Managing Sleep Problems after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

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Eric Zhou, PhD
Dana-Farber Cancer Institute
MANAGING SLEEP PROBLEMS AFTER TRANSPLANT

BMT InfoNet

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Sleep is Important

\[ \frac{1}{3} \]
• Insomnia disorder
• Obstructive sleep apnea
• Central sleep apnea
• Sleep related hypoventilation disorder
• Sleep related hypoxemia disorder
• Narcolepsy (Type I/II)
• Idiopathic hypersomnia
• Kleine-Levin syndrome
• Delayed sleep-wake phase disorder
• Advanced sleep-wake phase disorder

• Non-24 sleep-wake disorder
• Shift work disorder
• Jet lag disorder
• Confusional arousals
• Sleepwalking
• Sleep terrors
• Sleep related eating disorder
• REM sleep behavior disorder
• Sleep enuresis
• Restless legs syndrome
Table 1. DSM-V Criteria for Insomnia Disorder

- Complaint of dissatisfaction with quantity or quality of sleep occurs at least 3 nights a week for at least 3 months, associated with one or more of the following:
  - Difficulty falling asleep
  - Difficulty staying asleep, with frequent awakenings or difficulty falling back asleep
  - Early morning awakening

- The sleep disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

- The sleep disturbance occurs even when there is enough time for sleep.

- The sleep disturbance does not occur exclusively during the course of narcolepsy, breathing-related sleep disorder, circadian rhythm sleep disorder, or a parasomnia (an unusual behavior or event that occurs during sleep that may lead to intermittent awakenings).

- The sleep disturbance does not occur exclusively during the course of another mental disorder.

- The sleep disturbance is not due to the direct physiologic effects of a substance such as a drug of abuse or a medication, or from a general medical condition.

**DSM-V, Diagnostic and Statistical Manual of Mental Disorders, 5th Ed.**
INSOMNIA SYMPTOMS ARE COMMON
Insomnia is Trivialized
Health Consequences

- ✖ Cardiovascular disease
- ✖ Diabetes
- ✖ Obesity

- ✖ Depression
- ✖ Anxiety
- ✖ Behavioral problems
- ✖ Suicide attempts
- ✖ Alcohol use
- ✖ Quality of life
America’s Sleep Crisis Is Making Us Sick, Fat, and Stupid. But There’s Hope.

Sleep deprivation now rivals obesity and smoking as our greatest public health crisis. Here’s what everyone (including America’s businesses) needs to do to help stop our massive sleep debt and get more shut-eye.
Rates of the 10 leading causes of death in the United States in 2016 (per 100,000 population)*

- Heart disease: 165.5
- Malignant neoplasms: 155.8
- Accidents (unintentional injuries): 47.4
- Chronic lower respiratory diseases: 40.6
- Cerebrovascular diseases: 37.3
- Alzheimer’s disease: 30.3
- Diabetes mellitus: 21
- Influenza and pneumonia: 13.5
- Nephritis, nephrotic syndrome and nephrosis: 13.1
- Intentional self-harm (suicide): 13.5

Source:
CDC
© Statista 2018

Additional Information:
United States; CDC; NCHS (NVSS)
Sleep, sleepiness and motor vehicle accidents: a national survey

Abstract
Objective: To assess the role of sleep-related factors, ethnicity and socio-economic deprivation in self-reported motor vehicle accidents while driving, after controlling for gender, age and drinking exposure.

Phillippa H. Gander, Nathaniel S. Marshall
Sleep/Wake Research Centre, Massey University, Wellington, New Zealand

Ricci B. Harris, Papaarangi Reid
Eru Pohare Maru Health Research Centre, Department of Public Health, Cline University at Wellington School of Medicine and Health Sciences, New Zealand

Original Articles

Short Sleep Duration as a Risk Factor for Hypertension Analyses of the First National Health and Nutrition Examination Survey
James E. Gangwisch, Steven B. Heymsfield, Bernadette Boden-Alba, Ruud M. Buijs, Felix Kreier, Thomas G. Pickering, Andrew G. Rundle, Gary K. Zammit, Dolores Malaspina

Sleep Disturbance Preceding Completed Suicide in Adolescents
Tina R. Goldstein, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center
Jeffrey A. Bridge, and Columbus Children's Research Institute and Department of Pediatrics, The Ohio State University
David A. Brent
Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center

Behaviorally Assessed Sleep and Susceptibility to the Common Cold
Arti A. Prasher, PhD, Denise Janicki-Devons, PhD, Martin H. Hall, PhD, Sheldon Cohen, PhD
1Department of Psychiatry, University of California, San Francisco, CA; 2Department of Psychology, Carnegie Mellon University, Pittsburgh, PA; 3Department of Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, PA

Impact of Sleep on the Risk of Cognitive Decline and Dementia
Adam P. Spira1,2, Lenis P. Chen-Edinboro1, Mark N. Wu3, and Kristine Yaffe4
1Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
2Department of Psychiatry and Behavioral Sciences, Johns Hopkins School of Medicine, Baltimore, MD
3Departments of Neurology and Neuroscience, Johns Hopkins School of Medicine, Baltimore, MD
4Departments of Psychiatry, Neurology, and Epidemiology and Biostatistics, University of California, San Francisco and San Francisco VA Medical Center, San Francisco, CA

Sleep Duration as a Risk Factor for Incident Type 2 Diabetes in a Multiethnic Cohort
DEBORAH A. BEIHL, ANGELA D. LISE, PhD, MPH, AND STEVEN M. HAFFNER, MD
Rates of the 10 leading causes of death in the United States in 2016 (per 100,000 population)*

- Heart disease: 165.5
- Malignant neoplasms: 155.8
- Accidents (unintentional injuries): 47.4
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Source: CDC
© Statista 2018

Additional Information:
United States, CDC, NCHS (NVSS)
Our data suggest that

- an improvement in sleep efficiency by 10%
- among women with sleep efficiency <85%
- could potentially lead to a 32% increase in survival time
Prevalence and Treatment of Insomnia in General Practice
A Longitudinal Study

F. Hohagen¹, K. Rink¹, C. Käppler¹, E. Schramm¹, D. Riemann², S. Weyerer², and M. Berger²

¹Psychiatric Department, University of Freiburg, Hauptstrasse 5, W-7800 Freiburg, Germany
²Centre Institute of Mental Health, Mannheim, Germany

PCP Not Aware of Sleep Problems

<table>
<thead>
<tr>
<th>Insomnia Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td></td>
<td>91.2%</td>
<td>78.1%</td>
<td>60.8%</td>
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</table>
SO WHAT DO YOU DO?
National Use of Prescription Medications for Insomnia: NHANES 1999-2010

Suzanne M. Bertisch, MD, MPH^1,2,4; Shoshana J. Herzig, MD, MPH^1,4; John W. Winkelman, MD, PhD^3,4; Catherine Buettner, MD, MPH^1,4

^1Divisions of General Medicine and Primary Care, and ^2Pulmonary, Critical Care, and Sleep Medicine, Beth Israel Deaconess Medical Center, Boston, MA; ^3Department of Psychiatry, Sleep Disorders Clinical Research Program, Massachusetts General Hospital, Boston, MA; ^4Harvard Medical School, Boston, MA
Mortality Hazard Associated With Anxiolytic and Hypnotic Drug Use in the National Population Health Survey

Geneviève Belleville, PhD

Objective: Although widely used in the general population, sleeping pills and minor tranquilizers, also known as anxiolytic agents, have been associated with undesirable outcomes. Reports about the association of these drugs with an elevated mortality rate are inconsistent and controversial. This study was designed to assess the mortality hazard associated with anxiolytic and hypnotic drug use in the National Population Health Survey in Canada. It was hypothesized that anxiolytic and hypnotic drug use would be associated with an elevated mortality hazard.

Method: A population-based sample of 14,117 people aged 18 to 102 years participated in a longitudinal panel survey, with data collected every second year from 1994 to 2007. The primary outcome measures reported in this study are self-report use of anxiolytic and hypnotic drugs, and death.

Results: For respondents who reported anxiolytic or hypnotic drug use in the past month, the odds of mortality were 3.22 times more (95% CI 2.70 to 3.84) than for those who did not use anxiolytic or hypnotic drugs in the past month. After controlling for confounding sociodemographic, lifestyle, and health factors (including depression), the odds ratio was reduced to 1.36 (95% CI 1.09 to 1.70) but remained significant.

Conclusion: Sedative drug use is associated with a small but significant increase in mortality risk. Further research is required to confirm the mechanisms by which sedative drug use increases mortality risk. Where possible, physicians should systematically consider possibilities for nonpharmacological treatment of sleep disturbances and anxiety.

RESULTS

Melatonin content was found to be highly variable between samples and lots, with no pattern observed between brand, form of supplement, labelled value, or presence of other herbal extracts. The most variable sample, chewable tablet E1, showed a 478% increase from label claim containing almost 9 mg of melatonin, compared to the 1.5-mg label claim, though this was also highly variable between lots (465% difference). The supplement that showed the greatest decrease in melatonin content as compared to labelled values was the capsule G5 which contained lavender, chamomile, and lemon balm, with a decrease of 83%. The least variable products appeared to be those that contained the simplest mix of ingredients, generally tablets or sublingual tablets with melatonin added to a filler such as cellulose derivatives or silica (Table 1, Figure 1). The capsules generally showed the greatest variability, with the variability observed from E1 greatly distorting the mean results of the chewable category (Figure 1). The herbal extracts most commonly added to these capsules included valerian root, passion flower, chamomile, skullcap, and hops, though other extracts were also found in some supplements (Table 1). Surprisingly, lot-to-lot variability was as varied as deviation from the label claim, ranging from 0.37% up to 466% (Table 1, Figure 2), with little correlation with other descriptive factors, though again, the sublingual tablets and tablets were most reproducible. Liquid supplements, though suspected to be the least stable, due to melatonin's known instability at room temperature in solvent, were generally high to medium in their stability (Figure 1) with low lot-to-lot variability (Figure 2). These results were confirmed by MS in all cases with the exception of Q1 for which serotonin was found only by electrochemical detection, though this could be attributed to long storage of significant variability of melatonin content.

SCIENTIFIC INVESTIGATIONS

Melatonin Natural Health and Significant Variations

Lauren A. E. Erland, MSc; Praveen K. Saxena

Coating Research Institute for Plant Preservation, Norway

Study Objectives: Melatonin is an important available supplement for the treatment and prevention of commercial supplements, comprising different forms.

Methods: A total of 31 supplements were analyzed and serotonin. Presence of serotonin was confirmed by high-performance liquid chromatography (HPLC) and mass spectrometry (MS) detection. Table 1 summarizes the results of the analyses, showing the range of melatonin content in each supplement.

Results: Melatonin content was found to vary widely, with some samples containing up to 10 times the label claim. The variability was not related to the presence of serotonin, and other ingredients did not significantly affect melatonin content. The supplements were classified into three categories: tablets, capsules, and liquids.

Conclusions: Melatonin is a popular supplement for sleep and mood regulation. However, the variability in content and the lack of standardization make it difficult to determine the effectiveness of these supplements. Future research is needed to establish standardized production methods and quality control measures.

Keywords: melatonin, variability, supplement, serotonin, HPLC, MS.

Recommendation 1: ACP recommends that all adult patients receive cognitive-behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder.
WHAT IS CBT-I?
### WHAT IS CBT-I?

<table>
<thead>
<tr>
<th>Mayo Clinic</th>
<th>AASM</th>
<th>Wikipedia</th>
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- **Stimulus Control**
- **Sleep Restriction**
- **Sleep Hygiene**
- **Cognitive Therapy**
- **Relaxation Training**
- **Paradoxical Intention**
- **Biofeedback**
HOW MANY HOURS OF SLEEP PER NIGHT DO YOU GET?
It’s not about tonight.
COLLECT DATA
# SLEEP DIARIES

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<tr>
<th>Day</th>
<th>Date</th>
<th>Mid night</th>
<th>1am</th>
<th>2am</th>
<th>3am</th>
<th>4am</th>
<th>5am</th>
<th>6am</th>
<th>7am</th>
<th>8am</th>
<th>9am</th>
<th>10am</th>
<th>11am</th>
<th>Noon</th>
<th>1pm</th>
<th>2pm</th>
<th>3pm</th>
<th>4pm</th>
<th>5pm</th>
<th>6pm</th>
<th>7pm</th>
<th>8pm</th>
<th>9pm</th>
<th>10pm</th>
<th>11pm</th>
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<td>Fri</td>
<td>2-20</td>
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<td></td>
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<td>3am</td>
<td>3:30am</td>
<td>4pm</td>
<td>5:00am</td>
<td>6pm</td>
<td>7pm</td>
<td>8pm</td>
<td>9pm</td>
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<td>11pm</td>
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<td>Sat</td>
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<table>
<thead>
<tr>
<th>Day</th>
<th>Daytime Naps</th>
<th>Medication and/or Substance Use</th>
<th>Time to Bed</th>
<th>Time Taken to Fall Asleep</th>
<th>Number of Night Awakenings</th>
<th>Total Time Awake in Night</th>
<th>Time Woke Up</th>
<th>Time Intended to Wake Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>January 3</td>
<td>2 naps / 15 minutes each</td>
<td>Ambien 5mg and Benadryl</td>
<td>10:30pm</td>
<td>45 minutes</td>
<td>3</td>
<td>60 minutes</td>
<td>5:45am</td>
<td>6:30am</td>
</tr>
</tbody>
</table>
SLEEP RESTRICTION
A WAGER
SLEEP HYGIENE

1. Eliminate the bedroom clock
2. Exercise in the late afternoon/early evening
3. Avoid caffeine, alcohol, and nicotine
4. Eat a light bedtime snack
5. Reduce liquid consumption before bed
6. Reduce electronics use
If I don’t sleep well tonight, I don’t know how I’m going to be able to work tomorrow.

This has to stop. My _____ is going to come back if I don’t sleep.

I’m never going to fall asleep with so much to worry about right now.
SLEEP OCCURS IN CONTEXT OF LIFE
FINDING A SPECIALIST

www.behavioralsleep.org
“The amount of sleep required by the average person is 5 minutes more.”

- Wilson Mizner
Questions?

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