Original Article

Effect of Thiamine on Glycemic Control in Induced Diabetic Rat Model

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ABSTRACT

Objective: To evaluate the effect of high dose thiamine on postprandial blood glucose (PPBG) and hemoglobin A1C levels in induced diabetic albino rat model.

Study Design: Experimental/Analytical study

Place and Duration of Study: Animal House, Isra University Hyderabad from March to October 2013.

Materials and Methods: Forty adult albino rats were divided into four groups; Group I. Controls receiving normal diet, Group II. Controls receiving thiamine fortified diet, Group III. Diabetics receiving normal diet and Group IV. Diabetics receiving thiamine fortified diet. Diabetes mellitus was induced using Streptozocin. Thiamine was given at a dose of 1.6 g/kg body weight. Venous blood samples were drawn from animal's tail with a small bore cannula before and after 12 weeks of experimentation. The PPBG levels and Glycosylated HbA (HbA1c) were measured. The data was converted into database and analyzed on SPSS version 21.0 by ANOVA and Tukey-Kramer`s test. A p-value of ≤ 0.05 was taken statistically significant.

Results: The PPBG and HbA1c levels were found statistically significant in groups I vs. III (p=0.0001), I vs. IV (p=0.0001), II vs. III (p=0.0001), II vs. IV, (p=0.001) and III vs. IV (p=0.024) at 12th week of experimentation. The study shows significant reduction in the PPBG and HbA1c levels of rats taking thiamine compared to controls (p=0.001). Significant differences in HbA1c levels were observed between control groups I and II vs. experimental groups III and IV (p=0.024) (p=0.0001) respectively. A highly significant difference in HbA1c was observed in rats given thiamine fortified diet compared to those not given (p=0.001).

Conclusion: The thiamine improves glucose metabolism in induced diabetic rat models, hence it is concluded that the thiamine may be given along with anti- diabetic drugs to overcome defects of glucose metabolism.

Key words: Thiamine, Glycemic control, HbA1c, Diabetic rats

INTRODUCTION

The number of diabetic population older than twenty is estimated to rise from 285 million in 2010 to 439 million in 2030 as reported by International Diabetes Federation (IDF).[1] The current rise in diabetic population has put Pakistan at sixth position in the world.[2] According to an estimate, 15% of Pakistani population is diagnosed of having diabetes mellitus (DM) and millions more are unaware and undiagnosed of having DM.[3,4] According to the estimates of Pakistan National Diabetes Survey (PNDS), for each diagnosed case of DM, there are approximately two cases of undiagnosed DM and three cases of impaired glucose tolerance who remain unaware of it.[5,6] The DM is characterized by chronic hyperglycemia which in long term causes damage in the target organs like kidney, nerves, eyes, heart and blood vessels.[7,8] The DM is a multifactorial metabolic disorder, mainly characterized by abnormal glucose metabolism which is responsible for most of its symptoms and complications. But the thiamine deficiency is also linked with the pathogenesis and complicaitons of DM as has been reported in many studies.[9, 10,11] The thiamine is known as vitamin B_1. Thiamine forms an indispensable co-enzyme and participates in several steps of glucose and intermediary metabolisms. In human body it plays role in glucose metabolism by forming co-enzymes essential for functioning of enzymes of glycolysis ad citric acid cycle. The DM has been characterized by thiamine deficiency due to amplified glucose metabolism.[11] Thiamine deficiency causes disturbed glucose metabolism, and accelerates DM complications through various mechanisms.[11] The various mechanisms which have been postulated causing diabetic complications include the activation of polyol pathway, formation of advanced glycation end products (AGES), activation of protein kinase C (PKC) and increased flux through the hexosamine biosynthetic pathway (HBP).[11] These metabolic abnormalities are triggered through increased formation and elevated concentration of triose-phosphate intermediates of glycolysis.[12,13] Triose-phosphate can be suppressed by the activation of reductive pentose phosphate pathway (PPP) by high-dose thiamine therapy that would increase transketolase (TK) activity and stimulate the

conversion of glyceraldehyde-3-phosphate (GA3P) and fructose-6-phosphate (F6P) to ribose-5-phosphate (R5P), thus reducing the risk of the development of diabetic complications.[9] The present study hypothesizes that high doses of thiamine administration would be independently associated with glucose metabolism and that this association is modified by blood glucose level. The present experimental study aims to evaluate the metabolic effects of high dose thiamine on blood glucose and HbA1c in induced diabetic rat model.

MATERIALS AND METHODS

This experimental study was conducted at Animal House of Isra University Hyderabad from June 2012 to December 2013. Forty 12-week old male albino rats were selected through non-probability purposive sampling. The normal healthy rats of 150-250g body weight were included while sick rats and rats not feeding properly were excluded from study. Rats were habitated in stainless steel cages, at room temperature with 55-60% humidity. The rats were kept under standard conditions. Pelleted form of diet was given to animals throughout study period. The diet was made available freely to feed *ad-libitum*. Water was made available in separate containers. Pelleted diet was fortified with thiamine at a dose of 1.6 gms/ kg for the specified groups *as referenced*.[14] Twenty rats were separated as controls, while another twenty rats were injected streptozocin to damage β-cells to induce DM at a dose of 60mg intraperitoneally.[15,16] The rats (N=40) were divided into four groups by random selection, containing ten rats in each group. Group I (n=10) included normal healthy rats as controls receiving normal pelleted diet, Group II (n=10) included normal healthy rats as controls receiving normal diet, fortified with thiamine, Group III (n=10) diabetic rats given normal diet and Group IV (n=10) included diabetic rats given thiamine fortified diet. The study duration was twelve weeks. Venous blood samples were drawn from animal's tail with a small bore cannula, to measure random blood glucose and glycosylated HbA (HbA1c). Random blood glucose was measured by glucose oxidase method and HbA1c by enzyme calorimetric method on spectrophotometer (Hitachi, USA). Normal blood glucose level was taken as 52-105mg/dl. HbA1c range for rats was taken normal as 3-8.8%.[15] The data was converted into database onto SPSS version 21.0. The continuous variables were analysed by ANOVA and Tukey-Kramer`s test. The data was presented as mean±SD. A p-value of ≤ 0.05 was taken statistically significant.

RESULTS

The blood glucose level and HbA1c were measured before and after intervention in all groups of rats. The continous variables are presented as mean±SD in Table I for groups. The difference in blood glucose level and HbA1c in control groups I and II and experimental groups III and IV were found statistically non-significant before intervention ($p > 0.05$). However, the blood glucose level and HbA1c were found statistically significant in groups I vs. III ($p=0.0001$), I vs. IV ($p=0.0001$), II vs. III ($p=0.0001$), II vs. IV, ($p=0.001$) and III vs. IV ($p=0.024$) after intervention at twelve weeks of experimentation. The study shows significant reduction in the blood glucose level and HbA1c of rats taking thiamine compared to controls ($p=0.001$). Although the study duration was twelve weeks, still significant differences in HbA1c levels were observed between control groups I and II vs. III and IV ($p=0.024$) ($p=0.0001$) respectively. A highly significant difference in HbA1c was observed in rats taking thiamine fortified diet compared to those not taking thiamine ($p=0.001$). From the observations of present study, it is concluded that thiamine has a definitive role in regulating glucose metabolism. The thiamine shows positive effect in reducing blood glucose level through enhanced metabolism and reduces formation of HbA1c. The observations of thiamine effect on blood glucose level are of practical importance while treating diabetic subjects by clinicians.

Table No.I. Postprandial blood glucose (PPBG) level and Hemoglobin A1c in study animals (n=40)

Variable	**Group I** Control group (Thiamine $^{-ve}$ diet)		**Group II** Control group (Thiamine $^{+ve}$ diet)		**Group III** Diabetic group (Thiamine $^{-ve}$ diet)		**Group IV** Diabetic group (Thiamine $^{+ve}$ diet)	
	Before	After	Before	After	Before	After	Before	After
PPBG level (mg/dl)	79±4.7	80±3.9	80±1.5	80±3.5	78±2.5	153±15.6	80±2.7	145±13.5
HbA1c (%)	3.48±0.23	3.49±0.22	3.49±0.24	3.51±0.21	3.47±0.24	5.98±0.89	3.49±0.21	5.13±0.79

DISCUSSION

The studies regarding the effect of high dose thiamine therapy on blood glucose and HbA1c are lacking in medical literature of Pakistan. A few studies are reported on role of thiamine in diabetics.[9,15] It is reported by various studies that diabetics are thiamine deficient.[9,10,15-17] The present study shows that high doses of thiamine improves blood glucose level and results are comparable to previous studies.[9,10,15] In present study we found statistically significant

differences in blood glucose levels among in all four groups after intervention. The blood glucose levels are significantly elevated in group IV diabetics compared with group I controls and group II controls taking thiamine (p=0.0001) (Table I). Statistically significant differences in blood glucose levels are observed between group III diabetics and groups IV diabetics taking thiamine in diet. (p=0.001). The present study also observes statistically significant differences in HbA1c levels among controls, diabetics and diabetics with thiamine intake. (p=0.001). The statistically significant differences in HbA1c observed in present study are contrary to previous studies.[9,15] The differences are observed because of long duration of present study compared to previous study[15] i.e; 4 vs. 12 weeks. A previous study reported that the thiamine intake was inversely associated with blood glucose levels and this shows improved glucose metabolism.[17] The findings support our present study. Babaei-Jadidi et al.[18] conducted experimental study on diabetic rats and reported positive effects of thiamine intake on blood glucose and lipid levels. Our findings support this previous study regarding improved blood glucose levels. In that previous study, it was concluded that the hepatic expression of thiamine dependent enzymes is sensitive to decrease transketolase (TK) and pyruvate dehydrogenase (PDH) activities,[18] both of which are important in regulating intracellular glucose metabolism. The Berrone E et al.[19] conducted study on role of thiamine and benfotiamine on intracellular glucose and polyol pathway in cultured vascular cells and reported improved glucose uptake and metabolism by vascular cell cultures. The previous study concluded that high doses of thiamine and benfotiamine may prevent development of microvascular complications of diabetics.[19]

The findings are in keeping with the present study as we observed better glucose metabolism in *thiamine-fed* rats. The present study shows that the thiamine improves blood glucose levels and HbA1c in induced diabetic rat models.

CONCLUSION

The thiamine improves glucose metabolism in induced diabetic rat models as observed in present study. The present study concludes that the thiamine may be given along with antidiabetic drugs to overcome defects of glucose metabolism as it improves glycemic control.

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