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Melatonin Inhibits Oxidative Stress in Heart Tissue in Aged Diabetic Female Rats

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AIM:

Melatonin is a largely neurotransmitter-like compound derived principally from the pineal gland. The diverse range of actions and biological functions of melatonin suggest the potential for a number of clinical and health improving uses. Therefore, melatonin has attracted increasing attention for the therapeutic management of various diseases.

Many scientific studies have demonstrated that melatonin can reduce lipid peroxidation through a free radical scavenging effect and also by directly raising antioxidant activity. In parallel with this, oxidative stress, which has an important role in the induction of various complications of diseases such as diabetes, is effectively attenuated by the anti-oxidative activity of melatonin.

Melatonin, an effective antioxidant, is therefore thought to prevent harmful effects on the heart caused by diabetes. The purpose of this study is was to investigate the effects of melatonin administraton on heart tissue damage in a diabetic elderly female rats.

METHODS:

The study was performed on female aged rats (16 months old) which were provided by The Experimental Medicine Research and Application Center of Selçuk University. The study protocol was approved by the Selcuk University Experimental Medicine Researchand Application Center ethics committee of the latter. In the study conducted on 24 female old Wistar rats the animals were divided into 4 groups in equal numbers.

Group 1:General Control Group: the group which was not subjected to any procedure and fed on a normal diet.

Group 2:Melatonin-Supplemented Control Group: the group fed on a normal diet and supplemented with 5 mg/kg/day subcutaneously melatonin for 4 weeks.

Group 3:Diabetes Group: the group in which diabetes was induced by subcutaneous injection of “40 mg/kg” streptozotocin (STZ).

Group 4: Melatonin-Supplemented Diabetic Control Group: the group in which diabetes was induced by subcutaneous injection of “40 mg/kg” streptozotocin (STZ) and which was supplemented with 5 mg/kg/day subcutaneously melatonin for 4 weeks.

Inducement of Diabetes in Experimental Animals

In order to induce diabetes, 12 rats were picked as the diabetes groups. The rats were injected with 40 mg/kg subcutaneous streptozotocin (STZ) “Sigma, S-0130”. 6 days after injection, blood glucose levels of the animals were determined from the tail vein using a diagnostic glucose kit. The animals whose blood glucose rose to or above 300 mg/dlt were accepted as diabetic.Also, to rats, 5mg/kg/day resveratrol (intraperitoneal) and melatonin (subcutaneously) were given for 4 weeks.

Melatonin Supplementation

After dissolving 40 mg of melatonin (Sigma M-5250) in 3 ml pure ethanol, this suspension was sealed and stored in dark in the deep freeze until the time of use. From the stock solution 0.1 ml was added 0.4 ml NaCl (5 mg/kg/day) and injected to the rats through the intraperitoneal route at 09.00 a.m. Melatonin supplementation was carried out at the same hours for 4 weeks.

Biochemical Analyses

At the end of the experiment, in cardiac tissue samples taken under general anesthesia as well as MDA and GSH levels of were determined by ELISA method. Levels of MDA were expressed as nmol/gr tissue. GSH levels were presented as mg/gr tissue.

Statistical Evaluations

Computer package software was used in the statistical evaluation of results. Arithmetic means and standard deviations of all parameters were calculated. Variance analysis was used to determine differences between groups. The Least Significance Difference (LSD) test was employed to compare group means in variance analysis results which were found significant. Differences for which $p<0.05$ were considered significant.

RESULTS:
In our study, the highest heart MDA values were found in the diabetes group (G3; P <0.05). Heart tissue MDA levels in groups 1,2 and 4 were lower than the levels in groups 3 (P <0.05). Groups 1,2 and 4 had the highest heart GSH values (P <0.05). The lowest GSH levels in heart tissue were found in the diabetes group (P <0.05, Table 1).

Table:Levels of MDA and GSH in the heart tissue of groups

Groups	N	MDA (nmol/gr tissue)	GSH (mg/gram tissue)
G1 Control	6	82,92±2,97^{b}	4741,24±426,21^{a}
G2 Melatonin Control	6	81,74±3,16^{b}	4543,18±221,06^{a}
G3 Diabetes	6	110,60±1,70^{a}	513,56±93,92^{b}
G4 Diabetes + Melatonin	6	95,06±5,01^{b}	4475,99±290,65^{a}

*Means with different superscripted letters in the same column are statistically significant (a>b) (p<0,005).

CONCLUSION: Many investigators have reported that melatonin may protect heart function in cardiomyopathy caused by diabetes. These effects of melatonin occur by increasing the activity of antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase. In accordance with the reports presented above the reults of our study showed that oxidative stress in heart tissue can be prevented by melatonin supplementation in diabetic elderly female rats. Chronic melatonin therapy can improve heart tissue damage caused by diabetes in the aged rat model.