A Cross-Sectional Study Examining the Correlation between Nocturnal Melatonin Level and Sleep Quality in Patients Admitted To the Cardiac Care Unit

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Abstract

BACKGROUND: Quality of sleep, as a basic need, is an important factor for surviving patients in hospitals. Many factors may contribute to disturbing patients sleep, such as continuous ambient light, is required for healthcare providers to monitor patients. Ambient light can influence patients' quality of sleep due to melatonin secretion.

AIM: Study aimed to determine the correlation between nocturnal melatonin levels and sleep quality in patients admitted to the Cardiac Care Units (CCU).

MATERIAL AND METHODS: This cross-sectional study was done on inpatients of CCUs at Amir-Almomenin Hospital in Kordkoy city, a cardiac referral hospital in the northeastern of Iran in 2015. Sixty-eight inpatients were selected through convenience sampling. Before data gathering light level of CCUs was measured every one hour in 2 days, the quality of nocturnal sleep was investigated through Verran and Snyder-Halpern (VSH) Sleep Scale at the second night of admission urinary melatonin level was measured at the same night in all urine excreted between 22:00 pm and 07:00 am.

RESULTS: The mean and standard deviation (SD) score of sleep quality in three dimensions of sleep disturbance, sleep effectiveness and sleep supplementation were 336.6 ± 149.9, 269.0 ± 82.2, and 175.2 ± 30.7, respectively. Also, the mean and SD of nocturnal urinary melatonin levels was 323.02 ± 136.21 pg/ml. There was not a significant correlation between level of nocturnal melatonin and three domains of sleep quality; sleep disturbance (r = 0.005, P = 0.968), sleep effectiveness (r = 0.090, P = 0.464), and sleep supplementation (r = -0.037, P = 0.763).

CONCLUSION: According to the result, most CCUs patients suffer from sleep disturbance. However, there was no correlation between the level of melatonin and sleep quality. There is a need for recognising the reasons for sleep disturbances in Cardiac Care Units. It is imperative for care providers to be able to recognise the causes of sleep disturbances and to modify environmental factors such as ambient light to improve sleep quality in hospitalised patients.

Introduction

Coronary Artery Disease (CAD) is the most common type of cardiovascular disease which frequently causes hospital readmission [1]. It is a major cause of death and disability in developed countries [2]. Cardiovascular diseases cause nearly one-third of all deaths worldwide [3]. According to the Centers for Disease Control and Prevention (CDC), more than 370,000 people die from CAD each year in the United States. CAD has an impact on 110 million people and as a consequence 8.9 million deaths globally [4]. It is estimated that CAD will be the most common cause of deaths up to 2020 [5]. The incidence of Cardiovascular diseases is increasing in the developing country. According to the Ministry of

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Health and Medical Education report, the number of CAD is increasing in Iran which is affected 15 million people and accounts for approximately 46% of deaths in patients over 35 years old. It is the first leading cause of mortality [2], [6], [7]. In some situation, patients required to be admitted in Cardiac Care Units (CCUs) to prevent complication which leads to improving quality of life. When patients stay in the hospital, some patient-related factors; such as pain, anxiety, and primary illness and environment factors; such as continuous ambient light exposure, equipment noise, alarm, and beepers may cause sleep disruption. Also, physician intervention and nursing care; including checking vital signs, diagnostic testing and other procedures, are the leading cause of disturbed sleep pattern of patients [5], [8], [9]. Although the research findings indicate that quality of sleep is a basic human need and one of the important factors for surviving patients, evidence shows that they suffer from sleep disturbance [10] [11]. More than fifty percent of hospitalized patients experience sleep disturbance during the early days of admission [12]. Sleep disturbances may increase epinephrine and norepinephrine secretion and considering that heart rate, respiratory rate, blood pressure and myocardial oxygen demand will be increased. As a result, heart ischemic would be expanded independently [13], therefore, sleep disruptions is associated with the symptoms of the cardiovascular disease and rate of mortality [14].

Research findings indicate that multiple factors may contribute to disturbing the sleep of patients in the hospital, and continuous ambient light is significant contributors to sleep disruption [11], [14], [15], [16]. Given the fact that continuous ambient light is required for health care providers to monitor patients, light can influence on patients' quality of sleep and circadian rhythm due to nocturnal secretion of melatonin [14], [15], [17].

Melatonin (N-Acetyl-5-methoxytryptamine) secretion as crucial biomarker follows a stable circadian rhythm in healthy individuals [15]. Research findings indicate that light-induced neural and endocrine signals that regulate behavioural and physiological circadian rhythms associated with melatonin secretion of patients in intensive care units, which is often accompanied by sleep disturbance [18]. Thereby, light can disturb circadian rhythm and suppress melatonin release, in consequence, sleep deprivation will be occurred and hinder the progress of patients' treatment and recovery. As a result, it can make more problems which increase the cost of health care services [19].

Serum concentrations of melatonin vary from 80 to 120 pg/ml. About 80 per cent of the melatonin is produced at night. The lowest level of melatonin is 10-20 pg/ml in daylight hours [14]. In healthy individuals, melatonin as a pivotal biomarker acts by a stable circadian rhythm. Findings of the study demonstrate that light-induced–melatonin secretion of patients in

critical care units associated with sleep problems [17], [18]. Thereby, light can disturb circadian rhythm and suppress melatonin release, in consequence, sleep deprivation will be occurred and hinder the progress of patients' treatment and recovery. As a result, it can increase the cost of health care services [19]. Research finds, which assessed the pattern of melatonin secretion and its relation with sleep impairment in different groups of patients, has been discussed. Also, there is a controversy about the correlation between severity of disease and the amount of melatonin secretion [16], [17], [19].

By determining the affecting factors on melatonin secretion such as continuous light, the health care providers can do suitable interventions to improve patients' quality of sleep. This study was done to determine the correlation between nocturnal melatonin levels and sleep quality in patients admitted to the CCUs.

Methods

This cross-sectional study was conducted at CCUs of Amiralmomenin Hospital, a cardiac referral hospital in the northeastern of Iran, in 2015. Sixty-eight eligible patients with CAD were selected via convenience sampling which was admitted to the CCU, a day before the study. Inclusion criteria were age more than 18 years old, ability to complete the sleep assessment questionnaires, the absence of psychiatric disorders or illness that led to sleep loss or disruption during the last two months and non-attendance to work in a night shift with daytime sleeping.

For data gathering first, 2 days, a day of weekday and a day of the weekend, was chosen randomly. Then light levels were measured every hour of 2 days. Light levels were recorded in 25 patient's bedsides one meter high (next to the head of patients) and 2 nursing stations, using lux-meter TES-1339 made in Taiwan.

The consenting patients were given written informed consent. They were assured about the confidentiality of private information and they're volunteers for participation. Potential participants were asked fulfilling the questionnaire to capture information pertaining to patient demographics, pre-admission sleep pattern and sleep quality. On the second night of hospitalization in CCU, patients completed a checklist to record pre-admission sleep characteristics, and Verran and Snyder-Halpern (VSH) Sleep Scale. The level of nocturnal urinary melatonin (MT) was measured for the same night. Pre-admission sleep characteristics were assessed through a checklist which was developed to monitor sleep pattern and factors affecting sleep, and to

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identify the causes of sleep disturbance in patients prior to hospitalization [20]. The VSH sleep scale was developed in order to assess the subjective sleep quality of hospitalized individuals – those without preexisting sleep difficulties. The 15-item VSH scale evaluates three main sleep domains; disturbance (including sleep latency and fragmentation), effectiveness (including sleep quality and length), and supplementation which are scored 0-700, 0-500, and 0-400 respectively. The validity and reliability of the Persian version of VSH sleep scale was evaluated by Mashayekhi [21]. To measure nocturnal urinary melatonin, urine was collected through the indwelling urine catheter for a total period of 9 hours starting at 22 in the night (from 10 p.m to 7 a.m in next day). Samples of 5 mL of urine were obtained from urine portion and transferring to a laboratory for analyzing. 6-hydroxymelatonin, as a metabolite of melatonin (N-Acetyl-5-methoxytryptamine), was excreted in urine. It was determined from urine samples by Enzyme-Linked Immunosorbent Assay (ELISA) using EASTBIOPHARM ELISA kit made in USA [22].

Data were analysed using Statistical Package for the Social Sciences (SPSS; version 16). Descriptive statistics were used to describe patients' demographic and to analyse the frequencies of pre-admission sleep characteristics. Normality of scores was assessed by Shapiro-Wilk and distribution was not normal; therefore, data were analysed using Kruskal Wallis test. Spearman correlation coefficients were calculated to assess the correlation between melatonin level and Quality of sleep. Significant level was considered 0.05.

Results

The findings showed that the majority of the patients were male (51.5%); the mean age was 56.2 ± 8.5 years (range from 25 to 65 years). Most of the patients had a diagnosis of Acute Coronary Syndrome (66.2%) and had a history of hospitalisation in Cardiac Care Units (51.5%). Fifty per cent of the patients were illiterate, and only 5.9% of them graduated from university, and 23.5% of them reported that they had no comorbid disease. An overview of the demographic characteristics of patients is given in Table 1.

Table 1: Socio-demographic characteristics of the patients (n = 68)

Variables		N	%
Gender	Male	35	51.5
	Female	33	48.5
History of hospitalisation	Yes	35	51.5
	No	33	48.5
Patients' diagnosis	ACS*	52	76.5
	UA**	16	23.5
History of comorbidity	Yes	52	76.5
	No	16	23.5

* Acute coronary syndrome; ** Unstable angina

The mean of light levels in a day of weekday and weekend was 244.4 and 261 Lux, respectively and in a night of weekday and weekend were 104.1 and 130 Lux, respectively (Table 2).

Table 2: The mean of light levels in a weekday and weekend in CCUs

Time of evaluation	Light Level (Lux)	
	Night	Day
Weekend	104.1	244.4
Weekday	130	261
Standard	100	300

The results revealed 45.6% of patients had well-ordered sleep pattern before admission. Majority of them reported that light and noise effect on their sleep during the night, only 1.5 per cent of patients reported that light and noise never impact on their nocturnal sleep and 86.8% of them were awakening for going to the toilet more than once in a night. Only 2.9% of patients pointed out that they woke up to take the drug. Most patients (94.1%) had less than 2 hours of daily sleep (Table 3).

Table 3: Frequency distributions of the patients' sleep pattern and sleep affecting factors

Items		N	%
Sleep pattern	Well ordered	31	45.6
	Partly disordered	18	26.5
	Disorderly	19	27.9
The effect of light on sleep	Never	1	1.5
	Rarely	14	20.6
	Sometime	34	50
	Always	19	27.9
The impact of noise on nocturnal sleep	Never	1	1.5
	Rarely	17	25
	Sometime	31	45.6
	Always	19	27.9
Waking up to take the drug	Never	52	76.5
	Rarely	14	20.6
	Mostly	2	2.9
To take a nap during the day	Never	13	19.1
	Once in a day	50	73.5
	Twice or more in a day	5	7.4
Duration of daily sleep	2 hours or less	64	94.1
	More than 2 hours	4	5.9
Awakening for going to the toilet	Never	9	13.2
	Once in a night	31	45.6
	Twice or more in a night	28	41.2

According to finding, the mean score of sleep disturbance was 336.6 ± 149.9; sleep effectiveness was 269.0 ± 82.2, sleep supplementation was 175.2 ± 30.7, and mean nocturnal urinary melatonin levels was 323.02 ± 136.21 pg/ml (Table 4).

Table 4: The means of patients' melatonin level and scores of sleep quality (n = 68)

Domains of sleep quality scale	Mean	Standard deviation
Sleep disturbance	336.6	149.9
Fragmentation	244.4	108.5
Latency	92.2	43.4
Sleep effectiveness	269.4	82.2
Quality	13.3	62.4
Length	13.7	27.2
Sleep supplementation	175.2	30.7
Melatonin level (pg/ml)	323.02	136.21

Results of the correlation between nocturnal melatonin level and sleep measurements showed there was not a significant correlation between the level of nocturnal melatonin and three domains of sleep quality(P > 0.464) (Table 5).

Table 5: The correlation of sleep quality domains with nocturnal melatonin levels (n = 68)

	Supplementation Sleep	Sleep Effectiveness	Sleep Disturbance
R	0.005	0.090	-0.037
P-value	0.968	0.464	0.763

Discussion

The low mean score of sleep in domains of sleep disturbance, supplementary sleep and sleep efficiency indicates the low quality of sleep in the patients. Findings of several studies have shown that inpatients do not have sufficient sleep quantity and quality. According to the finding study that carried out by Redekeret et al., during the first five post-operative days after open heart surgery, although no significant change was observed in the duration of sleep, the quality of sleep reduced due to repeated sleep interruptions during the first three days [23]. Research finding on patients with heart disease showed that 51% of the patients had difficulty falling asleep, 44% had trouble sleeping, 40% had difficulty in the last phases of sleep, and 39% were waking up too early [24]. The findings are consistent with the results of several studies conducted on the quality of sleep in ICU patients over the past three decades [25], [26]. Study of Mashayekhi et al. on CCU patients demonstrated the short nighttime sleep-duration of the patients and the poor quality of sleep regarding efficiency and disturbance [27]. In intervention studies on the quality of sleep in ICU patients, the subject had poor sleep quality before the intervention, and controlling some environmental factors could improve the quality of sleep in the patients [2], [15], [28]. Findings of the sleep pattern showed that 27.9% of the patients had sleep problems before hospitalisation, and the majority of them reported noises, light and having to go to the bathroom as the main causes of sleep problem. A review study showed that noise, pain, discomfort, the severity of disease, nursing and medical interventions, and medications are the factors disrupting the sleep pattern of patients [11]. Parker reported that sleep problems are more prevalent in heart failure patients than in those without the disease, and factors such as respiratory problems, age, medications, anxiety and depression play a significant role in this regard [29].

In this study, the majority of patients pointed out that noise and light influenced their sleep. Freeman investigated the effect of environmental factors on sleep disorders in patients undergoing ventilation in ICUs. Findings of 24- and 48-hour polysomnography indicated that sleep-wake cycles of patients were disrupted, and the maximum amount of sleep was between 6:00 and 22:00, which is normally awake time [30]. This could be attributed to environmental factors such as continuous night light.

The findings of this study showed that the light intensity in ICUs was less than the standard limit during the daytime and higher than the standard limit at nighttime. Consistent with these findings, the study of Golmohammadi reported that the average intensity of artificial, general and local illumination during daytime was less than the recommended limit in hospitals of Hamadan [31]. Hu measured the light intensity in an ICU every hour for 24 hours under laboratory conditions. Although the average nightlight was 100 lux (near the standard), the light intensity varied from 5 to 2238 lux at different times of the day [15], [32]. Some studies have demonstrated the positive effect of increased light exposure on ICU patients, while other studies did not find a relationship between exposure to light and clinical outcomes in patients [33]. According to some studies, using eye masks overnight for prevention of overexposure to light improves the quality of sleep in patients [15], [26], [34]. Given that the standard light level is 300 lux during the day and 100 lux during the night, these contradictory results may be because none of these studies has considered the difference in the level of light during day and night.

Melatonin is secreted earlier at night when people are exposed to light in the morning. Low light levels throughout the day can delay the secretion of melatonin at night, while exposure to bright light in the evening can inhibit production of melatonin at night [35]. Therefore, the amount of light in ICUs can affect the secretion of melatonin in patients. In this study, the mean level of melatonin at night was 323.22 pg/ml during the second night of admission. However, there was no statistically significant relationship between melatonin level and patients' quality of sleep. Most interventional studies have investigated the effects of light exposure on patients' quality of sleep and melatonin, the relationship between melatonin levels and quality of sleep was not evaluated, while the amount of light is associated with melatonin level, circadian rhythm and sleep patterns. Melatonin affects the tendency to fall asleep and the duration and quality of sleep [35]. According to the findings of Bourne et al. consumption of melatonin increased the sleep time of patients admitted to the ICUs by one hour during nighttime [28]. Kakooei et al. monitored the level of melatonin in nurses for 24 hours (every three hours). They reported that the minimum and maximum 24-hour melatonin levels were 14.91 pg/ml at 4 a.m and 139.41 pg/ml at 4 p.m. In nurses with constant day shift, these values were 1.02 and 177.40 pg/ml, respectively. This indicates the association between melatonin and nighttime sleep [36]. Study of Shamir et al. measured the urinary melatonin levels in 19 patients with schizophrenia every 3 hours. Their findings indicated that the level of urinary melatonin was lower in patients with sleep problems [37], which is inconsistent with the findings of the present study. This difference between the results could be because the mentioned study measured melatonin levels at different times of a day, while we measured the mean

level of melatonin at nighttime. Patients in the CCU have disease-related problems such as pain, respiratory problems and side effects of drugs that can disrupt their sleep pattern. Also, the subjects in the mentioned study were over 50 years of age and often had sleep problems [38].

The limitation of this study was using a questionnaire to measure the quality of sleep since we were unable to use the standard objective method of polysomnography for measuring the quantity and quality of sleep due to the difficulty for use on CCU patients. Also, since half of the subjects in the study were illiterate, they might have completed the questionnaire inaccurately. It is recommended to use both subjective and objective methods in future studies.

According to the result, most CCUs patients suffer from sleep disturbance. However, there was no correlation between the level of melatonin and sleep quality. There is a need for recognising the reasons for sleep disturbances in Cardiac Care Units. It is imperative for health care providers to be able to recognize the causes of sleep disturbances and to modify environmental factors such as ambient light to improve sleep quality in hospitalised patients.

Acknowledgements

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