Sleep and Chronic Illness

John Park, MD
Assistant Professor of Medicine
Disclosure

• Speaker’s bureau for American Physician’s Institute
• Research grant with Dymedix, Corp.
Outline

• Normal sleep
• Chronic diseases and sleep
• Impact of poor sleep
• Treatment
Normal sleep
Normal Sleep Architecture
Normal Sleep

![Graph showing changes in sleep metrics with age](image-url)
Total Sleep

![Graph showing the relationship between age and total sleep]

Sleep 2004;27:1255
Arousals During Sleep

Graph showing the relationship between arousal index/TST and age (years), with a correlation coefficient of r = 0.852 (p < 0.00001).
Sleep Duration

Total Sleep Time (in hours)

Mean
- Workday/Weekday: 6 hrs 40 min
- Non-Workday/Weekend: 7 hrs 25 min

Sleep in America Poll, National Sleep Foundation, 2008
Sleep Needed

Hours of Sleep Needed to Function at Best During Day vs. Hours Slept on Workdays/Weekdays

- Less than 6: 15% needed, 16% slept
- 6 to less than 7: 22% needed, 28% slept
- 7 to less than 8: 30% needed, 32% slept
- 8 to less than 9: 26% needed, 18% slept
- 9 or more: 5% needed, 2% slept

Mean
- Hours needed: 7 hrs 18 min
- Hours slept: 6 hrs 40 min

Sleep in America Poll, National Sleep Foundation, 2008
Normal Sleep: Summary

• Most probably need about 7 – 7.5 hours of sleep
• Most get about 6.5 hours of sleep during the week
• Normal to have about 20 – 30 minutes of wake time after falling asleep
• Normal to see up to 15 – 20 arousals/hour of sleep
Chronic Disease and Sleep
Sleep Deprivation

- Insufficient sleep duration to support full level of functioning the next day (in alertness or performance)
  - Insufficient sleep
    - Most common
    - Sleep debt is cumulative
  - Poor quality of sleep
    - Due to sleep disturbances
Fatigue

• Different from sleepiness

• Types:
  • Difficulty in initiating activity due to weakness without objective causes
  • Difficulty in maintaining activity
  • Difficulty in concentrating or recall
Fatigue and Inflammatory Bowel Disease

Substantial Fatigue
- Ulcerative Colitis
- Crohn's Disease

Chronic Fatigue
- Ulcerative Colitis
- Crohn's Disease

Percent

Inflamm Bowel Dis 2011;17:1564
Fatigue and Inflammatory Bowel Disease

- Factors affecting fatigue
  - Disease symptoms
  - Hemoglobin
  - Altered sleep
  - Smoking
    - Crohn’s disease
    - Correlated with physical fatigue scores
  - Perceived stress
Sleep and Inflammatory Bowel Disease

Sleep Disruption

Inflamm Bowel Dis 2011;17:1564
Sleep Disturbance and IBD

- Urination: 60%
- Bowel Movement: 50%
- Breathing Problems: 40%
- Too hot/cold: 50%
- Bad dreams: 50%
- Anxiety: 30%

J Gastroenterol Hepatol 2007;22:1748
Sleep and Depression

Percent with chronic depression

Sleep Duration

<5  6  7  8  >9

Sleep 2011;34:1173
Fatigue and PSC

• Sense of well being, fatigue and depression was worse if you had inflammatory bowel disease in addition to PSC

• Fatigue was not related to severity of the liver disease but was related to gastrointestinal symptoms (reflux, abdominal pain, constipation, indigestion, and diarrhea) and depression

Scand J Gastroenterol 2004;39:961
Delayed Circadian Rhythm in Cirrhosis

Am J Gastroenterol 2010;105:1773
Chronic Disease and Sleep

• Disease states, hemoglobin, and altered sleep are among main contributors of fatigue
• Disease itself often cause interrupted sleep
• Co-existing depression will also impact sleep
• There may be a delay in circadian rhythm in cirrhosis
Impact of Poor Sleep
Effect of Sleep Disruption

Percent of Sleep

- Wake
- Light sleep
- Deep sleep
- REM sleep

Baseline
Disruption

Sleep 1985;8:11
Effects of Sleep Deprivation

• Mood
• Cognitive function
• Accidents
• Quality of life
• Immune function
  • Poor immune response
  • Increased cytokines
• Appetite
• Effect on the heart
Sleep Deprivation
Antibody Response

Figure. Antibody Titers at Baseline and 10 Days Following Influenza Vaccination

Sleep Deprived Subjects (n=11)

Control Subjects (n=14)

Mean Anti-Influenza IgG Titers, × 10^6

Time Relative to Influenza Vaccination
- Day 0
- Day 10

Subject

Mean (SD)

JAMA 2002;288:1471
Treatment
Conservative Management

- Maintain adequate sleep hygiene
  - Preparation for sleep
    - Slow down and dim the lights
    - Avoid mentally or physically stimulating activities
    - Use of thinking time
    - Caffeine and alcohol
  - Sleep environment
    - TV off or at least on a timer
    - Noise and light reduction in the room
    - Temperature adjustment
  - Bootzin technique
    - Stimulus control
Conservative Management

• Adequate bedtime
  • Goldilocks of sleep
  • Naps

• Watch your routine during your “sleep time”
  • Snacking, smoking, internet/working

• Avoid clock watching

• Individualized approach
Exercise: Acute

- Stage 1
- Stage 2
- Stage 3
- Stage 4
- SWS
- REM

Sleep onset latency
REM latency
Total sleep time
Awake time

Effect Size
Exercise: Chronic
Exercise

A. PSQI Score

- Exercise vs. Non-Physical Activity

B. CES-D Score

- Exercise vs. Non-Physical Activity

C. ESS Score

- Exercise vs. Non-Physical Activity

Sleep Med 2010;11:934
Exercise

• Moderate intensity
  • 30 – 60 minutes few days a week
  • Strength training
  • Start slow and gradually build up to target
  • If pain or symptoms worsen, reduce the intensity and slowly increase
Cognitive Behavior Therapy: Fibromyalgia

- Corrections of thoughts, behaviors, and beliefs that may negatively impact disease
- Many programs combine graded increase in activity

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CBT N</th>
<th>Mean(SD)</th>
<th>Usual care N</th>
<th>Mean(SD)</th>
<th>Std. Mean Difference IV, Fixed, 95% CI</th>
<th>Weight</th>
<th>Std. Mean Difference IV, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditional CBT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Huib</td>
<td>30</td>
<td>6.27 (2.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>O'Dr.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prins</td>
<td>170</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sharq</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Cochrane Database of Systematic Review 2008
Treat Co-existing Sleep Disorders

• Restless leg syndrome
  • Periodic limb movement disorder

• Obstructive sleep apnea

• Depression/anxiety disorder
Gabapentin and Pregabalin

- Pregabalin is FDA indicated for fibromyalgia
- Both have shown to:
  - Improve sleep
  - Improve pain
  - Improve fatigue
  - Improve quality of life

---

### Study or sub-category

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>N</th>
<th>PGB and GBT Mean (SD)</th>
<th>Placebo Mean (SD)</th>
<th>SMD (random) 95% CI</th>
<th>Weight %</th>
<th>SMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>02 Sleep - Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crofford Preg 300 mg</td>
<td>123</td>
<td>45.26 (19.20)</td>
<td>121</td>
<td>54.16 (19.20)</td>
<td>8.90</td>
<td>-0.46 [-0.72, -0.21]</td>
</tr>
<tr>
<td>Crofford Preg 450 mg</td>
<td>121</td>
<td>40.44 (19.20)</td>
<td>121</td>
<td>54.16 (19.20)</td>
<td>8.68</td>
<td>-0.71 [-0.97, -0.45]</td>
</tr>
<tr>
<td>Crofford Preg 150 mg</td>
<td>123</td>
<td>45.66 (19.30)</td>
<td>121</td>
<td>54.16 (19.20)</td>
<td>8.92</td>
<td>-0.44 [-0.69, -0.19]</td>
</tr>
<tr>
<td>Arnold Gabapentin</td>
<td>57</td>
<td>33.40 (19.50)</td>
<td>62</td>
<td>47.80 (20.90)</td>
<td>5.22</td>
<td>-0.71 [-1.08, -0.34]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>425</td>
<td></td>
<td>425</td>
<td></td>
<td>31.72</td>
<td>-0.56 [-0.71, -0.42]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2 = 3.35$, df = 3 ($P = 0.34$), $\beta = 10.4\%$
Test for overall effect: $Z = 7.54$ ($P < 0.00001$)

<table>
<thead>
<tr>
<th>03 Sleep - Mean change</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Arnold Preg 300 mg</td>
<td>183</td>
<td>-11.39 (18.80)</td>
<td>180</td>
<td>-6.65 (18.78)</td>
<td>11.32</td>
<td>-0.25 [-0.46, -0.05]</td>
</tr>
<tr>
<td>Arnold Preg 450 mg</td>
<td>185</td>
<td>-12.85 (18.63)</td>
<td>180</td>
<td>-6.65 (18.78)</td>
<td>11.31</td>
<td>-0.33 [-0.54, -0.12]</td>
</tr>
<tr>
<td>Arnold Preg 600 mg</td>
<td>188</td>
<td>-15.09 (18.92)</td>
<td>180</td>
<td>-6.65 (18.78)</td>
<td>11.30</td>
<td>-0.45 [-0.65, -0.24]</td>
</tr>
<tr>
<td>Mease Preg 300 mg</td>
<td>184</td>
<td>-19.14 (20.07)</td>
<td>187</td>
<td>-14.32 (20.10)</td>
<td>11.45</td>
<td>-0.24 [-0.44, -0.04]</td>
</tr>
<tr>
<td>Mease Preg 450 mg</td>
<td>183</td>
<td>-20.45 (20.16)</td>
<td>187</td>
<td>-14.32 (20.10)</td>
<td>11.41</td>
<td>-0.30 [-0.51, -0.10]</td>
</tr>
<tr>
<td>Mease Preg 600 mg</td>
<td>187</td>
<td>-19.52 (20.23)</td>
<td>187</td>
<td>-14.32 (20.10)</td>
<td>11.49</td>
<td>-0.26 [-0.46, -0.05]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1110</td>
<td></td>
<td>1101</td>
<td></td>
<td>68.28</td>
<td>-0.30 [-0.39, -0.22]</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2 = 2.72$, df = 5 ($P = 0.74$), $\beta = 0\%$
Test for overall effect: $Z = 7.11$ ($P < 0.00001$)

Total (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Placebo Mean (SD)</th>
<th>SMD (random) 95% CI</th>
<th>Weight %</th>
<th>SMD (random) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favours treatment</td>
<td>1535</td>
<td>1526</td>
<td>100.00</td>
<td>-0.39 [-0.48, -0.29]</td>
<td></td>
</tr>
</tbody>
</table>
Duloxetine

- Antidepressant

![Graph showing pain improvement with Duloxetine](image_url)

*Pain 2005;119:5*
Hydroxyzine in Cirrhosis

- Histamine blocker
- Caution in those with overt hepatic encephalopathy

Am J Gastroenterol 2007;102:744
Sodium Oxybate
Alternative Medicine: Insomnia

- Acupuncture and Acupressure: Insomnia
  - May improve sleep quality
  - Limited in size of the study and some inconsistencies in different studies

  Cochrane Database of Systematic Review 2007

- Yoga: Fatigue
  - Improved fatigue and vigor among breast cancer survivors

  Cancer 2011
Spa Therapy

RAND-36

Physical  Mental

Spa  Control  Spa  Control

Baseline  One month

Rheum 2005;44:539
Treatments

• Treatment of underlying disease
• Conservative treatments in sleep hygiene
• Exercise
• Cognitive Behavior Therapy
• Medications: from fibromyalgia managements
  • Pregabalin
  • Duloxetine
  • Others
• Some evidence for alternative medicine
When all else fails...
Thank you!