Sleep Health and the Appropriate Use of OTC Sleep Aids in Older Adults

GSA Webinar: Results from a National Summit
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Rutgers Institute
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Clinical Solutionz
KOL, LLC
Quick Poll of the Audience
Webinar Agenda

• Introductions
• Background on aging and sleep disturbance
• Current state of OTC therapeutics for sleep disturbance
• Pharmacist perspective on gaps in therapies and clinical practice
• Conclusions
• Questions
• National Summit on OTC Sleep Aids and Sleep Health in Older Adults
• Grand Hyatt, Washington, DC
• October 17, 2013
Full-day conference intended to raise understanding of issues and risks related to OTC sleep aid use in older adults, and frame future efforts to address barriers affecting health care professionals, older adults, and caregivers.

Over 20 stakeholders convened for the Summit drawing from the public and private sectors; trade, professional, and advocacy organizations; and academia. Thought leaders with varied interests, experience, and expertise in OTC sleep aids and sleep health in older adults participated.
Objectives of the Summit—Overall

• Increase understanding of sleep health and OTC sleep aid use in older adults (ages 65 years and older).
• Identify opportunities for improving understanding among health care practitioners, consumers, and caregivers regarding use of OTC sleep aids in older adults.
• Enable networking to create new connections and deepen existing relationships with individuals having a common interest in older adult sleep health and sleep aid use.
Summit Dissemination

National Summit: OTC Sleep Aids and Sleep Health in Older Adults
October 2013

White Paper: Sleep Health and the Appropriate Use of OTC Sleep Aids in Older Adults
November 2013

Press Briefing: Fact Sheets and FAQs about OTC Sleep Aids and Sleep Health in Older Adults
November 2013

Webinar: Sleep Health and the Appropriate Use of OTC Sleep Aids in Older Adults
January 2014

GSA Annual Meeting Symposium
Washington, DC
November 2014

GSA Webinar on Sleep Health and the Appropriate Use of OTC Sleep Aids in Older Adults
Background on Aging and Sleep Disturbance

Phyllis Zee, MD, PhD, Northwestern University Feinberg School of Medicine
Sleep, Circadian Rhythms, and Health

Sleep disorders
- Insomnia
- Sleep apnea
- Restless legs
- Narcolepsy

Genetic predisposition

Sleep Deficiency Circadian Dysfunction

Aging
- Circadian disruption
- Behavioral lifestyle
- Work schedules
- Physical activity level

Cognitive performance

Obesity
- Diabetes
- Heart disease
- Lung disease
- Mood disorders
- Neurologic disorders

Appetite
- Inflammation
- Metabolism
- Heart, lung functions

HEALTH

SAFETY and PRODUCTIVITY

Sleep Disturbances Increase with Age: Insomnia Prevalence

Large-scale community survey of non-institutionalized American adults, ages 18 to 79 years old

Reported Sleep Problems: Survey

(n = 9,282; mean age 74 years)

- Waking Not Rested
- Waking Too Early
- Trouble Falling Asleep
- Daytime Napping
- Insomnia
- Nocturnal Waking
- Initiating/Maintenance

Duration of Insomnia in the National Comorbidity Survey Replication


n = 2,578
### Prevalence of Sleep Disturbance in Persons with Dementia and Their Family Caregivers

#### Caregivers

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCurry and Teri</td>
<td>68%</td>
</tr>
<tr>
<td>Pruchno and Potashnik</td>
<td>22–41% (men), 53–67% (women)</td>
</tr>
<tr>
<td>Wilcox and King</td>
<td>67% (women only)</td>
</tr>
</tbody>
</table>

#### Persons with Dementia

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carpenter et al.</td>
<td>40%</td>
</tr>
<tr>
<td>Craig et al.</td>
<td>42–54%</td>
</tr>
<tr>
<td>Lyketsos et al.</td>
<td>20–27%</td>
</tr>
<tr>
<td>McCurry et al.</td>
<td>35%</td>
</tr>
<tr>
<td>Moran et al.</td>
<td>25%</td>
</tr>
<tr>
<td>Pang, et al.</td>
<td>35–54%</td>
</tr>
<tr>
<td>Rabins</td>
<td>33%</td>
</tr>
<tr>
<td>Ritchie</td>
<td>19–44%</td>
</tr>
<tr>
<td>Thommessen et al.</td>
<td>25%</td>
</tr>
</tbody>
</table>

Possible Underlying Causes of Sleep Disturbance and Insomnia Symptoms

Common Conditions \(^1,^2\)

- Altered Sleep Regulation & Circadian Rhythms\(^1\)
  - Difficulty Initiating & Maintaining Sleep
  - Sleep Loss
- Medical, Neurologic, & Psychiatric Conditions\(^1\)
  - Chronic Pain Pulmonary Disease
  - Depression
  - SDB (Sleep Apnea) Restless Legs
- Psychosocial Factors\(^2\)
  - Late-Life Stressors


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Poor Health Impacts Prevalence of Insomnia in Older Adult Population

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Normal age-associated changes in sleep are

**NOT**

primarily responsible for increased prevalence of insomnia and other sleep disorders in older adults

Highest contribution is physical and mental health
Impact of Poor Sleep in Elderly Adults

- Difficulty Sustaining Attention & Slowed Response Time
- Decreased Ability to Accomplish Daily Tasks
- Impairments in Memory & Concentration
- Increased Consumption of Health Care Resources
- Increased Risk of Falls
- Shorter Survival
- Inability to Enjoy Social Relationships
- Increased Incidence of Pain
- Cardiometabolic Disease Risk? Depression Risk?

Cognitive Decline and Insomnia in Older Adults

* Adjusted for baseline cognitive function, age, race, education, income, and marital status


n = 6,444; age ≥65 years
Impact of Insomnia on Quality of Life

Axes represent subscales of the SF-36. All $P$ values < .05 (range .000-.023).

Days-Out-of-Role Associated with Insomnia and Comorbid Conditions in America Insomnia Survey

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total Sample</th>
<th>Ages 18-34 Yrs</th>
<th>Ages 35-59 Yrs</th>
<th>Ages 60+ Yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Days(^a)</td>
<td>(SE)</td>
<td>Days(^a)</td>
<td>(SE)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>.42(^b)</td>
<td>(.10)</td>
<td>.12</td>
<td>(.15)</td>
</tr>
<tr>
<td>Cardiovascular Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>.25(^b)</td>
<td>(.10)</td>
<td>-.18</td>
<td>(.25)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>.63</td>
<td>(.71)</td>
<td>-.05</td>
<td>(.23)</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seasonal allergies or hay fever</td>
<td>-0.18(^b)</td>
<td>(.07)</td>
<td>-.06</td>
<td>(.14)</td>
</tr>
<tr>
<td>Chronic bronchitis, emphysema, other</td>
<td>-.11</td>
<td>(.15)</td>
<td>-.22</td>
<td>(.12)</td>
</tr>
<tr>
<td>COPD</td>
<td>.80(^b)</td>
<td>(.35)</td>
<td>.04</td>
<td>(.24)</td>
</tr>
<tr>
<td>Musculoskeletal Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis (osteo or rheumatoid)</td>
<td>.16</td>
<td>(.14)</td>
<td>-.20</td>
<td>(.18)</td>
</tr>
<tr>
<td>Back or neck pains</td>
<td>.20(^b)</td>
<td>(.09)</td>
<td>.16</td>
<td>(.20)</td>
</tr>
<tr>
<td>Other Pain Disorders</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraine headaches</td>
<td>.11</td>
<td>(.10)</td>
<td>.05</td>
<td>(.11)</td>
</tr>
<tr>
<td>Other frequent or severe headaches</td>
<td>.29</td>
<td>(.14)</td>
<td>.05</td>
<td>(.16)</td>
</tr>
<tr>
<td>Chronic pain of any sort including</td>
<td>.48(^b)</td>
<td>(.09)</td>
<td>.43(^b)</td>
<td>(.17)</td>
</tr>
<tr>
<td>muscle, joint or nerve</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sleep Difficulties in Older Adults: Under-recognized in Medical Practice

Conclusions

- Although sleep patterns change with age, it is the change in the ability to sleep and co-morbid medical and psychiatric disorders that result in most sleep complaints in older adults.
- Sleep — similar to nutrition and physical activity — is an essential part of a healthy lifestyle for all.
- A potentially modifiable risk factor for age-associated impairments in mental and physical function.
Current State of OTC Therapeutics for Sleep Disturbance

Thomas Roth, PhD, Sleep Disorders and Research Center, Henry Ford Health System
Types of Sleep Aids

- Prescription drugs
- OTC drugs

- Herbal supplements: Cannot say anything about treating medical conditions because these supplements are not subject to clinical trials or manufacturing standards
- Alcohol
Indication

• Prescription hypnotics
  – Used for treatment of insomnia; no limitation on duration
• OTC agents
  – For occasional sleeplessness for 2 to 3 days
Longest Period of OTC and Rx Sleep Aid Use

### Number of Days in Last Month

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt;1</th>
<th>1-4</th>
<th>5-19</th>
<th>20+</th>
</tr>
</thead>
<tbody>
<tr>
<td>60+</td>
<td>9.1%</td>
<td>24.1%</td>
<td>31.2%</td>
<td>35.6%</td>
</tr>
<tr>
<td>65+</td>
<td>8.3%</td>
<td>24.7%</td>
<td>31.4%</td>
<td>35.6%</td>
</tr>
<tr>
<td>75+</td>
<td>7.4%</td>
<td>19.3%</td>
<td>31.6%</td>
<td>41.7%</td>
</tr>
</tbody>
</table>

Base: Experiencing sleep difficulties, reporting one or more symptoms of sleeplessness, and use OTC for sleep difficulties

NHWS US 2012: (SQ6) Thinking of the sleeplessness or difficulty sleeping that you experience, which of the following sleep problems or symptoms do you **regularly** experience?

NHWS US 2012: (HH10) Which of the following have you experienced in the past 12 months? <Sleep difficulties>

NHWS US 2012: (SD75) Do you use an over-the-counter or herbal products to treat your sleep condition?

NHWS US 2012: ((SD90) How many days did you use the following product(s) in the past month?

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Doxylamine

- Unisom SleepTabs, Equaline Sleep Aid, Good Sense Sleep Aid, etc.
- Very weak H1 antagonist; H1/M1 potency ratio low to moderate
- Pregnancy Category B
- No published placebo-controlled trials
US FDA Permitted OTC Sleep Aids

- **Diphenhydramine**
  - Nytol, Sominex, Tylenol PM, Excedrin PM, Advil PM, Unisom SleepGels, ZzzQuil, etc.
  - Very weak H1 antagonist; H1/M1 potency ratio low to moderate
  - Pregnancy Category B
  - 1 crossover study in 20 elderly patients with insomnia; decreased only awakenings vs placebo; AEs vs placebo: dry mouth (80% vs 65%), dizziness (25% vs 10%), and headache (20% vs 5%)


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Diphenhydramine

$1/\text{Relative Selectivity} \times 10,000$

**Beers Criteria**

**TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults**

<table>
<thead>
<tr>
<th>Organ System/Therapeutic Category/Drug(s)</th>
<th>Recommendation, Rationale, Quality of Evidence (QE) &amp; Strength of Recommendation (SR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergics (excludes TCAs)</td>
<td></td>
</tr>
<tr>
<td>First-generation antihistamines (as single agent or as part of combination products)</td>
<td>Avoid.</td>
</tr>
<tr>
<td>- Brompheniramine</td>
<td>Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity.</td>
</tr>
<tr>
<td>- Carbinoxamine</td>
<td></td>
</tr>
<tr>
<td>- Chlorpheniramine</td>
<td></td>
</tr>
<tr>
<td>- Clemastine</td>
<td></td>
</tr>
<tr>
<td>- Cyproheptadine</td>
<td></td>
</tr>
<tr>
<td>- Dexbrompheniramine</td>
<td></td>
</tr>
<tr>
<td>- Diphenhydramine (oral)</td>
<td>Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate.</td>
</tr>
<tr>
<td>- Doxylamine</td>
<td></td>
</tr>
<tr>
<td>- Hydroxyzine</td>
<td>QE = High (Hydroxyzine and Promethazine), Moderate (All others); SR = Strong</td>
</tr>
<tr>
<td>- Promethazine</td>
<td></td>
</tr>
<tr>
<td>- Triprolidine</td>
<td></td>
</tr>
<tr>
<td>Antiparkinson agents</td>
<td>Avoid.</td>
</tr>
<tr>
<td>- Benztrpine (oral)</td>
<td>Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease.</td>
</tr>
<tr>
<td>- Trihexyphenidyl</td>
<td></td>
</tr>
</tbody>
</table>

Residual Effect of Diphenhydramine 50 mg on PET

FIGURE 1. Images of BPR of $^{11}$C-doxepin in the human brain. The BPR images taken from healthy male subjects (n = 8) using PET 12 hours after oral diphenhydramine 50 mg (left), bepotastine 10 mg (middle), or placebo (right) administration, and their MRI-T1 images (far right) are shown in the transaxial (top), coronal (middle), and sagittal (bottom) sections for each treatment. White circles indicate the ROIs. The brain image of each subject was transformed to fit stereotaxic brain space (spatial normalization) and was averaged across each treatment to generate the mean images. Note that treatment with diphenhydramine results in significantly lower BPRs than the other 2 treatments.

Diphenhydramine Pharmacokinetics and Age

### Table 4. Tests of Neurologic Function

<table>
<thead>
<tr>
<th>NEUROLOGIC TEST</th>
<th>TEMAZEPAM VS. PLACEBO</th>
<th>DPH VS. PLACEBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word list</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Vocabulary</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Tapping board</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cancellation test-time</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Cancellation test-omissions</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Digit span forward</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Digit span reverse</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Digit symbol substitution</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

*Plus sign indicates better score on test during week when this agent was administered.*

Conclusions

• Duration of action of diphenhydramine increases with age
• Efficacy data in general are not available and almost no efficacy data in elderly
• Safety concerns relate to potential residual effects and anticholinergic side effects
Pharmacist Perspective on OTC Sleep Aids: Gaps in Therapies and Clinical Practice

Michael Toscani, PharmD, Rutgers Institute for Pharmaceutical Industry Fellowships, Ernest Mario School of Pharmacy
Review of Today’s Pharmaceutical Care

- Increase access to health care for consumers/patients
- Provide advice/direction
- Provide education/information
- Coordinate essential health information
- Manage/coordinate OTC sleep aid use with prescription medication dispensing and other pharmacist patient care services
- Perform patient triage and make referrals
• Pharmacists make an average of 28 OTC product recommendations per week and counsel 27 patients

• On average, 77% of patients purchase the OTC product recommended by the pharmacist

• On average, pharmacists spend 3.6 minutes with patients requesting OTC information

• After counseling patients on OTC products, most pharmacists refer them to another health care professional – Refer 73% of the time

• 44% of older adults experience disturbed sleep at least a few nights each week (National Sleep Foundation 2013)

• 23% report taking sleep medications in past 4 weeks (NHANES 2013)

• 15% to 18% use OTC sleep aid; 40% concurrently taking 1+ anticholinergic medication (Kantar 2013)
OTC Sleep Recommendations: *Pharmacy Today* Survey

**Sleep Aids (n = 1,256)**
- Unisom SleepTabs (doxylamine): 22%
- Unisom SleepGels (diphenhydramine): 21%
- ZzzQuil (diphenhydramine): 7%
- Nytol (diphenhydramine): 6%
- Sominex (diphenhydramine): 5%
- MidNite (herbal): 2%
- Other: 38%

Assessment of sleep health and use of OTC sleep medications should be part of the routine examination in all patients

- How many hours of sleep do you get, on average?
- Do you have problems falling asleep or staying asleep? How often?
- Do you feel sleepy, drowsy, or tired during the day?
- Do you take OTC medications to help you sleep?

** It takes less than 1 minute! **
Areas to Be Addressed in Older Adults: Sleep

• Is this occasional sleepiness (2-3 days) or a chronic problem? (OTCs are not indicated for chronic insomnia)

• OTC recommendations (i.e., diphenhydramine- and doxylamine-containing agents)

• What other conditions or treatments does the individual have that increases the potential risk in using these OTCs?
  – BPH, glaucoma, anticholinergic medication effects, alcohol, herbals, etc.

• What are the pharmacokinetic and pharmacodynamic considerations that may effect pharmacologic activity and adverse events?
  – Drug accumulation, daytime sleepiness, falls, driving, etc.
Contributions of Pharmacists

• Through pharmacists’ contributions, patients:
  – Will be better informed/educated
  – Will potentially avoid problems associated with these medications (e.g., decreased falls, fewer side effects)
  – Will be less likely to engage in risky medication behaviors
  – Will have better management of their condition
  – Will have a potentially improved quality of life
Thank You and Q&A

www.geron.org/otc
Publications and Toolkits

GSA Webinar on Sleep Health and the Appropriate Use of OTC Sleep Aids in Older Adults
In an effort for continual improvement, we would like to hear your thoughts. Please provide feedback by clicking the survey link at the end of the webinar.

Thank you again and we hope you enjoyed the program!