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Original Article

Comparison of objective and subjective sleep time and quality in hospitalized recipients of hematopoietic stem cell transplantation

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A R T I C L E I N F O

Keywords:
Sleep time
Sleep efficiency
Hematopoietic stem cell transplantation
Insomnia
Actigraphy

A B S T R A C T

Objective: In this study, the sleep time and efficiency of recipients of hematopoietic stem cell transplantation (HSCT) were investigated throughout treatment and compared objective measurements with subjective self-reported data.

Methods: Sleep time and efficiency were measured using both objective and subjective methods throughout the treatment period in inpatients receiving HSCT. The participants were recruited among HSCT inpatients at a tertiary hospital in Seoul, South Korea, between August 2019 and August 2020. Actigraphy was used to measure objective sleep time and efficiency. Subjective sleep time and quality were measured using the sleep diary and Insomnia Severity Index. Measurement data from 40 patients were analyzed. Repeated-measures analysis of variance was used to compare the differences between objective and subjective values in total sleep time and sleep efficiency.

Results: The total sleep time was the lowest during the administration of anticancer drugs before stem cell transplantation. The total sleep time of patients with HSCT differed significantly over time when offsetting the difference in the measurement method. There were no significant differences between subjective and objective results for sleep time, and the interaction between the two methods over time was not significant. However, meaningful differences were found among the groups in sleep efficiency throughout the treatment period and between objective and subjective methods, as well as a statistically significant interaction between the two methods over time.

Conclusions: Actigraphy misclassified patients' low-energy state with little movement due to immune system impairment during treatment as sleep, resulting in high measured sleep efficiency, whereas their self-reported sleep efficiency was very low. Therefore, subjective measures might be more accurate for measuring sleep efficiency in HSCT patients.

Introduction

Sleep is a natural biological and physiological phenomenon, and adequate sleep is critical for maintaining good health and well-being. Sleep disorders may lead to undermined physical and mental functioning, chronic pain, respiratory failure, obesity, stress, and anxiety.[1] Hospitalized patients require longer periods of high-quality sleep to promote faster recovery. However, the quality of sleep is often overlooked in the inpatient environment, where treatment and care are prioritized over quality sleep.[2] A majority of patients with cancer experience sleep disorders to varying degrees throughout the treatment process. Patients with cancer who receive anti-cancer treatment experience particularly severe sleep disorders during treatment; these disorders are also exacerbated as their treatment is prolonged.[3]

Hematopoietic stem cell transplantation (HSCT) can be divided into two ways: autologous and allogenic. Auto transplantation is the transplanting of one's hematopoietic stem cells, which have been collected in advance, and allogenic transplantation is the transplanting of another's. Patients who receive HSCT are hospitalized for 3–4 weeks on average and often experience emotional distress, such as frustration, anxiety, and isolation, as a result of being separated from their families for isolation treatment during hospitalization.[4] The intense anti-cancer treatment, total radiation therapy, and side effects of HSCT are factors that contribute to disrupted sleep during hospitalization.[5,6] Upon being

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admitted to the hospital, patients with HSCT receive high-dosage of chemotherapy and a large amount of intravenous (IV) fluids during a roughly 1-week pre-transplantation conditioning period, and often experience side effects such as infection, gastrointestinal disorders, and pain during the immunosuppressed period, leading to sleep disorders.[5] Treatment-related sleep disturbance factors such frequent visits with medical staff, and frequent use of toilets due to large amounts of fluid injection interfere with the sleep of transplant patients.[5] Previous studies on patients with HSCT reported that 70%–80% of patients experienced sleep disruption and disorders during hospitalization and that 26% of patients were clinically diagnosed with insomnia.[7,8] Sleep disorders in patients with HSCT can reduce their quality of life, cause tumor-related fatigue and a weakened immune system, diminish their cognitive function, exacerbate depression and anxiety, and in the worst cases may negatively affect the transplantation outcomes due to an increased inflammatory response.[6,9,10]

Various objective and subjective measurement tools have been developed to evaluate sleep disorders. On one hand, subjective self-reporting tools have traditionally been used to measure sleep disorders. On the other hand, objective physiological methods such as actigraphy have been recommended to identify sleep disorders and understand the various characteristics of sleep.[11] It would be ideal to use both subjective and objective measures to complement each other because patients' self-reporting may not be sufficient to understand the overall sleep patterns.[8]

In a previous study that investigated the extent of sleep problems among patients with HSCT 2 weeks after being hospitalized in the transplantation ward, 26% of patients experienced clinical insomnia and 74% of the patients had at least mild insomnia.[7] Another study that analyzed patients' sleep quality during the immunosuppressed period reported that a majority of the patients showed sleep deprivation and irregular sleep patterns, which were highly correlated with the number of days hospitalized.[8] The same study reported that sleep deprivation and irregular sleep patterns were more prominent in objectively measured data than in subjectively perceived data reported by patients.[8]

Previous studies show that most sleep quality research on patients undergoing HSCT used self-reporting measures, while no study used both objective and subjective methods to measure sleep patterns and compare the results. The present study used actigraphy as an objective measure together with the self-reported Insomnia Severity Index (ISI) as a subjective measure to evaluate the quantity and quality of sleep and investigated the differences between the two sets of results.

Methods

Design

This descriptive survey-based study measured sleep time and efficiency among patients undergoing HSCT in each transplantation period using objective and subjective measures and compared the results obtained using the two methods.

Participants

Forty participants were recruited from the HSCT ward of a tertiary hospital in Seoul between June 2019 and June 2020. The sample size was calculated using the G*Power 3.1 program. The sample size of 40 participants was determined based on preceding studies with an effect size of 0.5, significance level (α) of 0.05, and statistical power (1-β) of 0.80 for analysis of variance (ANOVA), and considering a 10% drop-out rate. Participants were selected from patients who understood the purpose of this study and voluntarily agreed to participate. The specific criteria for selecting participants are listed below:

(1) Patients aged 19 and above undergoing HSCT due to leukemia, malignant lymphoma, multiple myeloma, myelodysplastic syndrome, amyloidosis, aplastic anemia, or other rare blood disorders
(2) Patients who were able to communicate and understand the questionnaire sufficiently to provide responses

Patients who received total-body irradiation treatment as a pretreatment had been receiving mental health treatment due to existing sleep problems or taking psychiatric drugs daily to induce sleep, were moved to the intensive care unit from the transplantation unit due to an aggravated condition, or had experienced mental or neurological changes such as depression and delirium during their hospitalization were excluded from the study, as these conditions may have impacted the results.

Outcome measurements

Objective measurements

Actigraphy (Actigraphy-Spectrum™): Actigraphy is a simple-to-use, cost-effective method that is more appropriate than polysomnography for measuring sleep patterns for multiple days.[12] The actigraph includes a multi-directional accelerometer that detects motion, which distinguishes sleep and arousal according to the level of motion worn on the wrist. Data from the actigraph can be converted into a format which allows for processing with the Actiware analysis software.[13] Actiware software uses algorithms to process data based on one of three actiware sleep-wake threshold settings (Low, Medium and High). According to Madisen et al., 's 2015 systematic review, it can be seen that actigraphy was used in a number of studies to examine the quality of sleep-in cancer patients.[2]

Actigraphy was used to measure total sleep time, sleep efficiency, and wake after sleep onset. Total sleep time referred to the duration from sleep onset to offset. The average recommended sleep time per day for adults is 7–8 h. Sleep onset latency is the starting point of the first awake state of 1 min or less during a 20-min sleep state in the actigraphy data and the offset period is the last point recorded as the sleep state. Sleep efficiency denotes the percentage of total sleep time during the total duration of the sleep episode. The duration of the sleep episode is the total of sleep onset latency, total sleep time, wakefulness after sleep onset (WASO), and time attempting to sleep after final awakening.[14] A sleep efficiency of at least 80% is considered to be an indicator of adequate sleep.[15] The average WASO for adults without insomnia is 42 min out of 7 h (ie., 0.7 h or less).[15] Indicators such as total sleep time, sleep efficiency, and WASO are all transformed into analog electric signals based on the movements of the participants, and then transformed into digital signals through actigraphy programs, generating graphs and numerical data.[16]

Subjective measurements

The ISI is a patient self-reporting tool for subjective sleep patterns that consists of seven questions regarding difficulty falling asleep, difficulty staying asleep, problems waking up too early, satisfaction with current sleep patterns, interference with daily functioning, anxiety about insomnia, and the level of sleep problems that are noticeable to others.[17] The ISI survey requires a relatively short time to complete (within 3 min) and is easy to use as a measurement of sleep quality over a short period of time.

Each question is scored with a Likert scale between 0 and 4. The total score can range from 0 to 28, with a higher score indicating a higher level of insomnia.[17] The results are classified into four categories according to the total score: 0–7 = no clinically significant insomnia, 8–14 = subthreshold insomnia, 15–21 = clinical insomnia (moderate severity), and 22–28 = clinical insomnia (severe).[17] The sleep efficiency measured by actigraphy means that the higher the score, the better the quality of sleep. But the ISI result value means that the higher the score, the worse the quality of sleep. Therefore, for the ease of comparison, the ISI result was inversely transformed so that the higher the ISI score, the higher the quality of sleep. The reversed total score of 0–19 indicated moderate to severe insomnia.

ISI was originally designed to evaluate sleep patterns in the past month, but in this study, it was confirmed that it could be used even if the period of 1 month was reduced to the period of 3 days with the approval of the developer. Therefore, the remaining period excluding the period before hospitalization (T1) was adjusted to 3 days. The Cronbach alpha of ISI was 0.92 by the scale developer[17] and 0.78 in this study.

Data collection and procedures

Researchers recruited participants from their affiliated hospital among inpatients with scheduled HSCT or patients hospitalized for transplantation and asked them whether they were willing to participate in the study after explaining the purpose and procedures of the study. The researchers conducted the study among patients who expressed willingness to participate and signed a written consent form. And a reward of 30,000 won was provided to the study participants.

Data on participants' demographic and disease-related characteristics were collected based on their medical records. The participants were asked to complete the ISI on the day of hospitalization to understand their pre-treatment sleep efficiency (T1). Changes in sleep patterns after being hospitalized were measured in three different periods: the conditioning period (the period of receiving anti-cancer treatment, 2–3 days prior to transplantation: T2), the immunosuppressed period (absolute neutrophil count of 500/mm^3 or less, 4–8 days after transplantation: T3), and the engraftment period (absolute neutrophil count of 1000/mm^3 or higher, at discharge: T4).

The ISI was administered each time the actigraph unit was removed; therefore, objective sleep quality was measured a total of three times using actigraphy and subjective sleep quality was measured four times using the ISI (including baseline). At each period, participants started wearing the actigraphy unit on their non-dominant wrist at noon and removed it 48 h later at noon. In addition, the subjects were asked to keep a sleep diary. The sleep log was recorded directly after waking up at a time when the subject thought he had slept within 48 h of wearing the actigraphy. And subjectively perceived sleep time was also measured through one-on-one interviews and records of when they woke up in the morning.

Data analysis

The collected data were processed using SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). Frequencies and percentages were calculated for participants' general characteristics and disease-related characteristics, and the average and standard deviation were estimated for objective and subjective sleep patterns by transplantation period. Objective sleep patterns measured with actigraphy were analyzed using Actiware. Repeated-measures ANOVA was used to compare the differences between objective and subjective values in total sleep time and sleep efficiency in each period. In this study, Cronbach's alpha was calculated for the reliability analysis, and the significance level was 0.05 or less.

Ethical considerations

Data collection was carried out after obtaining approval by the Institutional Review Board of the tertiary hospital in Seoul with which the researchers were affiliated (Approval No. 2019-05-014). The content and purpose of the study, the advantages and disadvantages of participating, and the fact that the results of this study would be used only for the purpose of this study were explained to the participants. The participants signed a written consent form after being explained that their anonymity and confidentiality would be protected, that their participation was voluntary and that they could decide to withdraw at any time. The collected data were stored and managed in a place that could only be accessed by researchers after deleting all information that could be used to identify individuals. The data will be discarded after keeping them for the stipulated period by the IRB upon completion of the study.

Results

General and disease-related characteristics of the participants

The participants consisted of 23 men (57.5%) and 17 women (42.5%), with a mean age of 52.6 years. A majority were diagnosed with lymphoma ($n = 18$, 45.0%); 25 participants (62.5%) received autologous transplantation and 15 participants (37.5%) received allogeneic transplantation. Most patients ($n = 26$, 65.0%) were staying in a room shared by five persons, while the others were in single rooms ($n = 14$, 35.0%). All but one participant ($n = 39$, 97.5%) had been hospitalized previously (Table 1).

Changes in sleep patterns by HSCT periods

Objective results of sleep patterns

The mean total sleep time, efficiency, and WASO measured by actigraphy in each HSCT period are illustrated in Table 2. The total sleep time was the lowest during T2 (the conditioning period) compared to T3 (the immunosuppressed period) and T4 (the engraftment period), and sleep efficiency was the highest at 77.28% during T3 (Table 2). The average WASO was the highest at 1.39 h in T2 and the lowest at 0.71 h in T3 (Table 2).

Subjective results of sleep patterns

The mean ISI at T1 did not indicate insomnia, but most participants developed moderate or higher insomnia during T2, where the reversed ISI scores were all 19 and lower (Table 3). The quality of sleep was lowest during T3 and started to recover as they moved on to T4 (Table 3).

Table 1
Demographic and disease-related characteristics of the HSCT patients ($n = 40$).

Characteristics	Categories	*n* (%)
Gender		
	Male	23 (57.5)
	Female	17 (42.5)
Age (year) (Mean = 52.6)		
	≤ 39	6 (15.0)
	40–49	6 (15.0)
	50–59	16 (40.0)
	60–69	12 (30.0)
Diagnosis		
	Acute myeloid leukemia	9 (22.5)
	Acute lymphocytic leukemia	2 (5.0)
	Myelodysplastic syndrome	2 (5.0)
	Multiple myeloma	8 (20.0)
	Lymphoma	18 (45.0)
	Amyloidosis	1 (2.5)
Marital status		
	Married	37 (92.5)
	Never married	3 (7.5)
Religion		
	Yes	29 (72.5)
	No	11 (27.5)
Type of transplantation		
	Autologous	25 (62.5)
	Allogenic	15 (37.5)
Type of rooms		
	Single	14 (35.0)
	Shared	26 (65.0)
Hospitalization experience		
	Yes	39 (97.5)
	No	1 (2.5)

HSCT, hematopoietic stem cell transplantation.

Table 2
Objective sleep time, efficiency and WASO by actigraphy according to the HSCT periods ($n = 40$).

	T2	T3	T4	Total
	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)
Sleep time (h)	4.28 ± 1.43	5.28 ± 1.41	5.33 ± 1.82	4.96 ± 1.63
Sleep efficiency (%)	64.35 ± 11.38	77.28 ± 10.07	75.24 ± 10.44	72.29 ± 11.98
WASO (h)	1.39 ± 0.81	0.71 ± 0.28	1.16 ± 0.75	1.10 ± 0.71

HSCT, hematopoietic stem cell transplantation; T2, conditioning period; T3, immunosuppressed period; T4, engraftment period; Sleep time, total sleep time per day; Sleep efficiency, percentage of total sleep time during the total duration of the sleep episode; WASO, Wakefulness after sleep onset.

Table 3
Subjective sleep time by sleep diary and subjective sleep efficiency by ISI according to the HSCT periods ($n = 40$).

Item	T1	T2	T3	T4	Total
	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)
ISI scores*	23.43 ± 5.5	17.28 ± 6.57	16.55 ± 5.54	18.77 ± 5.50	19.00 ± 6.33
% ISI scores**	80.60 ± 18.94	59.57 ± 22.67	57.07 ± 19.11	64.74 ± 18.99	65.49 ± 21.83

HSCT, hematopoietic stem cell transplantation; T1, at admission time; T2, conditioning period; T3, immunosuppressed period; T4, engraftment period; ISI, Insomnia Severity Index; *reversed ISI scores; ** converted "reversed ISI scores" into a percentage.

Comparison of objective and subjective sleep time

As a result of the Shapiro-Wilks test for normality test and repeated measurement analysis, the p value was 0.05 or more, and as a result of the Mauchly test for the sphericity test, the value for sphericity test was less than 0.05, so a value assumed for sphericity test was used. The total sleep times were significantly different by the period after accounting for the differences in measurement methods ($P < 0.001$), while there were no significant differences in the results between objective and subjective sleep time ($P = 0.414$). There were no interactions between the different methods over time ($P = 0.345$) (Table 4; Fig. 1).

Comparison of objective and subjective sleep efficiency

The sleep efficiency results showed significant differences by period ($P = 0.001$), and between objective and subjective data, even excluding the effect of time ($P < 0.001$). The levels of objective and subjective sleep efficiency were found to be correlated with time and measurement method ($P = 0.002$) (Table 5; Fig. 1).

Discussion

This study was conducted with the goal of investigating objective and subjective sleep time and efficiency and their changes over four transplantation periods (pre-treatment [T1] and during treatment [T2-T4]) of patients hospitalized for HSCT and to evaluate the differences between the objective and subjective measures. The average objective daily sleep time of the participants was only 4.96 h (4 h and 57 min) and their average sleep efficiency was 72.29%. These results showed a comparatively lower average sleep time, but a higher sleep efficiency, than the values reported by Hacker et al (5.6 h and 55%, respectively).[7]

According to the results of this study, both sleep time and efficiency demonstrated significant differences by period (T2-T4); in particular, less sleep time, lower efficiency, and more frequent WASO were observed at T2. This is most likely due to the increased need for urination from the large amount of IV fluids infused during T2. It should also be kept in mind that T2 is one of the earliest periods of treatment, and the unfamiliar devices and environment may have diminished the patients' sleep quality; in other words, the possibility of the first-night effect cannot be ruled out.

Through this study, it was found that the subjective quality of sleep in hematopoietic stem cell transplant patients also deteriorated. Subjective sleep quality measurements using the ISI showed that 75% of the participants experienced some level of insomnia between subthreshold and moderate levels. This result corresponds with a preceding study that reported that 74% of HSCT patients demonstrated subjective sleep problems in subjective measurements.[6] Among the ISI items, participants found it most difficult to stay asleep and gave generally low scores for sleep satisfaction. This reflects the circumstances in which the participants were frequently interrupted during sleep by needing to urinate or being interrupted by visits from the medical staff after getting in bed, which also explains the high WASO time at every stage of the transplant process. The ISI scores showed significant gaps by period, as the reversed mean ISI score was 23.43 pre-hospitalization, indicating no insomnia, but the scores subsequently dropped to 16–18 during their hospital stay, indicating that they had subjective sleep problems.

Sleep time and efficiency showed different results depending on the measurement method. The sleep times measured by actigraphy and self-reported sleep times did not show significant differences in this study, unlike the significant gaps in sleep efficiency between actigraphy and ISI results. The gap between the objective and subjective measures of sleep efficiency was most prominent during the neutropenic period because actigraphy may have incorrectly recorded times when patients were simply laying and resting in bed as sleep, as actigraphy detects movement to determine the state of sleep. This result proves that there are limitations in measuring sleep efficiency using actigraphy, providing support for a preceding study suggesting that subjective and objective sleep quality were not significantly correlated in patients with anxiety and depression and that actigraphy was less sensitive in measuring sleep patterns of patients with socio-psychological symptoms.[18] Another study of patients with colorectal cancer prior to starting anti-cancer treatment suggested that objective and subjective measurements were not significantly correlated, as they represent different aspects of sleep, but concluded that taking both objective and subjective measurements is useful when evaluating sleep quality because subjective sleep problems are relevant to objective changes in the circadian rhythm.[19] As such, objective and subjective measurement methods may include different aspects of sleep, so they should be used as a way to complement each other.

This study found that most patients undergoing HSCT experienced objective and subjective sleep disorders during the transplantation period. More active and persistent interventions will be needed to improve the sleep quality of patients with HSCT. This study also

Table 4
Repeated measures ANOVA of objective and subjective sleep time ($n = 40$).

Variables	T2	T3	T4	Sources	F	*P*
	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)			
Objective (h)	4.28 ± 1.43	5.28 ± 1.41	5.33 ± 1.82	Group	0.674	0.414
Subjective (h)	3.86 ± 1.51	4.95 ± 1.38	5.45 ± 1.63	Time	24.668	0.000***
t (*P*)	0.37 (0.709)	1.78 (0.083)	1.33 (0.998)	Group*Time	1.072	0.345

T2, conditioning period; T3, immunosuppressed period; T4, engraftment period; objective, data from actigraphy, subjective: data from ISI, ***$P < 0.001$.

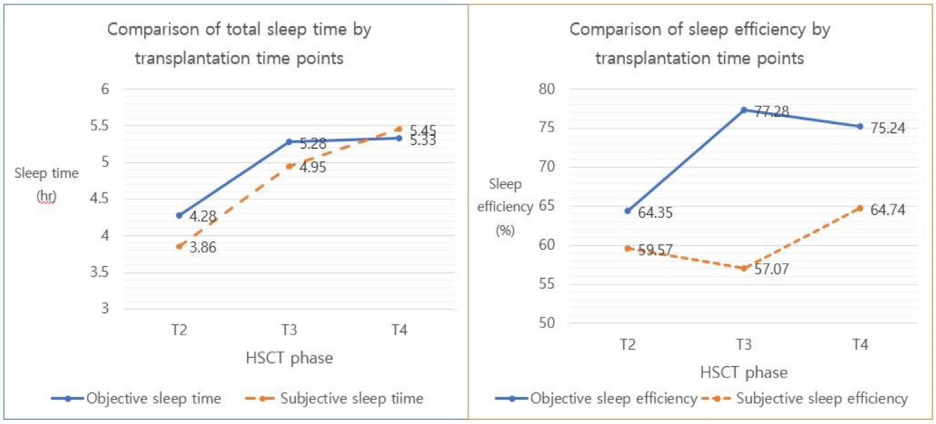

Fig. 1. Repeated measures ANOVA comparisons over the phase of HSCT. ANOVA, analysis of variance; HSCT, hematopoietic stem cell transplantation; T2, conditioning period; T3, immunosuppressed period; T4, engraftment period.

Table 5
Repeated measures ANOVA of objective and subjective sleep efficiency ($n = 40$).

Variables	T2	T3	T4	Sources	F	*P*
	(Mean ± SD)	(Mean ± SD)	(Mean ± SD)			
Objective (%)	64.35 ± 11.38	77.28 ± 10.07	75.24 ± 10.44	Group	20.858	0.000***
Subjective (%)	59.57 ± 22.67	57.07 ± 19.11	64.74 ± 18.99	Time	6.864	0.001
t (*P*)	1.95 (0.168)	2.65 (0.002)	2.17 (0.035)	Group*Time	6.284	0.002

T2, conditioning period; T3, immunosuppressed period; T4, engraftment period; objective, data from actigraphy, subjective, converted scores into percentage of revised ISI scores, ***$P < 0.001$.

confirmed that actigraphy, which determines sleep and awake states from the level of movement, may not always be reliable when used with hospitalized patients who spend most of their time lying in bed. Medical staff should keep in mind that patients lying in bed with their eyes closed may not always be asleep, especially during the neutropenic period. Measuring subjective sleep time and efficiency to complement actigraphy measures will help reduce potential errors.

While preceding studies of HSCT patients examined sleep patterns at only one point or cross-sectionally, the present study investigated sleep patterns using both objective and subjective methods in each transplantation period among participants who were admitted to the stem cell transplantation unit at the hospital on a long-term basis. It also provided significant findings for nursing professionals by identifying the severity of the sleep disruption suffered by patients with HSCT, underscoring the need for more active interventions. The results of this study have limitations in generalization as the participants were recruited by convenience sampling from a single tertiary hospital and the sample size was small. As a result of the analysis, there was no difference in sleep time and quality according to the type of room or transplant type, so it was not included in the results. However, if the number of subjects increases, different results may be shown, so the possibility of variables that can act as bias cannot be excluded.

Conclusions

The outcomes of this study demonstrated that a majority of the patients undergoing HSCT experienced significant decreases in sleep time during the transplantation period in both objective and subjective results. During the T3 period, where energy level of patients with HSCT is the lowest, actigraphy results falsely suggested high sleep efficiency by interpreting patients' low movement state while awake as a sleep state, showing the largest gap between objective and subjective measurements. This result confirmed that actigraphy may misinterpret a low-energy state as sleep in patients who are receiving treatment for severe blood cancer.

Based on these findings, we propose that a new method that can measure sleep patterns without confusing a low-energy state for a sleep state should be developed and applied for patients with HSCT. Moreover, further research should be conducted with the goal of developing effective nursing interventions to enhance sleep efficiency in patients with severe blood cancer who are undergoing treatment.

Authors' contributions

Conceived and designed the research: E. Suh, & M. Park.
Data collection: M. Park.
Data analysis: E. Suh, & M. Park.
Wrote the paper: E. Suh, & M. Park.

Declaration of competing interest

None declared.

Founding

Nil.

Ethics statement

This study was approved by the Ethics Board of Samsung Medical Center in Seoul (Approval 2019-05-014).

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