Characterization of the day-night fluctuations of serum melatonin in young boys and girls with different body mass indexes within normal range according to World Health Organization classification

Dünya Sağlık Örgütüne göre normal aralıkta, değişik vücut kitle indekslerine sahip genç erkek ve kızlardaki gündüz-gece serum melatonin dalgalanmalarının karakteristikleri

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Melatonin (5-methoxy-N-acetyltryptamine) is a neurohormone that is mainly produced in the pineal gland. Its release is synchronized with day-light cycle by a multisynaptic pathway. It plays a role in energy expenditure and body mass regulation in mammals (1). In Djungarian and Syrian hamsters, the melatonin-induced decrease in fat mass has been associated with thermogenic activation of brown adipose tissue (2). Effects of melatonin on adipose tissue may be start from the early stage of development. Body-mass index (BMI) is defined as the weight in kilograms divided by the square of the height in meters (kg/m^2). Normal range of BMI is 8.50-24.99 kg/m^2 according to World Health Organization (WHO) (3). It is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. In human adults, obesity is not accompanied by significant modifications of melatonin production (4). However, to our knowledge, the possible correlation of young boys and girls with different BMI within normal range with melatonin production has not been examined so far. To better characterize a possible melatonin fluctuations in this people, we studied in young boys and girls with different BMI within normal range according to WHO.

Twenty-three (15 boys and 8 girls) participants who were nonsmokers and were not on any medications and who had not consumed any alcohol were studied. All participants were healthy, as determined by their medical history and a routine examination. Written informed consent was obtained from all participants. Participants had regular sleep-wake schedules and typically consumed low amounts of caffeine (less than 50 mg daily), as indicated by logs the week before the study. All participants were requested to relax in a supine position, in a low noise, low light and constant temperature (20°C to 24°C) environment after consuming a light meal free of caffeine-containing beverages. The sleeping period was scheduled from 23:00 to 08:00. A full clinical evaluation was performed one week before the start of the study. To measure melatonin, blood samples were taken with a two-way stopcock, heparinized, polyethylene cannula inserted into a vein in the forearm. The samples were centrifuged at 2000 rpm for 15 min and stored at -20°C until further analysis. Plasma was taken to measure the concentrations of melatonin while the subjects were in the supine position at two time points, namely from 01.30-02.30 and 13:30-14:30 hours. In each subject arterial blood pressure and BMI (kg/m^2) were measured by the same observer. In each subject two blood pressure measurements were performed, and their mean was considered for analysis.

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

Assessment of plasma melatonin levels was performed within one month from the blood sampling. Melatonin levels were measured with a commercially available radioimmunoassay kit (RE29301, IBL, Germany). Samples of each participant's plasma were processed in the same assay, thus eliminating interassay variability. The assay has a sensitivity of less than 3.5 pg/mL and an intra-assay coefficient of variation of less than 8%.

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Statistics were obtained using the ready-to-use software SPSS (version 8.0, SPSS Inc, USA). All the values are expressed as means ±Standard Deviation. Mann-Whitney test was used to examine gender differences in measured anthropometric, hemodynamic and biochemical variables. Relations between variables were calculated using Pearson correlation tests. P<0.05 was considered significant.

Anthropometric, hemodynamic and biochemical values in boys and girls were presented in Table 1. Although hip circumference was significantly higher in girls than in boys (p=0.02), body weight, body height, BMI, waist circumference and waist-hip ratio were significantly higher in boys (p=<0.001, p=0.001, p=0.03, p=0.001, p=<0.001) than in girls (Table 1). We didn't find any correlation among the levels of melatonin and BMI in all subjects [BMI-Melatonin (day): p=0.65, r=-0.09; BMI-Melatonin (night): p=0.41, r=0.18].

We found that the day-night fluctuations of serum melatonin are not significantly different in young boys and girls with different BMI within normal range (18.50-24.99 kg/m^2) according to WHO (3). Overweight and obesity are important health problem for adolescent (4). Approximately, about 1/3 adolescent are considered under the risk for overweight. At the present day, rates of overweight in adolescence have increased markedly. The associations with melatonin and weight and/or BMI are controversial. Röjdmark et al. (5) showed that increased weight was not accompanied by significant modifications of melatonin production, as in our study. However, Burgess et al. (6) demonstrated that it was an association between weight and melatonin such that people with increased weight secreted less melatonin. This finding is consistent with report of increasing weight and higher BMI being associated with lower amounts of 6-sulfatoxymelatonin in urine (7). The mechanism behind this association has not been clearly explained in the literature (7).

Table 1. Anthropometric, hemodynamic and biochemical values in boys and girls

Variables	Boys	Girls	*p
Age, years	22.9±2.9	23.0±2.4	0.94
Weight, kg	71.00±6.54	56.00±5.97	<0.001
Height, m	176.86±4.54	163.37±8.27	0.001
Body mass index, kg / m^2	22.67±1.71	20.95±1.45	0.03
Waist circum, cm	82.33±6.77	72.00±3.96	0.001
Hip circum, cm	94.40±3.90	99.00±4.62	0.02
Waist / hip ratio	0.87±0.01	0.72±0.01	<0.001
Systolic blood pressure, mmHg, d	111.66±6.72	106.25±11.87	0.35
Systolic blood pressure, mmHg, n	100.33±8.54	95.00±10.69	0.36
Diastolic blood pressure, mmHg, d	62.00±6.76	65.00±10.35	0.52
Diastolic blood pressure, mmHg, n	58.33±5.23	62.50±10.69	0.20
Mean blood pressure, mmHg, d	78.52±5.34	78.70±10.22	0.97
Mean blood pressure, mmHg, n	72.31±5.77	73.31±10.39	0.62
Heart rate, beat/min, d	73.60±10.00	76.25±9.40	0.47
Heart rate, beat/min, n	59.06±7.99	65.25±13.77	0.46
Melatonin, pg/mL, d	5.30±6.40	4.61±4.76	0.72
Melatonin, pg/mL, n	77.22±52.24	74.69±65.19	0.60
Glucose, mg/dL	74.06±9.78	74.25±12.11	0.64
Cholesterol, mg/dL	145.46±20.29	145.12±24.74	0.84
HDL, mg/dL	38.53±8.15	44.25±10.95	0.17
LDL, mg/dL	81.06±23.61	86.00±19.33	0.49
Triglyceride, mg/dL	117.80±38.51	93.12±30.53	0.14

All the values are expressed as means±standard deviation
*Mann-Whitney test
d - day, HDL - high - density lipoprotein, LDL - low-density lipoprotein, n - night

The amount of the melatonin synthesized in the pineal gland is influenced by age. Peak nighttime serum levels of melatonin decrease rapidly between the ages of 6 and 20 years, remain stable between 20 and 40 years, and then slowly decline (8). In advanced age, especially during post-menopause, pineal secretion declines (8). Through melatonin levels remain stable between 20 and 40 years, we designed this study between 20 and 26 years for investigating gender differences. Endogenous synthesis of melatonin during the night depends on β- and α_1-adrenergic receptor stimulation by sympathetic system (9). Melatonin mediates its effects through high affinity G protein-coupled receptors. It mainly has two membrane receptors called MT1 and MT2. Recently, Brydon et al. (10) showed that melatonin may act directly at MT2 receptors on human brown adipocytes to regulate adipocyte physiology and body mass regulation.

In conclusion, the day-night fluctuation of serum melatonin is not significantly different in young boys and girls with different BMI within normal range (18.50-24.99 kg/m^2) according to WHO.

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References

1. Morgan PJ, Ross AW, Mercer JG, Barrett P. Photoperiodic programming of body weight through the neuroendocrine hypothalamus. J Endocrinol 2003; 177: 27-34. [CrossRef]
2. Viswanathan M, Hissa R, George JC. Effects of short photoperiod and melatonin treatment on thermogenesis in the Syrian hamster. J Pineal Res 1986; 3: 311-21. [CrossRef]
3. WHO expert consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. The Lancet 2004; 363: 157-63. [CrossRef]
4. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006; 295: 1549-55. [CrossRef]
5. Röjdmark S, Berg A, Rössner S, Wetterberg L. Nocturnal melatonin secretion in thyroid disease and in obesity. Clin Endocrinol (Oxf) 1991; 35: 61-5. [CrossRef]
6. Burgess HJ, Fogg LF. Individual differences in the amount and timing of salivary melatonin secretion. PLoS One 2008; 3: e3055. [CrossRef]

7. Levallois P, Dumont M, Touitou Y, Gingras S, Mâsse B, Gauvin D, et al. Effects of electric and magnetic fields from high-power lines on female urinary excretion of 6-sulfatoxymelatonin. Am J Epidemiol 2001; 154: 601-9. **[CrossRef]**
8. Markantonis SL, Tsakalozou E, Paraskeva A, Staikou C, Fassoulaki A. Melatonin pharmacokinetics in premenopausal and postmenopausal healthy female volunteers. J Clin Pharmacol 2008; 48: 240-5. **[CrossRef]**
9. Scheer FA, van Doornen LJ, Buijs RM. Light and diurnal cycle affect human heart rate:possible role for the circadian pacemaker. J Biol Rhythms 1999; 14: 202-12. **[CrossRef]**
10. Brydon L, Petit L, Delagrange P, Strosberg AD, Jockers R. Functional expression of MT2 (Mel1b) melatonin receptors in human PAZ6 adipocytes. Endocrinology 2001;142: 4264-71. **[CrossRef]**