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Original Article

Correlation of Plasma Melatonin Concentration and Alertness Level Among Female Nurses in Jakarta Indonesia

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ABSTRACT

Background Working in shifts, especially night shifts could alter alertness levels, increase fatigue, and working accidents. One of the factors that affect the circadian rhythm were melatonin. Melatonin was a hormone that regulates the wake and sleep cycle that have an impact on alertness levels. This study aimed to find the correlation between plasma melatonin and alertness level.
Methods A cross-sectional study was conducted on 40 female night shift nurses. Individual characteristics were obtained by a self-administered questionnaire. Plasma melatonin concentrations and alertness level was collected twice at night time (11 pm – 00 am) and in the morning (7 am − 8 am). The correlation test was used to find the correlation between melatonin concentrations and Psychomotor Vigilance Test (PVT).
Results Mean age was 28.4 (±4.9) years with working experience varied from 1-16 years. Plasma melatonin concentrations among female night shift nurses were higher before working hours than after duty. The range of plasma melatonin value was 10-240 pg/ml and Alertness was in the same manner with the average alertness level at night being 301.2 ± 51.6 ms and 293.2± 49.7 ms in the morning. There was a weak correlation between plasma melatonin concentration and alertness level difference before and after duty ($r = 0.37$; $p = 0.016$).
Conclusion There was a weak correlation between plasma melatonin and alertness level in night shift workers before and after duty. To Maintain alertness level reduction and melatonin secretion, night shift workers should rest at least 30 minutes during their working hours, always keep the lights on while on duty, and should not work more than one shift on the same day, and provide healthy foods.

INTRODUCTION

Working in a shift is a common working pattern. This pattern could develop negative effects on the workers, especially on night shifts. Their health and safety could be affected because they had to fight their own biological rhythm or circadian rhythm.[1] Nurse who works in the hospital, including in Cipto Mangunkusumo National Hospital had a working shift pattern, especially in some units such as the intensive care unit, emergency room, operating theatre, cardiac center, perinatology ward, and general ward.

Night shift will disrupt the natural circadian rhythm so people will develop symptoms such as fatigue, health disorder, sleep disorder (sleepiness), decreasing level of alertness, cognitive impairment, and increasing human error. Data showed that the decreasing level of alertness and fatigue on the night shift are the main factors contributing to work accidents.[2] Lack of sleep could increase the risk of work accidents. Many studies stated that working in night shift could increase the rate of work accidents by 50-100%. Moreover, workers that sleep less than six hours will increase working accidents than workers that sleep seven to eight hours per day.[3] In the health aspect, sleep deprivation could increase human error. A study stated that there was 2 − 3 times increase in errors to give medication to nurses who work more than 12.5 hours. The same thing happened to post-graduate medical residents who work more than or work five shifts more than 24 hours per month. A study in America recorded needlestick injury in nurses is 31% and increase to 61% for workers who work overtime.[3] In the health aspect, the prevalence of working accidents at night time is still high. In Indonesia, a study done in Kendari Regional Public Hospital recorded needlestick injury was 42.2%.[4] This finding will affect the safety of the workers or patients. It happened because of circadian rhythm disharmony inside the body, and it was also affected by melatonin. Melatonin secretion is regulated by the endogen clock located in suprachiasmatic nuclei (SCN) in the hypothalamus and dimmer light. From the literature, an artificial light source around 2000 − 2500 lux given for two hours will suppress melatonin secretion at all.[5]

Melatonin is a hormone secreted by the pineal gland. Melatonin production is influenced by the retina, gut, skin, bone marrow, and other organs. The pineal gland has proven as an active neuroendocrine transducer in animals, especially in photoperiodic species. The main function of melatonin is to regulate circadian rhythm. Melatonin also regulates body temperature, produces cortisol hormone, and affects alertness level.[5] Alertness level will decrease with the increasing awake time on the first night shift or when people force themselves to sleep outside their circadian rhythm.[6] In one of the studies, the worst alertness level was at 04.00 − 06.00 comparable to the melatonin peak level.[7] Besides the melatonin hormone, alertness level is also related to fatigue.[8]

In the previous studies, there were inconclusive results between melatonin and alertness level. Chellapa SL. et al found moderate correlation (r=-0.51; p=0.040) between saliva melatonin and alertness level.[9] Another study by Ganesan S, et al found a weak correlation (r=0.38; p=0.001) between urine melatonin and alertness level.[10] These findings could be caused by low levels of melatonin in saliva and urine that could be detected. This study was done in a hospital where medical care was provided for 24 hours. The sample of this study was female nurses who work in shifts, especially the second night shifts. The female has slower motoric responses than the male.[11] It is important because the prevalence of work accidents usually rises at night time, so we wanted to study the relationship between melatonin plasma level with alertness level assessed with Psychomotor Vigilance Test (PVT).

METHODS

Research Design

This study was a cross-sectional study conducted in Cipto Mangunkusumo National Hospital, Jakarta, from December 2019 until January 2020.

Research Subjects

Based on the calculation of the minimum sample size formula using a single sample correlation coefficient plus 10% additional in case of a blood specimen cannot be analyzed, 39 respondents were obtained. 40 respondents were eligible for this study. The study population was female nurses in Cipto Mangunkusumo National Hospital who were on duty in the General and Executive Ward, Perinatology Ward, Intensive Care Unit, Emergency Unit, and Cardiac Centre. Inclusion criteria were female nurses between 20 − 40 years old, nurses who work the second night shift, and have one-year working experience. Exclusion criteria in this study were caffeine consumption six hours before the test, pre-menopause or menopause, and taking antidepressant or antihistamine medication.

Data Collection

Total sampling (all of the nurses who were agree to participate in the study, meet the inclusion criteria, and did not fit in the exclusion criteria) was applied in this study. Alertness level was determined using Psychomotor Vigilance Test (PVT).[12,13] Plasma melatonin was drawn from a venous blood sample. Blood sampling was done twice, at night time at 23.00-24.00 and in morning time at 07.00-08.00. Samples were stored at -20ºC and transported to DKI Jakarta Province Laboratory.[14]

Information about age was obtained based on the ID card, and body weight and height were measured by calibrated weight and height scale to calculate the body mass index, working experience as a nurse, working time break, and marital status data were obtained using a self-administered questionnaire and interview.

Instruments

Psychomotor Vigilance Test is a tool developed by The Biotechnology High-Performance Computing Software Applications Institute (BHSAI) to determine simple alertness levels and it was validated by Basner.[13] In this study, we used psychomotor vigilance task application in a notebook for 3 minutes, with deviation around 355 ms and 1 − 4 seconds interstimulus. Respondents were asked to prepare, then they were given time to do the trial test by pressing the mouse button when the counter number on the screen appear.[12,13] After the trial session, any results were recorded as the data. Plasma melatonin values were obtained after the blood sample was analyzed with Liquid Chromatography Mass Spectrometry (LC-MS).[14]

Data Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences program, version [20]. Univariate analysis showed participant characteristics. Age, body mass index, alertness level, and plasma melatonin data showed in mean and standard deviation (SD) if they distributed normally. If they didn't, then the data showed in median and interquartile. Bivariate analysis was used to find the relationship between plasma melatonin and alertness level at night time before and after working hours. If the data was distributed normally, the Pearson test would be used. However, the Spearman test would be done if the data didn't distribute normally.

Ethical Clearance

Ethical Clearance was obtained from the Research Ethics Committee of the Faculty of Medicine Universitas Indonesia Research with the approval letter No. KET-867/UN2.F1/ETIK/PPM.00.02/ 2019.

RESULTS

In this study, 40 subjects were obtained. Data in this study showed mean age of participants was 28.4, with working experience varied from 1 to 16 years. The higher proportion of the subjects were nurses from the general ward (37.5%), executive general ward (17.5%), and perinatology ward (15%) respectively. Detailed information on the basic characteristics of the subjects can be seen in Table 1.

Melatonin and Alertness Level in Workers

Morning and night plasma melatonin were varied. Morning melatonin ranged from 10-190 pg/ml and night melatonin was 10-240 pg/ml. Alertness level measured by PVT was also varied in the morning and night time. Morning response times were 225-426 ms with a median value of 279 ms and night-time alertness levels ranged from 224-460 ms with a median value of 288.5 ms.

The study showed that there was a weak correlation (r=0.37; p=0.016) between plasma melatonin and alertness level before and after working hours as shown in Table 2. Data showed with standard deviation if they distributed normally, or with median (minimum-maximum) if they didn't distribute normally.

There were four respondents stationed at Emergency Operation Room, Perinatology Ward, General Ward, and Executive Ward who experience melatonin secretion alteration in the morning-time. However, there was one respondent with night time low melatonin concentration (10 pg/ml), but in the morning rose to 190 pg/ml even though she barely slept.

There were also three respondents with alertness levels between 361 ms to 460 ms in the night-time and 370 ms to 426 ms in the morning time. Two of the three participants had low levels of plasma melatonin 10 and 20 pg/ml which rose in the morning to 40 and 60 pg/ml with alertness levels of 431 ms and 361 ms at night time, and 426 ms and 370 ms in the morning respectively.

Table 1. Distribution of demographic characteristics of the nurses (n=40)

Characteristics	Description	Frequency n (%)
Age, year*	28.4 (±4.9)	
Working experience, year**	5 (1−16)	
Body Mass Index (BMI), kg/m^2*	22.8 (±3.8)	
Working time break, hour**	2 (0−4)	
Marriage Status		
Unmarried		19 (47.5)
Married		21 (52.5)
Working Unit		
Executive ICU		5 (12.5)
Emergency Room (ER)		2 (5)
Executive ER		2 (5)
Operation Theatre		1 (2.5)
Cardiac Unit		2 (5)
Perinatology		6 (15)
General Ward		15 (37.5)
Executive General Ward		7 (17.5)

*= Mean (± Standard Deviation)
**= Median (Minimum-Maximum)

Table 2. Plasma melatonin and alertness level before and after working hours comparison

Variable	Night Time (23.00 – 24.00)	Morning Time (07.00 – 08.00)	Mean difference (CI 95%)	p Value
Melatonin*	50 (10−240)	10 (10−190)		0.003^w
Alertness Level**	301.2 (±51.6)	293.2 (±49.7)	8.00 (0.69−15.13)	0.033^t

w = Wilcoxon
t = Paired t-Test
*= picogram/milliliter (pg/ml); median (minimal-maximum)
**= millisecond (ms); mean (±SD)

Correlation of Melatonin, Alertness Level with Age, Working Experience, Body Mass Index

In Table 3, we described the correlation of plasma melatonin and alertness level with various factors. We found there was no correlation between night time, morning time plasma melatonin with age, body mass index, and working experience. However, there was a moderate correlation between night-time alertness level with age (r = 0.57; p < 0.001) and night-time alertness level with working experience (r = 0.55; p < 0.001), and morning-time alertness level with age (r = 0.50; p = 0.001). There was a weak correlation between morning time alertness level with working experience (r = 0.45; p = 0.004), but there was no correlation between alertness level with age (r = -0.19; p =0.219), body mass index (r = -0.02; p = 0.893), and working experience (r = -0.16; p = 0.305).

Table 3. The correlation of plasma melatonin and alertness level with age, body mass index, and working experience

Variable	Age	Body Mass Index	Working Experience
Night time melatonin	r = -0.09 (p=0.560)^s	r = 0.22 (p=0.180)^s	r = -0.14 (p=0.360)^s
Morning time melatonin	r = -0.04 (p=0.790)^s	r = -0.04 (p=0.780)^s	r = -0.15 (p=0.340)^s
Melatonin Difference*	r = 0.02 (p=0.890)^s	r = -0.20 (p=0.170)^s	r = 0.03 (p=0.830)^s
Night-time alertness level	r = 0.57 (p<0.001)^p	r = 0.29 (p=0.070)^p	r = 0.54 (p<0.001)^s
Morning time alertness level	r = 0.50 (p=0.001)^p	r = 0.29 (p=0.650)^p	r = 0.44 (p=0.004)^s
Alertness level difference*	r = -0.19 (p=0.219)^p	r = -0.02 (p=0.893)^p	r = -0.16 (p=0.305)^s

*= Morning time – night time difference
p = Pearson test
s = Spearman test

Correlation of Plasma Melatonin, Alertness Level, and break during working hours

From the normality test, plasma melatonin variable data did not distribute normally, so the correlation between alertness level and plasma melatonin concentration was tested using the nonparametric test, i.e., the Spearman test. There was no correlation between night-time alertness level and plasma melatonin concentration before work (r = 0.07; p = 0.640). No correlation was also found between morning time alertness level after work melatonin concentration (r = 0,17; p = 0.270). As shown in Table 4, there was a weak correlation between the pre-post-shift plasma melatonin concentrations and pre-post-shift alertness levels (r = 0.37; p = 0.016).

Table 4. Melatonin and alertness level correlation

Variable	Night time alertness level	Morning time alertness level	Alertness level differentiation*	Resting time
Night time melatonin	r = 0.07 (p = 0.640)			r = -0.08 (p=0.630)
Morning time melatonin		r = 0.17 (p = 0.270)		r = 0.10 (p=0.530)
Melatonin difference*			r = 0.37 (p = 0.016)	r = 0.09 (p=0.570)
Night time alertness level				r = -0.01 (p=0.923)
Morning time alertness level				r = -0.06 (p=0.701)
Alertness Level difference*				r = 0.05 (p=0.754)

Night-time: 23.00 – 24.00
Morning-time: 07.00 – 08.00
Resting time: unsure between 01.00 – 04.00
*= Morning – Night time difference

DISCUSSION

This study shows that melatonin and alertness levels cannot be correlated with just one time. At least two measurements are required by taking into account other factors that can influence and the impacts that may be caused.

There were acute and chronic effects of working in shifts, such as effects on cardiac health, metabolism, mental health, and cancer.[1] Muzio MD, et al compared "Morning-Afternoon-Night- Off-Off" with "Afternoon-Morning-Night-Off-Off" in nurses working in the hospital, and found nurses worked in "Morning-Afternoon-Night" shifts were better in alertness level, fatigue, and sleepiness. This happens as circadian rhythm adaptation is easier and resembles a physiologic rhythm.[16] Yu San Chang, et al proved that two nights rotation schedule had lower performance than four nights rotation schedule. This difference could explain why circadian rhythm adaptation runs slower.[2] A study by Boivin DB, stated that there were 2−3 times medication errors in nurses who worked more than 12.5 hours.[3]

Plasma melatonin measurement found the mean level of night melatonin before work was 57.7 pg/ml and the mean level of morning melatonin after work was 29.5 pg/ml. From statistical analysis, there was a significant reduction of plasma melatonin concentration at night time to morning time after working hours. This finding was similar to a study done by Benloucif S, et al.[16] which stated that melatonin secretion was more active at 24.00 than at 08.00. This means peak melatonin secretion in most workers happen during night-time and is not disturbed by shifting schedule. In this study, some working units turn off or reduced the light in the night-time when we drew the blood for the sample. From the correlation study between melatonin in the night-time or morning time, we did not find any correlation with age, body mass index, and resting time in the night. This could happen because our population samples were quite similar, between 20−40 years old, and which literature stated that melatonin secretion is stable until 40 years old.[17]

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Alertness level measurement by Psychomotor Vigilance Test at night-time before working hours found mean reaction time was 301.2 and in the morning after work was 293.2. We found there was a statistically significant difference in reaction time 0.60-15.13 ms, with a mean value of 8 ms ($p < 0.050$). Our finding was not in line with a study by Kazemi R, et al at control room workers in the biggest petrochemical company in Iran,[2] that found reaction time at 24.00 was better than what could happen because participants in the company still get two until four hours of rest depend on their workloads. Centers for Disease Control and Prevention (CDC) recommendation stated that 30 minutes rest for 8 hours working time could improve alertness level, and 2-3 hours rest for 12−16 working hours the night.[18]

Our study found there was a weak correlation between melatonin and alertness level at night time or in the morning time, this finding was not in line with our hypothesis first, however, we found a weak correlation between melatonin difference and alertness level difference. These proved that melatonin measurement should not be done just once, Migut−BR and Paprocka J recommended serial melatonin sampling would give a better understanding of melatonin secretion. Their study found a weak correlation in melatonin concentration difference.[19]

We also found four respondents with plasma melatonin lower at night time (10−50 pg/ml) and rose in the morning (40−190 pg/ml). They had two hours of night's rest. This could happen because there is a delay in melatonin secretion caused by light exposure. R. Robert Auger, et al in their study also found workers exposed to light all night will have a decrease in melatonin secretion and the peak melatonin secretion will shift to morning time.[17] Another factor that could cause melatonin secretion shifting is dawn time sleeping habit because there is circadian rhythm alteration and melatonin will be secreted late. Minors and Waterhouse, and Moore-Ede et al. stated that circadian rhythm adaptation in workers working in shifts usually will run slower.[20]

Of those four respondents, one nurse worked in Emergency Operating Room, she usually didn't have enough sleep time due to her activity. Melatonin secretion increased in this nurse happened because of working duty which force her to stay awake and she was usually exposed to high-intensity light in the operating theatre. We did not measure light intensity in the operation table at Cipto Mangunkusomo Hospital, but by the Minister of Health's decision in 2004 about the Healthy Hospital Environment Requirement, light intensity in the operating theatre is about 300−500 lux and at the operation table is about 10,000−20,000 lux.[21] Study done by Clustrat B, found that exposure to 2000−2500 lux could depress melatonin secretion completely.[5] Another study by Gooley et al also proved that person exposed to light with intensity <200 lux at night time for at least 90 minutes could reduce melatonin secretion.[22] The increase in plasma melatonin was not followed by an increase in alertness level. From the sample, we found 300 ms at night time and 274 ms in the morning. This could happen because some factors, such as an increase in melatonin secretion is not significant to decrease alertness level, activity, or working duty which made the nurses still awake before sampling.

There were also three respondents with alertness levels over the cut-off point (355 ms). Those three were stationed in the perinatology unit, general ward, and executive ward. One of the factors affecting alertness level is age. Thomann J, et al in the study also found increasing age and working experience will slower alertness levels because cells in the brain and nerve conduction system will age and become atrophy naturally.[23]

Another factor that influences alertness level is body mass index, but in this study, we did not find any correlation between alertness level in the night and morning with body mass index. This is in line with a study by Galioto R, et al which compared the alertness level of obesity and normal weight population. They found population with obesity had worse alertness levels compared to the normal or overweight population.[24]

Many factors are affecting plasma melatonin, such as daily activity, diet, workload, environmental factors, and regular sleep schedule in the morning after the night shift. Based on the above discussion, we consider the possibility that the night shift nurses should rest at least 30 minutes during their working hours, always keep the lights on while on duty, and should not work more than one shift on the same day. These occupational measures together with nutritional interventions such as providing them with healthy foods may be beneficial for reducing melatonin secretion and increasing alertness levels. However, more research should be done in order to determine various factors associated with alertness level reduction and melatonin secretion during shift work.

The limitation of our study was, we did not have any detailed respondent activity throughout the day. We also did not know their sleep history before shift not only in the day, but also in the afternoon, and we also did not know their nutrition status. Respondent activity and sleep history could affect their activeness on the night shift, where nurses could stay awake and be more active, so plasma melatonin would be lower. Nutrition also played a role in plasma melatonin. Different nutrition intake resulted in plasma melatonin production. There was only a little literature about melatonin measurement using the LCMS method so our analysis of melatonin was minimal, especially LCMS normal range, and sampling time was not done at the same time, but we minimized the deviation of sampling time.

CONCLUSION

Working in shifts could disrupt the circadian rhythm regulated by the melatonin hormone. From our study, we concluded that plasma melatonin in night shift workers was higher before working hours than after duty, this means that there was a decreased level of alertness found mainly during night shift. Alertness levels were in the same manner, it was higher before working hours than after duty. And there was a weak correlation between plasma melatonin and alertness level in night shift workers before and after duty. Some workplace measures together with nutritional interventions may be beneficial for reducing melatonin secretion and increasing alertness levels.

DECLARATION

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