***Open Access Maced J Med Sci*** **electronic publication ahead of print,**
**published on December 17, 2018 as https://doi.org/10.3889/oamjms.2018.451**

ID Design Press, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences.
https://doi.org/10.3889/oamjms.2018.451
eISSN: 1857-9655
***Clinical Science***

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

Mohammad Zaman Kamkar[1], Sommayeh Rezvani Khorshidi[2], Seideh Mahrokh Alinaghi Maddah[3], Amir Emami Zeydi[4], Mahnaz Modanloo[5*]

*[1]Department of Psychiatry, Golestan Research Center of Psychiatry, Golestan University of Medical Sciences, Gorgan, Iran; [2]Department of Medical-Surgical Nursing, Faculty of Nursing and Midwifery, Golestan University of Medical Sciences, Gorgan, Iran; [3]Department of Anesthesiology, Faculty of Medicine, Golestan University of Medical Sciences, Gorgan, Iran; [4]Department of Medical-Surgical Nursing, Nasibeh School of Nursing and Midwifery, Mazandaran University of Medical Sciences, Sari, Iran; [5]Nursing Research Center, Golestan University of Medical Sciences, Gorgan, Iran*

**Citation:** Kamkar MZ, Rezvani Khorshidi S, Alinaghi Maddah SM, Emami Zeydi A, Modanloo M. A Cross-Sectional Study Examining the Correlation between Nocturnal Melatonin Level and Sleep Quality in Patients Admitted To the Cardiac Care Unit. Open Access Maced J Med Sci. https://doi.org/10.3889/oamjms.2018.451

**Keywords:** Sleep Quality; Melatonin; Light; Cardiac Care Unit

***Correspondence:** Mahnaz Modanloo. Nursing Research Center, Golestan University of Medical Sciences, Gorgan, Iran. E-mail: modanloo.mahnaz@goums.ac.ir

**Received:** 28-Sep-2018; **Revised:** 09-Nov-2018; **Accepted:** 10-Nov-2018; **Online first:** 17-Dec-2018



**Funding:** This research did not receive any financial support

**Competing Interests:** The authors have declared that no competing interests exist

**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 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 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

This article was extracted from an MSc thesis of Critical Care Nursing in Golestan University of Medical Sciences. The study has been approved by the Ethics Committee of the Deputy of Research at Golestan University of Medical Sciences, Iran (project no. 394592122510). The authors wish to thank all patients for their kind cooperation. We extend special thanks to the nursing staff of Amiralmomenin Hospital for their efforts in data collection.

## References

1. Modanloo M, Sharifi H. Do depressed elderly heart failure patients benefit from yoga? A future direction for research. J Cardiovasc Nurs. 2018; 33(5):420-1. https://doi.org/10.1097/JCN.0000000000000512 PMid:30095754

2. Moeini M, Khadibi M, Bekhradi R, Mahmoudian SA, Nazari F. Effect of aromatherapy on the quality of sleep in ischemic heart disease patients hospitalized in intensive care units of heart hospitals of the Isfahan University of Medical Sciences. Iran J Nurs Midwifery Res. 2010; 15(4):234-9. PMid:22049287 PMCid:PMC3203283

3. Wong ND. Epidemiological studies of CHD and the evolution of preventive cardiology. Nat Rev Cardiol. 2014; 11(5):276-89. https://doi.org/10.1038/nrcardio.2014.26 PMid:24663092

4. Moran AE, Forouzanfar MH, Roth G, Mensah GA, Ezzati M, Flaxman A, et al. The global burden of ischemic heart disease in 1990 and 2010: the Global Burden of Disease 2010 study. Circulation. 2014; 129(14):1493-501. https://doi.org/10.1161/CIRCULATIONAHA.113.004046 PMid:24573351 PMCid:PMC4181601

5. Bansilal S, Castellano JM, Fuster V. Global burden of CVD: focus on secondary prevention of cardiovascular disease. International journal of cardiology. 2015; 201:S1-7. https://doi.org/10.1016/S0167-5273(15)31026-3

6. Sadeghi M, Haghdoost AA, Bahrampour A, Dehghani M. Modeling the burden of cardiovascular diseases in Iran from 2005 to 2025: The impact of demographic changes. Iran J Public Health. 2017; 46(4):506-516. PMid:28540267 PMCid:PMC5439040

7. Mirkarimi A, Khoddam H, Vakili MA, Sadeghi MB, Modanloo M. Effect of life style modification on adherence to diet and hypertension in hypertensive patients. Koomesh. 2018; 20(2):192-202.

8. Li SY, Wang TJ, Vivienne Wu SF, Liang SY, Tung HH. Efficacy of controlling night-time noise and activities to improve patients' sleep quality in a surgical intensive care unit. J Clin Nurs. 2011; 20(3-4):396-407. https://doi.org/10.1111/j.1365-2702.2010.03507.x PMid:21219521

9. Patel M, Chipman J, Carlin BW, Shade D. Sleep in the intensive care unit setting. Crit Care Nurs Q. 2008; 31(4):309-18. https://doi.org/10.1097/01.CNQ.0000336816.89300.41 PMid:18815477

10. Emami Zeydi A, Jannati Y, Darvishi Khezri H, Gholipour Baradari A, Espahbodi F, Lesani M, et al. Sleep quality and its correlation with serum C-reactive protein level in hemodialysis patients. Saudi J Kidney Dis Transpl. 2014; 25(4):750-5. https://doi.org/10.4103/1319-2442.134962 PMid:24969183

11. Tembo AC, Parker V. Factors that impact on sleep in intensive care patients. Intensive Crit Care Nurs. 2009; 25(6):314-22. https://doi.org/10.1016/j.iccn.2009.07.002 PMid:19880319

12. Daneshmandi M, Neiseh F, SadeghiShermeh M, Ebadi A. Effect of eye mask on sleep quality in patients with acute coronary syndrome. J Caring Sci. 2012; 1(3):135-43. PMid:25276688 PMCid:PMC4161075

13. Fontana CJ, Pittiglio LI. Sleep deprivation among critical care patients. Crit Care Nurs Q. 2010; 33(1):75-81. https://doi.org/10.1097/CNQ.0b013e3181c8e030 PMid:20019513

14. Tordjman S, Chokron S, Delorme R, Charrier A, Bellissant E, Jaafari N, et al. Melatonin: Pharmacology, Functions and Therapeutic Benefits. Curr Neuropharmacol. 2017; 15(3):434-43. https://doi.org/10.2174/1570159X14666161228122115 PMid:28503116 PMCid:PMC5405617

15. Hu RF, Jiang XY, Zeng YM, Chen XY, Zhang YH. Effects of earplugs and eye masks on nocturnal sleep, melatonin and cortisol in a simulated intensive care unit environment. Crit Care. 2010; 14(2):R66. https://doi.org/10.1186/cc8965 PMid:20398302 PMCid:PMC2887188

16. Tamburri LM, DiBrienza R, Zozula R, Redeker NS. Nocturnal care interactions with patients in critical care units. Am J Crit Care. 2004; 13(2):102-12. PMid:15043238

17. Scheer FA, Van Montfrans GA, van Someren EJ, Mairuhu G, Buijs RM. Daily nighttime melatonin reduces blood pressure in male patients with essential hypertension. Hypertension. 2004; 43(2):192-7. https://doi.org/10.1161/01.HYP.0000113293.15186.3b PMid:14732734

18. Challet E. Minireview: Entrainment of the suprachiasmatic clockwork in diurnal and nocturnal mammals. Endocrinology. 2007; 148(12):5648-55. https://doi.org/10.1210/en.2007-0804 PMid:17901231

19. Meyer TJ, Eveloff SE, Bauer MS, Schwartz WA, Hill NS, Millman RP. Adverse Environmental Conditions in the Respiratory and Medical ICU Settings. Chest. 1994; 105(4):1211-6. https://doi.org/10.1378/chest.105.4.1211 PMid:8162751

20. Reza H, Kian N, Pouresmail Z, Masood K, Sadat Seyed Bagher M, Cheraghi MA. The effect of acupressure on quality of

sleep in Iranian elderly nursing home residents. Complement Ther Clin Pract. 2010; 16(2):81-5. https://doi.org/10.1016/j.ctcp.2009.07.003 PMid:20347838

21. Mashayekhi F, Mirzai Saifabad R, Baghery P. Validity and Reliability of the Verran and Snyder-Halpern Sleep Scale in Iranian population. J Mazandaran Univ Med Sci. 2016; 25(132):200-9.

22. Mundigler G, Delle-Karth G, Koreny M, Zehetgruber M, Steindl-Munda P, Marktl W, et al. Impaired circadian rhythm of melatonin secretion in sedated critically ill patients with severe sepsis. Crit Care Med. 2002; 30(3):536-40. https://doi.org/10.1097/00003246-200203000-00007 PMid:11990911

23. Redeker NS, Hedges C. Sleep during hospitalization and recovery after cardiac surgery. J Cardiovasc Nurs. 2002; 17(1):56-68. https://doi.org/10.1097/00005082-200210000-00006

24. Erickson VS, Westlake CA, Dracup KA, Woo MA, Hage A. Sleep disturbance symptoms in patients with heart failure. AACN Clin Issues. 2003; 14(4):477-87. https://doi.org/10.1097/00044067-200311000-00009 PMid:14595207

25. Stanchina ML, Abu-Hijleh M, Chaudhry BK, Carlisle CC, Millman RP. The influence of white noise on sleep in subjects exposed to ICU noise. Sleep Med. 2005; 6(5):423-8. https://doi.org/10.1016/j.sleep.2004.12.004 PMid:16139772

26. Weinhouse GL, Schwab RJ. Sleep in the critically ill patient. Sleep. 2006; 29(5):707-16. https://doi.org/10.1093/sleep/29.5.707

27. Mashayekhi F, Arab M, Pilevarzadeh M, Amiri M, Rafiei H. The effect of eye mask on sleep quality in patients of coronary care unit. Sleep Sci. 2013; 6(3):108-11.

28. Bourne RS, Mills GH, Minelli C. Melatonin therapy to improve nocturnal sleep in critically ill patients: encouraging results from a small randomised controlled trial. Crit Care. 2008; 12(2):R52. https://doi.org/10.1186/cc6871 PMid:18423009 PMCid:PMC2447606

29. Parker KP, Dunbar SB. Sleep and heart failure. J Cardiovasc Nurs. 2002; 17(1):30-41. https://doi.org/10.1097/00005082-200210000-00004

30. Freedman NS, Gazendam J, Levan L, Pack AI, Schwab RJ. Abnormal sleep/wake cycles and the effect of environmental noise on sleep disruption in the intensive care unit. Am J Respir Crit Care Med. 2001; 163(2):451-7. https://doi.org/10.1164/ajrccm.163.2.9912128 PMid:11179121

31. Golmohamadi R, Shafiee Motlagh M, Jamshidi Rastani M, Salimi N, Valizadeh Z. Assessment of Interior and Area Artificial Lighting in Hospitals of Hamadan City. Journal of Occupational Hygiene Engineering (JOHE). 2014; 1(1):47-56.

32. Hu RF, Hegadoren KM, Wang XY, Jiang XY. An investigation of light and sound levels on intensive care units in China. Aust Crit Care 2016; 29(2):62-7. https://doi.org/10.1016/j.aucc.2015.08.001 PMid:26307553

33. Gershengorn HB. Shedding light on light in the intensive care Unit. J Crit Care. 2013; 28(1):101-2. https://doi.org/10.1016/j.jcrc.2012.07.009 PMid:22999482

34. Richardson A, Allsop M, Coghill E, Turnock C. Earplugs and eye masks: do they improve critical care patients' sleep? Nurs Crit Care. 2007; 12(6):278-86. https://doi.org/10.1111/j.1478-5153.2007.00243.x PMid:17983362

35. Farud D, TAhavorgar A. Melatonin Hormone, Metabolism and its Clinical Effects: A Review. Iranian Journal of Endocrinology and Metabolism. 2013; 15(2):211-23.

36. Kakooei H, Zamanian Ardakani Z, Karimian S, Ayattollahi S. Twenty Four-hour circadian melatonin profile among women shift work nurses. Journal of Zanjan University of Medical Sciences. 2009; 17(68):75-84.

37. Shamir E, Laudon M, Barak Y, Anis Y, Rotenberg V, Elizur A, et al. Melatonin improves sleep quality of patients with chronic schizophrenia. J Clin Psychiatry. 2000; 61(5):373-7. https://doi.org/10.4088/JCP.v61n0509 PMid:10847313

38. Chisholm EJ, Kuchai R, McPartlin D. An objective evaluation of the waterproofing qualities, ease of insertion and comfort of commonly available earplugs. Clin Otolaryngol Allied Sci. 2004; 29(2):128-32. https://doi.org/10.1111/j.1365-2273.2004.00795.x PMid:15113295