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Research Article

**AN EXPERIMENTAL RESEARCH ON THE TOXIC NATURE
OF THE LITHIUM CARBONATE USED AS A COMMON MOOD
STABILIZATION AGENT**¹Dr. Asif Iqbal, ²Dr. Abdullah Zaka, ³Dr. Ilsa Maryam¹Medical Officer, BHU Jandraka, Hafizabad²Ameer-ud-din Medical College Lahore³Nishtar Medical College Multan**Abstract:**

Background: To stabilize the mood a commonly used agent is lithium carbonate but its nature is very toxic that toxicity can be the outcome of its small dose. We aimed in this research that this agent causes any reduction effect on the glutathione found in the erythrocytes of human.

Material & Methods: Research was by nature experimental which was carried out in the Service Hospital, Lahore (Research Laboratory) in the month of September, 2017. Research sample comprised on the six volunteers who were in the age bracket of 21 – 24 years. Fresh samples of blood were drained from all the volunteers. Every participated was drained an equal amount of blood which measured exactly fifteen (15 ml). GSH of Erythrocyte's was taken with various lithium carbonate concentrations. We also applied one-way ANOVA to observe statistical difference.

Results: The erythrocytes GSH decrease was observed as low to high (31.68, 34.16, 37.02, 38.90, 40.91 & 43.01) percent for various lithium carbonate concentration. There was also a significant decrease in the level of GSH observed as lowest lithium carbonate concentration with a significant p-value of (< 0.005) a GSH decreased was observed about 31.68% and we also further observed as the time passed in the depletion of the lithium toxicity, erythrocytes GSH is dependent on the time and dose hence an in-time measures for lithium detoxification which guarantee the safety of the patient.

Conclusion: No doubt lithium is widely used to stabilize the mood as well as to treat manic depressive psychosis; on the same time, it is to be kept in the mind by the experts in the erythrocytes GSH depletion so precautions are mandatory in the course of lithium therapy.

Key Words: Lithium Carbonate; Erythrocytes; Mood stabilizing agent and Therapeutic.

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INTRODUCTION:

To stabilize the mood a commonly used agent is lithium carbonate but its nature is very toxic that toxicity can be the outcome of its small dose; no doubt lithium is widely used to stabilize the mood as well as to treat manic depressive psychosis [1, 2, 3, 6]. Data that we extracted is highly effective to favor the maintenance through lithium [7 – 12]. In the list of drawbacks of the lithium therapy there are poor tolerability when high level dose is managed with another associated risk of the “Rebound Mania” on withdrawal [13]. In the list of various general unwelcoming lithium effects are polydipsia, tremor, long-term hypothyroidism and polyuria. In the presence of all the side effects, a good treatment standard is considered for the lithium with additional, anti-suicidal effects as well [14, 15].

An overdose of the lithium results in the shape of lithium toxicity as narrow therapeutic index is associated with the lithium [16]. Lithium toxicities in thyroid function, kidneys, intestine, brain, liver and various other vital organs which have been observed in numerous other research studies [17, 18]. With many other associated changes in the brain (L + 1) alerts enzymes glutathione peroxides activities and super oxides dismutase; whereas, in the kidneys the levels of malondialdehyde were increased treatment of the lithium [19, 20]. In the event of lithium in the form of carbonate, we observed that selective increase is caused by the carbonate (L+1 & Na+1) permeability; which is because of the carbonate ability to form pairs of ion with sodium and lithium [21, 22]. It has been observed in various in vitro research studies that lithium is extruded against a gradient which is electrochemical by mechanism which is counter transport depending on the availability of opposite directed sodium ion gradient [23, 24]. The gradient of lithium across the red blood cells of the human can be sustained in the low permeability of the passive lithium. Lithium sodium counter transport in large amounts is found in bovine which is different from the red blood cells of human in lesser amounts [25, 26].

RESULTS:

Detailed outcomes of GSH and LC concentration comparison and concentration of GSH and incubation time have been respectively shown in Table – I and Table – II.

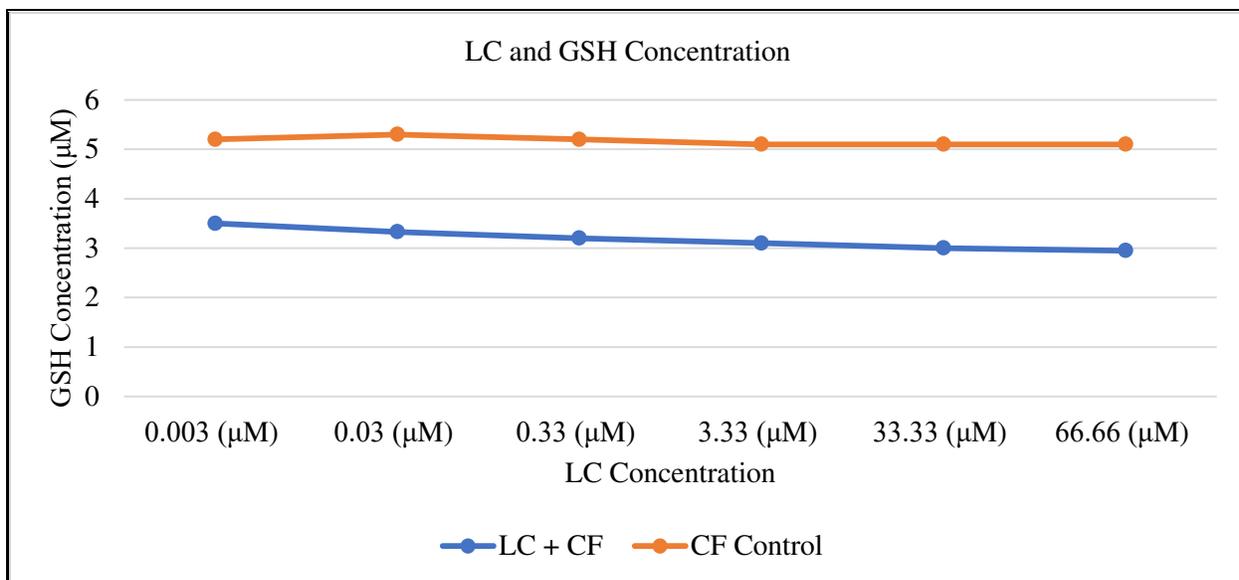
Table – I: LC and GSH Concentration

LC Concentration (µM)	GSH Concentration	
	LC + CF	CF Control
0.003	3.5	5.2
0.03	3.33	5.3
0.33	3.2	5.2
3.33	3.1	5.1
33.33	3	5.1
66.66	2.95	5.1

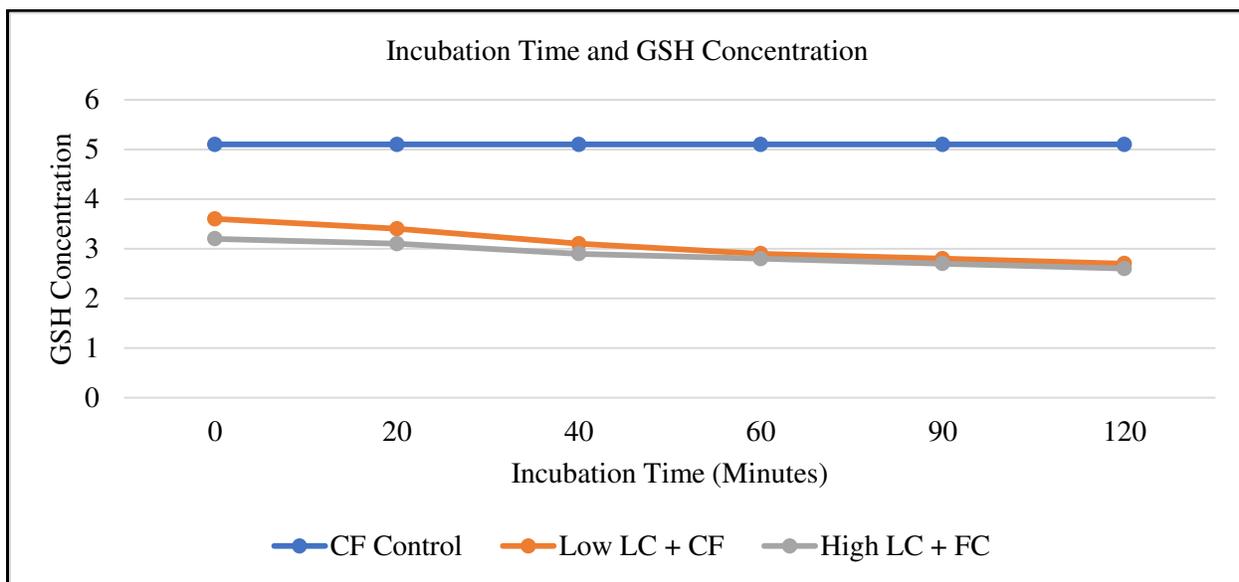
To stabilize the mood a commonly used agent is lithium carbonate but its nature is very toxic that toxicity can be the outcome of its small dose. We aimed in this research that this agent causes any reduction effect on the glutathione found in the erythrocytes of human.

MATERIAL AND METHODS:

Research was by nature experimental which was carried out in the Service Hospital, Lahore (Research Laboratory) in the month of September, 2017. Research sample comprised on the six volunteers who were in the age bracket of 21 – 24 years. Fresh samples of blood were drained from all the volunteers. Every participated was drained an equal amount of blood which measured exactly fifteen (15 ml). GSH of Erythrocyte's was taken with various lithium carbonate concentrations. We also applied one-way ANOVA to observe statistical difference. After the separation through centrifugation of various components of blood, we prepared one set which comprised of six test tubes for the cytosolic fraction which was obtained through erythrocytes. In this set of six tubes (2000 µl) for the cytosolic fraction was added to various concentrations (2000 µl) of LiI was incubated and mixed for ten minutes. These are actually the reactive mixtures of cytosolic fraction added with various (Li + I) concentrations. We prepared another set of six tubes containing phosphate (2300 µl) buffer saline (pH – 7.6) and in every test tube (200µl) cytosolic fraction plus various Lithium carbonate concentrations added in the (500 µl) DTNB with five minutes incubation. At the end of incubation time, each sample mixture absorbance was documented at a wavelength which was fixed (λ max: 412 nm) under Ultra Violet visible spectrophotometer. Every sample absorbance was also converted in to GSH concentration. We used various instruments and chemicals such as Ellman's reagent, r glutathione (GSH) in reduced form (Fluka), chloroform, ethanol, Lithium carbonate (sigma), potassium dihydrogen phosphate (sigma), UV-visible spectrophotometer (Shimadzu model-1601), centrifuge model H-200, NaOH, disodium edetate, HCl (Kolchlight) and NaCl (Merk).

**Table – II:** Incubation Time and GSH Concentration

Incubation Time (Minutes)	GSH Concentration		
	CF Control	Low LC + CF	High LC + FC
0	5.1	3.6	3.2
20	5.1	3.4	3.1
40	5.1	3.1	2.9
60	5.1	2.9	2.8
90	5.1	2.8	2.7
120	5.1	2.7	2.6



DISCUSSION:

Though lithium very effective in the management of the manic and depressive episodes which are linked with the bipolar disorder and it is also used in the long-term maintenance by the physicians about the general awareness of the toxicities cause by the intake of lithium. These mood stabilizers also act as the anti-suicidal agents [21, 22]. In the patients who had bipolar disorder these mood stabilizers are also effective [23]. A recommended target level of the therapeutic serum is (0.6 – 0.75 m Eq/L) in order to treat prophylaxis and bipolar depression against the depressive relapses [23, 24]. More effective level of serum is (0.75 – 1.2 m EQ/L) to treat mania in the patients. Lithium toxicity is also linked with the levels of Serum above (1.2 m Eq/L). It is observed in the outcome of our research that lithium is responsible for the depletion of reduced glutathione in erythrocytes in the course of lithium therapy generally and in particular for the toxicities of lithium. Higher dose pf the serum brings frequent side effects at any level of the dose.

Nausea, diarrhea, vomiting, thirst, tremor, weight gain, polyuria, acne and a benign leukocytosis are some of the associated side effects. Lithium is potent to cause deterioration and hypothyroidism of renal function in the patients (20%) [25, 26]. Outcomes of this research also suggest better awareness of the physicians about anti-manic lithium effects which may not be established in the time span of seven to ten days. In the same time the sedative medications including benzodiazepines and antipsychotics are not necessary in the acute manic state. As the patient stabilizes additional medical treatment is to be stopped as lithium is to be continued as only option. GSH erythrocytes level dropped with the passage of time indicating the in the course of lithium therapy their precursors or antioxidants must be managed with an adjunctive therapy and in the course of lithium toxicities along with associated lithium detoxification treatments, patients must be treated with antioxidant.

CONCLUSION:

No doubt lithium is widely used to stabilize the mood as well as to treat manic depressive psychosis; on the same time, it is to be kept in the mind by the experts in the erythrocytes GSH depletion so precautions are mandatory in the course of lithium therapy.

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