L-Arginine as a Protective Adjuvant in the

 Treatment of Bipolar Disorders

with Hepatotoxic Agent Lithium

{Original Article (Anatomy)}

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ABSTRACT

Objective: The purpose of this randomized experimental study was to explore the beneficial effects of L-arginine on lithium carbonate induced liver toxicity.

Study Design: This study is randomized, interventional, prospective and experimental in nature.

Place and Duration of Study: This study was conducted in the department of anatomy, Basic medical sciences institute, Jinnah post graduate medical centre, Karachi. Animals were obtained from the animal house of BMSI, JPMC, Karachi. The duration of this study comprises of two to twelve weeks.

Materials and Methods: Sixty albino adult rats of 90 – 120 days of age weighing about 200 – 300 grams were used for this study. These were divided into four major groups A,B, C & D each comprising 15 rats. Each major group was sub-divided into three sub-groups 1, 2 & 3 on the basis of 02 weeks, 6 weeks and 12 weeks duration of treatment respectively. 4 um thick sections of rat liver were cut using rotary microtome for H&E. The statistical significance of the differences of various quantitative changes between lithium carbonate and lithium carbonate + L-arginine treated rats from the control rats were evaluated by the student T-test
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Results: Lithium treated group exhibited significant augmentation in absolute and relative liver

weight. Histopathological findings of liver revealed dilatation of central and portal veins, congestion of sinusoids, increment in mononuclear cell infiltration, microvesicular fatty change, swelling and hydropic degeneration of hepatocytes leading to pyknosis of nuclei, disintegration of organelles consequently leading to cell apoptosis and necrosis. Rats fed on co-administration of lithium plus L-arginine displayed significant improvement in the altered histology of liver lobules.

Conclusion: This study revealed that concomitant administration of L-arginine with lithium considerably reduces lithium's adverse effects.

Key Words: L-arginine, lithium carbonate, rat liver, bipolar disorder, hepatotoxicity.

REFERENCES

1. Tajes M, Gutierrez-Cuesta J, Folch J, Ferrer I, Caballero B and Smith MA. Lithium treatment decreases activities of kinases in a murine model of senescence. J Neuropathol Exp Ndeurol 2008; 67:12-13.

2. Kumar V, Cotran S, Collins T. Pathologic basis of diseases. 6th ed. Philadelphia: WB Saunders Company; 1999.p.1-17.

3. Kowska KM, Pasternak K, Music I, Wronskatyra J, Hordyjewska A. The influence of different doses of lithium administered in drinking water on lipid peroxidation and the activity of antioxidant enzymes in rats, Department of General Chemistry, Feliks Skubis Zewski Medical University of Lublin-ul-Staszica, Poland, 2006, e-mail: malgorzata.kietczykowska@am.lublin.pol .

4. Vijaimohan K, Mallika J and Devi SCS. Chemoprotective effect of sobatum against lithium induced oxidative damage in rats. J Lung Pharmacol 2010; 2CD:68-73.

5. Chadha DV, Bhalla P and Dhawan DK. Zinc modulates lithium induced hepatotoxicity in rats. Liver Intern 2008; 28:558-565.

6. Kolachi GM. A morphological study of lithium- induced nephrotoxicity with the role of L-arginine in albino rats. J Postgraduate Med Center Karachi 2007;65-67.

7. Shami PJ, Moore JO, Gockerman JP, Hathorn JW, Misukonis MA and Weinberg JB. Nitrix oxide modulation of the growth and differentiation of freshly isolated acute non-lymphocytic leukemia cells. Leukemia Res 1995; 19(8):527-533.

8. Kaibori M, Sakitani K, Oda M, Kamiyama Y, Masu Y and Okumura T. Immunosuppressant FK506 inhibits inducible nitric oxide synthase gene expression at a step of NF-kB activation in rat hepatocytes. J Hepatol 1999; 30(6):1138-1145.

9. Surks HK. cGMP dependent protein kinase 1 and smooth muscle relaxation: a tale of two isoforms. Circulation Res 1999; 101:12-13.

10. Wikipedia free enzyclopedia 2006, Arginine available at http://ex.wikipedia.org/wiki/lithium.

11. Takeuchi K, Tomohisa O, Shinichi K and Susumu O. Cytoprotective action of L-arginine against HCl-induced gastric injury in rats. J Pharmacol 1993; 61:13-21.

12. Mahmoud M, Daba MH, Ali G, Ammb A and Haleem AA. Protective effect of L-arginine against nephrotoxicity induced by cyclosporine in normal rats. Pharmacol Res 2002; 45:441-446.

13. Glaser AN. High yield biostatistics. Philadelphia, Lippincott Williams and Wilkins 2001; pp.28-30.

14. Sharma SD, Iqbal M. Lithium induced toxicity in rats: A hematological, biochemical and histo-pathological study.2005.Biol. Pharma. Bull 2005:28(5):834 – 837

15. Kumar V, Abbas AK, Fausto N and Mitchell RN. Robbins and Cotran Pathologic Basis of Disease. 8 th ed. Philadelphia: Saunders Elsevier; 2007.p. 632-633.

16. Nakayushi H and Uemitsu N. Evaluation of liver weight changes following a single oral administration of carbon tetrachloride in rats. Toxicology Appl Pharmacol 1984; 75:127.

17. Kubes P, Suzuki M and Granger DN. Nitric oxide: An endogenous modulator of leukocyte adhesion. Proc natt Acad Sci 1991; 88:4651-4655.

18. Lin MS, Miao HL, Gong XG and Bao ST. Effect of L-arginine on calcium in hepatic mitochondrion in rats with obstructive jaundice. Hepatobiliary Pancreat Dis Int 2006; 5(3):433-435.

19. Chattopadhyay P, Shukla G and Wahi AK. Protective effect of L-arginine against necrosis and apoptosis induced by experimental ischemic and reperfusion injury in rat liver. Saudi J Gastroenterol 2009; 15:156-162.

20. Ozsoy Y, Ozsoy M, Coskun T, Namli K, Var A, Ozyurt B. The effects of L-arginine on liver damage in experimental acute cholestasis, an immunohistochemical study. HPB Surgery 2011.

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