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Protective Effect of Melatonin on Bone Tissue in Elderly Diabetic Female Rats

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Abstract – The aim of this study was to investigate the effects of melatonin administraton on bone tissue damage in a diabetic elderly female rat model.
The study was performed on female aged rats (16 months old) who were provided by The Experimental Medicine Research and Application Center of Selçuk University. A total of 24 elderly female rats were divided into 4 groups: Group 1. Control, Group 2. Control + Melatonin, Group 3. Diabetes, Group 4. Diabetes + At the end of the study, MDA ve GSH levels were determined by ELISA, on bone tissue samples obtained from the animals sacrificed under general anesthesia.
In our study, the highest bone MDA values were found in the Diabetes Group. MDA values of the Diabetes + Melatonin group were significantly lower than all the other groups. In our study, the highest bone GSH values were found in the Diabetes + Melatonin group and the lowest bone GSH levels were found in the Diabetes Group.
The findings of our study show that oxidative stress in bone tissue can be prevented by melatonin supplementation in diabetic elderly female rats.

Keywords *– old female rats, diabetes mellitus, melatonin, bone tissue, oxidative stress*

I. Introduction

In patients with diabetes mellitus, higher risks of impaired bone metabolism are widely reported [1]. Long-term exposure to a diabetic environment leads to changes in bone metabolism and impaired bone micro-architecture through a variety of mechanisms on molecular and structural levels [2]. These changes predispose the bone to an increased fracture risk and impaired bone healing [2]. As a result impaired bone quality and increased fracture risk have become recognized complications of diabetes mellitus [1],[2]. It was demonstrated in a study which included rats with streptozotocin-induced diabetes that diabetes caused bone destruction by significantly increasing urinary excretion of calcium-phosphorus [3]. Consequently numerous studies also attest to the fact that diabetes has a negative effect on bone metabolism [1],[3]. Melatonin hormone, which is secreted by the pineal gland in darkness and according to the circadian rhythm, has a part in the regulation of many physiological functions in the body [4]. As it is both fat-, and water-soluble, melatonin can reach all cell organelles, including the nucleus [5]. This property gives melatonin an advantageous position in the protection of DNA against oxidative stress [6]. Consequently, melatonin is regarded to be a strong antioxidant which prevents the oxidative damage resulting from lipid peroxidation [6]. It has been argued that melatonin which is known to contribute to the carbohydrate mechanism may play a protective role against diabetes as well [7].

The aim of this study was to investigate the effects of melatonin administraton on bone tissue damage in a diabetic elderly female rat model.

II. Materials and Method

The study was performed on elderly female rats (16 months) obtained from Selçuk University Experimental Medicine Research and Application Center. The ethics committee of the same center approved the study. A total of 24 elderly female rats were divided into 4 groups.

The study was performed on elderly female rats (16 months) obtained from Selçuk University Experimental Medicine Research and Application Center. The ethics committee of the same center approved the study. A total of 24 elderly female rats were divided into 4 groups.

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

Group 2. Control + Melatonin: The group which was fed on a normal diet and was additionally administered 5 mg/kg/day intraperitoneal (ip) melatonin for 4 weeks.

Group 3. Diabetes: The group which was induced diabetes with intraperitoneal “50 mg/kg” streptozotocin (STZ)

Group 4. Diabetes + Melatonin: The group which was induced diabetes with intraperitoneal “50 mg/kg” streptozotocin (STZ) injection and which was then

administered 5mg/kg/day intraperitoneal (ip) melatonin for 4 weeks.

A. Experimental animals

Experimental animals were kept in special steel cages which were washed and cleaned every on a daily basis. They were fed from special steel bowls and water (normal tap water) was given by glass feeding bottles. They were fed on 10 g feed per 100 g body weight daily. They were kept in an environment with 12 hour dark/12 hour light cycles and standard room temperature (21±1ºC). All injections were given at 09:00-10:00 a.m.

After 4-weeks melatonin treatment period, MDA ve GSH levels were determined by ELISA, on bone tissue samples obtained from the animals sacrificed under general anesthesia.

B. Experimental procedures

Induction of diabetes in experimental animals

In order to induce diabetes in experimental animals, 40 rats were used as diabetes groups. The rats were injected with 40 mg/kg intraperitoneal streptozotocin (STZ) "Sigma S-0130". Blood glucose levels of the animals were determined in the blood taken from the tail vein of the animals 6 days after the injection by using a diagnostic glucose kit. Animals with blood glucose at or above 300 mg/dlt were accepted diabetic [8].

Melatonin supplementation

After 40 mg of melatonin (Sigma M-5250) was dissolved in pure ethanol, this suspension was kept capped and in the dark in a deepfreeze, until it was used. Of the stock solution, 0.1 ml was taken, added 0.9 ml NaCl (5 mg/kg/day) and injected to rats at 09:00 a.m. through intraperitoneal route. Melatonin supplementation was carried out at the same hour for 4 weeks.

C. Statistics

A computer software package was used in the statistical evaluation of results. Arithmetic means and standard errors of all parameters were calculated. Variance analysis was used to determine differences between groups. The Least Significant Difference "LSD" Test was employed to compare group means in the statistically significant variance analysis results. Differences for which $p<0.05$ were accepted significant.

III. RESULTS

In our study, the highest bone MDA values were found in the Diabetes Group. MDA values of the Diabetes + Melatonin group were significantly lower than all the other groups. In our study, the highest bone GSH values were found in the Diabetes + Melatonin group and the lowest bone GSH levels were found in the Diabetes Group (Table 1).

Table 1. Bone Tissue MDA and GSH levels of the Study Groups

Groups (n=6)	MDA (nmol/gr tissue)	GSH (mg/gram/tissue)
G1 Control	40,87±13,83^{b}	122,89±11,79^{b}
G2 Control+Melatonin	36,06±7,82^{b}	138,17±13,81^{b}
G3 Diabetes	183,07±23,01^{a}	82,78±17,92^{c}
G4 Diabetes+Melatonin	23,61±3,00^{c}	179,95±21,49^{a}

a,b.c: *Means with different superscripted letters in the same column are statistically significant ($p<0.05$).

IV. CONCLUSION

The findings of our study show that oxidative stress in bone tissue can be prevented by melatonin supplementation in diabetic elderly female rats.Melatonin supplementation may be beneficial in diabetes.

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