Supplementation of taurine attenuates cataract formation in alloxan-diabetic New Zealand White rabbits

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Abstract: To investigate the protective effect of taurine on the progression of diabetic cataract formation induced by alloxan. Diabetes was induced in New Zealand white rabbits by intravenous injection of alloxan (100mg/kg) and the control rabbits received vehicle alone. While a set of diabetic animals received distilled water, another set received 1% taurine dissolved in distilled water for a period of 24 weeks. Body weight and blood glucose of all animals were measured once a week for a period of 24 weeks. Cataract progression was monitored by slit-lamp biomicroscope. The results showed that alloxan-induced diabetes caused a significantly ($p < 0.05$) body weight loss, hyperglycemia, and cataract formation as compared with normal control group. By contrast, administration of taurine for 24 weeks significantly ameliorated the elevated levels of blood glucose and the progression of diabetic cataract formation in lens that was induced by alloxan in rabbits. Overall, the studies demonstrate that taurine exhibits potent protective effects on alloxan-induced diabetic cataract and hyperglycemia in rabbits.
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1. Introduction

Cataract, characterized by cloudiness of the eye lens, is one of the earliest secondary complications of diabetic patients (1,2) and approximately 42% of the world's blind population is attributed to diabetic cataract (3,4). Diabetic cataract is a major cause of blindness or visual impairment, and the incidence and progression of cataract are elevated in diabetic (2).

In experimentation, the drugs of alloxan cause chronic diseases of diabetes that are characterized by high levels of blood glucose and insufficient insulin (5,6). Long-drawn-out exposure to chronic hyperglycemia can lead to the complication of diabetic cataract (2). These models have been widely used effectively to induce diabetic complications of cataract in various experimental animals for evaluating the therapeutic potential of drugs and dietary antioxidants (7,8).

Taurine, a conditionally essential amino acid in mammalian tissues, plays an important role in protecting cells and organisms against the harmful effects. The main source of taurine *in vivo* is dietary intake and biosynthesis. Interestingly, taurine, function as an organic osmolyte, is the most abundant free amino acid in the lens of humans (9). In diabetic experimental rat's model, taurine also protects against alloxan-induced hyperglycemia in type I diabetes (10). Many studies have been reported that taurine is necessary for the normal vision, and deficiencies are associated with retinal degeneration (11,12). A previous study has suggested that taurine is depleted by taurine-deficient diet in cats that causes degeneration diseases of retina is similar to retinitis pigmentosa in human (13). Regarding to the retinal protection, taurine supplementation has reported to prevent and possibly reverse age-related cataracts (14). Additionally, taurine has been also reported to inhibit cataractogenesis in rabbit lens exposed to 30 mM galactose without significantly reducing polyol accumulation (15).

In consideration of excellent bioactivity of taurine, we hypothesized that taurine supplementation may provide against alloxan-induced diabetic cataract in rabbits. Therefore, the present study examined the protective effects of taurine on alloxan-induced diabetic cataract in male New Zealand White rabbits.

2. Material and Methods

Animals

Thirty male New Zealand White rabbits (10 weeks old) were obtained from a farm (Ta Tsung farm, Changhua City, Taiwan). Animals were quarantined and allowed to acclimate for one week prior to the beginning of experimentation. Animals were housed in 1-2 per cage under standard laboratory conditions with a 12 h light/dark cycle. The temperature of animal room was maintained at 25 ± 2ºC with a relative humidity of 55 ± 5%. Air handling units in the animal rooms were set to provide approximately 12 fresh air changes per hour. Food and water were available *ad libitum*. The experimental protocols for this study were approved by the Institutional Animal Care and Use Committee and the animals were cared for in

accordance with the institutional ethical guidelines. All procedures were performed by according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Experimental Design

Group I served as normal control (n=6). The experimental groups (Group II and III) received an intravenous injection of alloxan in 0.9% sodium chloride at a dose of 100 mg/kg body weight for induced diabetes. Blood glucose levels were monitored weekly. The animals having blood glucose levels > 200 mg/dl in a consecutive 3-week period were included in the experiment and were distributed into the following groups: Group II diabetes (diabetic rabbits untreated, n=6) and Group III diabetes + taurine (diabetic rabbits treated with 1% taurine in drinking water, n=6). Furthermore, food intake, water intake (daily) and body weights (weekly) were recorded throughout the study period.

Blood Glucose Measurement

Blood was collected once a week from the marginal ear vein for glucose estimation by using a commercially available glucometer (Accu-Chek Active blood glucose meter; Roche Diagnostics Gmbha, Germany) for a period of 24 weeks.

Slit Lamp Examination and Cataract Classification

Eyes were examined every week using a slit lamp biomicroscope (Topcon SL-1, Topcon Optical Co., Tokyo, Japan) with the methods of indirect retro-illumination on dilated pupils. Initiation and progression of lens opacity were graded, double-blind and recorded as follows: Grade 0, no cataract (clear lenses); Grade 1, slight nuclear opacity, Grade 2, lens with a partial nuclear opacity; Grade 3, nuclear opacity; Grade 4, opacity in entire lens.

Statistical analysis

All values are expressed as the mean ± SD. Comparison between any two groups was performed using a Chi-square or one way analysis of variance (ANOVA) followed by Dunnett multiple comparison tests using the statistical software SPSS (Drmarketing Co., Ltd. New Taipei City, Taiwan). Statistically significant differences between groups were defined as $p < 0.05$.

3. Results and discussion

Body weight loss and hyperglycaemia are frequently used as markers of alloxan-induced diabetes in experimental animals. We measured body weight and blood glucose level over the 24 weeks of experimentation and the results are shown in Table 1. There were significantly lower body weights ($p < 0.05$) in the diabetic rabbits with or without treatment 1% taurine as compared to the controls, suggesting that diabetes caused body weight loss. However, the body weight was no dissimilarity between the diabetic group and the taurine treated group over the 24 weeks of experimentation. With respect to blood glucose levels, effects of taurine on alloxan-induced blood glucose diversification were also investigated. Alloxan treatment significantly increased ($p < 0.05$) blood glucose levels as compared to control ($p < 0.05$), suggesting that alloxan efficacious induced diabetes in experimental animals. On the contrary, taurine treatment significantly decreased ($p < 0.05$) blood glucose levels as compared to the diabetic group without taurine treatment in the end of experiment.

Alloxan is a diabetogenic agent that frequently used to induce insulin-dependent diabetes mellitus and to study diabetic complications in various experimental animals. Many studies have shown that alloxan induces the production of reactive oxygen species such as H_2O_2, hydroxyl radical and superoxide anion, and it causes severe necrosis of β-cells of the islets of Langerhans, leading to massive reduction in insulin release and elevation the levels of blood glucose and finally to produce diabetes (6, 16). In the present study, we found that treatment with taurine significantly inhibited alloxan-induced hyperglycaemia as evidenced by attenuating hyperglycemic response. Our results are in agreement with previous study that administration of taurine to alloxan-induced type 1 diabetic rats resulted in significantly suppressed hyperglycemia (10).

Table 1. Effects of taurine on body weight and blood glucose in normal and diabetic rabbits.

Design of treatment	Body weight (kg)		Blood glucose (mg/dl)	
	Initial	Final	Initial	Final
Normal control	2.70 ± 0.56 [b]	3.18 ± 0.40 [b]	108 ± 6.63 [b]	111 ± 7.40 [b]
Diabetes	2.40 ± 0.21 [a]	2.67 ± 0.23 [a]	287 ±154 [a]	483 ± 55.2 [ac]
Diabetes + taurine	2.33 ± 0.12 [a]	2.60 ± 0.28 [a]	248 ± 66.5 [a]	152 ± 12.9 [abc]

Values are mean ± SEM
[a] p <0.05 compare with normal group.
[b] $p < 0.05$ compared with diabetes group.
[c] $p < 0.05$ compared with initial estimation.

Hyperglycaemia plays an important role in diabetes-associated changes in lens metabolism and cataract formation. The most serious health problems of concerning about the visual complications in the patients with diabetes mellitus are changes in lens opacity. In the present study, the onset of cataract was observed after thirteen weeks by slit lamp examination in the diabetic group. The incidence of lens opacity in the present study was recorded in Table 2. Photographs of the lens opacity by slit lamp examination occurred in alloxan-intoxicated rabbits lens and their prevention by treatment with taurine was observed, as shown in Figure 1. At the final experiment, most of the lens (91.7 %) in control group appeared to be clear and normal throughout the experimental period whereas in

diabetic group, only 50% of the lens was in grade 1, 18.8% in grade 2, 12.5% in grade 3, 12.5% in grade 4 of cataract formation and only 6.25% of them were clear. However, administration with 1% taurine had 37.5% of the lens in grade 0, 25% in grade 1, 25% in grade 2 and 12.5% in grade 3. The results clearly indicated that treatment with taurine attenuates progression of alloxan-induced diabetic cataract.

Table 2. Effects of taurine on lens opacity in normal and diabetic rabbits.

Design of treatment	Incidence of cataract (%)				
	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Normal control	91.67	8.33	0.00	0.00	0.00
Diabetes	6.25	50.00	18.25	12.50	12.50
Diabetes + taurine	37.50	25.00	25.00	12.50	0.00

In experimental examination and clinical diagnosis, cataract has often depended upon slit lamp biomicroscope examination of lens opacities. Using routine examining techniques such as direct focal illumination and indirect retro-illumination has its advantages in that experienced optometrists have reliably and consistently identify cataract classification (17,18).

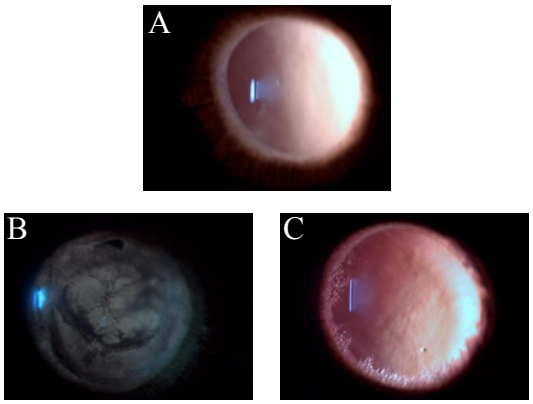

Fig. 1. Photographs of the lens opacity by slit lamp examination with indirect retro-illumination in alloxan-intoxicated rabbits lens. (A) control group; (B) Diabetes group; (C) Diabetes + taurine group.

In the present study, slit lamp biomicroscope examination with indirect retro-illumination in alloxan-induced diabetic rabbits lens showed significant cataract characteristics such as cloudiness (Fig.1B). However, treatment with taurine significantly decreased these cataract characteristics in rabbit lens (Fig. 1C), suggesting that taurine provided protection against alloxan-induced diabetic cataract. Through a semi-quantitative assessment (Table 2), the results were in agreement with the slit lamp biomicroscope observations that administration of taurine significantly reduced cataract in alloxan-induced diabetic rabbits. Our results were similar to those reported by Song et al. (19). They indicated that taurine supplementation to STZ-treated rabbits resulted in significant increasing of the taurine levels in lens and attenuating the progress of diabetic cataract. Several *in vitro* studies have demonstrated that administration taurine in lens culture system with high levels of glucose medium resulted in reducing oxidative stress in lens, involving both inhibited protein carbonylation and increased radical scavenging antioxidants (15,20). These studies indicate that taurine protects the lens from oxidative stress induced by hyperglycemia.

Taurine, the most abundant free amino acid in eye lens, plays an important role as antioxidant in protecting lens against the harmful effects of light, air and chemicals. The primary mechanism of action of this phenomenon appears to be the ability of taurine to quench excited sensitizer molecules and superoxide (20). In addition, taurine also protects lens against oxidative stress mediated by galactose as well as against lipid peroxidation caused by STZ-induced diabetes (15). Therefore, the taurine is expected to protect aloxan-induced type I diabetic cataract and lens damage. In conclusion, the results of this study demonstrate that the taurine was effective in prevention of aloxan-induced diabetic cataract and lens damage in rabbits. The inhibitory effects of a dietary taurine may be useful to an antidiabetic agent against chemical-induced diabetic cataract *in vivo*.

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