EXCELLENT PUBLISHERS

Effect of Coenzyme Q 10 on Blood Glucose Level in Streptozotocin Induced Diabetic Rats

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Abstract

Coenzyme Q-10 which is lipid-soluble, vitamin-like substance and are present in most eukaryotic cells, primarily in the mitochondria is a component of the electron transport chain and participates in aerobic cellular respiration. The capacity of this molecule to exist in a completely oxidized form and a completely reduced form enables it to perform its functions in the electron transport chain and as an antioxidant respectively. Hyperglycemia in DM generates free radicals by mechanisms that are thought to involve metal catalyzed oxidation of glucose, oxidative degeneration and protein glycation. The presence of free radicals may account for diabetes and its complication. On this background the plan of this research work was made. Healthy male Wistar rats weighing between 150-250 grams were divided in four groups containing six animals in each group. Normal and diabetic animals were treated by placebo and coenzyme Q10 1.8mg/kg body weight respectively and investigated for fasting blood glucose levels. Blood glucose level in diabetic rats was significantly decreased in three weeks period. Therefore we can conclude that Coenzyme Q10 reduces the fasting blood sugar level in streptozotocin induced diabetic rats and it is of statistical significance in long term use (at 21 days and later).

Introduction

Diabetes mellitus is a metabolic syndrome characterized by chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both (Danaei et al., 2011). Several distinct types of Diabetes mellitus are caused by a complex interaction of genetics and environmental factors. Diabetes is renowned as 'silent epidemic'. The slow progression and lack of symptoms in early stages of the disease preclude seeking medical attention and preventive care.

Coenzyme Q-10 which is also known as ubiquinone, is a lipid-soluble, vitamin-like substance and are present in most eukaryotic cells, primarily in the mitochondria (Ernster and Dallner, 1995). It is a component of the electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Ninety-five percent of the human body's energy is generated in this way (Dutton et al., 2000). Therefore, the organs which need the highest energy requirements; such as the heart, liver and kidney have the highest CoQ_{10} concentrations (Aberg et al., 1992). The capacity of this molecule to exist in a completely oxidized form

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and a completely reduced form enables it to perform its functions in the electron transport chain and as an antioxidant respectively (Shindo et al., 1994).

There are two major factors that lead to deficiency of Coenzyme Q -10. 1st is the reduced biosynthesis, and 2nd is its increased utilization by the body (Hyson et al., 2010). Toxicity is not usually observed with high doses of Coenzyme Q-10 up to 3600 mg per day in healthy as well as unhealthy persons (Hathcock and Shao, 2006). However, some adverse effects like abdominal discomfort, nausea, vomiting, etc. has been observed in very high doses.

Hyperglycemia in DM generates free radicals by mechanism that is thought to involve metal catalyzed oxidation of glucose, oxidative degeneration and protein glycation (Wolff and Dean, 1987). Recurrent high blood glucose concentration degenerates vital tissues and it is correlated with diabetes and its complications. Therefore chronic antioxidant therapy may be useful in decreasing the risk of diabetes and its complications. Coenzyme Q10 is an antioxidant, scavenges free radicals directly, inhibits biomolecule oxidation, regulates oxidative phosphorylation and prevents lipid per oxidation (Modi et al., 2006) that's why Coenzyme Q-10 treatment may produce antidiabetic effect. Some research work has been done but the result is confusing. In two randomized trial first done by Henriksen and co-workers in 1999, and second done by Eriksson and co-workers in1999 using 100 and 200 mg of coenzyme Q 10 in patient with type 1 and type 2 diabetes found no difference in glycemic control and insulin requirement. Considering all these facts the proposal of this experiment was made.

Materials and methods

Animals

Healthy male Wistar rats weighing about 150-250 g were selected for the present study. The animals were kept in clean and dry cages, with 12 h: 12 h light-dark cycle at room temperature and humidity. They were acclimatized to the available housing conditions and were fed with standard laboratory diet consisting of soaked black gram. Water was given *ad libitum*. Arrangements were made to ensure regular cleaning of cages and disposal of excreta and urine. The cages were floored with a layer of saw dust for absorption of urine of rats. The whole experiment was conducted in accordance with ethical norms approved by Institutional Animal Ethics Committee (IAEC) Guidelines. Drugs used in this experiment were coenzyme Q10 20 mg, (brand name Tab CoQ, Manufacturing Company: Universal Medicare), tab.metformin 500 mg (glyciphage, franco-Indian pharmaceuticals), Inj. streptozotocin 250 mg powder, Himedia, Mumbai and nicotinamide 100 g powder, Animed, Kolkata.

Study design

The experiment was done in "Department of Pharmacology & Therapeutics, Rajendra Institute of Medical Sciences, Ranchi". The animals used for the study were healthy and active male Wistar rats weighing about 150-250 grams. Only those rats were included in the study whose fasting blood sugar after induction of diabetes was in the range of 200-250mg/dl.

Experimental animals were divided into four groups having six animals in each group. The groups were as follows 1. Group A; normal control group, treated with1% gum acacia, 2.Group B; diabetic control group, streptozotocin induced diabetic rats treated with 1% gum acacia 3. Group C; non diabetic rats treated with Coenzyme Q10, 1.8mg/kg body weight, 4. Group D; Diabetic Control rats treated with Coenzyme Q10 1.8 mg/kg body weight.

All the cages were appropriately labeled. Animals in each cage were also labelled separately and colour coded with the help of permanent marker. Rats were given different treatment orally once daily for 28 days in the morning hour at 09:30-10:30 am.

Induction of diabetes mellitus

Diabetes was induced by freshly prepared single intraperitoneal injection of streptozotocin in the dose of 60 mg/kg. Just 15 minutes before the streptozotocin injection, nicotinamide was injected intraperitoneally in a dose of 120 mg/kg (Nayak, 2014). To administer streptozotocin and nicotinamide intraperitoneally, animal was held with its ventrum exposed and head pointed downwards. A 26 gauge needle with 1 ml syringe was inserted into the abdominal cavity in the lower right quadrant to avoid the injury to the caecum and urinary bladder. The needle was directed towards the animal's head at an angle of 15-20 degrees and inserted approximately 5 mm in depth. Following insertion of needle the drug solutions were gently

released. After intraperitoneal injections animals were allowed to drink 5% glucose solution overnight to overcome streptozotocin induced hypoglycemia.

The fasting blood glucose level was determined after 72 hrs of streptozotocin injection. The rats having blood glucose level in the range of 200-250 mg/dl were used for the study. The diabetic animals were allowed free access to tap water, normal laboratory diet, and were maintained at room temperature in their cages.

Though diabetes was confirmed after 72 hrs of streptozotocin induction, coenzyme Q10 was started on 8th day from induction and this 8th day was considered as day '0'. Then the treatment continued for 28 days. The blood samples were collected from all groups before induction of diabetes, after 72 hrs of diabetic induction as well as on day 0, 7, 14, 21, 28 day to determine the blood glucose level by glucometer.

Statistical analysis

Statistical analysis of data was carried out by employing analysis of variance. One way ANOVA test was used to compare the effect of drugs on different groups. Tukey's HSD test was used for post-hoc analysis of significant overall differences (Park, 2013).

Results and discussion

Effect of Coenzyme Q10 on fasting blood sugar level of non diabetic groups

The fasting blood glucose level in non diabetic and non diabetic coenzyme Q 10 treated groups was in stable range. In coenzyme Q10 treated group no significant decrease in blood sugar level was observed. Animal of this group did not develop hypoglycemia during the experimental period. Coenzyme Q10 has beneficial effects in diabetes and diabetes induced complications

(Modi et al., 2006). So the above mentioned observations are desirable.

Effect of Coenzyme Q10 on fasting blood sugar level in diabetic groups

Fasting blood sugar of diabetic rats treated by placebo (group B) gradually increased during the study period where as sugar level in group D (treated with coenzyme Q10) showed sequential decrease throughout the study (Table 1). Increase in blood sugar level in streptozotocin induced diabetic rats is expectable due to damage of beta cell. The statistical comparison between Group A and Group C is provided in Table 2. Statistically significant decrease FBS was observed in coenzyme Q 10 treated group on day 21 with *p*-value of 0.001 (Table 3). The possible mechanism by which chronic use of Coenzyme Q10 may be beneficial in diabetes is that Coenzyme Q10 works as an electron transporter in ATP synthesis by mitochondria. Coenzyme Q 10 decreases the oxidative stress by converting to a reduced state, scavenging the free radicals. It also regulates oxidative phosphorilation and prevents lipid peroxidation (Bargossi et al., 1994). In this way it prevents further damage of the pancreatic beta cell. This enzyme takes part in the generation of ATP. Those organs which have highest energy requirements such as the heart, liver, pancreas and kidney have the highest Co enzyme Q10 concentrations (Aberg et al., 1992). On day 28, p value was found highly significant that indicates its effects trying to achieving normal physiology probably *via* reducing the oxidative stress, and above mentioned mechanism (Ernster and Dallner, 1995). Result of this study resembles with the study done by Modi et al. (2006). In a randomized trial Hodgson et al. (2002) found modest improvement in A1C level by this drug in 200mg dose once daily in 12 weeks period which also support the result achieved in this experiments.

Table 1. Showing sequential changes in FBS in different groups throughout the study period. All the values are expressed as mean± standard deviation.

	Group A	Group B	Group C	Group D
Day 0	86.50± 1.87	206.17±2.71	87.00± 2.10	206.00± 2.19
Day 7	86.83± 1.47	207.33± 3.93	86.67± 2.34	205.33± 1.63
Day 14	87.17± 1.72	208.67± 3.56	84.33± 3.01	203.83± 2.48
Day 21	86.33± 3.01	209.83± 3.92	83.50± 2.66	201.00± 2.83
Day 28	86.67± 2.16	211.17± 3.87	82.67± 2.73	195.67± 2.73

Table 2. The statistical comparison between Group A and Group C.

	Day 0	Day 7	Day 14	Day 21	Day 28
Group A	86.50±1.87	86.83±1.47	87.17± 1.72	86.33±3.01	86.67± 2.16
Group C	87.00±2.10	86.67±2.34	84.33± 3.01	83.50±2.66	82.67± 2.73
Mean difference	0.5000	0.1667	2.8333	2.8334	4
p-value	0.998	1	0.539	0.654	0.137

Table 3. The statistical comparison between Group B and Group D.

	Day 0	Day 7	Day 14	Day 21	Day 28
Group B	206.17±2.71	207.33±3.93	208.67±3.56	209.83±3.92	211.17±3.87
Group D	206.00±2.19	205.33±1.63	203.83±2.48	201.00±2.83	195.67±2.73
Mean difference	0.1667	2	4.8333	8.8333	15.5000
p-value	1	0.839	0.067	0.001*	0.000*

Conclusion

From the results of the present study we can conclude that Coenzyme Q10 reduces the fasting blood sugar level in streptozotocin induced diabetic rats and it is of statistical significance in long term use (at 21 days and later). On the basis of this study we can also comment that Coenzyme Q10 has no hypoglycemic effect on normal rats. It may have supportive role in diabetes. Further more studies are needed to establish it as a novel anti diabetic drug.

Conflict of interest statement

Authors declare that they have no conflict of interest.

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