Journal of Women's Health Care

Kawano, J Women's Health Care 2018, 7:2
DOI: 10.4172/2167-0420.1000422

Research Article Open Access

The Influence of Sleep Status on Urinary Adrenaline, Noradrenaline, and Cortisol Levels in Women

Atsuko Kawano*

Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

***Corresponding author:** Atsuko Kawano, Associate Professor, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki 305-8575, Japan, Tel: +81-29-853-8431; E-mail: akawano@md.tsukuba.ac.jp

Received date: March 20, 2018; **Accepted date:** March 26, 2018; **Published date:** April 05, 2018

Abstract

Introduction: Postpartum depression, which occurs at high rates (10%-20%) in Japan, needs to be detected and treated early. An understanding of confounding factors is critical for determining early detection biomarkers of postpartum depression. This study examined urinary biomarkers and sleep status in women.

Methods: About forty non-pregnant women in their 20s and 30s were surveyed for the previous day's sleep status (hours slept, awakening time, falling asleep time and feeling of sleeping well) and urinary adrenaline, noradrenaline, and cortisol levels.

Results: Hours slept and urinary noradrenaline and cortisol levels did not correlate. Urinary adrenaline levels correlated negatively with hours slept. For falling asleep time, urinary cortisol levels differed significantly between the groups that went to sleep "before 12 p.m." and "after 12 p.m." Similarly, for awakening time, urinary cortisol levels differed significantly between the groups that woke up "before 8 a.m." and "after 8 a.m." In the comparison of the group that felt they slept well and the group that felt they had not slept well, only urinary adrenaline levels differed significantly.

Conclusion: Urinary adrenaline correlated with shortened sleep times and feeling of sleeping well, while urinary cortisol correlated with falling asleep time and awakening time differences.

Keywords: Women; Healthcare; Biomedical; Sleep; Stress

Introduction

Some studies have targeted adult males subjected to stress (such as giving presentations at academic meetings, taking tests, and exercise stress or load) by measuring saliva levels of stress-related substances before and after stress to determine if the markers were of practical significance [1-3]. As yet, little is known about these biomarkers, including their types, localization, and correlation to specific mental conditions, but research is ongoing. Studies on the relationship between biomarkers and chronic stress and mental fatigue have also been performed. A report by Phillips et al. [4] concluded that chronic stress influenced cortisol levels. However, this research is in an early stage since intensive studies of this type have only recently been conducted. Numerous indicators have been examined as stress biomarkers. Stimulation by stressors is first perceived in the cerebral cortex. After it is transmitted, the signal passes along the following two independent channels: cerebral cortex-hypothalamus-sympathetic nerves-adrenal medulla-catecholamine secretion, and cerebral cortex-hypothalamus-pituitary-adrenal cortex-cortisol secretion. Previous studies have identified hormones such as cortisol and catecholamine as stress indicators by measuring their levels. Measurement of stress indictors, however, requires sample collection using stress-free techniques; i.e., minimally physically invasive methods. As a result, some studies have measured saliva levels of stress indicators, including chromogranin [3], SIgA [2,5], cortisol [6,7], and alpha-amylase [8]. Obayash [9] reported that numerous factors such as collection method and conditions could affect saliva findings; the levels of indicators in saliva differ from blood components, where homeostasis is maintained. In other words, measurement errors are liable to occur due to (a) variations in saliva volume, viscosity, and composition according to collection conditions and environment, and (b) large individual differences. In addition, no components (such as creatinine in urine) have been identified that can correct for these variations. Sporadic reports have used sample types other than saliva, including urine [10], breast milk [11], and human hair [12,13]. Measurement of biomarkers in urine samples is useful since (a) the conditions and environments at the time of collection can be relatively easily standardized, and (b) urine has other components that can be used to correct the measurement values, making it less liable to cause data errors.

Studies in various fields have evaluated stress using urinary biomarkers, and a variety of indices has been used as stress indicators. Shimizu [14] described the relationship between urinary catecholamine and cortisol in postpartum women, and Castro et al. [15] reported on the relationship between psychosocial and socio-economic factors and urinary catecholamine and cortisol. Luiza et al. [16] published findings on the relationship between depression in the early stages of pregnancy and urinary cortisol levels. It is clear that urinary biomarkers are useful for measuring the psychological state of individuals. However, although biomarkers are attracting attention as an index to understand psychological state, studies of influence factors other than psychological state are still progressing. Previous studies on confounding factors have reported relationships between serum cortisol and body mass index (BMI) [17], salivary cortisol and sleep

deprivation [18], and mental status that may affect biomarker concentration. In addition, previous studies on the relationship between biomarkers and sleep states included studies evaluating the relationship between sleep deprivation and urinary cortisol levels [19] and the relationship between sleep deprivation and serum cortisol levels [20]. Both studies revealed the relationship with sleeping time. Postpartum women are breastfeeding and child rearing at night, sleeping is interrupted or intermittent, so sleep at night is different from normal. Therefore, we considered that the measurement of biomarkers targeting postpartum females should take full account of the effects of sleep states on biomarkers. Postpartum women often have breastfeeding and child rearing without distinguishing between day and night, and it is often that waking time and bedtime are different. In this research, in order to make full use of postpartum women's research in the future, we will focus on healthy women in their 20s and 30s not only about the relationship with sleeping time which has been clarified so far, but also sleep state, sleeping time, sleeping In consideration of time, subjective sleepiness, etc., the relationship between concentration of urinary biomarkers (adrenaline, noradrenaline, urinary cortisol) and sleep state was examined.

Materials and Method

Subjects

We targeted women living in cities in the suburbs of Tokyo who provided their consent, and enrolled females who were in their 20s to 30s who were not pregnant at the time of the investigation, were not caring for infants (since this may affect nighttime sleep), were not nighttime workers, had no chronic illnesses, and were non-smokers. The sample size was more than 34 cases as a result of expectation in the effect quantity with a two-sided test, detection power of 80%, significance level of 5% expected, so we considered subjects considering the missing person.

Measurement samples and methods

- **Subject characteristics**

We collected information on age, weight, height, and sleep status (hours of sleep during the previous day, waking and sleeping times, and if they felt that they had slept soundly) from subjects who provided consent to participate in the research.

- **Urinary adrenaline, noradrenaline, and cortisol**

Due to daily variation of biochemical indicators, we avoided times of day subject to wide variations, and asked the subjects to collect their urine between 1:00 p.m. and 3:00 p.m., using a sterile paper cup. The urine samples were transferred to a sterile Spitz tube, which was placed in a cooling box maintained at 4°C and immediately transported to an analysis agency.

Procedures

The subjects were recruited using posters. Women who volunteered to take part in the investigation received a full explanation from the researcher, who used documents to describe the need for research as well as the method and what would be required of the participants. A written explanation sheet containing this explanation was handed out to the women, and they were asked to sign an agreement form to confirm their informed consent to take part in the study. The dates and investigation schedule were determined after consulting with the subjects. The investigation took place on a single day, with researchers interviewing the subjects, gathering information, and collecting urine samples from the participants.

Analysis Methods

Measurement of urinary adrenaline, noradrenaline, and cortisol levels specimen analysis was performed by LSI Medience Corporation.

Statistical analysis

SPSS 19.0J was used for statistical analysis. We analyzed the relationship between subject backgrounds (age and BMI), the hours slept, and their urinary adrenaline, noradrenaline and urinary cortisol levels using Spearman's rank correlation coefficient. The subjects were divided into two groups based on the time they woke in the morning ("Before 8:00 a.m." or "After 8:00 a.m."), the time they went to bed ("Before midnight" or "After midnight"), and their sense of having slept soundly ("Yes" or "No"). Differences in urinary adrenaline, noradrenaline, and cortisol levels between each set of groups were compared using the Mann-Whitney-test, with $p>0.05$ regarded as statistically significant.

Results

Subject characteristics

Of 43 women who participated in this study, 40 provided all data and were included in the analysis. Their ages ranged from 20 to 39 years (mean age: 29.5 ± 7.1), with BMI between 17.1 and 24.8 (mean BMI 20.1 ± 1.5). They were not raising infants, had no chronic illnesses, were non-smokers, and did not work during the night. Their hours of sleep the night before ranged from 4-8 hours, with a mean of 6.1 ± 1.1 hours. When asked if they felt they had slept soundly, 31 women said "yes" (77.5%) and nine said "no" (22.5%). About 19 (47.5%) and 21 women (52.5%) had gone to bed the previous night before and after midnight, respectively, ranging from 9 p.m. to 3 a.m. Meanwhile, 24 women (60%) reported waking before 8:00 a.m. that morning and 16 (40%) woke after 8:00 a.m., a time of waking that ranged from 5 a.m. to 11 a.m.

Concentrations of urinary adrenaline, noradrenaline, and urinary cortisol

Table 1 shows concentrations of urinary adrenaline, noradrenaline, and urinary cortisol. The mean adrenaline, noradrenaline, and cortisol concentrations were 16.8 ± 13.5, 152.8 ± 143.3, and 63.7 ± 59.5 μg/mL, respectively.

Variables	Adrenaline	Noradrenaline	cortisol
age	-0.237	-0.161	-0.442
BMI	-0.063	-0.051	-0.22
Spearman's rank correlation coefficient (n=40)			

Table 1: Relation of age, BMI and urinary biomarkers.

Relationship between subject backgrounds and urinary adrenaline, noradrenaline, and urinary cortisol levels

There was no significant correlation between subject age and urinary concentrations of adrenaline and noradrenaline (Table 2), but the concentration of urinary cortisol was negatively correlated with age (r=–0.442, p=0.004). However, there was no relation between BMI and urinary adrenaline, noradrenaline or urinary cortisol levels (Table 2).

Variables	Mean ± SD	Min	Max
Adrenalin (μg/day)	16.8 ± 13.5	4	52.4
Noradrenalin (μg/day)	152.8 ± 143.3	18.4	7900
Cortisol (μg/day)	63.7 ± 59.5	7	297

Table 2: Urinary Biomarkers data (n=40).

Relationship between sleep state and urinary adrenaline, noradrenaline, and urinary cortisol levels

Although no correlation was seen between the hours of sleep the previous day and noradrenaline and cortisol concentrations, the concentration of adrenaline was negatively correlated with hours of sleep (r=–0.445, p=0.005). Moreover, although there were no significant differences between adrenaline and noradrenaline concentration in subjects had gone to bed before or after midnight, there was a significant difference in cortisol concentration between these two groups (p=0.002). Likewise, a significant difference was seen only in adrenalin concentration between the group whose subjects woke up before 7:59 a.m. and the group whose subjects woke after 8:00 a.m. (p=0.003). Comparison of the group that felt they had slept soundly compared to those who did not showed a significant difference only in adrenaline concentration (p=0.025) (Table 3).

Variables	n			
Hours of sleep*	40	-0.445	-0.317	-0.160
The hour of rising				
before 7:59 a.m.	24	0.161	0.143	0.002
after 8:00 a.m.	16			
The hour of sleeping**				
before midnight	19	0.078	0.481	0.003
after midnight	21			
Feeling refreshed after sleep				
Yes	31	0.025	0.198	0.932
No	9			

Table 3: Relation of a sleep state and the urinary biomarkers [*The relation of hours of sleep and biomarker was analyzed in spearman's rank correlation coefficient, and showed the correlation coefficient; **About the relation of the hours of rising the hour of sleeping and feeling refreshed after sleep, and biomarker, it analyzed in Mann-Whitney test, and P value was shown].

Discussion

Subject selection

We compared their urinary data to reference values: their average adrenaline, noradrenaline, and cortisol concentrations were 16.8 ± 13.5 μg/mL (reference value: 3-41 μg/mL), 152.8 ± 143.3 μg/mL (reference value: 31-160 μg/mL), and 63.7 ± 59.5 μg/mL (reference value: 26-187 μg/mL), respectively, indicating that the mean of each biochemical indicator was within the range of the reference values in this study population. Because this study targeted healthy women who are not working at night and no chronic illnesses and are non-smokers, they are healthier than women in their 20s to 30s on average, and they have no problem in their sleeping state women became the subject of this study, We feel that this data is representative of the population only for healthy women.

Relationship between subject backgrounds and catecholamine and cortisol levels

As a result of the negative correlation between age and urinary cortisol levels, it was assumed lower cortisol levels would be associated with increased age. Pal et al. [21] has reported that secretion of adrenaline, noradrenaline, and cortisol increase with age, while the cortisol level decreases. Their findings are similar to our study results. However, urinary adrenaline and noradrenaline levels were not correlated with age, likely because the age range of the subjects in this study was relatively narrow (20-39 years). Moreover, although there is a report showing that BMI is related to biological indicators [17], no such relationship was seen in our study, perhaps because the BMIs of the subjects in our study were between 17.1 and 24.8, within the normal range, and were not related to urinary biomarker concentrations.

Relationship between sleep status and urinary catecholamine and cortisol levels

Researchers have reported that chronic sleep disorders are related to increased secretion of salivary interleukin-6 and noradrenaline [22], and that the sympathetic nervous system activated if the quality of sleep is low, as measured by using the Pittsburgh Sleep Quality Index (PSQI) [23]. In our study, there was a negative correlation between hours of sleep and urinary adrenaline levels, meaning that shorter hours of sleep were associated with increased urinary adrenalin concentration, similar to findings of prior studies. To investigate the relationship with the quality of sleep in our study, we asked the subjects to subjectively describe if they felt they had slept soundly by answering, “Yes” or “No”.

Subjects who reported sleeping soundly had higher adrenaline levels than those who had not, similar to findings reported by Huang, who suggested that sympathetic nerves are activated when sleep quality is low. In addition, although urinary cortisol levels were not correlated to sleep duration or quality, it was related to the time of waking up in the morning and going to bed at night. Therefore, even with sufficient hours of good quality sleep, irregular or disrupted times of waking and going to sleep were influenced by cortisol concentrations. This observation is believed to be due to changes in circadian rhythm. Another report found that that cortisol concentrations increase for 2 hours after waking and remain relatively constant thereafter. Urinary samples were collected from 1 p.m. to 3 p.m. in our study, more than 2 hours after participants reported waking in the morning. We therefore

believe that daily variations in cortisol levels attributable to differences in waking time had no effect on cortisol concentrations in this study.

However, unlike previous studies that claim that sleep disorders affect the sympathetic nerves, noradrenaline concentration in our study was unrelated to differences in hours of sleep, time of waking, and time of going to bed, or the sense of having slept soundly. The reasons for this may have been that the total hours of sleep ranged 4-8 hours among participants in this study, the subjects did not include those with extreme sleep disorders, and that there were relatively few differences in the sleep status among all subjects. Our study found that hours and subjective quality of sleep influenced adrenaline concentrations, and disruptions in sleep schedules influenced the cortisol concentrations. However, these findings must be validated in future studies with subjects with a broader range of states of sleep.

Ethical Procedures

Before starting this study, we submitted a study plan to the Medical Ethics Board of the Faculty of Medicine at the University of Tsukuba and obtained their approval (Approval No.: 666-2). We feel that, except for the minor inconvenience attributable to the time restrictions, the procedure caused little or no physical invasions to the subjects.

Study Limitations and Challenges

The subjects in this study showed little or no differences in their sleep status, and had a narrow range of characteristics such as age and BMI; a limitation in our study of the relationship between biomarkers and sleep status. There is a need, therefore, for additional studies with subjects who show a broader range of sleep status.

Conclusion

Urinary adrenaline correlated with shortened sleep times and feeling of sleeping well, while urinary cortisol correlated with falling asleep time and awakening time differences.

Acknowledgement

This work was supported by JSPS KAKENHI Grant Number 15K11655.

References

1. Nakane H, Asami O, Yamada Y (1998) Salivary chromogranin A as an index of psychosomatic stress response. Biol Res 19: 401-406.
2. Lowe G, Urquhart J, Greenman J (2000) Academic stress and secretory immunoglobulin A. Psychol Res 87: 721-722.
3. Reshma AP, Arunachalam R, Pillai JK, Kurra SB, Varkey VK, et al. (2013) Chromogranin A: Novel biomarker between periodontal disease and psychosocial stress. J Indian Soc Periodontol 17: 214-218.
4. Phillips AC, Carroll D, Evans P, Bosch JA, Clow A, et al. (2006) Stressful life events are associated with low secretion rates of immunoglobulin A in saliva in the middle aged and elderly. Brain Behav Immun 20: 191-197.
5. Satoshi T, Kanehisa M (1999) Secretory IgA in saliva can be a useful stress marker. Environ Health Prev Med 4: 1-8.
6. Eck M, Berkhof H, Nicolson N, Sulon J (1996) The effects of perceived stress, traits, mood states, and stressful daily events on salivary cortisol. Psychosom Med 58: 447-458.
7. Wolff S, Peter S, Juliane H, Arthur AS, Dirk HH (2006) Trait anxiety moderates the impact of performance pressure on salivary cortisol in everyday life. Psychoneuroendocrinology 31: 459-472.
8. Nater UM, Rohleder N, Gaab J, Berger S, Jud A, et al. (2005) Human salivary alpha-amylase reactivity in a psychosocial stress paradigm. Int J Psychophysiol 55: 333-342.
9. Obayashi K (2013) Salivary mental stress proteins. Clin Chim Acta 21: 196-201.
10. Fabregas M, Servio L, Castro J, Malmagro M, Antonio J, et al. (2013) Chronic stress and calcium oxalate stone disease: Influence on blood cortisol and urine composition. Urology 82: 1246-1252.
11. Maureen G, Mitzi D, Kathryn S (2004) Associations between human milk SIgA and maternal immune, infections, endocrine, and stress variables. J Hum Lact 20: 153-158.
12. Wosu AC, Valdimarsdottir U, Shields AE, Williams DR, Williams MA (2013) Correlates of cortisol in human hair: Implications for epidemiologic studies on health effects of chronic stress. Ann Epidemiol 23: 797-811.
13. Lee DY, Kim E, Choi MH (2015) Technical and clinical aspects of cortisol as a biochemical marker of chronic stress. BMB Rep 48: 209-216.
14. Shimizu Y (2003) Psychological stress that mothers experience due to childcare and coping styles: Relationship with urinary stress hormones. Maternal Health 44: 372-373.
15. Diehl C, Roux AV, Seeman T, Shea S, Shrager S,et al. (2014) Associations of socioeconomic and psychosocial factors with urinary measures of cortisol and catecholamines in the Multi-Ethnic Study of Atherosclerosis (MESA) Psychoneuroendocrinology 41: 132-141.
16. Luiza JW, Gallaher MJ, Powers RW (2015) Urinary cortisol and depression in early pregnancy: Role of adiposity and race. BMC Pregnancy Childbirth 15: 466.
17. Odeniyi IA, Fasanmade OA, Ogbera AO, Ohwovoriole AE (2015) Body mass index and its effect on serum cortisol level. Niger J Clin Pract 18: 194-197.
18. Klumpers UM, Veltman DJ, Tol MJ, Kloet RW, Boellaard R (2015) Neurophysiological effects of sleep deprivation in healthy adults, a pilot study. PLoS One 21: 10.
19. Bouhuys AL, Flentge F, Hoofdakker RH (1990) Effects of total sleep deprivation on urinary cortisol, self-rated arousal and mood in depressed patients. Psychiatry Res 34: 149-162.
20. Leproult R, Copinschi G, Buxton O, Cauter E (1997) Sleep loss results in an elevation of cortisol levels the next evening. Sleep 20: 865-870.
21. Pal R, Singh SN, Chatterjee A, Saha M (2014) Age-related changes in cardiovascular system, autonomic functions, and levels of BDNF of healthy active males: Role of yogic practice. Age 36: 9683.
22. Faraut B, Nakib S, Drogou C, Elbaz M, Sauvet F, et al. (2015) Napping reverses the salivary interleukin-6 and urinary norepinephrine changes induced by sleep restriction. J Clin Endocrinol Metab 100: E416-E426.
23. Huang Y, Mai W, Hu Y, Wu Y, Song Y, et al. (2011) Poor sleep quality, stress status, and sympathetic nervous system activation in nondipping hypertension. Blood Press Monit 16: 117-123.