Sweet Dreams – HIV + Sleep

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HIV and Sleep Problems

An Accredited, Case Based Discussion

By

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## Disclosure – Dr. Moscovitch

<table>
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<tr>
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<td>Transport Canada, US DOT, FMCSA, WSIB</td>
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Learning Objectives

After completing this program, participants should be able to:

• Incorporate sleep assessment as a regular component of follow-up of patients with HIV
• Screen for sleep problems among patients with HIV, including use of standardized tools
• Prescribe medications, when appropriate, to improve sleep in patients with HIV
• Know when to refer patients with HIV to specialist care to manage their sleep problems
Program Outline

1. Presentation of two case studies
   – discussion about what to do in each case

2. Overview of sleep problems in HIV patients
   – epidemiology
   – impact
   – screening (including sleep questionnaire and how to interpret its results)
   – management

3. Revisit the case studies to discuss management in light of new information
William: Patient Overview

- 18-year-old male
- Diagnosed HIV+ two months ago
  - baseline CD4+: 390/mm³
  - baseline viral load: 330,000 copies/mL
  - no resistance mutations
  - prescribed single-tablet efavirenz, emtricitabine and tenofovir as ART
William: Presentation

- Patient returned two weeks after initiating ART
- Reported new-onset severe nightmares
  - vivid, caused him to relive sexual abuse suffered during childhood
  - frightened to go to sleep
  - new symptom since starting ART
William: Considerations for Management

- He is not receptive to changing therapy: strongly expresses wish to continue receiving ART in one pill
- Combined emtricitabine/rilpivirine/tenofovir is not an option since:
  - viral load > 100,000 copies/mL
  - patient eats at irregular and unpredictable hours
  - not covered by patient’s drug plan
Discussion

• How would you further investigate William’s sleep disturbances? What questions would you ask him?
Lucien: Patient Overview

• 47-year-old male
• Immigrant from Senegal
• Being treated for pulmonary tuberculosis
• Recent diagnosis of HIV+
  – baseline CD4+: 135/mm³
  – baseline viral load: 175,000 copies/mL
  – prescribed single-tablet efavirenz, emtricitabine and tenofovir as ART
Lucien: Other Medical History

- **Comorbidities**
  - overweight (BMI 32.2)
  - type 2 diabetes
  - dyslipidemia
  - hypertension
  - pulmonary tuberculosis (two months)

- **Medications**
  - metformin
  - atorvastatin
  - HRZE (isoniazid, rifampin, pyrazinamide and ethambutol) for tuberculosis; responding well
Lucien: Presentation
6 Months After Starting ART

• HIV status:
  – viral load: < 40 copies/mL
  – CD4+: 260/mm³

• Reports increasing fatigue since starting ART therapy: is now exhausted
  – blames his ART and would like to switch regimens

• Other laboratory analyses normal (hemoglobin, TSH/free T4, free + AM testosterone, LFTs, A1C)
Discussion

• What do you think is causing Lucien’s fatigue?
HIV and Sleep Problems

Overview of Sleep Problems in HIV patients
Sleep Problems in HIV: Overview

- Effects on the central nervous system may be among the first physical manifestations of HIV infection
- Sleep problems are experienced by 30% to 100% of HIV-positive adults (depending on definitions)
- Fragmented sleep may not be perceived by patients and is rarely accompanied by initial insomnia (difficulty falling asleep), but commonly causes daytime sleepiness or fatigue
  - can lead to difficulty concentrating, poor cognitive functioning, depressive symptoms, loss of daytime productivity
- Sleep problems may be substantially underdiagnosed in HIV patients

Sleep Problems Are Highly Prevalent in HIV

Systematic sample of outpatient HIV/AIDS clinic:¹
• 73% had a sleep disturbance according to PSQI

Cross-sectional study of adults with HIV:²
• 45% slept < 6 hours per night
• 34% had difficulty falling asleep
• 56% had fragmented sleep

BEA HIV national Canadian survey:³
• 62% had difficulty falling asleep and half of these (31% of total) reported this as bothersome

PSQI = Pittsburgh Sleep Quality Index; BEA HIV = Behaviour and Attitudes in HIV.
Possible Causes of Sleep Problems in HIV

- Primary sleep disorders (e.g., Sleep Apnea, RLS, PLMS, Primary Insomnia)
- Psychiatric disorders
- Psychosocial stressors
- Immune dysregulation
- Virus progression
- Neuronal damage
- Comorbid medical conditions
- Adverse drug effects

Proposed Associations

HIV Infection → Immune Responses → Sleep → Neuro-cognition

Picture of Normal Sleep

8-hour EEG recording in a healthy person

Wake
REM sleep
Stage 1 sleep
Stage 2 sleep
Slow-wave sleep

0 1 2 3 4 5 6 7 8
Hours in bed

EEG = electroencephalogram; REM = rapid eye movement.
Hypnogram in a Patient
## Differential Diagnosis of Insomnia in HIV


<table>
<thead>
<tr>
<th>Etiologies</th>
<th>Considerations</th>
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<tbody>
<tr>
<td>Primary insomnia not related to underlying condition/treatment</td>
<td>Should be treated with consideration given to the role of sleep hygiene counselling and to concomitant medications</td>
</tr>
<tr>
<td>Non-HIV medications that may cause insomnia side effects</td>
<td>Beta-blockers, bronchodilators, calcium channel blockers, corticosteroids, decongestants, immunomodulators (e.g., interferons), trimethoprim-sulfa, dapsone, amphotericin, fluconazole, isoniazid, diuretics taken at bedtime, varenicline</td>
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<tr>
<td>Medical conditions</td>
<td>Hyperthyroidism, chronic renal failure, lung disease, congestive heart failure, pain, diarrhea, incontinence, fever, dyspnea &amp; sleep apnea, periodic limb movements in sleep or restless limb syndrome</td>
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<tr>
<td>Mental health etiologies</td>
<td>Side effects of psychotropic medications, including SSRIs; psychiatric disorders, including mood and anxiety disorders, mania &amp; psychosis</td>
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<tr>
<td>Substance-use etiologies</td>
<td>Illicit drug use, particularly stimulant drugs; alcohol and caffeine consumption; nicotine</td>
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<tr>
<td>ARV medications</td>
<td>[See following slides]</td>
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SSRIs = selective serotonin reuptake inhibitors.
Sleep Problems in HIV: Impact

• Sleep problems have been linked to:
  – reduced quality of life
  – treatment non-adherence
  – neurocognitive impairment

### Self-reported Symptoms, Including Insomnia, Impact Adherence to ART

<table>
<thead>
<tr>
<th>Self-reported Symptom</th>
<th>Odds Ratio for Non-adherence (95% CI)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Vision problems</td>
<td>6.06 (1.92 – 19.1)</td>
<td>0.002</td>
</tr>
<tr>
<td>Nausea</td>
<td>5.80 (2.38 – 14.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Confusion</td>
<td>4.27 (1.74 – 10.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Taste perversion</td>
<td>3.31 (1.24 – 8.91)</td>
<td>0.03</td>
</tr>
<tr>
<td>Anxiety</td>
<td>3.30 (1.80 – 6.04)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Anorexia</td>
<td>3.07 (1.23 – 7.71)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Insomnia</strong></td>
<td><strong>2.32 (1.19 – 4.48)</strong></td>
<td><strong>0.02</strong></td>
</tr>
<tr>
<td>Abnormal fat accumulation</td>
<td>2.06 (1.06 – 4.06)</td>
<td>0.04</td>
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Univariate analysis.
HIV and Sleep Problems

Screening for Sleep Problems in HIV
Screening for Sleep Problems Should be Routine in HIV Management

- Healthcare professionals should ask patients, at routine monitoring visits, about quality of sleep and difficulty initiating or maintaining sleep.

- Healthcare professionals should determine whether a patient’s insomnia is acute, chronic, primary, or secondary.

Adapted from: New York State Department of Health AIDS Institute. Mental Health Approach and Differential Diagnosis.
Insomnia: Time-based Classification

- Acute
  - transient or short-term insomnia (< 1 months)

- Chronic
  - persistent insomnia (≥ 1 month)
  - Lasting frequently for years

Primary Insomnia

• Diagnosis of exclusion
• Common characteristics:
  – “light” sleepers
  – inability to relax
  – often sleep better away from home
  – insomnia becomes pronounced during stress

Secondary Insomnia

- Associated with:
  - medical, psychiatric, and neurological disorders
  - certain medications
  - alcohol/stimulants
  - specific sleep disorders
    - restless legs syndrome
    - sleep apnea
    - circadian rhythm sleep disorder

Jiva TM. Sleep Rev 2003; 4.
Sleep & Fatigue Wellness Screening Questionnaire

Consider Recommending a Sleep Diary

http://www.sleeplab.ca/SleepDiary.pdf
Sleep Hygiene Program:

Dr. Adam’s Commandments for Better Sleep

Patient Name: ________________________________  Date: _____________________________

Start this program only after you have filled out one week of the accompanying sleep log, as your baseline (starting point).

1. Time in bed is restricted to _____ hours, between _____ and _____. Keep this schedule 7 days per week, within reason.

2. Two hours before bed begin to disengage from the day’s activities. You can have a hot bath to slightly raise your body temperature. Do something relaxing after that until bedtime.

3. Your bedroom should be dark, quiet and comfortable. Use it only for sleep and sex. Remove the clock from your bedroom or at the very least, turn it around so you can’t see it. If you get up during the night, DO NOT look at the clock.

4. If you have not fallen asleep within 20-30 minutes (just estimate), or if you wake up and can’t get back to sleep again, get up and go to another room, to do something relaxing and non-stimulating. Go back to bed only when you feel sleepy. If you are not sleepy, don’t go back to bed.

5. Within two hours of awakening in the morning, get approximately 30 minutes of direct sunlight (outside, no sunglasses), or discuss with your Dr. use of a light unit to be prescribed. Do not use one without medical supervision.

6. Eat regular meals and a balanced diet. Avoid heavy, spicy meals close to bedtime.

7. Try to get some exercise every day, but nothing strenuous within 4 hours of bedtime.

8. Either stop smoking totally or do not smoke after 7PM or during the night. Avoid caffeine or drink no more than 3 cups of caffeinated beverages a day, none later than 2PM. Have no more than 2-3 drinks of alcohol on any given day.

9. Learn simple relaxation methods to help you get to sleep and turn your mind off, such as progressive relaxation techniques, self-hypnosis, meditation etc. Our therapist can help guide you with that.

10. □ Do not nap during the day  □ Take naps consistently around _____ for 20-30 minutes. Discuss the catnap tape with your sleep clinician.

11. Take Calcium 500 mg and Magnesium 250 mg approximately 30 minutes before bedtime with a light snack and a glass of apple or grape juice.

12. Medications – sleeping pills are used as an aid only, until the non-medication measures become effective.

13. Take _______ mg of ______________________ □ at bedtime □ 30 minutes before bedtime.

14. Other Instructions: _______________________________________________________________________

BE PATIENT. The first few weeks can be quite difficult, but most people will notice some improvement in the first month. However, it usually takes between 3-6 months to obtain the full benefits from this program. Your sleep problem did not develop overnight. There are no instant fixes either.

DON’T GIVE UP! YOU CAN HAVE A RESTFUL AND REFRESHING SLEEP.

If you have any questions or concerns, call Debbie at (416) 784-1430
### Considerations for Pharmacotherapy (1)

Select the agent with the best likelihood of addressing (or at least not exacerbating) the underlying symptoms contributing to the patient’s insomnia

- e.g., depression, anxiety, neuropathic pain

Ensure that the agent selected does not have potentially deleterious effects on comorbid conditions

- e.g., benzodiazepines: contraindicated in untreated obstructive sleep apnea; may cause cognitive impairment which also impacts sleep; have long half-lives which contribute to increased adverse effects in patients with liver disease

HIV and Sleep Problems

Case Studies Revisited
William: Review

- 18-year-old male
- Returned two weeks after initiating single-tablet efavirenz, emtricitabine and tenofovir
- Reported new-onset severe nightmares
  - vivid; caused him to relive sexual abuse suffered during childhood
  - frightened to go to sleep
  - insists on single-tablet therapy
Discussion

• Given what we have just discussed, how would you recommend managing William’s nightmares?
William: Management

- Information and counselling about sleep hygiene
- Short-term benzodiazepine (lorazepam 1 mg po qhs x 2 weeks)
  - plan to treat to desired effect, then attempt to wean the patient back off the medication
- With lorazepam therapy, the nightmares stopped
  - at end of 2 weeks, dose reduced to 0.5 mg qhs for 1 week and then, with no return of the nightmares, cessation of lorazepam
- Nightmares have not returned
Lucien: Review

- 47-year-old man from Senegal
- Reports increasing fatigue since starting single-tablet efavirenz, emtricitabine and tenofovir; is now exhausted
  - blames his ART and would like to switch regimens
Discussion

• Given what we have just discussed, how would you recommend managing Lucien's fatigue?
• Responses to sleep questionnaire indicated high risk for sleep apnea
• Assessment by a sleep specialist was recommended
  – patient was receptive to this suggestion
• Sleep study showed that the patient had obstructive sleep apnea
  – sleep specialist recommended management with a continuous positive airway pressure (CPAP) device
• Once this treatment was initiated, the patient reported a resolution of his fatigue
Sleep Apnea on PAP Treatment
Specialized Sleep Centres

- Approximately 150 sleep labs/clinics in Canada (about 125 in Ontario)
- Most consultations and many specialized services at these clinics are covered by provincial healthcare with appropriate referrals
- **Multidisciplinary** labs/clinics tend to be those based in universities or major teaching hospitals
- Canadian Sleep Society website provides a listing/map of sleep clinics
  - [www.canadiansleepsociety.ca/usermap/action/nationalmap](http://www.canadiansleepsociety.ca/usermap/action/nationalmap)
HIV and Sleep Problems: Summary

• When faced with HIV-positive patients with sleep-related complaints, use a sleep questionnaire and take a full history to fully understand the cause(s) of the sleep problems.

• An interdisciplinary approach is needed to diagnose and manage sleep problems in patients with HIV.