

Vitamin Thiamine and Glucose Homeostasis in Alloxan Induced Diabetes Mellitus

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ABSTRACT

Objective: valuating the vitamin B₁ (thiamine) on glucose homeostasis and Glycosylated hemoglobin A1 (HbA1c) in Alloxan induced diabetic rat model.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Animal House, Isra University Hyderabad from September 2014 to March 2015.

Materials and Methods: 60 adult albino rats were divided into four groups; Group 1. Controls, Group 2. Rats receiving thiamine added diet, Group 3. Diabetics rats on normal diet and Group 4. Diabetic rats receiving thiamine added diet. Alloxan (120 mg/kg) was introduced intraperitoneally to induce diabetes. Vitamin B₁ was given orally at 1.6 g/kg body weight for 12 weeks. Venous blood was taken from tail vein by small bore cannula at the baseline and after 12th week. Blood glucose and HbA1c were detected at baseline and after 12th week. Data was saved in proforma and analyzed on SPSS 22.0 using paired student t-test at 95% confidence interval.

Results: Blood glucose and HbA1c levels were found statistically significant in groups 1 vs. 3 (p=0.0001), 1 vs. 4 (p=0.0001), 2 vs. 3 (p=0.0001), 2 vs. 4, (p=0.001) and 3 vs. 4 (p=0.024) at the end of experiment period. Significant improvement in blood glucose and HbA1c was noted in the vitamin thiamine treated rats.

Conclusion: Vitamin thiamine improved the blood glucose homeostasis and reduced Glycosylated Hemoglobin A1 effectively in experimental rats. It is recommended to supplement diabetic subjects with vitamin thiamine.

Key Words: Vitamin thiamine, Glucose homeostasis, HbA1c

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INTRODUCTION

Vitamin thiamine is also known as the vitamin B₁. Thiamine functions as a coenzyme in the glucose metabolism and plays pivotal role in glucose homeostasis. Thiamine pyrophosphate co-enzyme catalyzes several steps of glucose and intermediary metabolism. Thiamine is essential for the normal glucose metabolism and homeostasis as it is necessary for the biochemical reactions of glycolysis and Krebs cycle. Diabetes mellitus (DM) is characterized by abnormal glucose homeostasis. Thiamine deficiency causes abnormality of glucose metabolism in DM subjects.¹¹ Vitamin thiamine deficiency disturbs the glucose homeostasis resulting in hyperglycemia and accelerated microvascular and macrovascular complications.¹¹

DM is increasing these days as estimated by the International Diabetes Federation (IDF). IDF estimates show a rise of diabetics of 439 million by the year 2030.¹ Currently, Pakistan is suffering diabetes epidemic and ranks 6th position as reported.² Previous studies from Pakistan had reported 15% population of country is suffering from DM, and many millions are undiagnosed.^{3,4} Crude estimates of Pakistan National Diabetes Survey (PNDS) reported that for each diagnosed case of DM; there are 3 cases of pre-diabetes (impaired glucose tolerance) and 2 cases of undiagnosed DM.^{5,6}

Chronic hyperglycemia is the hallmark of DM which damages the vital organs like eyes, kidneys, nerves, blood arteries.^{7,8} Thiamine deficiency is linked with damage of these organs in diabetics as reported previously.^{9,10,11}

Chronic hyperglycemia, in the presence of thiamine deficiency, activates protein kinase C, accelerated hexosamine synthesis, and formation of advanced glycation end products (AGEs). AGEs are involved in the pathogenesis of micro- and macrovascular complications in diabetics.¹¹ AGEs synthesis is increased through triose-phosphate intermediates of glycolysis in the presence of thiamine deficiency.^{12,13} High doses of thiamine suppresses the AGEs pathways through improved glucose homeostasis, thus reducing the risk of diabetic complications.⁹

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The present study aimed to evaluate the effect of high doses of thiamine on glucose homeostasis and Glycosylated HbA1c in Alloxan induced albino rat model.

MATERIALS AND METHODS

The present experimental study was carried out at the Animal House, Isra University Hyderabad from September 2014 to March 2015. A sample of 60 male albino rats was selected according to well delineated criteria of inclusion and exclusion. A male albino rat of 200-250g body weight was the inclusion criteria. Female rats, sick rats and rats not feeding were the exclusion criteria. Rats were kept in standard environment of room temperature with normal humidity (55-60%). Normal chow diet and water was freely available. Rats were exposed to 12/12 hour dark-light cycle. Intraperitoneal injection (i.p.) of Alloxan (120mg/kg body weight) was administered to induce diabetes mellitus.^{15,16}

Sixty male albino rats were divided into four groups by random selection, containing 15 rats in each group.

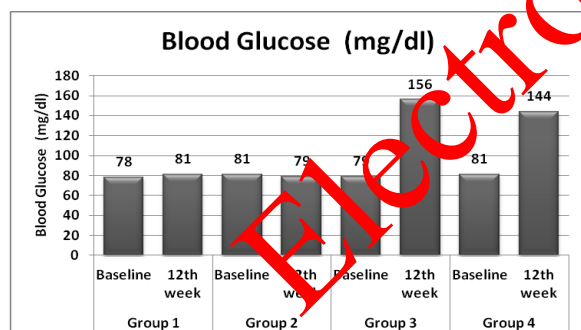
Group 1 Controls (n=15), Group 2 Rats receiving thiamine added diet (n=15), Group 3 Diabetics rats on normal diet (n=15) and Group 4 Diabetic rats (n=15) receiving thiamine added diet. Vitamin B1 was given orally at 1.6 g/kg body¹⁴ weight for 12 weeks. Venous blood was taken from tail vein by small bore cannula at the baseline and after 12th week. Blood glucose and HbA1c were detected at baseline and after 12th week. Normal blood glucose for rats was taken at 52-105mg/dl. HbA1c range for rats was taken normal as 3-8.8%.¹⁵ Data was saved in proforma and analyzed on SPSS 22.0 using paired student t-test at 95% confidence interval ($p \leq 0.05$).

RESULTS

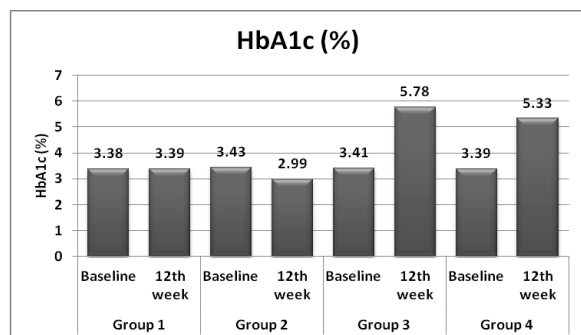
Blood glucose and HbA1c levels were found statistically significant in groups 1 vs. 3 ($p=0.0001$), 1 vs. 4 ($p=0.0001$), 2 vs. 3 ($p=0.0001$), 2 vs. 4, ($p=0.001$) and 3 vs. 4 ($p=0.024$) at the end of experiment period. Significant improvement in blood glucose and HbA1c was noted in the thiamine treated rats. The findings are summarized in table 1 and graphs 1 and 2.

Table No. I: Blood glucose level and Glycosylated hemoglobin A (HbA1c) in experimental animals (n=60)

	Group 1 Control group (Normal diet)		Group 2 Control group (Normal diet+ Vit.B ₁)		Group 3 Diabetic group (Normal diet)		Group 4 Diabetic group (Normal diet+ Vit.B ₁)	
	Baseline	12 th week	Baseline	12 th week	Baseline	12 th week	Baseline	12 th week
Blood Glucose (mg/dl)	78±4.34	81±3.3	81±0.5	79±4.4	79±1.5	156±17.6	81±3.5	144±12.4
HbA1c (%)	3.38±0.21	3.39±0.2	3.43±0.21	2.99±0.11	3.41±0.4	5.78±0.99	3.39±0.2	5.33±0.69



Graph No.1: Bar graph showing blood glucose levels in rat groups



Graph No.2: Bar graph showing Glycosylated HbA1c in rat groups

DISCUSSION

The present study reports on the effect of high dose thiamine intake on glucose homeostasis and HbA1c in Alloxan induced diabetic albino rat model. A search of literature of showed a few studies have been conducted previously, although the topic is of clinical importance as the burden of DM is increasing in Pakistan.^{9,15} Previous studies had reported vitamin thiamine deficiency is prevalent in the diabetic subjects.^{9,10,15-17} Vitamin thiamine is necessary for the glucose metabolism. The present study reports high dose of vitamin thiamine improved glucose homeostasis and HbA1c in Alloxan induced diabetes model of albino rats. The findings are in keeping with previous reports.^{9,10,15} Blood glucose and HbA1c showed statistically significant amelioration in the experimental diabetic rats compared to controls.

Glucose homeostasis and HbA1c showed significant improvement in diabetic rats fed thiamine rich diet (Group 4) compared to controls (Group 1) ($p=0.0001$) (Table I). Group 3 and 4 also showed significant amelioration of blood glucose as shown in table 1 and graph 1 and 2 ($p=0.001$). Glycosylated HbA1c was significantly reduced in the diabetics given thiamine

supplements ($p=0.001$). Significant reduction in HbA1c noted in present study in contradistinction to previous studies.^{9,15}

Reason is very logical, that above studies^{9,15} used vitamin thiamine therapy just for 4 weeks which is less compared to 12 weeks vitamin supplementation in the present study. It is suggested that the vitamin thiamine be prescribed for long durations for clinical effect to be elicited.

Thiamine supplementations inversely affected the blood glucose levels, has been reported in a previous study,¹⁷ this shows it's positive impact on correcting the blood glucose levels. Above findings are in keeping to present study.

A previous study¹⁸ reported improvement in blood glucose and blood lipid profile in diabetic rats supplemented with vitamin thiamine. The findings of above study support the present study. Above study¹⁸ concluded that the thiamine dependent enzymes transketolase (TK) and pyruvate dehydrogenase (PDH) activities are improved, hence this improved blood glucose regulatory mechanisms.

Another previous study was conducted with thiamine and benfotiamine on blood glucose polyol pathway. The study was conducted on cultured vascular cells. A significant improvement in blood glucose was noted. They concluded that the thiamine and benfotiamine may help to prevent and retard the microvascular complications of diabetes mellitus.¹⁹ Improved blood glucose levels of above study in agreement to the present study. The present study observed amelioration of blood glucose homeostasis and Glycosylated hemoglobin A1 (HbA1c) in thiamine supplemented diabetic rats.

CONCLUSION

Vitamin thiamine improved the blood glucose homeostasis and reduced Glycosylated Hemoglobin A1 effectively in experimental rats. It is recommended to supplement diabetic subjects with vitamin thiamine.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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