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Research article

LIGHT EXPOSURE AT NIGHT AND ROTATING NIGHT SHIFT ASSOCIATED WITH CIRCADIAN DISRUPTION OF 6-SULFATOXY MELATONIN

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ABSTRACT

Background: Alterations in the sleep-wake cycle leads to decreased melatonin secretion and it may be associated with sleep disorders and cancer risk. Exposure of light at night and rotating night shift decrease the melatonin production due to acute suppression of pineal melatonin secretion during night work has been suggested to increases cancer risks. **Aims & Objectives**: The objectives of the present study were to investigate the effect of light exposure at night on circadian pattern of 6-Sulfatoxy melatonin levels in night shift nursing professionals. **Material and Methods**: 62 healthy nursing professionals of both genders performing day and night shifts (continuous 9 days night shift with alternate day shifts) were recruited. Urine samples were collected at around 8 hour intervals (afternoon sample: between 13:00 to 15:00, night samples between 22:00 to 01:00 and morning samples between 05:00 to 08:00) while they were performing night duties and repeated when they were assigned day duties. Night melatonin level was decreased as compared to morning melatonin. **Results**: Night melatonin level was found declined as compared to morning level and this pattern was significant when compared night melatonin between night (16.71 ± 11.98) vs day shift (22.71 ± 13.25) and morning melatonin level between night (20.07 ± 14.13) vs day shifts (28.26 ± 14.14) ($p<0.001$). **Conclusion**: Light exposure at night disrupts the circadian rhythm of melatonin secretion during night shift leads to internal desynchronization.

Key words: Rotating night shift; Light at Night; Circadian rhythm; 6-Sulfatoxy melatonin.

INTRODUCTION

Rotating night shift disrupts the circadian rhythms and has been associated with fatigue, stress and sleep disturbances. Alterations in the sleep pattern leads to decreased melatonin which might be associated with sleep disorders, anxiety, depression, and stress and cancer risk. Those who work in night shift may attempt to sleep when their body clock is adjusted for the awakening phase.[1] This attempt disturbs the body clock resulting in a contradictory relationship between sleep time and circadian schedule. It is possible that the circadian sleep propensity rhythm and hormonal rhythm are under influence of circadian pacemaker as well as sleep habit.[2] Majority of the circadian rhythms in our body have both an endogenous component regulated by an internal clock, viz. the suprachiasmatic nuclei (SCN), and it synchronized with an exogenous component composed of a light-dark cycle.[3,4]

Melatonin is a hormone (N-acetyl 5 methoxy-tryptamine) synthesized and secreted principally by the pineal gland at night under normal environmental conditions. The pineal gland decides whether or not to secrete melatonin and the amount of melatonin secretion based on information directly sent from the retina of the eye. The Retina of the eye contains a unique subset of cells other than rods and cones, this unique subset of cells produce a pigment called melanopsin. Melanopsin allows a cell to detect light and dark. Information collected by the unique subset of cells is sent along the retinohypothalamic tract (RHT), a sort of information highway that extend from the retina to the hypothalamus. In hypothalamus, this information is transmitted to a cell called the suprachiasmatic nuclei (SCN). The SCN of the hypothalamus have melatonin receptors and melatonin may have a direct action on SCN to influence “circadian rhythm”.[5]

Melatonin secretion is enhanced in darkness and decreased by light exposure. Exposure to artificial light at night and disruption of the endogenous circadian rhythm with suppression of the melatonin synthesis has been suggested mechanisms.[6] Melatonin gives a measure of day length, it can reset the clock by acting as chemical zeitgeber. Melatonin is metabolized to 6-hydroxy-mel in the liver and the main metabolite excreted in urine is 6-Sulphatoxy-melatonin are more stable than 6-hydroxy melatonin in serum. The concentration of 6-Sulfatoxy melatonin or 6- hydroxyl melatonin sulphate in urine correlates with the total level of melatonin in the blood during the collection period. Melatonin levels in individuals with normal sleeping patterns begin to increase during the evening (~ 9:00 p.m.). Melatonin levels peak at around 2:00 a.m. and return to baseline around sunrise (~ 6:00 a.m.).[7] Irregular sleeping patterns can lead to circadian disruption and shift the amplitude and timing of peak melatonin levels. The hypothalamic-pituitary adrenal axis (HPA), has been identified as a potential mechanism of neuroendocrine system that influenced by night shift work through which circadian desynchrony may lead to stress and ill-health.[8] The present study was planned to investigate the effect on light exposure at night and rotating night on circadian pattern of 6-sulfatoxy melatonin in night shift nursing professionals.

MATERIAL & METHODS

The study was approved by the institutional ethic committee (Ref. code: XXXIV ECM/B-P3), a detailed proforma was explained to all volunteers; written informed consent was obtained from all the subjects. The study volunteers willing to participate in the study were recruited from Trauma Centre, GM and Associated Hospitals, KGMU, Lucknow, UP, India. Sixty two healthy night shift nursing professionals, aged 20-40 year, performing rotating night shift duties (continuous 9 days night shift with alternate day shifts) from past 5-6 years, the duration and pattern of shift work were same among all the subjects. **Inclusion criteria**: Subjects were working in continuous 9 days light at night exposure in each month. We recruited nurses of both genders, age between 20-40 yrs from different wards and units viz. Intensive care unit (ICU), surgical emergency, Neurosurgery, Neurotrauma, Orthopaedics emergency and Medicine emergency, who worked in rotating night shift.

Exclusion criteria: Subjects with any acute/chronic illness, known patients of diabetes mellitus, other endocrinal disorders, hypertension, coronary artery disease, subjects taking oral contraceptive pills and chronic renal diseases were excluded from this study.

Study design: The present prospective observational study was planned to investigate the effect of light exposure at night and rotating night shift on circadian pattern of 6-sulfatoxy melatonin in night shift nursing professionals and whether they are reversible in due course of time.

Collection of Urine samples: Urine samples were collected at around 8 hours interval in their night shift and day shift schedules (afternoon sample: between 13:00 to 15:00, night samples between 22:00 to 01:00 and morning samples between 05:00 to 08:00). The volunteers themselves collected the samples in different colour vials. For collection of urine samples, a notebook was provided to each subject with all details regarding the timing and procedure for sampling and their sleep-awake timing. Samples were analyzed for 6-Sulfatoxy Melatonin by the ELISA method.

RESULTS

There were total 62 (32 male and 30 females) night shift nursing professionals recruited in the present study. The effect of light at night exposure on rotating night shift was investigated by analyzing urinary 6-sulfatoxy melatonin levels. All the data were summarized as Mean± SD & baseline characteristics of male and female night shift workers are given in Table 1. Groups were compared by applying paired t test. A two tailed (α=2), $p<0.05$ was considered significant, $p<0.01$ moderate/very significant and $p<0.001$ highly significant. P value elucidate that if it is < 0.05, < 0.01, < 0.001 then the null hypothesis would be rejected at 5 %, 1 % or 0.1 % respectively. Statistical analysis was carried out by using INSTAT 3.0 (Graph pad prism software; San Diego, CA). Association of variable between different shifts was done by Pearson correlation analysis.

Table 1: Baseline characteristics of night shift workers.

Baseline Characteristics	**Night Shift Workers (*n* = 62)**
Age (years)	24.74 ± 3.81
Weight (kg)	53.21 ± 8.85
Height (cm)	160.44 ± 8.16
Body mass index (BMI)	20.59 ± 2.40
Marital Status	
Married	16 (25.80%)
Unmarried	46 (74.19%)
Diet	
Vegetarian	23 (37.10%)
Non-Vegetarian	39 (62.90%)

Data are presented as means ± SD.

Table 2: Correlation of Urinary Melatonin between Nights versus Day shift

Measured Variables	**Night Shift (NS) versus Day Shift (DS)**	**(n=62)**
6-Sulfatoxy Melatonin	Afternoon Melatonin: NS vs DS	$r = 0.13^{ns}$
	Night Melatonin: NS vs DS	r =0.51***
	Morning Melatonin:NS vs DS	$r = 0.18^{ns}$

ns= Non significant, ***p<0.001 highly significant

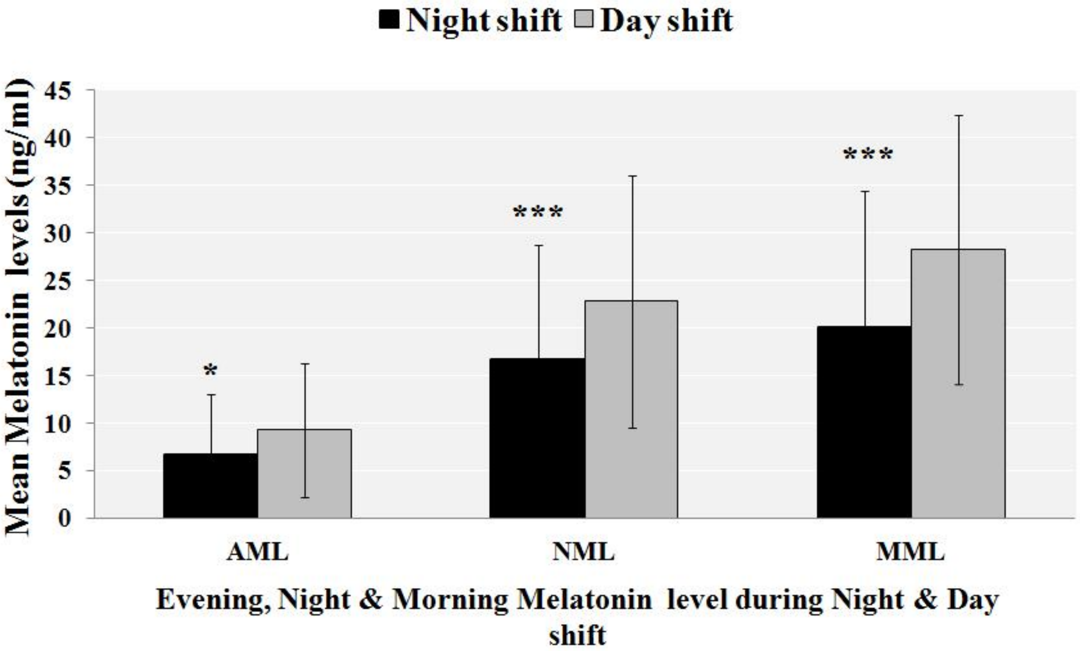

Fig 1: Mean Afternoon, Night and Morning melatonin during night and day shift
(AML: Afternoon Melatonin level; NML: Night Melatonin level; MML: Morning Melatonin level), (*p<0.05, ***p<0.001; By paired t test; I- Bar of the standard deviation).

Melatonin hormone also shows diurnal variation, its level increases from midnight to early morning and decreases in the late morning and in day hours. This pattern was found altered in rotating night shift workers during night shift. Melatonin synthesis directly depends upon transport of signal of light in the day time and conversion of serotonin into melatonin depends upon signals of darkness received at night. However, its level may differ from individual to individual. Normal range of melatonin is 0.8-40 ng/ml, its levels increases at midnight and declines in day time. Night 6-sulfatoxymelatonin level was found declined as compared to morning level and this pattern was significant when compared night 6-sulfatoxymelatonin between night (16.71 ± 11.98) vs day shift (22.71 ± 13.25) and morning melatonin level between night (20.07 ± 14.13) vs day shifts (28.26 ± 14.14) (p<0.001) (Figure 1). 6-sulfatoxy melatonin level of evening and morning time during night shift was positively associated with that of during day shift. Since the pattern of melatonin secretion was altered in early morning time during night shift hence this positive association did not reach at significant level (p>0.05);(Table 2). 6-sulfatoxy melatonin level of night time during night shift was positively associated with that of during day shift and this association was highly significant (p<0.0005). The result show that light exposure at night effect on melatonin production during night shift. Altered 6-sulfatoxymelatonin levels were found at night and in the morning samples during night shift.

DISCUSSION

Previous studies have reported that subjects exposed to light and who remain awake at night have lower levels of melatonin at night , as melatonin synthesis always occurs at night, particularly in the darkness. On the basis of the finding of the previous studies, it has been hypothesized that exposure of light at night (LAN) is one of potential mechanisms of breast carcinogenesis in the night shift workers through decreased melatonin synthesis.[6] Findings of the recent study indicates that two nights of rotating shift work may not change the timing of melatonin production to the day among those working at night.[9] While the results of the present and other studies indicate that working six to eight or more night shifts per month may disrupt the synthesis of melatonin.[6] Finding of our study in agreement with previous study indicate that night shift workers have substantially lower level of 6-sulfatoxymelatonin at night work and daytime sleep during night shift, and levels remain low when night shift workers sleep at night during day shift. Long term chronic reduction in melatonin among night shift workers may be an important carcinogenic mechanism, which could affect the cancer risk.[10,11] Other studies have also reported higher incidence of poorer sleep and its complications in night shift workers.[12-14] These findings reinforce previous studies which reported elevated exposure to cortisol on early shifts, relative to 'normal' later working days and rest days, might promote pathogenic processes including insulin resistance.[15] and help to elucidate the increased risks of cardiovascular diseases in rotating night shift workers.[16] In other study, the related neurotransmitters like Urinary nor- epinephrine and Epinephrine were higher during work than non-work in the day, but in evening shift and night shift workers, the difference was lesser and in opposite direction. Working evening or night shift are independent predictors of Non –dipper status.[17] During night shift the hormones are more sensitive to endogenous components like catecholamine, prolactin, and growth hormones which showed an immune response to the shifted sleep/activity cycle, evidencing a "masking effect" due to the work activity. In another study, hormones having stronger endogenous components, such as cortisol and Melatonin, showed a more stable pattern, with a slight tendency for partial adjustment of cortisol during the second night.[18] The onset of sleep was consistently followed by a decrease in concentration of cortisol. While both sleep-wake and light-dark transitions were consistently associated with cortisol secretary pulses.[19] It is also reported that the sleep factor (time of onset and/or period) seemed to be more potent in modifying the circadian rhythm of serum cortisol, especially with the night shift.[20] Sleep was initiated (on average) about three hours prior to the onset of melatonin production in night shift workers while in day-active subjects initiated sleep (on average) about three hours after their melatonin onset. Thus, the sleep times availed for night shift workers may not be well-synchronized to their melatonin secretion rhythm, assumed to mark the phase of their underlying circadian pacemaker.[21]

The change in the Acrophase of 6-sulfatoxy-melatonin was associated with different shifts.[22] The overall advance of Melatonin profile was primarily achieved during the initial exposure to an 8h period of darkness. The present data suggested that exposure to dark affects human circadian phase.[23] In the present study, subjects with rotating shifts of 12 hrs night works had complained of difficulty in sleep, decreased calculative tasks, impaired cognitive functions, decreased alertness, constipation, stress and mental fatigue which is in accordance with the other studies.[24, 25] Quality and quantity of sleep are also affected by rotating night shift. Duration of sleep was shorter during day time at night shift (3-4 hours less as compare to night time sleep during day shift). Night shift nurses have experience changes in aMT6s levels after six to eight nights in a month and the findings might be related to the increased cancer risk reported in night-shift workers and suggest that a short nap during night-shifts may exert a positive effect to night shift workers.[26] The long term higher intensity of light exposure during night work may have decreased total melatonin production, possibly by initiating re-entrainment and leads to internal desynchronization that could be the mediator between night shiftwork and cancer risks.[27] In brief, it is possible that rotating night shift appears to have adverse effects on body's physiological rhythm leads to hormone related disorders and cancer risk.

CONCLUSION

In present study, we concluded that rotating night shift disrupt the circadian pattern of melatonin particularly at night and in the morning time during night shift due to desynchronization. However, recovery was found when subjects went back to the day shift. Prolonged exposure of light at night leads to decreased melatonin level may be one factor contributing to an increased risk of cancer and other endocrinal disorders in rotating night shift workers.

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Conflicts of interest: The authors declare that there is no conflict of interest.

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