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Supplementation of Taurine Alleviates Oxidative Stress and Dyslipidaemia in Streptozotacin Induced Diabetic Rats

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Abstract

Context: Diabetes mellitus (DM) is a metabolic disorder characterised by chronic hyperglycaemia, oxidative stress and dyslipidaemia. Glycaemic control may not always normalize the dyslipidaemia and antioxidant status. *Aim:* To study the effect of taurine on glycaemic control, antioxidant status and dislipidaemia in streptozotocin (STZ) induced diabetic rats. *Settings and Design:* It is an experimental study done on Wistar rats. *Materials and Methods:* Thirty two Wistar male albino rats of 19±1 weeks of age weighing 200-220 grams were randomly divided into four groups and each group consisted of eight animals. Group I (control) standard chow diet; Group II (chow diet plus taurine) Group III (diabetes induced), Group IV (diabetic receiving taurine). At the end of 45th day, all animals were sacrificed by cervical decapitation after overnight fasting. Blood and liver tissue samples were collected for analyses of plasma glucose, plasma and hepatic thiobarbituric acid reactive substances (TBARS), lipid profile, activities of lipoprotein lipase (LPL) and Lecithin cholesterol acyl transferase (LCAT) and histopathological studies of liver for fatty changes. *Statistical analysis used:* One way analysis of variance (ANOVA) test was applied in order to evaluate any significant difference in the mean values. *Results:* The present study found that there was no significant change in plasma glucose levels and plasma and hepatic TBARS levels were significantly reduced while a significant positive modulation of lipid profile and reduction of hepatic fats in diabetic rats treated with taurine. *Conclusions:* The present study indicates that taurine supplementation might be beneficial in alleviating oxidative stress and dyslipidaemia in diabetes.

Keywords: Diabetes; Streptozotacin; Taurine; Antioxidant; Dyslipidaemia

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterised by chronic hyperglycaemia with derangement in carbohydrate, fat and protein metabolism arising from a defect in insulin secretion or action or both [1]. Based on the aetiology and pathogenesis; DM is classified into two types: type 1 and type 2 DM [2]. The risk of developing diabetic complications is associated with age, duration of diabetes and this is greater in young diabetic patients [3]. Chronic hyperglycaemia causes cellular damage through several pathways such as increased non enzymatic glycation and increased lipid peroxidation and reduced antioxidant status, which result in over expression of gene products causing cellular damage [4, 5]. Oxygen free radicals are formed disproportionately in diabetes by glucose oxidation, non-enzymatic glycation of proteins and subsequent oxidative degradation of glycated proteins [6]. Oxidative stress due to generation of free radicals and accumulated products of lipid peroxidation plays a major role in the development of complications in diabetes [7].

Diabetes, especially type 2 is often associated with disorders in lipid metabolism [8]. Diabetic dyslipidaemia in subjects with type 2 commonly consists of elevated levels of triacylglycerol (TGL), reduced levels of high density lipoprotein (HDL) and normal or slightly elevated levels of low density lipoprotein (LDL) [9]. Taurine, 2-aminoethane sulfonic acid is a sulfur containing amino acid that is widely distributed in various animal tissues [10, 11]. It was shown to have hypoglycaemic activity, antioxidant property by reducing lipid peroxidation

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[12,-14]. and beneficial effect on blood levels of TGL and HDL in animal models [9,15]. Glycaemic control such as intensive glycaemic control can prevent micro vascular and macrovascular complications in both types 1 and 2 diabetes [16]. Glycaemic control is as such beneficial in preventing these complications; however, there is a little evidence that it promotes the average health of the diabetes. Glycaemic control may not always normalise the status of antioxidant and dyslipidaemia [17,18]. Therefore, it is paramount importance to identify suitable agents to address these concerns in diabetes. Hence, the present study was designed to investigate the effect of taurine on glycaemic control, antioxidant status and dyslipidaemia in streptozotocin (STZ) induced diabetic rats as model.

Materials and Methods

Wistar strain male albino rats of 19±1 weeks of age weighing 200-220 grams were obtained from the Central Animal House, Rajah Muthiah Medical College and Hospital, Annamalai University. They were housed in polypropylene cages; three per cage and kept at 25±2°C with 12:12 hour light and dark cycles. The animals were maintained on standard chow diet and water ad libitum. They were randomly divided into four groups and each group consisted of eight animals. Group I (control) standard chow diet; Group II (chow diet plus taurine) Group III (diabetes induced), Group IV (diabetic receiving taurine).

Induction of diabetes

The animals were fasted for 24 hour before inducing diabetes with STZ. They were injected intraperitoneally with STZ at a dose of 50 mg/kg body weight in 0.1 M citrate buffer (pH 4.5). The control animals received citrate buffer alone. Diabetes was confirmed by measuring the fasting plasma glucose concentration 48 hour after STZ injection. Animals with plasma glucose concentration above 240 mg/dl were considered to be diabetic and they were taken up for the study. Taurine was administered orally once daily at a dose of 100 mg/kg body weight.

Sample collection

At the end of 45th day, all animals were sacrificed by cervical decapitation after overnight fasting. Blood samples were collected in plain and heparinized tubes. They were centrifuged at 3000 rpm at room temperature. The serum and plasma were used for analyses. The liver specimens were collected in homogenising buffer (0.1 M Tris-Hcl, pH 7.4) for homogenisation and in 10% formalin for histopathological studies.

Biochemical analyses

Plasma glucose was determined by enzymatic glucose oxidase peroxidase (GOD-POD) method, serum total cholesterol, TGL, HDL were estimated by using Boehringer Mannheim reagent kits in Erba Smart Lab analyzer, USA. LDL was calculated using the formula developed by Friedewald et al [19]. Lecithin cholesterol acyl transferase (LCAT) activity was estimated by the method of Legraud et al [20]. with the modification of Hitz et al. (1983) [21]. Lipoprotein lipase (LPL) activity was assayed by the method of Schrecker and Greter (1979) [22]. A portion of the liver was homogenised in homogenising buffer and the homogenate was used for the estimation of hepatic fats and assay of fat metabolizing enzyme as well as determination of thiobarbituric acid reactive substances (TBARS). Hepatic lipase activity was assayed by the method of krauss et al. (l973) [23]. TBARS in plasma and liver homogenate were estimated by the methods of Yagi (1987) [24] and Ohkawa et al. (1979) [25]. Histopathological examination of formalin fixed liver tissues was performed with Hematoxylin and Eosin stain for fatty changes.

Statistical Analysis

One way analysis of variance (ANOVA) test was applied in order to evaluate any significant difference in the mean values. All values used in analysis represent the mean±SD of eight rats in each group. The results were considered statistically significant if the *p* values were 0.05 or less.

Results

Table l shows food intake, body weight changes and plasma glucose levels in experimental animals. Body weight was significantly reduced in diabetic rats while minimally decreased in diabetic rats treated with taurine although there was no significant change in plasma glucose levels in the same group (Group IV). Table 2 shows plasma TBARS, hepatic TBARS, cholesterol and TGL in experimental animals. Plasma and hepatic TBARS levels were significantly reduced in diabetic rats treated with taurine. There was a significant decrease in hepatic cholesterol and TGL in diabetic rats treated with taurine (Group IV). Table 3 shows

serum lipid profile and lipoprotein metabolizing enzymes in experimental animals. There was a significant decrease in serum cholesterol, TGL and LDL in diabetic rats administered with taurine (Group IV). The activities of LPL and LCAT were increased in Group IV compared to Group III.

Figure 1 shows histopathological changes of liver. Hepatocytes were normal with portal triad and central vein in control rats (Group I). Hepatocytes were normal with mild congestion of central vein and sinusoidal dilatation with congestion in control rats treated with taurine (Group II). Hepatocytes showed

Table 1: Food intake, body weight and plasma glucose levels in experimental animals

Groups	Food Intake (gm)	Body weight (gm)	Plasma glucose (mg/dl)
Control	18.22±0.05	244.1 ± 8.94	103.75 ± 4.77
Control+Taurine	18.35 ±0.06*	241.5 ±l0.86*!	100.25 ±2.92*
Diabetic	20.82±0.14**	202.75±13.35**!	344.13 ±41.71**#
Diabetic+Taurine	19.53 ±0.16***	221.00± 11.01***#	329.5 2±27.4***

Values are expressed as mean ± SD ; * Group 2 compared with Group 1 ** Group 3 compared with Group 1; *** Group 4 compared with Group 3 !p<0.05; #p<0.001

Table 2: Plasma TBARS, hepatic TBARS, cholesterol and TGL in experimental animals

Groups	Plasma TBARS nmoles/ml	Hepatic TBARS nmoles/mg pro	Hepatic Cholesterol mg/l00gm	Hepatic TGL mg/100gm
Control	0.37±0.04	0.34±0.40	318.0± 5.86	335.5 ± 6.23
Control + Taurine	0.29±0.03*#	0.28±0.42*	310.0±6.23*	326.4 ±5.42*
Diabetic	0.61±0.04**#	0.49±0.06**#	534.13±15.15**#	480.4 ±9.23**#
Diabetic+Taurine	0.43±0.03***#	0.37±0.02***#	322.62±8.94***#	372.3± 4.34***!

Values are expressed as mean ± SD; *Group 2 compared with Group 1; ** Group 3 compared with Group 1 ***Group 4 compared with Group 3; !p<0.05 #p<0.001

Table 3: Serum lipid profile and lipoprotein metabolising enzymes in experimental animals

Group	Cholesterol mg/dl	TGL mg/dl	LDL mg/dl	LPL	LCAT	HDL mg/dl
Control	87.13±8.54	95.5±7.17	35.15±9.96	0.13±0.04	0.67±0.04	32.13±2.42
Control+Taurine	90.88±10.55*	93.25±16.32*	36.6±7.70	0.14±0.03*#	0.70±0.06*	35.38± 2.78*!
Diabetic	228.0±15.72**#	258.63±22.66**#	150.40±13.37	0.05±0.02**#	0.23±0.02**#	26.13± 3.19**#
Diabetic+Taurine	140.5±29.95***#	168.25±11.17***#	76.22±31.33	0.113±0.05*** #	0.58±0.02***#	30.38±3.02***!

Values are expressed as mean ± SD; *Group 2 compared with Group 1; ** Group 3 compared with Group 1 ***Group 4 compared with Group 3; !p<0.05; #p<0.001
LPL: µ moles of glycerol liberated/ml/hr;
LCAT: n moles of cholesterol esterified /ml/hr

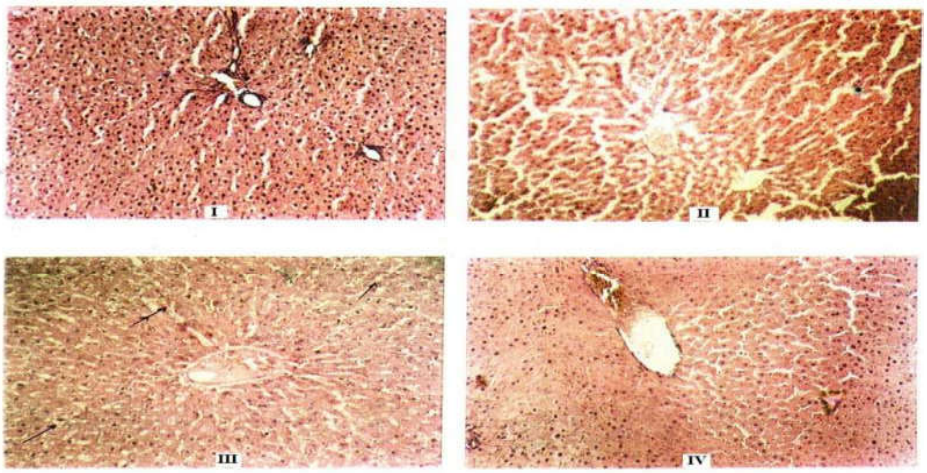

Fig. 1: Histopathology of liver H&E x 100

sinusoidal dilatation and congestion of central vein with micro vascular type of fatty changes in diabetic rats as indicated with black arrows (Group III). Hepatocytes showed congestion of central vein and focal sinusoidal dilatation with no fatty changes in diabetic rats treated with taurine (Group IV).

Discussion

The present study investigated the effect of taurine on hyperglycaemia, antioxidant and dyslipidaemia in STZ induced diabetic rats. It was found that taurine did not improve the glycemic status as taurine administration showed no significant effect on plasma glucose levels in taurine treated group. This is in contrast to earlier studies which reported that taurine was effective in reducing hyperglycaemia [26,27]. Taurine administration reduced the plasma and hepatic TBARS levels significantly which suggests the antioxidant role of taurine which is in good agreement with most other studies [14,28]. It is reported that that taurine plays a role as antioxidant by increasing the activity of super oxide dismutase (SOD) in serum and the expression of heme oxygenase-1 in liver tissue [29]. There was a significant increase in total cholesterol, LDL and TGL and decrease of HDL in diabetic rats when compared with the controls. Taurine administration reduced the blood cholesterol levels in STZ induced diabetic rats. This could be due to decreased dietary intake or decreased absorption of cholesterol. It could also be due to decreased synthesis or increased elimination or both. Decreased dietary intake could not be the cause as evident from table 1. There was no significant change in blood and hepatic lipids in control rats receiving taurine compared to control rats. Hence decreased absorption of cholesterol and decreased synthesis could be ruled out. Therefore, it might be due to enhanced elimination of cholesterol. It has been reported that taurine enhances 7-alpha hydroxylase, a key enzyme in bile acid synthesis [30,31] and hence enhanced elimination of bile acids.

Taurine administration reduced the serum and hepatic TGL levels significantly; it could not be due to decreased synthesis of TGL as taurine has no effect on insulin secretion, which is evident by insignificant change in plasma glucose levels. It suggests that taurine might reduce the lipolysis in the adipose tissue, causing lowering of serum and hepatic TGL and so only marginal weight loss was seen when compared to diabetic rats. This might be due to enhancement of LPL activity and increased utilization of TGL rich lipoproteins by peripheral tissues or due to decreased uptake by liver. Taurine administration enhanced the LCAT activity which shows that there is an increased uptake of cholesterol. But the hepatic cholesterol was significantly reduced which implies that cholesterol might be converted to bile acids which would be easily eliminated [32-34]. There was a significant reduction of hepatic fats which suggests the protective role of taurine against fatty changes due to diabetes in liver (Figure 1).

Conclusion

The present study indicates that taurine supplementation might be beneficial in alleviating oxidative stress and dyslipidaemia in diabetes.

Conflict of Interest: None

Key Messages

Diabetes mellitus is characterised by chronic hyperglycaemia. It is also characterised by lipid peroxidation and dyslipidemia. It is associated with complications such as micro and macro vascular complications. Taurine supplementation would be beneficial to these complications in diabetes.

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