

Vitamin E Ameliorates Renal Damage in Streptozotocin induced Diabetes in Albino Rats

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ABSTRACT

Aims and Objectives: This study was designed to find out the role of Vitamin E on serum glucose and Creatinine concentrations of male albino rats made diabetic by streptozotocin.

Study Design: Prospective study.

Place and Duration of Study: This study was conducted at the Department of Physiology; Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Center (JPMC), Karachi from Feb. 2010 to March 2010.

Materials and methods: In a 4 weeks study, 45 male albino rats were divided into 3 groups containing 15 animals each. Group A was treated as control, Group B and Group C received 45 mg/kg STZ once at the start of the experiment whereas Group C additionally received 600 mg/kg Vitamin E Intramuscularly 3 times weekly. Serum glucose and Creatinine concentrations were measured at the beginning of the experiment and once weekly.

Results: Serum glucose and Creatinine levels were significantly elevated in Group B as compared to control. In Group C, blood glucose was elevated but the levels of serum Creatinine were significantly reduced, when compared to group B.

Conclusions: Our findings conclude that Vitamin E supplementation may have protective effects against deterioration of renal function brought about by free radical toxicity in diabetes mellitus.

Key Words: Streptozotocin, Oxidative stress, Oxygen Free Radicals, Vitamin E, Creatinine, Diabetes Mellitus, Diabetic Nephropathy, Antioxidant.

INTRODUCTION

Diabetes Mellitus is a disease in which the hallmark feature is elevated blood glucose concentrations due to loss of insulin-producing pancreatic β -cells (type 1 diabetes) or through loss of insulin responsiveness of its targets issues like adipose and muscle (type 2 diabetes). Diabetic Nephropathy is one of the major long term complications of diabetes mellitus and has emerged as a leading cause of end-stage renal disease. According to World Health Organization, diabetes affects more than 170 million people worldwide and this number will rise to 370 million by 2030¹.

Several lines of evidence suggest the central role of oxidative stress in the development of diabetic nephropathy and the beneficial effects of antioxidants in renal injury owing to diabetes². The production of Reactive Oxygen Species (ROS) is central to the pathogenesis of diabetes and its complications³. It is suggested that there is a high correlation between oxidative stress in diabetes and the development of complications including diabetic nephropathy. As the disease progresses, anti-oxidant potential decreases and the plasma lipid per-oxidation products increase, depending upon the level of glycemic control⁴.

Streptozotocin (STZ) as an anti-biotic and anti-cancer agent has been widely used for inducing type 1 diabetes in a variety of animals by producing degeneration and necrosis of pancreatic beta cells⁵.

Vitamin E is an important lipid soluble, chain-breaking anti oxidant in tissues, red cells and plasma⁶. It is a

powerful anti oxidant that has been shown to decrease several outcomes of oxidative stress and oxidative damage in cell culture, in animal models of diabetes and in diabetic humans⁷.

This study was designed to observe the protective effect of Vitamin E on the renal functions in albino rats rendered diabetic by administration of STZ.

MATERIALS AND METHODS

This study was conducted at the Department of Physiology; Basic Medical Sciences Institute (BMSI), Jinnah Post Graduate Medical Center (JPMC), Karachi for a period of four weeks. In this study, 45 healthy male albino rats, 90-120 days old, weighing around 250-300 grams were obtained from the animal house of BMSI and divided into three groups, each group containing 15 animals. Group A was taken as control; Group B and C animals were fasted overnight and made diabetic by administering STZ intraperitoneally in a dose of 45 mg/kg dissolved in 1 ml of citrate buffer at 4 PH, only on the first day of the experimental study⁸. Group C additionally received 600 mg/kg of Vitamin E intramuscularly three times a week⁹.

All the animals were kept in propylene cages equipped with drinking water bottle and wood chip floor bedding under natural environments (12 hours light and 12 hours dark). Food and water were supplied *ad libitum*. Blood samples were collected from the tail vein.

Serum glucose was determined by glucose oxidase method using, Glucometer. 3 days after STZ

administration, rats having a serum glucose of >300 mg/dl were rendered diabetic.

Serum Creatinine was determined by colorimetric method using Elisa kit. It was measured as the parameter of renal function at the start of the experiment and once weekly for four weeks and the results correlated in all the three groups.

RESULTS

At the end of the 4th week, the fasting blood glucose levels were significantly higher in Group B and C as compared to control, indicating that Vit E did not significantly change the blood sugar levels in Group C. Serum creatinine levels were significantly increased in Group B as compared to control, whereas in Group C, there was a significant reduction in the levels of serum creatinine as compared to Group B (Table 1).

Table No.1 Mean serum glucose and serum creatinine values in different groups of albino rats:

Groups	Treatment Received	Serum Glucose (mg / dl)	Serum Creatinine (mg / dl)
A (n=15)	Control	125 ± 15	0.95 ± 0.07
B (n=15)	STZ	528 ± 43 **	2.16±0.24**
C (n=15)	STZ+ Vit E	519± 40 **	1.20±0.07 *

Values are mean ± SEM of 15 animals in each group.

*P < 0.05

** P < 0.01

DISCUSSION

Tight control of blood glucose can reduce clinical complications in diabetic patients. However, alternative treatment strategies are needed to prevent oxidative stress complications and to optimize recovery¹⁰. Oxidative stress in diabetic kidney is usually associated with tissue damage that interferes with proper organ function, causing an increase in urinary protein excretion and blood urea nitrogen¹¹.

At the end of experimental period, STZ diabetic rats showed elevated levels of serum creatinine, as reported in previous experimental studies^{12, 13}. Vitamin E failed to lower blood sugar levels in group C animals¹⁴, but the serum creatinine levels were almost reduced to control levels by the use of Vit E, which were significantly higher in group B.

In one study, Vit E Supplementation (1000 IU / kg diet) for 4 weeks after STZ induction of diabetes resulted in significant reductions of urinary protein excretion and Blood Urea Nitrogen (BUN) compared to diabetic rats on a control diet¹¹. Animal studies have shown Vit E supplementation to reduce oxidative stress in glomeruli of diabetic rats¹⁵. Other data has confirmed an effect of Vit E in reducing BUN and serum creatinine in diabetic rats, demonstrating a positive effect in kidney function⁹. Vitamin E, a membrane – bound, lipid-soluble antioxidant has been shown to protect biological

membranes against injury induced by reactive oxygen species¹⁶. At the cellular level, one mechanism of action proposed is the inhibition of oxidative stress induced NF – KB activation and apoptosis in rat kidney¹⁷. The levels of Vit E in plasma are significantly reduced in diabetic patients¹⁸. Vit E given to diabetic animals has been shown to exhibit effects in several tissues including kidney¹⁹, lens, peripheral nerve, brain and liver.

Data from clinical studies demonstrates a role for Vit E to decrease lipid peroxidation in diabetic humans. Subjects with metabolic syndrome who were supplemented for 6 weeks with 800 mg/day α -tocopherol, γ -tocopherol or both had lower blood malondialdehyde (MDA) and lipid peroxides than subjects supplemented with placebo²⁰.

CONCLUSION

Our findings conclude that dietary Vitamin E helps to preserve renal functions in STZ induced diabetic rats. So the supplementation of Vit E to Diabetic patients may help in preventing diabetic nephropathy brought about by free radical toxicity.

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