary teeth, showed a decrease in all the types of teeth except premolars, while Magnesium increased in incisors and a slight decreased was observed in molars (Figure 1).

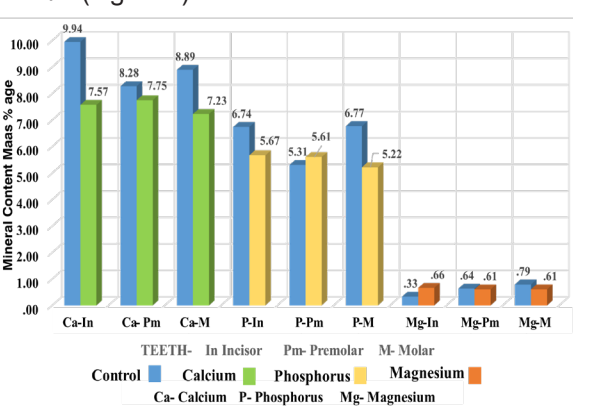

Figure 1: Comparison of minerals in Maxillary Teeth

Table 1: Effect of lithium on maxillary teeth (Mass percentage of minerals)

Teeth	Mineral	Mean ± SD		P-Value	Remarks
		Control	Treated		
Incisors	Calcium	9.94±3.46	7.57±3.36	0.07	Insig.
Premolars		8.27±3.13	7.74±3.24	0.66	Insig.
Molars		8.89±2.98	7.22±3.59	0.19	Insig.
Incisors	Phosphorus	6.74±2.66	5.67±2.11	0.25	Insig.
Premolars		5.30±1.83	5.60±1.98	0.68	Insig.
Molars		6.77±2.63	5.21±2.38	0.11	Insig.
Incisors	Magnesium	0.33±0.21	0.66±0.43	0.01	Sig.
Premolars		0.63±0.22	0.60±0.16	0.69	Insig.
Molars		0.79±0.32	0.60±0.24	0.10	Insig.

Table 2: Effect of lithium on mandibular teeth (Mass percentage of minerals)

Teeth	Mineral	Mean ± SD		P-Value	Remarks
		Control	Treated		
Incisors	Calcium	10.15±4.61	6.62±2.57	0.01	Sig.
Premolars		9.81±2.71	7.64±1.85	0.02	Sig.
Molars		10.39±3.39	6.96±4.82	0.03	Sig.
Incisors	Phosphorus	6.28±2.81	5.08±1.86	0.19	Insig.
Premolars		7.27±1.93	5.95±1.46	0.05	Sig.
Molars		7.42±2.65	5.35±3.60	0.09	Insig.
Incisors	Magnesium	0.60±0.58	0.56±0.15	0.81	Insig.
Premolars		0.70±0.29	0.60±0.22	0.31	Insig.
Molars		0.99±0.38	0.64±0.33	.017	Sig.

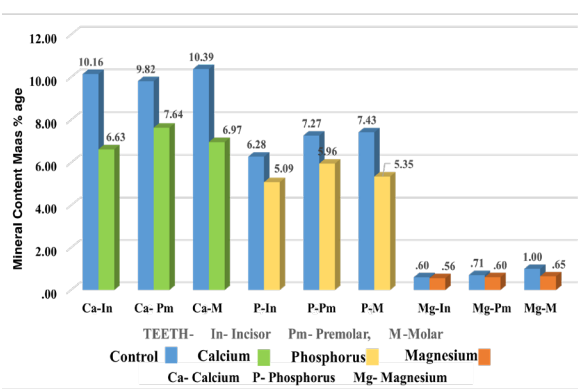

Figure 2: Comparison of minerals in Mandibular Teeth

Considering the magnitudes of drug's effect on the mandibular teeth which revealed that Calcium and Phosphorus decreased in all the three types of teeth, while observing the trend of Magnesium in mandibular teeth which slightly decreased in premolars and molars (Figure 2).

DISCUSSION

Lithium is a drug of choice for bipolar disorder and as well prescribed during pregnancy. Literature search revealed that it has a noteworthy positive effect on bone density.[8] In contrary, there is another study reporting that lithium caused a significant decrease in bone density.[10] According prior report success and survival of the restorations were calculated with the Kaplan Meier

method. A Cox regression analysis was performed to detect influencing parameters for the survival or the success of the restorations. The Lithium disilicate restorations showed a good clinical performance up to 8.5 years. The indirect posterior restorations demonstrated a high success and survival rate.[11]

Prior reports in term of treating bone defect and fracture, lithium seemed to be a good choice of microelement for improving the shortcomings of synthetic bone substitutes for their brittleness and insufficiency to promote osteogenesis.[15] Effect of Lithium on bone was reported in prior studies. [5-8,10-13,] but on the other hand the influence of Lithium on dental tissues has not been reported in the published literature. Regarding the clinical practice, the persuaded tooth drive related with chronic use of lithium carbonate in Wistar rats caused in poorer rate of tooth movement for the duration of 14-days period, probably to the decrease in the number of Osteoclasts.[16] In the present study, lithium was given during pregnancy being induced systemically and reporting the influence on inorganic component regarding Calcium, Phosphorus and Magnesium on the teeth of rabbit's offsprings. One of the prior studies concluded that the different doses of Li distressed tissue homeostasis of Mg. The surge in Mg tissue concentration was perceived in groups getting superior Li doses cane effect nervous-muscular excitability.[17] The researchers have focused on the Mg concentration influencing the nervous-muscular system. In contrast our results, reported the association between maternal use of lithium effecting the inorganic component of newborn's teeth. Parkin GM *et al*., strongly recommended that saliva may possibly be utilized for lithium checking, and unwrapped the access for the development and application of a point of-care salivary lithium scheme for the clinical practice.[18] The recommendation of Parkin GM *et al*., is very important and might be included in research protocols.

The hypo mineralized enamel surface may be considered regarding the bonding of brackets used in Orthodontic practice. The brand of adhesives and the enamel condition might regulate the result of bond to hypo mineralized enamel. Developmental defects of enamel (DDE) have been commonly perceived individually in pediatric and orthodontic dental practices. The usage of bonding agent ingredients in dental practice for reinforcing and attachment of the bands and brackets is important in modern orthodontic practice. The surface of hypo mineralized enamel and its abrasion is practically assessed by considering superficial enamel evenness, firmness and shade. Appropriate diagnosis and precautionary management might have some contribution to the pediatric dentistry along with the orthodontist challenged by the individuals with hypo mineralized teeth.[19] It was also revealed in a prior study that lithium chloride expressively decreases orthodontic tooth drive in rats.[20]

The report of an earlier study, revealed that autophagy-promoting the influence of LiCl on bone remodeling based osteoporotic environments for the period of tooth movement.[21] Orthodontic tooth movement (OTM) is determined dynamism which employed alveolar bone transformation, considered by jaw bone development on the strain side and bone resorption on the inflexibility side. For the period of orthodontic treatment, instable alveolar bone restoration take place in osteoporotic patients, causing enhanced tooth crusade, and unnecessary alveolar bone resorption which could lead to undesirable treatment results. Preventing the complications in osteoporotic patients in orthodontic treatment a previous study providing the consumption of LiCl in case of harmless orthodontic treatment to osteoporotic people with improved results.[22] The preclinical evidence disputes to possible progressive effects of perinatal exposure to lithium, which is not found in clinical surveys. This study has provided the systemic effect of lithium administered in pregnancy on the developing teeth of neonates, the reports could help the clinician for designing the treatment plan.

CONCLUSION

It could be determined that systemically used Lithium in pregnancy provoked aesthetically and operationally compromised teeth. Therefore, it must be considered mandatory that the medication taken during pregnancy should only be according to the doctor's prescription avoiding the risk of developmental imperfections on the newborn's dentition.

REFERENCES

1. Poels P, Bijma H, Galbally M. Lithium during pregnancy and after delivery: a review. Int J Bipolar Disord. 2018;6:26. https://doi.org/10.1186/s40345-018-0135-7
2. McKnight RF, Adida M, Budge K, Stockton S, Goodwin GM, Geddes JR. Lithium toxicity profile: a systematic review and meta-analysis. Lancet. 2012;379(9817):721-8. https://doi.org/10.1016/S0140-6736(11)61516-X
3. Da Silva V, Trevisan L, Michels A, Luiz S, Reis L, Brancher J, et al. Effect of the chronic use of lithium carbonate on induced tooth movement in Wistar rats. PLoS One. 2016;11(8):e0160400. https://doi.org/10.1371/journal.pone.0160400
4. Ishimoto K, Hayano S, Yanagita T, Kurosaka H, Kawanabe N, Itoh S, et al. Topical application of lithium chloride on the pulp induces dentin regeneration. PLoS One. 2015;10(3):e0121938. https://doi.org/10.1371/journal.pone.0121938
5. Kagioka T, Itoh S, Hue M. Lithium carbonate accelerates the healing of apical periodontitis. Sci Rep. 2023;13:7886. https://doi.org/10.1038/s41598-023-34700-z
6. Hallmann L, Ulmer P, Kern M. Effect of microstructure on the mechanical properties of lithium disilicate glass-ceramics. J Mech Behav Biomed Mater. 2018;82:355-70. https://doi.org/10.1016/j.jmbbm.2018.02.032

7. Duarte PM, Miranda TS, Marins LM, Da Silva JRB, De Souza F, De Vasconcelos B, et al. Lithium chloride stimulates bone formation in extraction socket repair in rats. Oral Maxillofac Surg. 2022;15. https://doi.org/10.1007/s10006-022-01124-4
8. Duarte PM, Miranda TS, Marins LM, Perez EG, Copes LG, Tonietto CB, et al. Systemic lithium chloride administration improves tooth extraction wound healing in estrogen-deficient rats. Braz Dent J. 2020;31(6):640-9. https://doi.org/10.1590/0103-6440202003595
9. Eren I, Yildiz M, Civi I. The effects of lithium treatment on bone mineral density in bipolar patients. Neurol Psychiatry Brain Res. 2006;13:175-80. https://doi.org/10.1016/S0924-977X(03)91885-2
10. Wadke A, Kommuri K, Talluri S, Kalladka M, Kalladka G, Khan J. Effect of lithium on orthodontic tooth movement: a systematic review of animal studies. Turk J Orthod. 2024;37(1):63-71. https://doi.org/10.4274/TurkJOrthod.2023.2022.149
11. Fotiadou C, Manhart J, Diegritz C, Folwaczny M, Hickel R, Frasheri I. Longevity of lithium disilicate indirect restorations in posterior teeth prepared by undergraduate students: a retrospective study up to 8.5 years. J Dent. 2021;105:103569. https://doi.org/10.1016/j.jdent.2020.103569
12. Eduardo P, Simões A, De Freitas PM, Arana V, Nicolau J, Gentil V. Dentin decalcification during lithium treatment: case report. Spec Care Dentist. 2013;33(2):91-5. https://doi.org/10.1111/scd.12000
13. Koren G. Special aspects of perinatal & pediatric pharmacology. In: Basic and Clinical Pharmacology. 10th ed. USA: McGraw-Hill; 2007. p. 971-82.
14. Shakila N, Naeem H, Masood A, Naema N. SEM-EDX analysis for surface aberrations of neonate's teeth influenced by the use of lithium in pregnancy. World J Dent. 2011;2(2):105-10. https://doi.org/10.5005/jp-journals-10015-1065
15. Wong SK, Chin K-Y, Ima-Nirwana S. The skeletal-protecting action and mechanisms of action for mood-stabilizing drug lithium chloride: current evidence and future potential research areas. Front Pharmacol. 2020;11:430. https://doi.org/10.3389/fphar.2020.00430
16. Da Silva V, Trevisan L, Michels A, Luiz ST, Reis L, Brancher J, et al. Effect of the chronic use of lithium carbonate on induced tooth movement in Wistar rats. PLoS One. 2016;11(8):e0160400. https://doi.org/10.1371/journal.pone.0160400
17. Kiełczykowska M, Musik I, Hordyjewska A, Boguszewska A, Lewandowska A, Pasternak K. Oral administration of lithium increases tissue magnesium contents but not plasma magnesium level in rats. Pharmacol Rep. 2007;59(3):291-5. PMID: 17652829.
18. Parkin GM, McCarthy MJ, Thein SH, Piccerillo HL, Warikoo N, Granger DA, et al. Saliva testing as a means to monitor therapeutic lithium levels in patients with psychiatric disorders: identification of clinical and environmental covariates, and their incorporation into a prediction model. Bipolar Disord. 2021;23(7):679-88. https://doi.org/10.1111/bdi.13128
19. Sapir S. Considerations in orthodontic bracket adhesion to hypomineralized enamel. In: Naretto S, editor. Principles in Contemporary Orthodontics. InTech; 2011. https://doi.org/10.5772/22252
20. Talebian R, Jafari F, Dehpour AR, Gruber R. Effects of lithium chloride and nitric oxide inhibitor on orthodontic tooth movement in the rat. Appl Sci. 2021;11(8):3607. https://doi.org/10.3390/app11083607
21. Huang L, Yin X, Chen J, Liu R, Xiao X, Hu Z, et al. Lithium chloride promotes osteogenesis and suppresses apoptosis during orthodontic tooth movement in osteoporotic model via regulating autophagy. Bioact Mater. 2021;6(10):3074-84. https://doi.org/10.1016/j.bioactmat.2021.02.015
22. Dai Q, Zhou S, Zhang P, Ma X, Ha N, Yang X, et al. Force-induced increased osteogenesis enables accelerated orthodontic tooth movement in ovariectomized rats. Sci Rep. 2017;7(1):3906. https://doi.org/10.1038/s41598-017-04422-0

CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.

AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	SN, AM
Acquisition, Analysis or Interpretation of Data:	SN, AM
Manuscript Writing & Approval:	SN, AM

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Copyright © 2025. Shakila Nazir, et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License, which permits unrestricted use, distribution & reproduction in any medium provided that original work is cited properly.