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Cancer Epidemiology, Biomarkers & Prevention

Null Results in Brief

No Effect of Exercise on Urinary 6-Sulfatoxymelatonin and Catecholamines in Young Women Participating in a 16-Week Randomized Controlled Trial

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Abstract

Background: Women with breast cancer have decreased levels of melatonin or its metabolite in plasma and/or urine.

Methods: We measured serum melatonin, urinary 6-sulfatoxymelatonin, catecholamines, and cortisol in 141 sedentary young female participants in a clinical trial comparing 150 min/wk aerobic exercise for 4 months to no-exercise controls. Demographics, health surveys, body composition, sleep quality, fitness levels, and blood and urine samples were obtained at baseline and 16 weeks.

Results: There were no differences between groups at baseline in demographics, exercise, sleep habits, or study hormones. There were also no significant differences between groups in any of the hormones at 16 weeks.

Conclusion: Sixteen weeks of exercise had minimal effects on melatonin secretion of young women.

Impact: There is convincing evidence that exercise protects against breast cancer, but this does not appear to occur through changes in melatonin secretion. *Cancer Epidemiol Biomarkers Prev; 22(9); 1634–6. ©2013 AACR.*

Introduction

Women with breast cancer have decreased levels of melatonin or its metabolite in plasma and/or urine (1). Short-term exercise has been shown to acutely affect plasma melatonin levels in healthy humans (2, 3), but the findings have been inconsistent due to differences in study designs, that is, lighting during exercise, time of day, exercise intensity, as well as subject characteristics. Furthermore, there have been no controlled clinical studies examining the effects of regular exercise on melatonin levels in humans. The purpose of this study was to determine the effect of regular exercise on melatonin secretion and excretion in young women.

Methods

Study samples were obtained from the Women In Steady Exercise Research (WISER) study, a previously described randomized clinical trial comparing the effects of a 16-week aerobic exercise intervention versus no exercise on markers associated with breast cancer risk (4) in previously sedentary young women. Participants were healthy women in the age range of 18 to 30 years, BMI 18.5 to 40 kg/m^2, not taking any hormonal contraceptives, and not dieting. This study was approved by the University of Minnesota Institutional Review Board.

Although the women randomized into the control group were asked to maintain their usual level of physical activity, those in the exercise group were asked to engage in 150 min/wk of aerobic exercise for 16 weeks. Exercise intensity increased every 4 weeks to reach 80% to 85% of maximum heart rate.

At baseline and 16-weeks postintervention, the following were collected: demographic and anthropometric data, body composition via DXA (Lunar Radiation Corp.), health habits, fitness level via a submaximal test, exercise logs including time of day of exercise, and blood and urine samples. The samples analyzed in this study were obtained from those participants who also filled out sleep journals to assess sleep duration and light exposure at night during urine collections, completed a sleep quality survey (Pittsburgh Sleep Quality Index – PSQI; ref. 5), and collected overnight urine samples (from 10 pm until 6 am) at baseline and 16 weeks.

Serum melatonin, urinary 6-sulfatoxymelatonin, cortisol, epinephrine, and norepinephrine were measured by commercially available ELISA kits, and intra- and inter-assay CVs were 7.4% and 9.1%, 7.1%, and 11.9%, 3.3%, and 2.3%, 8.4% and 6.4%, 8.7% and 7.2%, respectively. Sulfatoxymelatonin was measured in both overnight (10 pm until 6 am) and 24-hour urine. All other assays were conducted in 24-hour urine samples.

Baseline characteristics were compared by two sample t test or the χ^2 test. Hormone outcomes were transformed to the log scale for analysis and geometric means and their 95% confidence intervals are reported. Groups were

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Table 1. Baseline demographics ($N = 141$)[a]

	Exercise ($n = 77$)	Control ($n = 64$)	*P*
Age, y	25.5 ± .4	25.6 ± .4	0.834
Body mass index	25.0 ± .5	25.4 ± .6	0.611
% Body fat	37.1 ± 1	37.0 ± 1	0.986
White	58 (75%)	51 (80%)	0.141
Asian	9 (12%)	8 (13%)	
Black	4 (5%)	5 (8%)	
Other	6 (8%)	0	
Taking birth control	38 (49%)	41 (64%)	0.080
METS at baseline	6.7 ± .1	6.8 ± .2	0.627
Hours of sleep	7.4 ± .2	7.6 ± .2	0.445
Bedtime (24 hour: minutes)	00:04 ± 8	23:46 ± 9	0.153
PSQI ($n = 117$)	5.3 ± .3	6.0 ± .3	0.108
SMT 24 hour (μg/d)	12.2 (10–14)	11.4 (10–14)	0.588
SMT night (μg/d)	10.2 (9–12)	9.1 (8–11)	0.297
SMT 24 hour (ng/mg Cr)	10.8 (9–13)	9.0 (8–11)	0.098
SMT night (ng/mg Cr)	23.4 (20–27)	20.0 (17–23)	0.152
Serum melatonin (pg/mL)	28.9 (24–35)	26.5 (22–32)	0.505
Cortisol (ng/mg Cr)	56 (50–63)	62 (55–69)	0.220
Norepinephrine (ng/mg Cr)	20.2 (17–24)	22.2 (19–26)	0.422
Epinephrine (ng/mg Cr)	2.4 (1.9–3.0)	2.8 (2.2–3.6)	0.382

[a]Values are mean ± SE or number (%); for outcome variables, the values are geometric mean (95% confidence interval), adjusted for month of starting the study. SMT 24 hour, 6-sulfatoxymelatonin in urine collected over 24 hours; SMT night, 6-sulfatoxymelatonin in urine collected overnight. These are expressed in μg/d as well as in ng/mg creatinine.

compared by a general linear model, adjusted for calendar month of the final measurement. All analyses were conducted using SAS Version 9.2. Based on the adjusted SDs in the observed data, the study had 80% power to detect a difference greater than 1.4 and 1.4 μg/day in SMT 24-hour and SMT night, respectively.

There were no differences between groups at baseline in demographics, exercise, sleep habits, or study hormones (Table 1). There was no evidence of seasonal differences in the distribution of start dates between exercisers and controls (χ^2 $P = 0.138$) or that time of exercise affected the levels of any hormones. Although both groups reported a significant decrease in PSQI score, there were no differences between groups in sleep hours, bedtimes, or PSQI scores at the end of the study.

Baseline and follow-up samples were collected approximately 6 months apart for measurement of the study endpoints, which would have contributed significantly to

Table 2. Final treatment outcomes, adjusted for month of ending measurement[a]

	Exercise ($n = 77$)	Control ($n = 64$)	*P* value
SMT 24 hour (μg/d)	12.0 (10–14)	10.9 (9–13)	0.363
SMT night (μg/d)	9.4 (8–11)	8.4 (7–10)	0.347
SMT 24 hour (ng/mg Cr)	11.0 (10–13)	9.8 (8–11)	0.282
SMT night (ng/mg Cr)	22.5 (19–27)	19.2 (16–23)	0.192
Serum melatonin	27.2 (23–32)	24.7 (21–29)	0.410
Cortisol	56 (51–62)	59 (54–66)	0.389
Norepinephrine	23.5 (20–27)	21.1 (18–25)	0.343
Epinephrine	2.1 (1.7–2.6)	2.8 (2.3–3.5)	0.069

[a]Values are geometric mean (95% confidence interval). SMT 24 hour, 6-sulfatoxymelatonin in urine collected over 24 hours; SMT night, 6-sulfatoxymelatonin in urine collected overnight. These are expressed in μg/d as well as in ng/mg creatinine.

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the within-subject variation, had we looked at change in these endpoints. Therefore, we chose to compare the exercise and the control groups at follow-up only, and no significant differences between groups were found in end-of-study hormone levels (Table 2).

Discussion

There is convincing evidence that exercise protects against breast cancer, but the mechanisms involved are largely unknown. Although short-term physical exercise acutely increases plasma melatonin levels in healthy humans (2, 3), we found that 150 minutes per week of exercise for 4 months did not affect melatonin levels. Recently, it has been shown that 12 weeks of exercise at 70% does not alter sympathetic nervous system (SNS) activity in healthy people (6). This could be an explanation why we did not see any effects of exercise on melatonin levels, given that catecholamine secretion, which is directly related to the biosynthesis of melatonin by the pineal gland, is triggered by SNS activity. In addition, it is possible that the duration and intensity of the exercise training in this study was not sufficient to alter SNS activity and, thus, change melatonin levels. Strengths of this trial include excellent adherence to the exercise treatment (7), large sample size, and selecting an exercise intervention based on current public health guidelines (8).

Conclusion

Our findings suggest that the reported beneficial effects of exercise against breast cancer are not likely to involve changes in melatonin levels.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: A.Y. Arikawa, S.R. Patel, M.S. Kurzer
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): A.Y. Arikawa, M.S. Kurzer
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): W. Thomas, S.R. Patel
Writing, review, and/or revision of the manuscript: A.Y. Arikawa, W. Thomas, S.R. Patel, M.S. Kurzer
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): A.Y. Arikawa
Study supervision: A.Y. Arikawa, M.S. Kurzer

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