Prevalence of sleep aid medication use in patients receiving a hematopoietic cell transplant on an inpatient unit

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Prevalence of Sleep Aid Medication Use in Patients Receiving a Hematopoietic Cell Transplant on an Inpatient Unit

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Abstract

Background and objectives: There is a lack of research regarding the use of sleep aids after hematopoietic stem cell transplantation (HCT). We describe the prevalence of sleep aid administration in the HCT unit and identify associations with patient or clinical characteristics.

Patients and methods: In this retrospective analysis of sequential inpatient HCTs from July 1 to December 31, 2016 we describe whether and when patients were prescribed sleep aid medications. Chi-square tests determined significant differences between patient characteristics, sleep aid prescription, and time of prescription.

Results: Of the 225 patients identified, 193 (86%) were prescribed sleep aids. Significantly more women received prescriptions for sleep aids (90.4%) than men (81%; P = .047). One hundred patients (44%) received prescriptions exclusively while in the hospital.

Conclusion: Findings show a high prevalence of sleep medication use in patients undergoing inpatient HCT, primarily during hospitalization. Future efforts toward standardized recommendations to optimize peri-transplant sleep would help clinicians and patients.

Keywords: Sleep, Pharmaceutical prescription, Retrospective analysis, Hematopoietic stem cell transplantation, Inpatient

1. Introduction

Sleep disturbance is associated with impaired cognitive performance, immune dysfunction, and increased inflammation due to disrupted neurobehavioral functions [1]. For patients undergoing hematopoietic stem cell transplantation (HCT), it is one of the most distressing symptoms [2], significantly impairing overall quality of life [3]. Data show that 69% of HCT patients experience clinically significant sleep disturbance during the acute post-transplant recovery period and 46% of patients receiving an allogeneic HCT experience sleep disturbance even prior to transplant [4]. Contributing factors include extended hospitalizations disrupting normal sleep-wake patterns, treatment-related disturbances, sleep-disrupting medications, and psychological distress [5].

The inpatient setting is particularly problematic, with up to 80% of HCT patients experiencing sleep disruption, 68% of whom report stress as contributing to sleep difficulties while hospitalized [6]. In hospitalized patients, sleep deprivation is common due to environmental changes, medications, noise, and device alarms [7]. Two-thirds of patients are prescribed a pharmacologic sleep aid while inpatient [5], a rate double that of other non-HCT hospitalized patients [8]. Evidence demonstrates the efficacy of such medications for regulating sleep [9], but the incidence, frequency, and timing of most
sleep medications has not been studied in HCT patients [9,10].

Although factors associated with sleep disturbance in HCT patients have been well documented [5,6], there is a lack of research regarding the use of sleep aids before, during, and at hospitalization discharge [10]. Therefore, the objective of this study was to describe the prevalence of sleep aid administration in an inpatient HCT unit and identify associations with patient or clinical characteristics.

2. Patients and methods

To understand the prevalence and characterization of sleep aid medications prescribed to hospitalized HCT patients, we performed a retrospective analysis of sequential inpatient HCT patients from July 1 to December 31, 2016. The study was approved by the institutional review board at the Medical College of Wisconsin. A research team member reviewed medical charts of hospitalized patients receiving an autologous or allogeneic transplant. Demographic, transplant-specific, and medication prescription data were obtained from the HCT research database and from the hospital's electronic medical record. Prescription patterns at three timepoints were recorded: prior to, during, and after hospitalization (at time of discharge). Medications are often chosen for their multi-purpose benefit (e.g., benefitting GI concerns and sleep concerns). Therefore, medications where one of the potential benefits is sleep aid were included in the data extraction. Sleep aid medications were categorized as follows: benzodiazepines, non-benzodiazepine hypnotics, antidepressant sleep aids, and other sleep aids.

We categorized patients based on whether they were ever prescribed sleep aid medications (before, during, or after hospitalization vs. never prescribed) and based on when they were prescribed medication (those who were consistently prescribed vs. those who were only prescribed while hospitalized). We describe the number and percentage of patients prescribed each type of pharmaceutical sleep aid using counts and percentages. The Chi-square test was used to determine whether there was a statistically significant difference between patient characteristics significantly associated with sleep aid prescription (ever vs. never) and time of prescription (only in hospital vs. before, during, and after hospitalization).

3. Results

Demographics of patients by prescription status are displayed in Table 1. Of the 225 patients identified, 51% were over age 60 years, 54% were male, and 68% had a KPS <90 (68%). The most common underlying hematologic disease was a plasma cell disorder (44%), and the most common HCT type was autologous transplant (53%).

One hundred ninety-three (86%) patients were prescribed sleep aids either before, during, or after hospitalization (on discharge). Only 32 (14%) were never prescribed sleep aids. A significantly larger proportion of women received prescriptions for sleep aids (90.4%) than men (81%; P = .047). There were no other significant differences in clinical or demographic characteristics between patients prescribed and those never prescribed sleep aids. Table 1 also shows descriptive statistics of patients who were only prescribed sleep aids while in the hospital vs. those prescribed sleep aids before, during hospitalization, and at discharge. Among the 86% of patients who received sleep aids, 100 (44% of the full sample) were prescribed exclusively during their stay in the hospital, while 52 (23% of the full sample) received sleep aids before, during, and after treatment. There were no statistically significant differences between those who were consistently prescribed sleep aids and those who only received them in the hospital.

Thirteen different sleep medications were prescribed to patients. Four different drug classes (benzodiazepines, antidepressant sleep aids, non-benzodiazepine hypnotics, other sleep aids) and sleep aids of interest comprised 19 different medications including alprazolam, alprazolam ER, lorazepam, clonazepam, diazepam, temazepam, zolpidem, zolpidem CR, eszopiclone, trazodone, mirtazapine, amitriptyline, diphenhydramine. Of these patients, 84% were prescribed lorazepam while approximately 40% of patients were prescribed zolpidem and diphenhydramine.

4. Discussion

This retrospective study made the following important observations [1]: a large majority of transplant patients receive sleep aids during hospitalization [2]; a sizable minority of patients may be chronic sleep aid users given that they were prescribed at all timepoints assessed (30%) [3]; a wide variety of sleep aids were prescribed, though lorazepam, zolpidem, and diphenhydramine were most common.

First, consistent with previous findings, our findings show a high prevalence of sleep medication use in patients undergoing inpatient HCT. Sex was the only patient characteristic with significant differences between those prescribed vs. those not prescribed a sleep aid. A larger proportion of women received prescriptions than men. Previous research in the general population has shown that women
endorse better sleep quality than men while also reporting more sleep complaints [11]. However, research concerning female patients receiving HCT is mixed; one study noted that female patients were more likely to report sleep disturbances [12] while a more recent study did not note a statistically significant difference based on sex [5].

These data also suggest that the highest proportion of patients receiving sleep aids was only prescribed them during hospitalization. The second largest group among patients prescribed sleep aids are those who received prescriptions at all three time points, potentially indicating chronic users of sleep medications. Among those patients prescribed any sleep aids, about a quarter were prescribed sleep aids prior to hospitalization while a little over a third were prescribed a sleep aid at discharge, suggesting more patients are leaving the hospital during hospitalization.

Table 1. Patient Characteristics by Sleep Aid prescription status (ever prescribed compared to never prescribed and consistent prescription compared to only in hospital).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n = 225)</th>
<th>Prescribed Sleep Aids (n = 193; 86%)</th>
<th>Never Prescribed Sleep Aids (n = 32; 14%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-40</td>
<td>28 (12.4%)</td>
<td>25 (89.3%)</td>
<td>3 (10.7%)</td>
<td>.803</td>
</tr>
<tr>
<td>41-60</td>
<td>82 (36.4%)</td>
<td>70 (85.4%)</td>
<td>12 (14.6%)</td>
<td></td>
</tr>
<tr>
<td>61+</td>
<td>115 (51.1%)</td>
<td>98 (84.3%)</td>
<td>17 (15.7%)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>.047</td>
</tr>
<tr>
<td>Female</td>
<td>104 (46.2%)</td>
<td>94 (90.4%)</td>
<td>10 (9.6%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>121 (53.8%)</td>
<td>99 (81.0%)</td>
<td>22 (19.0%)</td>
<td></td>
</tr>
<tr>
<td>Disease</td>
<td></td>
<td></td>
<td></td>
<td>.272</td>
</tr>
<tr>
<td>Leukemia</td>
<td>53 (23.6%)</td>
<td>43 (81.1%)</td>
<td>10 (18.9%)</td>
<td></td>
</tr>
<tr>
<td>Plasma cell disorder</td>
<td>98 (43.6%)</td>
<td>81 (81.6%)</td>
<td>17 (18.4%)</td>
<td></td>
</tr>
<tr>
<td>Myelodysplastic Syndrome</td>
<td>29 (12.9%)</td>
<td>28 (96.5%)</td>
<td>1 (3.5%)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>39 (17.3%)</td>
<td>35 (89.7%)</td>
<td>4 (10.3%)</td>
<td></td>
</tr>
<tr>
<td>Severe Aplastic Anemia</td>
<td>4 (1.8%)</td>
<td>4 (100%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2 (.9%)</td>
<td>2 (100%)</td>
<td>0</td>
<td>.821</td>
</tr>
<tr>
<td>KPS &lt;90</td>
<td>153 (68%)</td>
<td>130 (85.0%)</td>
<td>23 (15.0%)</td>
<td>.365</td>
</tr>
<tr>
<td>KPS 90+</td>
<td>72 (32%)</td>
<td>63 (86.1%)</td>
<td>9 (13.9%)</td>
<td></td>
</tr>
<tr>
<td>HCT Type</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous</td>
<td>120 (53.3%)</td>
<td>101 (83.3%)</td>
<td>19 (16.7%)</td>
<td>.602</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>105 (46.7%)</td>
<td>92 (87.6%)</td>
<td>13 (12.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Caption: Table describing counts and percentages of patient characteristics (age, sex, disease, KPS score, and hematopoietic cell transplant type) for all patients in the sample and by subgroups: patients prescribed any sleep aids, patients prescribed no sleep aids, patients prescribed sleep aids only in the hospital, patients prescribed before, during, and after hospitalization. The right most column shows p-values for chi-square statistical comparisons across subgroups for each patient characteristic.
with sleep aids than those who enter. Understanding patients’ prior sleep patterns is important, as prior sleep disorders have been demonstrated to potentially impact transplant-related factors [3].

Our study shows large variation in the sleep aids prescribed. Ten of 13 medications were prescribed to less than 10% of patients. Zolpidem is the only sleep-specific medication, in contrast to lorazepam and diphenhydramine which have other uses. Lorazepam was prescribed to 84% of patients, which may indicate a consistency in sleep aids prescribed to HCT patients, or that other properties of lorazepam make it especially attractive in this population (e.g., anti-emetic, anti-anxiolytic). The current study is unable to distinguish indication for drug use.

This study’s findings are limited in several respects. These results are retrospective in nature; therefore, we were unable to obtain specific reasons for sleep aid prescription and/or characterize individual provider practices. Further, many sleep agents may have been used for reasons other than sleep, such as lorazepam that, in addition to sleep, is also prescribed for nausea and anxiety. Intent for prescription was not available in the data collected and is critical for future studies. In addition, over-the-counter drugs such as melatonin were not extracted from the patient’s records when recording sleep aid prescriptions. Information about the dose or frequency of medication prescribed was not collected in this study but is an important area of future research. Finally, these findings are representative of a single institution during a restricted duration of time, limiting the generalizability of these findings while providing important baseline information for HCT providers to consider in their individual practices.

Despite these limitations, this study is the first to our knowledge to identify the types of sleep aids prescribed to HCT patients as well as the prevalence of chronic use of sleep aid medications compared to the prevalence of patients who only use sleep aids during hospitalization. Circumscribed collection time period (six months) and a single institutional study limit the generalizability of these findings. Future studies should focus on defining the type and timing of sleep aid prescription to HCT patients and potential impacts on outcomes by qualitatively looking into the indication for sleep aid prescription. Future research should also evaluate provider-based information and patient perspectives to determine more specific reasons for sleep aids, frequency of use of sleep aids, and alternatives to sleep aid medications. There are several alternative intervention strategies (i.e., mindfulness, care environment control) that are not well understood in this patient population. Finally, future efforts toward standardized recommendations to optimize peri-transplant sleep would be helpful for both clinicians and patients.

Declaration of Competing Interest

Drs. Cusatis and Knight report no conflicts of interest.

Mr. Ibrahim reports no conflict of interest.

Dr. D’Souza reports no relevant conflicts of interest. The following are Dr. D’Souza’s financial conflicts of interest: Institutional research funding: Takeda, Sanofi, TeneoBio, CAELUM, Prothena Consulting/Advisory Board- Janssen, BMS, Prothena, Imbrium, Pfizer.

Dr. Shaw reports consulting for OrcaBio and Mallinckrodt.

References