Sleep and Falls

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• Conflicts of interest:
  – Consultant for Merck
Significance: Falls in older adults

• Falls occur in approximately a third of community-dwelling older adults each year\(^1\)
  – >50% of institutionalized elders fall each year\(^2\)

• A major cause of functional impairments due to fractures and other injuries\(^2\)

• Mortality risk increased among frequent fallers
  – 9-year mortality risk increased by 60% in older white women\(^3\)
  – Risk may be even greater in older men\(^4\)

Significance: Falls in older adults

• Causes of falls are multifactorial
  – Poor balance & reaction time/gait problems (e.g. in those with postural hypotension)
  – Frailty
  – Urinary incontinence
  – Effects of medications (e.g. hypnotics, antidepressants)
    – *Sleep problems*??

• Sleep may represent a modifiable behavior to target for reducing risk of falls in older adults
Significance: Sleep and Falls

• Insomnia and other sleep problems increase with advancing age
• Evidence suggests increased fall risk in older adults with sleep problems
• **Controversy**: is it the sleep problem, or medications (e.g. hypnotics) used to treat the sleep problem that is responsible for increased fall risk?
  – Most studies have not examined the independent effects of disturbed sleep and medications used to treat sleep
Prevalence of insomnia symptoms by age group

Large-scale community survey of non-institutionalized American adults, aged 18–79 years

Sleep characteristics and history of falling in Australian nursing home residents

- n=150 nursing home residents
- Mean age 81 years, 66% female
- 44% fallers, 56% nonfallers during 1 year
- In multivariate models that accounted for use of hypnotic medications and other fall risk factors, only significant contributor to risk of falls:
  - self-reported poor or very poor sleep quality (OR=3.2, 95% CI 1.04-10.0; p=.04)
  - Hypnotic use and sleepiness (ESS) were not associated with greater risk of falls

Self-reported sleep and nap habits predict risk of falls and fractures\textsuperscript{1}

• Older women who reported taking daily naps were...
  – 32% more likely to experience two or more falls during the subsequent year of follow-up (OR=1.32; 95% CI=1.03-1.69)
  – 33% more likely to suffer a hip fracture during 6 years of follow-up (OR=1.33; 0.99-1.78)

• Long sleep duration (>10 hours per 24 hour period) was also associated with increased hip and non-spine fracture risk

• \textit{Results persist after accounting for benzodiazepine use}

Actigraphic measures of nightly sleep duration and risk of falls in older women¹ (SOF)

Risk of falls*

<table>
<thead>
<tr>
<th>Sleep duration (hours)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>:=5</td>
<td>2.0 (1.2 - 3.3)</td>
</tr>
<tr>
<td>&gt;5 to 7</td>
<td>1.5 (0.9 - 2.6)</td>
</tr>
<tr>
<td>&gt;7 to 8</td>
<td>1.0 (Reference)</td>
</tr>
<tr>
<td>&gt;8</td>
<td>1.1 (0.6 - 1.9)</td>
</tr>
</tbody>
</table>

n=2,978, mean age=83y


* Falls were ascertained by tri-annual questionnaire. 549 women (18.4%) suffered 2+ falls during approximately one year after sleep assessment. Results adjusted for age, race, BMI, depression, exercise, instrumental activities of daily living, comorbidities, cognitive function, and use of benzodiazepines and antidepressants.
Actigraphic measures of sleep and risk of falls in older women\(^1\) (SOF), additional results

- Results between sleep duration and fragmentation and risk of falls were unchanged by adjustment for benzodiazepine use
- Use of short-acting benzodiazepine use was associated with increased risk of frequent falls, even after accounting for objectively measured sleep
  - OR=1.53, 95% CI=1.00–2.32
- Use of long-acting benzodiazepines was not associated with increased risk of frequent falls, but use was less common and study power may have been an issue

Sleepiness, Urinary Incontinence, and Falls in Older Women

• 782 ambulatory, community-dwelling women aged 75 to 86 (Australian study, subjects selected at random from the electoral roll)

• Collected subjective data on daytime sleepiness, night-time sleep problems, urinary incontinence and falls (retrospective, past year)

• In multivariate analysis, significant risk factors for falls:
  – Urge incontinence: OR=1.76; 95% CI 1.29 – 2.41
  – Abnormal daytime sleepiness: OR=2.05; 1.21 – 3.49

State-of-the-Art Knowledge

• Non-vertebral fractures and dislocations increased after initial prescription for hypnotics\(^1\):
  – Large retrospective cohort study.
  – Community-based HMO members with initial prescription for zolpidem, alprazolam, lorazepam, or diazepam identified from pharmacy databases
  – Rates of hospitalization for fracture compared before and after prescription

## Hypnotics Prescriptions and Fracture\(^1\):
### Rate Ratio Post-treatment Compared to Pre-treatment

<table>
<thead>
<tr>
<th></th>
<th>Zolpidem</th>
<th>Alprazolam</th>
<th>Lorazepam</th>
<th>Diazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>10,857</td>
<td>20,429</td>
<td>42,080</td>
<td>16,372</td>
</tr>
</tbody>
</table>

### Non-vertebral fractures

<table>
<thead>
<tr>
<th></th>
<th>Rate Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zolpidem</td>
<td>2.55</td>
<td>(1.78 - 3.65)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>1.14</td>
<td>(0.80 - 1.64)</td>
<td>0.42</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>1.53</td>
<td>(1.23 - 1.91)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diazepam</td>
<td>1.97</td>
<td>(1.22 - 3.18)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

### Hip fractures

<table>
<thead>
<tr>
<th></th>
<th>Rate Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zolpidem</td>
<td>3.11</td>
<td>(1.96 - 4.91)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>1.46</td>
<td>(0.91 - 2.35)</td>
<td>0.1</td>
</tr>
<tr>
<td>Lorazepam</td>
<td>2.05</td>
<td>(1.58 - 2.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diazepam</td>
<td>2.03</td>
<td>(1.03 - 4.00)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

State-of-the-Art Knowledge, continued

• Nonbenzodiazepine Sleep Medications and Fractures in Nursing Home Residents¹:
  – Case-crossover study
  – 15,528 long-stay US nursing home residents, age 50+
  – Hip fracture documented in Medicare claims data (2007-2008)
  – Odds ratios for hip fracture compared exposure to meds during 0=29 days prior, compared with 60-89 and 120-149 days before (control periods).

Nonbenzodiazepines and Fractures in Nursing Home Residents

• Nonbenzodiazepine drug use 0-29 days before hip fracture increased risk by 66% (OR=1.66; 95% CI 1.45 – 1.90)

• Greater increase in risk observed for new prescriptions (OR=1.90; 1.60 – 2.26)

• Greater increase in those with urinary incontinence, and those requiring minimal supervision to transfer.

State-of-the-Art Knowledge, continued

• Nocturnal hypoxemia is related to increased risk of falls and fractures among older men\(^1\):
  – Older men with 10% or more of sleep time at O\(_2\) saturation of 90% or below had 43% increase in risk of experiencing 2+ falls in the subsequent year
  – 30-40% increase in risk of non-spine fracture among those with greater levels of nocturnal hypoxemia

• Sleep apnea may be another sleep disorder (other than insomnia/short sleep) related to increased fall risk.

Knowledge Gaps

• Does improving sleep result in fewer falls?
  – Which insomnia treatments offer best ‘balance’ for older adults in terms of improved sleep with fewest side effects
  – Do newer hypnotics (e.g. nonbenzodiazepines) result in decreased fall risk compared to benzodiazepines?

• What are the primary mechanisms linking disturbed sleep with risk of falls?
  – Although we have some good candidates (e.g. frailty, balance, hypnotic use, urinary incontinence, comorbidities), there is still no concrete evidence
Knowledge Gaps, continued

• Besides insomnia, what other sleep disturbances are related to increased fall risk, and what are the mechanisms?
  – Altered circadian rhythms?
  – Sleep apnea?
  – Restless legs syndrome?

• Extending findings to falls resulting in injury such as fractures
Research Opportunities

• Testing whether sleep interventions are effective in reducing the risk of falls in older adults
  – Comparative effectiveness studies of alternative insomnia treatments for insomnia/sleep problems in older adults, with falls as a major outcome
  – Especially testing hypnotics vs cognitive behavioral therapy and other non-pharmacological treatments

• Observational studies with comprehensive assessment of sleep (objective and subjective) and well-characterized for medication use, urinary incontinence, and other potential mediating factors
Research Opportunities, continued

• More comprehensive characterization of the falls outcome, to help understand mechanisms:
  – Night-time falls vs daytime falls
  – Circumstances of falls
  – Did a fracture or other injury result?