

## Effects of Lipoic Acid Supplementation on Activities of Cyclooxygenases and Levels of Prostaglandins E2 and F2 Alpha Metabolites in the Offspring of Rats with Streptozocin-Induced Diabetes

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**Abstract :** Background: Uncontrolled diabetes mellitus (DM) is an etiological factor for recurrent pregnancy loss and major congenital malformations in the offspring. Antioxidant therapy has been advocated to overcome the oxidant-antioxidant disequilibrium inherent in diabetes. The aims of this study were to evaluate the protective effect of lipoic acid (LA) on fetal outcome and to elucidate changes that may be involved in the mechanism(s) implicit diabetic fetopathy. Methods: Female rats were rendered hyperglycemic using streptozocin and then mated with normal male rat. Pregnant non-diabetic (group1; n=9; and group2; n=7) or pregnant diabetic (group 3; n=10; and group 4; n=8) rats were treated daily with either lipoic acid (LA) (30 mg/kg body weight; groups 2 and 4) or vehicle (groups 1 and 3) between gestational days 0 and 15. On day 15 of gestation, the rats were sacrificed, and the fetuses, placentas and membranes dissected out of the uterine horns. Following morphological examination, the fetuses, placentas and membranes were homogenized, and used to measure cyclooxygenases (COX) activities and metabolisms of prostaglandin (PG) E2 (PGEM) and PGF<sub>2</sub> (PGFM) levels. Maternal liver and plasma total glutathione levels were also determined. Results: Supplementation of diabetic rats with LA was found to significantly (P<0.05) reduce resorption rates in diabetic rats and increased mean fetal weight compared to diabetic group. Treatment of diabetic rats with LA leads to a significant (P<0.05) increase in liver and plasma total glutathione, in comparison with diabetic rats. Decreased levels of PGEM and elevated levels of PGFM in the fetuses, placentas and membranes were characteristic of experimental diabetic gestation associated with malformation. LA treatment to diabetic mothers failed to normalize levels of PGEM to the non-diabetic control rats. However, the levels of PGEM in malformed fetuses from LA-treated diabetic mothers was significantly (P < 0.05) higher than those in malformed fetuses from diabetic rats. Conclusions: We conclude that LA can reduce congenital malformations in the offspring of diabetic rats at day 15 of gestation. However, LA treatment did not completely prevent the occurrence of malformations, other factors, such as arachidonic acid deficiency and altered prostaglandin metabolism may be involved in the pathogenesis of diabetes-induced congenital malformations.

**Keywords :** diabetes, lipoic acid, pregnancy, prostaglandins

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