

**EFFECT OF TAURINE ON CAROTID INTIMA MEDIA THICKNESS IN  
PATIENTS WITH TYPE 2 DIABETES MELLITUS.**

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**ABSTRACT**

**Background :** Carotid intima-media thickness (CIMT) has been proposed as a surrogate marker to identify diabetic patients at higher risk for CAD. Oxidative stress has been postulated to be involved in the development of atherosclerosis.

**Objective:** The present study was to evaluate the effect of taurine on serum lipids, lipid peroxidation and RBC antioxidant status and vessel changes in type 2 diabetes.

**Design :** Twenty individuals T2DM, aged 35 -50 were enrolled. Twenty age and sex-matched healthy individuals served as controls. Taurine was given to both controls and diabetics at a dose of 500mg / day for a period of 30 days. Blood glucose, serum lipids, TBARS in plasma, RBC, antioxidant status in RBC were estimated before and after taurine supplementation. Intima media thickness in both common carotid arteries were assessed by using Doppler B mode ultrasonography. **Results:** Taurine significantly reduced the serum lipids, lipid peroxidation and improved the antioxidant enzymes in diabetics. Intima media thickness was significantly high in type 2 diabetics. Taurine significantly reduced the intima media thickness in both common carotid arteries in type 2 diabetics. **Conclusion:** Taurine by its antioxidant effect could be useful in retarding atherosclerosis in diabetics and thereby preventing the complications.

**INTRODUCTION**

Cardiovascular diseases are the major cause of mortality in patients with diabetes mellitus (1). Identification of asymptomatic patients with diabetes mellitus (DM) at increased risk for coronary artery disease (CAD) remains a challenge. Carotid intima-media thickness (CIMT) has been proposed as a surrogate marker for CAD but only limited data are available (2). Carotid artery intima-media thickness (CIMT) represents the simplest measurable parameter for pre-atherosclerotic lesions in extra-cranial arteries (3). Measurement of the IMT of the CCA by ultrasound was found to be a suitable noninvasive method to visualize the arterial walls and to monitor early stage of the atherosclerotic process. An increased carotid IMT was observed in type 2 diabetic patients (4). Furthermore asymptomatic hyperglycemic subjects were shown to have significant IMT in comparison with healthy control subjects. Aortic intima media thickness (aIMT) is an earlier marker than carotid intima media thickness (cIMT) of preclinical atherosclerosis in children with type 1 diabetes mellitus and relates to known cardiovascular risk factors and metabolic control (5). Diabetes mellitus, especially type 2 diabetes often associated with disorders in lipid metabolism (6). Diabetic dyslipidemia in patients with type 2 diabetes commonly consists of elevated triglyceride levels, low HDL-C levels and normal or slightly elevated LDL-C levels.

This atherogenic lipoprotein profile contributes to the development of atherosclerosis and increasing the risk of cardiovascular events, the most common cause of death in type 2 diabetes (7). Increase in lipid peroxidation and decrease in the level of antioxidant enzymes in diabetic animals and in diabetic subjects were reported in many studies (8,9). Taurine, 2-aminoethane sulfonic acid is a sulfur containing amino acid that is widely distributed in various animal tissues. Taurine has been shown to have antioxidant property by reducing lipid peroxidation (10,11,12). Studies have reported that taurine reduces the atherogenic VLDL and LDL cholesterol and triglyceride levels in rats fed with a high cholesterol diet triglyceride (13,14). Taurine also has a beneficial effect on atherosclerosis by increasing HDL-C levels (15). Few studies have reported the relationship between asymptomatic carotid atherosclerosis, as defined by carotid intima-media thickness (CIMT), plasma lipids and RBC antioxidant status. This study has been taken to explore the effect of taurine supplementation on the atherosclerotic changes of carotid vessels using Doppler, plasma lipids and RBC antioxidant status in both controls and diabetic subjects.

## MATERIALS AND METHODS

Twenty number of type 2 diabetes patients in the age group 35- 55 yrs diagnosed on the basis of WHO criteria attending Rajah Muthiah Medical college Hospital Annamalai University , India were selected for this study. The criterion of inclusion was T2DM receiving glibenclamide 5 mg per day. Patients were excluded if they had any previous history of ischemic stroke, hypertension, familial hyperlipidemia, history of angina, myocardial infarction, angioplasty, congestive heart failure, atrial fibrillation, coronary bypass, carotid or peripheral vascular surgery, or renal insufficiency. All subjects were normotensives, nonsmokers, nonalcoholic. Subjects on any drugs such as aspirin, lipid lowering agents or supplemental vitamins were excluded from the study. Female subjects were premenopausal. In addition to ethical committee approval, written consent was obtained from all subjects.

Twenty subjects in the same age group with normal glucose tolerance and no history of first degree relatives with diabetes mellitus and who were nonsmokers, nonalcoholic, not on any drugs were selected as controls.

Taurine was given to both controls and patients at a dose of 500mg / day for a period of 30 days. Fasting and postprandial venous blood samples were collected in heparinized tubes.

The following biochemical investigations were carried out before and after taurine supplementation.

Blood glucose

Serum lipid profile

Plasma TBARS

RBC TBARS and

Erythrocyte antioxidant status

Ultrasonography was performed with B-mode images of a high-resolution ultrasound scanner equipped with a 7 MHz linear array transducer. Arterial diameter and IMT measurements were done for both common carotid arteries on the first day and 30<sup>th</sup> day following taurine supplementation.

## Biochemical estimations

Blood samples were collected in heparinized tubes and plasma was separated by centrifugation at 3000 rpm for 15 min. Blood glucose and lipid profile were analyzed by using Boehringer Mannheim kits by Erba smart lab analyzer, U.S.A. LDL-C was calculated using the formula developed by friedewald et al. (16).

TBARS in plasma and RBC were assayed according to the methods of Yagi (17), and Ohkawa et al (18) respectively. RBC antioxidant enzymic activities viz., SOD, Catalase, Glutathione peroxidase and non enzymic antioxidant reduced glutathione were assayed by Kakkar et al (19), Sinha (20), and Beutler and Kelley (21) respectively.

### Statistical Analysis

The data were expressed as means  $\pm$  SD. Statistical comparisons were performed by one way analysis of variance (ANOVA) followed by student's t-test. The results were considered statistically significant if the p values were 0.05 or less.

### RESULTS

Table 1 indicates the levels of serum cholesterol, triglycerides, HDL-C, LDL-C. The level of serum total cholesterol, LDL-C and triglycerides were significantly increased in diabetes in comparison with controls. Taurine treatment at a dose of 500mg/day significantly reduced the total cholesterol, LDL-C and triglycerides in diabetics. The decrease in HDL-C in diabetics was brought back to near normal range in both control and diabetics.

Table 2 depicts the TBARS in plasma and RBC and the RBC antioxidant status.

There was significant decrease in TBARS in diabetics after taurine supplementation. The antioxidant enzymes viz catalase, glutathione peroxidase, SOD and nonenzymic antioxidant GSH were markedly decreased in diabetics and returned to near normal with taurine.

Table 3 and 4 presents the vessel changes in LCCA and RCCA. The carotid intima media thickness was significantly high in diabetics which was markedly reduced after taurine treatment.

**Table 1: Levels of serum cholesterol, triglycerides, HDL-C, LDL-C**

Parameters	Control	Control after Taurine	Diabetes	Diabetes after Taurine	P value
Cholesterol (mg/dl)	180.20 $\pm$ 28.04	172.60 $\pm$ 26.23	228.25 $\pm$ 27.08	189.50 $\pm$ 25.35	NS* 0.001**
TGL (mg/dl)	121.70 $\pm$ 25.70	90.00 $\pm$ 12.97	167.2 $\pm$ 48.1	129.3 $\pm$ 38.5	0.002* 0.001**
HDL-C (mg/dl)	42.00 $\pm$ 4.03	48.43 $\pm$ 4.92	40.45 $\pm$ 2.50	45.85 $\pm$ 2.49	0.001* 0.001**
LDL-C (mg/dl)	118.86 $\pm$ 29.83	106.00 $\pm$ 26.04	154.48 $\pm$ 31.69	118.49 $\pm$ 27.24	NS* 0.001**

Values are given as mean  $\pm$  SD, \*control vs control after taurine, \*\*Diabetes vs diabetes after taurine

**Table 2. Lipid peroxidation and RBC antioxidant status**

Parameter	Control	Control after Taurine	Diabetes	Diabetes after Taurine	P value
Plasma TBARS	3.19 $\pm$ 0.79	2.61 $\pm$ 0.65	6.98 $\pm$ 1.47	5.01 $\pm$ 0.67	NS* 0.01**
RBC TBARS	6.74 $\pm$ 0.60	5.42 $\pm$ 0.67 <sup>b</sup>	9.49 $\pm$ 0.71	5.77 $\pm$ 1.12	0.04* 0.03**
Catalase	15.62 $\pm$ 0.58	17.90 $\pm$ 1.62	9.35 $\pm$ 0.17	14.06 $\pm$ 1.75	0.002* 0.001**
Gpx	11.84 $\pm$ 0.64	13.97 $\pm$ 1.30	6.82 $\pm$ 0.65	9.75 $\pm$ 0.98	0.003* 0.001**
Reduced glutathione	11.44 $\pm$ 0.72	12.28 $\pm$ 0.43	5.99 $\pm$ 0.86	10.14 $\pm$ 1.04	0.001* 0.001**
SOD	6.07 $\pm$ 0.31	6.77 $\pm$ 0.43	3.91 $\pm$ 0.42	5.18 $\pm$ 0.44	0.01* 0.01**

Values are given as mean  $\pm$  SD, \*control vs control after taurine, \*\*Diabetes vs diabetes after taurine  
Plasma TBARS - nmoles/ml, RBC TBARS – nmoles /mg of Hb, Catalase-  $\mu$ moles of H<sub>2</sub>O<sub>2</sub> utilized/min/ mg of Hb, GPx –  $\mu$ g of GSH consumed / min/ mg of Hb, SOD- 50% inhibition of NBT reduction/min / mg of Hb, GSH- mg/ 100 ml of RBC

**Table 3- Vessel changes in LCCA**

Parameter	Control	Control after Taurine	Diabetes	Diabetes after Taurine	P value
Total vessel size (mm)	7.59 ± 0.56	7.54 ± 0.47	7.91 ± 0.55	7.73 ± 0.60	NS* 0.01**
Lumen size (mm)	5.56 ± 0.51	6.05 ± 0.41	5.38 ± 0.65	5.78 ± 0.63	0.01* 0.01**
Intima media thickness (mm)	0.97 ± 0.07	0.74 ± 0.05	1.28 ± 0.14	0.90 ± 0.12	0.01* 0.01**

Values are given as mean ± SD, \*control vs control after taurine, \*\*Diabetes vs diabetes after taurine

**Table 4 - Vessel changes in RCCA**

Parameter	Control 1	Control after Taurine 2	Diabetes 3	Diabetes after Taurine 4	P value
Total vessel size (mm)	7.84 ± 0.72	7.66 ± 0.47	7.89 ± 0.81	7.67 ± 0.83	0.04* 0.01**
Lumen size (mm)	5.56 ± 0.51	6.05 ± 0.41	5.38 ± 0.65	5.78 ± 0.63	0.01* 0.01**
Intima media thickness (mm)	0.97 ± 0.07	0.74 ± 0.05	1.28 ± 0.14	0.90 ± 0.12	0.01* 0.01**

Values are given as mean ± SD, \*control vs control after taurine, \*\*Diabetes vs diabetes after taurine

## DISCUSSION

Diabetes mellitus is often associated with dyslipidemia (22). In the present study there was significant increase in total cholesterol, LDL-C and TGL and significant decrease in HDL-C in diabetics when compared with the control. Taurine supplementation reduced the blood cholesterol level diabetic which might be due to enhanced elimination of cholesterol. It has been reported that taurine enhances 7-alpha hydroxylase, a key enzyme of bile acid synthesis and thus enhanced elimination of bile acids (23). The resultant bile acid synthesis and the enhancement of LDL receptor binding may retard the development of atherosclerosis (24). Taurine supplementation decreased the serum TGL levels in both group.

Reactive oxygen species induced oxidative damage has been implicated in the pathogenesis of several disorders including diabetes mellitus (25). Elevated TBARS observed in the diabetic subjects could therefore be related to overproduction of lipid peroxidation byproducts (26). Taurine is a semiessential amino acid, and its deficiency is involved in retinal and cardiac degenerations. In recent years, it was found that diabetes mellitus (DM) is associated with taurine, and many in vivo experimental studies showed that taurine administration is able to reduce the alterations induced by DM in the retina, lens, and peripheral nerve (27). There were overwhelming evidence that taurine treatment diminishes the severity of complications among the major targets of diabetes namely, the retina the neuron, and the kidney. Taurine supplementation reduced the plasma and RBC TBARS levels which suggest the antioxidant role of taurine as reported in early studies (28,29). Taurine treatment brought back the activities of GPx, CAT, SOD and the level of GSH to near normal range in the present study. The beneficial effect of taurine appears to be primarily linked to attenuation of oxidative stress. Measurement of carotid intima media thickness (IMT) using high-resolution B-mode ultrasonography is a noninvasive, well validated method to assess early cardiovascular disease (30).

Carotid IMT is an independent, significant parameter for the prediction of significant coronary artery disease. In type-2 diabetes mellitus (T2DM), carotid IMT was significantly higher than in corresponding healthy, age- and sex-matched nondiabetic subjects as found in several studies. Taurine administration significantly reduced the carotid intima media thickness in both common carotid arteries. Taurine therapy may thus represent a novel approach towards diminishing the severity of diabetic complications with its antioxidant activity.

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