THE EFFECT OF TAURINE ON BLOOD GLUCOSE, TISSUE GLYCOGEN AND SERUM C-PEPTIDE LEVELS ON GLUCOCORTICOID ADMINISTERED RATS.

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SUMMARY : *In this study, we planned to observe the effects of taurine treatment on blood glucose, c-peptide and tissue glycogen levels in rats with glucocorticoid induced hyperglycemia. Pretreatment with taurine attenuated the rise in serum glucose levels and prevented the decrease in muscle and liver glycogen content after glucocorticoid administration. These effects of taurine were shown not to be dependent on serum c-peptide concentration. Taurine does not have hypoglycemic effect in rats without glucocorticoid induced hyperglycemia.*

Key Words : *Taurine, Hypoglycemic Effect, Glucocorticoid Administration.*

INTRODUCTION

Taurine (2- aminoethanesulfonic acid) is found in high concentration in mammalian tissues (3, 5). This amino acid is found in heart, skeletal muscle, nervous system and in the liver (6). Although its physiological roles are not clearly defined, its effect on carbohydrate metabolism is well described.

The antiarrythmic effect of taurine following digoxin and epinephrin induced arrythmias, its antiepileptic properties and central nervous system depressant action indicate its potential future clinical applications (9, 15).

The hypoglycemic effect of taurine on hyperglycemia, induced by cold, immobilization, streptozotocin and ditisone has been studied in different experimental models in the literature (6, 11, 15).

In the present study the effect of taurine on glucocorticoid induced hyperglycemia and its relation to blood glucose level, glycogen content of liver and skeletal muscle and serum c-peptide levels were studied in the rats.

MATERIALS AND METHODS

Male and female rats weighing 216 ± 10.6 gram were used. They were housed 7-8 to a cage under a controlled thermal environment, allowed to feed ad libitum till 18 hours to the study and exposed to 12 hour light and dark schedule with illumination between 8 am. and 8 pm.

Five rats were used to show the changes in blood glucose concentration following single dose (16 mg/kg) subcutaneous injection of methylprednisolone. Periodic blood glucose determinations were made in these rats through their tail veins to establish the time when the blood glucose concentration reach to the maximum. With this information in mind 6 control rats received subcutaneous saline injections at the begining of the experiment and intraperitoneal saline injections at the 30^{th} minute (Gro-

up 1).

Ten rats which constituted the second group received 16 mg/kg subcutaneous methylprednisolone injection at the beginning and intraperitoneal saline solution at the 30^{th} minute of the experiment. The third group of rats also 10 in number received subcutaneous saline injections at the beginning and 200 mg/kg taurine (4 % in saline) intraperitoneally at the 30^{th} minute of the experiment. The fourth group of rats received 16 mg/kg subcutaneous methylprednisolone injections at the beginning of the experiment and 200 mg/kg taurine intraperitoneally at the 30^{th} minute.

All of the animals were killed at the 60^{th} minute (which is the expected time for the highest blood glucose concentration following glucocorticoid administration and the peak-time for the hypoglycemic effect of taurine treatment) with decapitation, and blood, liver and muscle tissue specimens were obtained. Glucose and c-peptid levels were studied from the sera of the animals. Tissue glycogen contents were studied from muscle and liver tissues of the rats by Siu Lo method (8). Serum c-peptide levels were studied by RIA (14) while serum glucose levels were measured by glucose oxidase method with Technicon RA-1000 auto analyzer (1).

The averages of the parameters were analyzed by one way ANOVA test. The significance of the differences between the groups were tested by Student's t test. Additionally Kruscal Wallis test was used to retest the parameters, as the number of the subjects were less than 10 in some groups. The additional comparison between the pairs were done by Mann - Whitney - U test.

RESULTS

As described earlier in the text, blood glucose reached to the maximum level 60 minutes after subcutaneous methylprednisolone injection at the dose of 16 mg/kg (Fig 1).

The serum glucose concentrations of the control and the other three groups are shown in the table 1. The difference between these groups was significant ($p<0.05$). When compared as pairs only the difference between the groups 1 and 3 was again insignificant ($p>0.05$).

Glycogen content of the liver tissue is shown in table 2 for both control and test groups. The difference between the groups was found to be signifi-

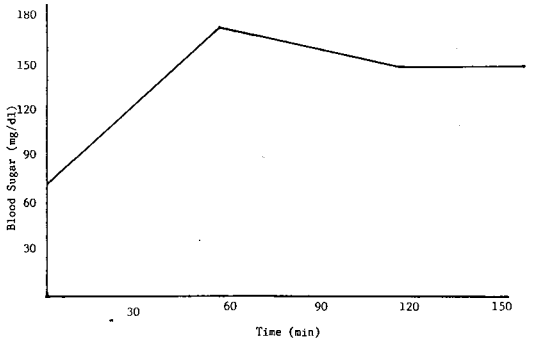

Fig - 1 : Following glucocorticoid (methylprednisolone 16 mg/kg sc.) administration, blood sugar reaches to the maximum level at the 60^{th} min (160 mg/dl).

Groups	$\bar{x}$	sd	n
Control	97.1 ± 2.7	6.6	6
Methylprednisolone	154.4 ± 6.1	18.5	9
Taurine	115.7 ± 8.4	23.5	9
Methylprednisolone Taurine +	137.6 ± 1.6	4.8	9

Table 1 : Serum glucose (mg/dl) results of the control and the experiment groups. The difference between groups revealed to be significant ($p<0.05$). When compared as pairs only the difference between the groups 1 and 3 was insignificant ($p>0.05$).
F : 18.9805 $p < 0.05$ KW : 20.02 $p < 0.05$

Groups	$\bar{x}$	sd	n
Control	4.75 ± 0.19	0.48	6
Methylprednisolone	1.12 ± 0.13	0.39	9
Taurine	4.29 ± 0.69	1.96	8
Methylprednisolone Taurine +	1.44 ± 0.08	0.24	8

Table 2 : Liver glycogen (gr/100 gr) contents of the control and the experiment groups. The difference between groups revealed to be significant ($p<0.05$). When compared as pairs only the difference between the groups 1 and 3 was insignificant ($p>0.05$).
F : 72.5521 $p < 0.05$ KW : 20.92 $p < 0.05$

cant ($p<0.05$). When compared in pairs the difference between the groups 1 and 3 was again insignificant ($p>0.05$).

Glycogen content of the skeletal muscle is shown in the table 3. The results were found to be similar to the previous table.

C-peptide levels of the groups are demonstrated in table 4 and no significant difference was found between the groups ($p>0.05$). All the data is shown together in table 5 for comparison.

DISCUSSION

The effect of pharmacologic doses of taurine on carbohydrate metabolism is well known (7, 10, 11, 15). Kulakowski et al. have shown the hypoglycemic effect of taurine following bolus glucose injection in rats. In that study, taurine also prevented the rise in serum immunoreactive insulin levels (6). These data suggest that, the action of taurine is unrelated to a direct stimulation of pancreatic insulin release.

Groups	$\bar{x}$	sd	n
Control	3.89 ± 0.26	0.64	6
Methylprednisolone	1.18 ± 0.12	0.38	9
Taurine	3.51 ± 0.28	0.74	7
Methylprednisolone + Taurine	2.33 ± 0.28	0.74	7

Table 3 : Skeletal muscle glycogen (gr/100 gr) content of the control and the trial groups. The difference between groups revealed to be significant ($p<0.05$). When compared in pairs only the difference between the groups 1 and 3 was insignificant ($p>0.05$).
F : 72.5521 $p < 0.05$ KW : 22.92 $p < 0.05$

Groups	$\bar{x}$	sd	n
Control	0.041 ± 0.01	0.024	5
Methylprednisolone	0.049 ± 0.012	0.029	5
Taurine	0.031 ± 0.002	0.0059	5
Methylprednisolone + Taurine	0.0035 ± 0.003	0.0079	5

Table 4 : Serum c-peptide (pmol/lt) levels of the control and the experimental groups. There is no statistical difference between the groups ($p>0.05$).
F : 12.0144 $p > 0.05$ KW : 11.94 $p > 0.05$

In this study we investigated the effect of taurine on the alteration of glucose metabolism induced by glucocorticoid administration. In our model blood glucose concentration reached to its maximum level at 60^{th} minute (160 mg/dL) and returned below 140 mg/dL by 100^{th} minute. This finding is in agreement with the literature (12, 13). The antagonistic effect of taurine on stress induced increases in blood sugar occurs at 30^{th} minute following its administration to hyperglycemic subjects (11). Other studies have shown the hypoglycemic action of taurine in different hyperglycemic conditions such as alloxan, ditisone, streptozotocin administration, or cold and immobilization stress (6, 11, 15). In our acute study we found that, taurine not only inhibited the rise in serum glucose levels following glucocorticoid administration but also prevented the rise in serum c-peptide levels. Since taurine enhances glucose uptake without increasing serum c-peptide it appears that taurine may have a direct action on the cell membrane to enhance glucose transport. As the

Groups	Blood Sugar (mg/dl)	Liver Glycogen (gr/100 gr)	Muscle Glycogen (gr/100 gr)	Serum C-peptide (pmol/lt)
Control	97.1 ± 2.7	4.75 ± 0.19	3.89 ± 0.26	0.041 ± 0.010
Methylprednisolone	154.4 ± 6.1	1.12 ± 0.13	1.18 ± 0.12	0.049 ± 0.012
Taurine	115.7 ± 8.4	4.29 ± 0.69	3.51 ± 0.28	0.031 ± 0.002
Methylprednisolone + Taurine	137.6 ± 1.6	1.44 ± 0.08	2.33 ± 0.28	0.035 ± 0.0035

Table 5 : Serum glucose, tissue glycogen and serum c-peptide results of the control and the trial groups.

clearence of c-peptide is longer than insulin it is more reliable to follow the insulin response. Corresponding to the initial rise in serum glucose levels following glucocorticoid administration we were unable to demonstrate a rise in serum c-peptide levels in group 2 in this experiment. This finding is in contradiction with the literature, and could be explained by the faster metabolic clearence of c-peptide in rats than in humans (4). For this reason we do question the value of serum c-peptide measurements as a reliable indicator of insulin response in rats, as we could not demonstrate significant differences in the c-peptide levels for both the control and the other 3 groups.

The enhanced taurine mediated glucose clearence from the serum appears to be associated with increased glucose accumulation in skeletal muscle and liver in our study. It has been described that taurine increased the glycogen synthesis in the liver both in diabetic and normal rats (6). In our model glucocorticoid administration led to a decrease in tissue glycogen content acutely. Single dose of taurine and taurine plus glucocorticoid administration increased liver and muscle glycogen content compared to glucocorticoid only treated group. Our comment on this result is that, taurine helps glucose to accumulate in the liver and muscle in the form of glycogen during this process. In a previous study, measurements of key metabolic intermediates revealed that, taurine stimulated glycolysis by enhancing flux through phosphofructokinase. Similarly it was shown that glycogenesis was promoted because of the increase in glycogen synthase I and decrease in phosphorylase A activity (6). Other investigators have shown increased utilization of glucose by rat heart following taurine administration in hyperglycemic conditions (7).

Tokunaga et al. have shown that continuous pretreatments of mice with taurine significantly suppress streptozotocin - induced hyperglycemia. Since animals pretreated with taurine exhibited significantly less decrease of immunoreactive insulin in pancreas and less damage of beta-cells in the islets of Langerhans than those found in animals treated with streptozotocin alone, it is likely that the site of protective action of taurine resides at the islets of Langerhans in pancreas. Mechanisms underlying protective actions of taurine against the damage of beta-cells are not clear at present (15). In Nakagawa and Kuriyama's study rats that were exposed to immobilized cold stress, adrenaline content in the adrenal gland as well as noradrenaline content in the brain stem were reduced drastically, while noradrenaline content in the atria was not altered by the application of stress. Oral administration of taurine prevented the stress induced decline of adrenaline in the adrenal gland. The stress induced elevation of the blood level of corticosterone was not affected by taurine administration. These findings indicate that taurine antagonizes the stress induced elevation of blood sugar by reducing adrenaline output from the adrenal gland (11).

As a conclusion we can state that taurine prevents glucocorticoid induced hyperglycemia in rats. At present we are unable to show the role of insulin in this process. Single dose of taurine and taurine plus glucocorticoid treatments prevent the decrease in tissue glycogen levels compared to the group which was treated only with glucocorticoid.

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