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Original Article

The Relationship of Endogenous Nocturnal Melatonin Levels and Heart Rate in Healthy Young Males

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Abstract

Objectives: Light inhibits the secretion of melatonin produced in the pineal gland, while darkness increases its release. Melatonin may affect cardiologic functions, including heart rate and blood pressure. In this study, we evaluated the relationship between endogenous nocturnal melatonin levels and heart rate in healthy young males.

Methods: Twenty-four healthy males [mean age: 22.4±2.4 (18–26) years] who did not have any disease and did not smoke, drink alcohol, or use drugs were included in the study. While the subjects were in the supine position at a time point between 02:30 and 04:30 am, plasma samples were taken to measure melatonin concentrations. After centrifugation, plasma samples were immediately frozen at -20°C until analysis. In each subject, heart rate and arterial blood pressure were measured by the same observer.

Results: Although we found a significant negative correlation between nocturnal melatonin levels and age (p=0.02, r=-0.46), we did not find any correlation between melatonin and body mass index (p=0.80, r=0.05), waist circumference (p=0.12, r=-0.31), hip circumference (p=0.77, r=-0.06), systolic blood pressure (p=0.79, r=-0.05), diastolic blood pressure (p=0.71, r=-0.07), mean blood pressure (p=0.95, r=-0.01), or pulse pressure (p=0.51, r=-0.14). Additionally, we found a negative correlation between nocturnal melatonin levels and heart rate, which did not reach statistical significance (p=0.86, r=-0.038).

Conclusion: The current study demonstrated a negative correlation that did not reach statistical significance between endogenous nocturnal melatonin levels and heart rate in healthy young males.

Keywords: Healthy male; heart rate; melatonin.

Sağlıklı Genç Erkeklerde Endojen Gece Melatonin Düzeyleri ile Kalp Hızı Arasındaki Ilişki

Özet

Amaç: Işık, pineal bezde üretilen melatonin salgısını engellerken karanlık salınımı artırır. Melatonin, kalp hızı ve kan basıncı gibi kardiyolojik fonksiyonları etkileyebilir. Bu çalışmada, sağlıklı genç erkeklerde endojen nokturnal melatonin düzeyleri ile kalp hızı arasındaki ilişkiyi değerlendirdik.

Gereç ve Yöntem: Herhangi bir hastalığı olmayan, sigara, alkol ve ilaç kullanmayan yirmi dört sağlıklı erkek [ortalama yaş: 22.4±2.4 (18–26) yıl] çalışmaya alındı. Denekler sabah 02:30–04:30 arasında sırtüstü pozisyondayken melatonin konsantrasyonlarını ölçmek için plazma örnekleri alındı. Santrifüjlemeden sonra plazma örnekleri analiz edilene kadar hemen -20°C'de dondurulduu. Her denekte kalp hızı ve arteriyel kan basıncı aynı gözlemci tarafından ölçüldü.

Bulgular: Gece melatonin düzeyleri ile yaş arasında anlamlı negatif korelasyon bulunmasına rağmen (p=0,02, r=-0,46), melatonin ile vücut kitle indeksi (p=0,80, r=0,05), bel çevresi (p=0,12, r=-0,31), kalça çevresi (p=0,77, r=-0,06), sistolik kan basıncı (p=0,79, r=-0,05), diyastolik kan basıncı (p=0,71, r=-0,07), ortalama kan basıncı (p=0,95, r=-0,01) ve nabız basıncı (p=0,51, r=-0,14) arasında anlamlı bir korelasyon bulunmadı. Ek olarak, gece melatonin seviyeleri ile kalp hızı arasında istatistiksel anlamlılık sınırına ulaşmayan negatif yönde bir korelasyon bulundu (p=0,86, r=-0,038).

Sonuç: Mevcut çalışma, sağlıklı genç erkeklerde endojen gece melatonin seviyeleri ile kalp hızı arasında istatistiksel anlamlılığa ulaşmayan negatif bir korelasyon olduğunu göstermiştir.

Anahtar sözcükler: Sağlıklı erkek; kalp atış hızı; melatonin.

This article is an adaptation of Mustafa Yıldız's thesis.

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Introduction

Melatonin, N-acetyl-5-methoxytryptamine, is an indole hormone synthesized from the essential amino acid tryptophan.[1] It is secreted by the pineal gland during the night and plays important roles in regulating the cardiovascular system.[1] Melatonin receptors are present throughout the cardiovascular system, including the left ventricle, cardiomyocytes, coronary arteries, and blood vessels.[1] It affects many cardiovascular parameters, including heart rate, blood pressure, and arterial resistanc.[1–3] Melatonin use can decrease heart rate and arterial blood pressure via its effects on the autonomic nervous system and vascular function.[3] Heart rate, which can be easily measured, predicts adverse outcomes such as death and disease development in normal and healthy individuals. The relationship between endogenous nocturnal melatonin levels and heart rate in healthy young males is investigated in the current study.

Materials and Methods

Study Population

Twenty-four healthy males [mean age: 22.4±2.4 (18–26) years] who did not have any disease and did not smoke, drink alcohol, or use drugs were included in the study. All participants' hemogram and biochemistry values [glucose, urea, creatinine, cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride, alanine transaminase (ALT), aspartate aminotransferase (AST), thyroid-stimulating hormone, calcium] were within normal limits. Written informed consent was obtained from all participants, and the study design was in accordance with the guidelines issued by the ethics committee (date: 04.06.2002, decision no: 02). The investigation conformed to the principles outlined in the Declaration of Helsinki.

Study Protocol

Participants had regular sleep–wake schedules and typically consumed low amounts of caffeine (<50 mg per day). Participants' sleep time was scheduled from 11:00 pm to 8:00 am. A complete clinical evaluation, including measurements of vital signs such as blood pressure and heart rate, and routine laboratory tests including glucose, lipids, and complete blood count, was performed one week before the start of the study. Blood samples were collected for melatonin measurement via a double-stopcocked, heparinized polyethylene cannula inserted into a vein in the forearm. Samples were centrifuged at 2000 rpm for 15 minutes and stored at -20°C until further analysis. Plasma was collected for melatonin concentrations between 2:30 am and 4:30 am with the subjects in the supine position.

Blood pressure measurements were taken twice for each subject and averaged for analysis.

Mean blood pressure = [systolic blood pressure + 2 × diastolic blood pressure] / 3

Pulse pressure = systolic blood pressure − diastolic blood pressure

Table 1. Anthropometric, hemodynamic and nocturnal melatonin values in healthy males

	Male
Age (years)	22.4±2.4
Body mass index (kg/m^2)	23.49±2.21
Waist circumference (cm)	82.75±8.84
Hip circumference (cm)	95.87±5.98
Systolic blood pressure (mmHg)	99.37±10.96
Diastolic blood pressure (mmHg)	59.79±6.67
Mean blood pressure (mmHg)	73.24±6.16
Pulse pressure (mmHg)	40.41±9.54
Heart rate (beat/min)	59.25±8.60
Melatonin (pg/mL)	94.78±64.32

Assays

Plasma melatonin levels were assessed within one month of blood sampling. Melatonin levels were measured with a commercially available radioimmunoassay kit (RE29301, IBL, Germany). Samples of plasma from each participant were processed in the same assay, eliminating inter-assay variability. The assay has a sensitivity of <3.5 pg/ml and an intra-assay coefficient of variation <8%.

Statistical Analysis

Statistics were obtained using the ready-to-use software SPSS (version 20.0, SPSS Inc., USA). All values are expressed as means±SD. Relations between melatonin and anthropometric and hemodynamic parameters were calculated using Pearson correlation tests. Values below $p<0.05$ were considered significant.

Results

Anthropometric and hemodynamic values in healthy males were presented in Table 1. Although we found a significant negative correlation between nocturnal melatonin levels and age ($p=0.02$, $r=-0.46$), we did not find any correlation between melatonin and body mass index ($p=0.80$, $r=0.05$), waist circumference ($p=0.12$, $r=-0.31$), hip circumference ($p=0.77$, $r=-0.06$), systolic blood pressure ($p=0.79$, $r=-0.05$), diastolic blood pressure ($p=0.71$, $r=-0.07$), mean blood pressure ($p=0.95$, $r=-0.01$), or pulse pressure ($p=0.51$, $r=-0.14$). Additionally, we found a negative correlation between nocturnal melatonin levels and heart rate, which did not reach the limit of statistical significance ($p=0.86$, $r=-0.038$).

Discussion

In this study, although we found a significant negative correlation between nocturnal melatonin levels and age, we found a negative correlation between nocturnal melatonin levels and heart rate that did not reach the limit of statistical significance. Production and release of melatonin in the pineal gland are stimulated by darkness and suppressed by light.[1,4] With the onset of darkness, photoreceptors stimulate the suprachiasmatic nucleus, which is the biological circadian clock in mammals, in the hypothalamus.[5] The increase in melatonin level in humans begins immediately after dark (20:00–23:00). Then, in the second half of the night, melatonin levels gradually decrease. Serum

melatonin levels change according to age. In newborns, blood melatonin levels are low. The highest melatonin levels occur between the third and fifth years.[1] In general, nocturnal melatonin release decreases with advanced age, as in our study, in which we also found a negative correlation between age and nocturnal melatonin levels that did not reach statistical significance.

According to different times of day and various physiological or environmental conditions, heart functions change. In this adaptation, many neuronal and hormonal factors play a role. The most important parameters of the cardiovascular system that show circadian rhythm are changes in heart rate—which predicts adverse outcomes such as death and disease development in normal and healthy individuals—blood pressure, and vascular tone.[1] Heart rate, blood pressure, and vascular tone decrease at night.[1,2,4] This condition is associated with autonomic activity. The circadian rhythm of heart rate in pinealectomized rats exposed to constant light was found to be more disrupted than in the pinealectomized control group.[6] Similarly, in humans, the circadian rhythm of heart rate is disrupted by nighttime light exposure.[7] These findings suggest that melatonin may play a role in circadian heart rate changes.[1,4,6,7] In the supine position, after oral melatonin intake, heart rate and blood pressure decreased due to increased cardiac vagal tone and decreased plasma norepinephrine and dopamine levels. This effect is due to melatonin's suppression of sympathetic tone.[3] Chuang JI et al.[8] also demonstrated that intravenous administration of melatonin (30–60 mg/kg) or vehicle (10% alcohol) decreases brain serotonin release and results in sympathetic inhibition or parasympathetic stimulation, which leads to hypotension and bradycardia in rats.

Study limitations

We cannot provide a clear explanation for the results of this study, namely the relationship between endogenous nocturnal melatonin levels and heart rate in healthy young males. Studies with larger numbers of participants are needed to better understand the possible interactions between nocturnal melatonin levels and heart rate.

Conclusion

In conclusion, the current study demonstrated a negative correlation, which did not reach statistical significance, between endogenous nocturnal melatonin levels and heart rate in healthy young males.

Disclosures

Ethics Committee Approval: The study was approved by the Trakya University Ethics Committee (no: 02, date: 04/06/2002).

Informed Consent: Informed consent was obtained.

Conflict of Interest Statement: All authors declared no conflict of interest.

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