Indian J Physiol Pharmacol 2000; 44 (4) : 500–502

LETTER TO THE EDITOR

INCREASE IN CIRCULATING PRODUCTS OF LIPID PEROXIDATION (MALONALDEHYED) IN STREPTOZOCIN INDUCED DIABETIC MICE

Sir,

(Received on January 27, 1999)

Morbidity and mortality in diabetes is typically associated with the development of atherosclerotic cardiovascular diseases and diabetes related complications. In these pathological events peroxidation of cellular structures, consequence of increased free radical activity is thought to play an important role. Oxidative stress has been increasingly implicated in atherosclerosis (1-3), in accelerated atheroclerosis and microvascular complications of diabetes (2, 4, 5). Oxidative stress can result in widespread lipid, protein and DNA damage (6), including oxidative modification of LDL cholesterol, believed to be central in the pathogensis of atherosclerosis and endothelial dysfunction (1-3,5). Oxidative stress as assessed by index of lipid peroxidation has been shown to be elevated in diabetics (7-14), even in patients without complications (9,11-13). The mechanism underlying the apparent increased oxidative stress in diabetes is not entirely clear. Accumulating evidence points to many, often interrelated mechanisms (2,4,5); increased production of free radicals or decreased antioxidant defences. With this background knowledge we have assessed the oxidative stress as measured by a widely used index of lipid peroxidation (Malonaldehyde) in streptozocin induced diabetic mice and in normal healthy mice. The effect of Vitamin E administration on lipid peroxidation in these mice is seen Malonaldehyde (MDA) is the most abundant individual aldehyde resulting from lipid peroxidation (15) and its determination by thioborbituric acid (TBA) (16) which is a common method of estimating lipid peroxidation. After fasting for 48 hours young healthy mice (n=12) were anaesthetized with Ether and given i/p injection of freshly prepared solution of streptozozin (Sigma, St Louis, Mo) 50 mg/ml in 0.1 m citrate buffer pH 4.5 making final dose of 50mg/kg body weight. Control mice (n=8) received 0.23-0.25 ml of citrate buffer. Streptozocin treated animals were allowed to drink 5% glucose solution overnight to overcome drug induced hypoglycemia. Streptozocin induced animals were periodically monitored by testing blood glucose level. Control mice and streptozocin induced diabetic mice were given Vitamin E in dose of 10 mg/kg daily i/p for six weeks. For estimation of MDA in plasma, 0.5ml of plasma (blood was taken from tail vein in healthy and streptozocin induced diabetic mice before and after giving vitamin E for 3 and 6 weeks) was added to an equal volume of isotonic saline and to it was added 2.0 ml of 50% Trichloacetic acid in cold and shaken to precipitate the protein. After `30 min it was centrifuged at

800xg for 15min at 4°C; into 1.0ml of supernatant was added 2.0ml of 0.67% aqueous TBA and the mixture was heated in boiling water for 15 min and rapidly cooled. The pink chromophore that developed was read at 535 nm.

A greater than two fold higher levels of plasma TBARS (Thiobarbutric acid reacting substances); a widely used indirect measure of lipid peroxidation was found in streptozocin induced diabetic mice (1.024 umol/ml) which is significantly higher than healthy control mice (plasma malonaldehyde 0.450 umol/ml) Table 1. The level of plasma M.D.A. tends to normalize in streptozocin induced diabetic mice after giving vitamin E for six weeks. There was no significant change seen in level of plasma malonaldehyde in control mice after giving vitamin E for three and six weeks. Increased level of circulating products of lipid peroxidation (TBARS) in streptozocin induced diabetic mice suggests increased oxidative stress in diabetic and aggress with a large number of studies finding increased plasma TBARS or MDA in diabetic patients (7-14). These investigations are suggestive that supplementation of lipid peroxidation chain breaking antioxidants such as vitamin-E (alpha- tocopherol), significantly reduces ther level of lipid peroxidation in diabetes; hence the development of diabetic vascular complications can be significantly prevented by giving vitamin E in diabetic patients.

TABLE I: Plasma M.D.A. µmol/ml mean ± SD.

Group	*Before Vit. E administrartion*	*After Vit. E administration*	
	0 day	*3rd week*	*6th week*
Streptozocin induced Diabetic mic (n=12)	1.024±0.124	0.862±0.096	0.642±0.050
Healthy mice (n=8)	0.450±0.050	0.402±0.386	0.86±0.078

Showing level of plasma M.D.A. in streptozocin induce diabetic mice and healthy mice before and after administration of Vitamin E for 3 and 6 weeks.

VANI GUPTA,* SANDEEP BHATTACHARYA, VANDANA GUPTA*** AND S. M. NATU**

*Departments of *Physiology and **Pathology, K.G. Medical College Lucknow – 226 003 and ***G. S. V. M. Medical College, Kanpur – 208 002*

*Corresponding Author

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