



INSOMNIA in the Primary Care Practice: Is there time? 1st Live Lunchtime Webcast

THE VALUE OF SLEEP

Sleep is Essential to Physical Health

Poor sleep increases the risk of:

- High blood pressure
- Metabolic syndrome
- Overweight/obese status
- Elevated C-Reactive protein
- Impaired immune response
- Diabetes

References:

Gangwisch JE et al., *Hypertension*, 2006; 47(5):833-9
Vorona RD et al., *Arch Intern Med.*, 2005; Jan 10; 165(1):25-30
Spiegel K et al., *Ann Intern Med.*, 2004; 141(11):846-850
Hall MH et al., *Sleep*, 2008; 31(5):635-643
Meier-Ewert HK et al., *J Am Coll Cardiol*, 2004; 43:678-683
Gangwisch JE et al., *Sleep*, 2007; 30(12):1667-73

Sleep is Essential to Mental Health

Insomnia is a risk factor for depression, anxiety and suicide.

Ford DE and Kamerow DB, *JAMA*, 1989; 262(11):1479-84
Neckelmann et al., *Sleep* 2007; 30(7):873-880
Perlis et al., *J Affect Disord* 1997; 42(2-3):209-12
Hall RC et al., *Psychosomatics* 1999; 40(1):18-27

Poor Sleep May Increase Pain

In patients with chronic pain, sleep disturbance is associated with more severe pain and greater disability.

In patients with chronic pain, concomitant depression and insomnia may worsen physical symptoms.

McCracken LM and Iverson GL, *Pain Res Manag*, 2002 Summer; 7(2):75-9
Wilson KG et al., *Clin J Pain* 2002 18(2):77-83

Note: this is a condensed version of Webcast available through www.TriadCME.com

Poor Sleep Impacts Performance

Sleep loss is associated with:

- Worker absenteeism
- Reduced productivity
- Driving impairment

Among medical interns, sleep loss is associated with more errors, adverse events and attention failures.

Ozminkowski et al., *Sleep* 2007 Mar 1; 30(3):263-73

National Sleep Foundation 2008 *Sleep in America* poll

Czeisler et al., *PLoS Medicine*, Vol. 3, No. 12

Pack et al., *Am J Respir Crit Care Med*. 2006 Aug 15; 174(4):446-54

Poor Sleep is Expensive

A 2007 study found that average direct and indirect costs for younger adults with insomnia were about \$1,253 greater than for patients without insomnia.

Among the elderly, direct costs were about \$1,143 greater for insomnia patients.

Ozminkowski RJ et al., *Sleep* 2007; 30(3):263-73

INSOMNIA OVERVIEW

Insomnia Prevalence

- Sleep disruption in general population ~30%
- Sustained insomnia with daytime functional impairment (= insomnia diagnosis) ~10%
- Symptoms in general practice ~50%

National Institutes of Health State of the Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults June 13-15, *Sleep* 2005 Vol. 28

Who is most at risk for insomnia?

Primary care physicians should have a high index of suspicion in at-risk patient groups, including:

- Elderly
- Women (esp. during perimenopausal, pregnancy)
- Patients with medical and psychiatric disorders
- Patients who work long hours (>50 hours per week) and/or shift workers

National Sleep Foundation 2008 *Sleep in America* poll

NIH Consensus State Sci Statements. 2005; 22:1-30.

Akerstedt T et al., *Sleep* 2002; 25(5):585-8

Medical/Psychiatric Conditions Associated with Complaints

Note: this is a condensed version of Webcast available through www.TriadCME.com

- Cardiovascular disease
- Obesity
- Diabetes
- Rheumatoid arthritis
- Fibromyalgia
- Epilepsy
- Cancer
- COPD
- Depression
- Anxiety Disorders
- Schizophrenia
- Dementia

NIH Consens State Sci Statements. 2005;22:1-30
Moldofsky H, *Rheum Dis Clin North Am.* 2002;28(2):353-65.
Mendez M, *J Clin Neurophysiol* 2001 (2):106-27
Spiegel K, *Ann Intern Med.* 2004;141:846-50
Kawakami MD, *Diabetes Care* 2004;27(1):282-3
Beszterczey A, *Can Med Assoc J* 1997 116(4):355
Klink M, *Chest* 1987; 91: 540-546

Why Should Insomnia Be Diagnosed and Treated?

Insomnia is a clue to patient health

- Sleep is sensitive to medical and psychiatric infirmity
- Nature, duration, and severity of sleep trouble is an indicator of a patient's physical and mental well-being

Insomnia is a disorder

- Has unique physiological distortions
- Leads to functional impairment

Insomnia is a risk factor

- Medical problems
- Psychiatric problems

TREATING INSOMNIA

When to Ask Patients about Their Sleep

Acute visits

- Sleep is an indication of overall well-being

Regular visits for medical/psychiatric problems

- Insomnia is OFTEN comorbid

Complete physical exams - ROS should include two questions:

- Do you have trouble falling asleep or staying asleep?
- Do you feel alert throughout the day?

If necessary, bring patients back to the office for a separate visit if not enough time

- Interview bed Partner

Note: this is a condensed version of Webcast available through www.TriadCME.com

- Use sleep diaries

Tools for Insomnia Screening and Diagnosis

[Insomnia Severity Index](#)

- Evaluates sleep symptoms and daytime functioning
- Self-report questionnaire (1-2 minutes)

[Epworth Sleepiness Scale](#)

- Evaluates daytime sleepiness
- Self-report questionnaire (1-2 minutes)

Sleep diaries (see Physician Kit or visit www.TriadCME.com)

Polysomnography

- Useful when sleep apnea is suspected
- Requires referral to sleep specialist

When to Treat Insomnia

- Initiate treatment when insomnia persists for more than 3-4 weeks or when sleep trouble is likely to cause daytime impairment
- When insomnia is comorbid with major psychiatric disorder, insomnia-specific therapy should be initiated concurrent with treatment of the psychiatric condition
- Sleep hygiene should be used for all patients
- Behavioral strategies can be employed alone or in combination with pharmacotherapy

NIH Consensus State Sci Statements. 2005;22:1-30

Fava M, et al. *Biol Psychiatry* 2006 59(11):1052

When to Refer to a Sleep Specialist

Refer patients for polysomnography when insomnia complaints are accompanied by snoring, breathing pauses during sleep and daytime symptoms such as sleepiness and fatigue.

How to Begin Insomnia Treatment

If the problem is acute (< 4 weeks):

- Identify precipitant and reverse where possible (e.g., new medication, incomplete post-op pain control, acute stress)
- Educate patients about sleep hygiene
- Short course of medications if insomnia is likely to pose risks

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For Chronic or Recurrent Insomnia

Develop a longer-term strategy:

- Identify precipitants/exacerbants and reverse where possible (e.g., medications)
- Identify comorbidities and optimize current treatment (e.g., DM, depression)
- Educate patients about sleep hygiene
- If another sleep disorder is suspected or patient fails to respond to therapy, consider polysomnography

Are Daytime Symptoms Present?

If there are no evident daytime consequences, educate patient about sleep hygiene and follow conservatively.

If daytime symptoms are present:

- Consider behavioral therapy in all patients with chronic insomnia, but particularly in those who will not or should not take hypnotics
- Consider pharmacologic therapy

Current Components of Insomnia Treatment

Behavioral therapy

- sleep hygiene
- cognitive behavioral therapy (CBT)

Off-label pharmacotherapy

Approved pharmacotherapy

***Cognitive Behavioral Therapy for Insomnia**

- Addresses factors that may perpetuate insomnia
- Incorporates multiple modalities that can be tailored to the patient's sleep symptoms
- As effective as prescription medications for treating insomnia in the short-term, may be more effective in the long-term
- Usually 5 weekly sessions (individual or group)
- No adverse effects

*See "Guide to CBT in Primary Care" in the Triad physician kit and at www.TriadCME.com under the Resources tab.

Who Can do CBT?

- Sleep center
- Psychologist
- Internet
- YOU and/or your staff
 - Training available at sleep centers
 - Certification

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Pharmacologic Approaches to Insomnia

- Prescription agents
- Approved hypnotics
 - benzodiazepine receptor agonists
 - benzodiazepines
 - nonbenzodiazepines
 - melatonin receptor agonist
- Non-approved for insomnia
 - sedating antidepressants
 - antipsychotics
 - anticonvulsants

- Nonprescription agents
- OTC agents
 - sedating antihistamines
- Others
 - valerian*
 - melatonin*
 - herbals*
 - alcohol*
 - dietary supplements*

**Not approved for this use*

NIH Consensus Development Program

- 2005 Chronic Insomnia SOS panel did not endorse as insomnia treatments
 - Complementary and alternative preparations
 - Antihistamines (OTC and prescription)
 - Antidepressants
 - Antipsychotics

NIH Consensus State Sci Statements 2005;22: 1-30.

OTC Sleep Aids (e.g., diphenhydramine)

- FDA regulated, but NOT approved for insomnia
- Antihistamines
 - Diphenhydramine
 - Doxylamine
- Alone or combined with analgesics
- Significant potential for adverse effects (diphenhydramine):
 - Residual sedation
 - Psychomotor impairment
 - Dizziness
 - Fatigue
 - Tinnitus

Note: this is a condensed version of Webcast available through www.TriadCME.com

Kryger, et al. Eds *Principles and Practice of Sleep Medicine* 4TH Philadelphia: Elsevier Saunders. 2005

Off-Label Insomnia Medications

Trazodone is among the most commonly prescribed medications for insomnia

- Not FDA-approved for insomnia
- No long-term use studies
- Broad array of side effects relative to insomnia medications

Medications Indicated for Insomnia

- Benzodiazepines (temazepam, triazolam, flurazepam, quazepam, estazolam)
- Selective benzodiazepine receptor agonists (BzRAs) (zolpidem, zaleplon, eszopiclone, zolpidem ER)
- Melatonin receptor agonists (MelRAs) (ramelteon)

BzRA Efficacy: Daytime Improvements

Recent studies with intermediate-acting BzRAs (e.g., eszopiclone and zolpidem ER) suggest that these drugs can improve daytime function (e.g., alertness) in patients with insomnia relative to placebo.

Krystal et al., 2003 *Sleep* Vol. 26., No. 7

Krystal et al., 2008 *Sleep* Vol. 30, No.1

Melatonin Agonists: Ramelteon*

- High selectivity and potency for MT1/MT2
- Negligible affinity for other active binding sites, including Bz, DA, and opiate receptors

**Ramelteon should not be used in patients with severe hepatic impairment or in combination with fluvoxamine.*

Kato K et al. *Neuropsychopharmacology* 2005 48:301-310

Melatonin Agonists: Efficacy

Recent studies with ramelteon suggest that this drug can reduce sleep latency in patients with insomnia relative to placebo.

Zammit G et al. *Sleep* 2005 28: Abstract Supplement A229. Abstract no. 0680

Medications Indicated for Insomnia...

- May be used alone or in conjunction with behavioral approaches
- Older agents are approved for short-term use
- Newer agents (e.g., eszopiclone, zolpidem ER and ramelteon) may be prescribed without limitation on duration of use

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Safety Data for Insomnia Medications

- Newer agents (e.g., eszopiclone, ramelteon, zaleplon, zolpidem ER) have 6-12 month placebo controlled safety studies
- None of the medications showed evidence of tolerance or duration-dependent AE risk

Insomnia Medications: Potential for Adverse Effects

- Potential adverse effects
 - Residual sedation
 - Related to dose and elimination half-life
 - Potential impairment of psychomotor skills in BzRAs
 - Tolerance
 - Some require progressively larger doses to achieve same results
 - Risk of symptoms on withdrawal
 - Potential for abuse in scheduled meds
 - Especially in those with history of drug abuse
- Anaphylaxis, rare
- Complex sleep-related behaviors (e.g., sleep driving and sleep eating)

Charney DS et al. In: Hardman JG, Limbird LE, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*, 10th ed; New York, NY: McGraw-Hill; 2001: 399

FDA Requests Label Change for All Sleep Disorder Drug Products, March 14, 2007: <http://www.fda.gov/bbs/topics/NEWS/2007/NEW01587.html> (accessed 3.11.2008)

Insomnia Medications: Potential for Drug Interactions

- Relatively low potential for overdose when taken alone (ramelteon has no potential for overdose)
- Potentially toxic or lethal when taken in combination with alcohol, other drugs
- Potential for worsening of depression

Kryger, et al. Eds *Principles and Practice of Sleep Medicine* 4TH Philadelphia: Elsevier Saunders. 2005, pages 448-449.

Advantages of Newer Agents Over Benzodiazepines

- Lower risk of adverse events (e.g., ataxia, amnesia, respiratory suppression) due to:
 - Greater selectivity
 - Average shorter half-life
- Lower abuse potential (ramelteon has no abuse liability; BzRAs are schedule IV controlled substances)

NIH Consens State Sci Statements 2005;22:1-30.

Kryger, et al. Eds *Principles and Practice of Sleep Medicine* 4TH Philadelphia: Elsevier Saunders. 2005, pages 448-449.

Kryger, et al. *Sleep Breath*. 2007; 11:159-64

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Abuse Liability of Hypnotics

- Abuse liability assessed as:
 - Likelihood of abuse
 - Consequences of abuse (toxicity)
- All BzRAs = class IV controlled substances
- MeIRAs = non-scheduled

Griffiths, R. R. and M. W. Johnson *Clinical Psychiatry* 2005 66 Suppl 9: 31-41

When to Reconsider a Therapeutic Approach

- Inadequate efficacy:
 - Review sleep hygiene, add CBT?
 - Alternate drug class (BzRA vs. MeIRA)
- Daytime sedation, psychomotor symptoms:
 - Reconsider CBT
 - Switch to MeIRA
- "Pharmacokinetic phailure:"
 - Tailor duration of action to sleep complaint and morning function

Summary

- Insomnia is prevalent in primary care practice, especially among women, older adults and people with medical and psychiatric conditions
- Insomnia is associated with low productivity, high healthcare costs and reduced quality of life
- Insomnia is responsive to treatment and treatment of insomnia effectively addresses nocturnal symptoms, improves daytime function, and may improve comorbid psychiatric and medical conditions



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