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Regulatory Effect of Melatonin Supplement on Cardiac Contraction Parameters in Diabetic Aged Female Rat Model

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Poster # PC45

AIM:

Diabetes-associated changes in myocardial structure and function, unrelated to coronary artery disease, arterial hypertension, valvular heart disease, or congenital heart disease, are called diabetic cardiomyopathy. Several mechanisms are involved in diabetic cardiomyopathy including metabolic changes, myocyte hypertrophy, myocardial interstitial fibrosis, apoptosis, microvascular disease, autonomic dysfunction, energy production deterioration, intracellular calcium homeostasis alterations, and myocardial contractile proteins

Melatonin, a multi-faceted molecule secreted rhythmically by the pineal gland, plays a cardioprotective role especially in conditions such as ischemia-reperfusion injury, atherosclerosis, diabetic cardiomyopathy, pathological hypertrophy and heart failure. Melatonin can protect diabetic myocardium from diastolic dysfunction. Melatonin can alleviate cardiac fibrosis, pathological fibrosis causes accumulation of extracellular matrix, and melatonin contributes to its reduction. Thus, there is substantial evidence that melatonin could potentially play a critical role in the treatment and prevention of fibrosis present in cardiac hypertrophy. However, the effects of melatonin on diabetic heart muscle are still controversial.

The aim of this study was to investigate the effects of melatonin supplementation on myocardial papillary muscle contraction parameters in a diabetic elderly female rat model.

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

Group 2 (CM):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 (D): Diabetes Group: the group in which diabetes was induced by subcutaneous injection of “40 mg/kg” streptozotocin (STZ).

Group 4 (DM): 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.

Electrophysiological Measurements

At the end of the experiment, for the electrophysiological recordings in the isolated organ bath, the hearts of the animals were quickly removed under anesthesia and the left ventricular papillary muscles were isolated in the solution adjusted to pH 7.2. As a result, the contraction force and durations of the papillary muscles of all animals were measured in an isolated organ bath.

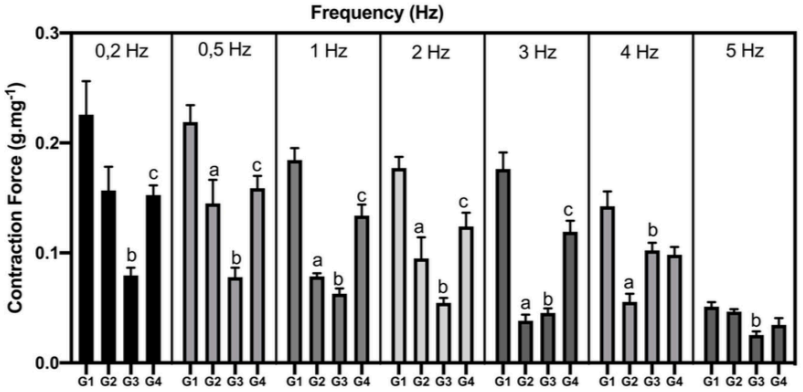
Statistical Evaluations

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:

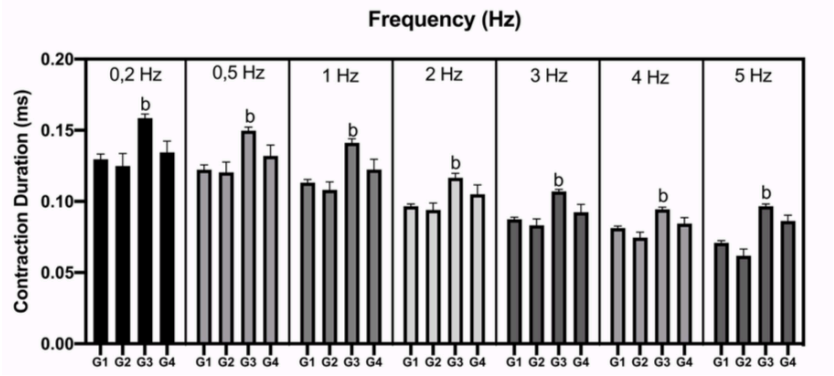
In our study, the responses of the myocardial papillary muscles of diabetic rats to stimuli at frequencies of 0.2, 0.5, 1, 2, 3, 4 and 5 Hz in the isolated organ bath were evaluated. At all frequencies of stimulation, the contraction force of the animals decreased significantly, while the contraction duration was significantly prolonged ($p<0.05$). Melatonin supplementation significantly increased the animals' decreased contractile strength ($p<0.05$), but did not affect the duration of contraction. Graphics (1-2).

Graphic 1: The stimulus frequency - contraction relationship of the contractile force values.



Response values of the contraction force to stimuli at different frequencies were given as mean ± standard error. It shows the significance between a, G1 and G2; b, G1 and G3; c, G3 and G4 groups.

Graphic 2: Stimulus frequency - contraction relationship of the contractile duration values



Response values of the contraction duration to stimuli at different frequencies were given as mean ± standard error. It shows the significance between b, G1 and G3 groups.

CONCLUSION: The findings of our study show that the reduction in myocardial papillary muscle contraction force can be restored with melatonin supplementation in a diabetic elderly female rat model. Based on the findings we have obtained, we can say that; Melatonin supplementation modulates the cardiac contractile force of diabetic rats.