

# EPEEC-O

Education in Palliative and End-of-life Care - Oncology

## **Participant's Handbook**

Module 31:

**Symptoms –**

**Insomnia**

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**EPEC-O: Education in Palliative and End-of-life Care for Oncology.**  
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**ISBN: 0-9714180-9-8**

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The EPEC Project™ was created with the support of the American Medical Association and the Robert Wood Johnson Foundation. The EPEC-O curriculum is produced by The EPEC Project™ with major funding provided by the National Cancer Institute, with supplemental funding provided by the Lance Armstrong Foundation. The American Society of Clinical Oncology partners with the EPEC-O Project in dissemination of the EPEC-O Curriculum. Acknowledgment and appreciation are extended to Northwestern University's Feinberg School of Medicine, which houses The EPEC Project.

Special thanks to the EPEC-O Team, the EPEC-O Expert Panel, and all other contributors.

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## Case\*

A.P. is 53-year-old woman who is admitted to a home hospice program with metastatic breast cancer, mild dyspnea, and bone pain. She is still able to walk with assistance and enjoys visiting with family and friends and playing with her two small grandchildren. Her hospice nurse reports that she is not sleeping well at night and the family has requested a sleeping medication. Her sleep problems began within the past two weeks. She has difficulty falling asleep and wakes up at least twice during a typical night, but does not have early morning awakening. She often takes brief naps in the daytime. Further history reveals that she is reluctant to take sustained-release oral morphine as prescribed (60mg twice daily) for fear of addiction and sedation, and uses caffeinated beverages to prevent sedation from the 10mg immediate release breakthrough doses she does take. Daytime pain control is acceptable (usually a 2 out of 10), but pain flares late at night are common. She has recently moved to her daughter's home after a recent discharge from hospital to facilitate her hospice care. With encouragement, she agrees to try taking the sustained-release morphine as prescribed, augmented by a nonsteroidal anti-inflammatory agent. She requests that her bed be moved to her daughter's home for her use. She is also advised to avoid caffeine and daytime naps (if possible), and to do her best to maintain a consistent sleep schedule. She achieves reliable pain relief and is able to sleep without interruption most nights. Though a benzodiazepine hypnotic is prescribed for PRN use, it is only rarely needed.

\* This case is not on an EPEC-O Curriculum trigger tape.

## Introduction

Insomnia is *an experience of inadequate or poor quality sleep characterized by one or more of the following: difficulty falling asleep, difficulty maintaining sleep, early morning awakening, non-refreshing sleep or daytime consequences of inadequate sleep, eg, tiredness or fatigue, anergia, poor concentration, or irritability.*<sup>1</sup>

Insomnia is a largely subjective symptom. From a pragmatic perspective, insomnia is significant if it causes consequences. The goal of insomnia management in the cancer patient is to restore the quality and restfulness of sleep.

Insomnia has a negative impact on quality of life in sufferers. Poor sleep has obvious effects on fatigue, energy, and mental and physical stamina. Insomnia interferes with a patient's ability to enjoy relief that may be gained from effective management of other symptoms. Additionally, inadequate sleep has been associated with increases in pain and perceived discomfort, diminished coping capacity, and reductions in measures of global quality of life.<sup>2,3,4,5</sup>

## Prevalence

Insomnia is a very common complaint. Some 30-40% of adults in the general primary care population report difficulty sleeping at some time over a 12-month period, and 10-

15% report chronic problems with insomnia.<sup>1</sup> The prevalence of insomnia increases with age and is associated with physical illness such as cancer. In most studies of insomnia among cancer patients, the majority of respondents reported insomnia. Studies show prevalence rates as high as 63%.<sup>6,7,8,9</sup> In one study of patients on a palliative care unit, 77% were taking sedative-hypnotic medications at the time of admission.<sup>10</sup>

## Prognosis

With effective intervention, restful sleep can be restored. However, as in the general population, a significant subset of cancer patients who complain of difficulty sleeping may have chronic insomnia. Published studies suggest that a substantial majority of cancer patients with sleep problems may have long-standing problems with sleep.<sup>8, 11</sup> In such instances, insomnia may predate the cancer diagnosis. The impact of disturbed sleep or sleeplessness on cancer prognosis is unclear.

## Pathophysiology

Insomnia can be caused by a variety of factors, ranging from disruptions of the neurophysiology of sleep to the consequences of physical or mental disorders to simple interruption of normal sleep habits.

During a typical night of restful sleep, an adult cycles through physiologic stages of sleep multiple times.<sup>12</sup> These stages progressively deepen until rapid eye movement (REM) sleep is achieved. Many primary sleep disorders, eg, sleep apnea, restless legs syndrome, periodic limb movement disorder, cause disruptions in the normal architecture of sleep and can be detected readily by observation and polysomnography, as performed in a clinical sleep lab.

Physical symptoms common in advanced cancer, eg, pain, dyspnea, cough, nausea, or pruritus, whether due to the tumor itself or treatment prescribed for the tumor, are likely to interfere with sleep. Prescription medications, eg, psychostimulants, corticosteroids, over-the-counter medications, or other substances with stimulating effects can interfere with restful sleep. Caffeine, even in modest amounts, can interfere with sleep. Also consider withdrawal from sedating substances, eg, alcohol, benzodiazepines.

Non-physical factors can also lead to disturbed sleep. Depression is commonly associated with or complicated by insomnia. One of the most common signs of a major depressive episode is sleep disturbance characterized by early morning awakening.<sup>13</sup> Worry, tension, or anxiety can cause insomnia by interfering with the ability to relax and fall asleep. Patients with chronic insomnia often develop poor sleep habits, and attention to improving these habits, ie, practicing good sleep hygiene, can lead to improved sleep.<sup>1</sup> Patients who are hospitalized or must sleep away from home for cancer treatments may suffer from sleep disturbance as a consequence of being in an unfamiliar environment at night, with unfamiliar surroundings, or intrusive ambient noises.

## Assessment

While diagnostic instruments for insomnia exist especially for specific types or causes of insomnia, the best approach to diagnosing insomnia in the clinical oncology setting is the clinical, subjective approach noted above – insomnia is present if the quality or restfulness of sleep is disturbed to the extent that it causes consequences.

Focus on determining the course and pattern of the sleep problem. If insomnia is a problem of fairly recent onset, focus on concurrent nighttime symptoms, eg, pain, dyspnea, recent medication changes, changes in substance use (especially caffeine and alcohol), stress related to recent life events, or any necessity of sleeping away from home. More chronic sleep problems may indicate an underlying problem such as a primary sleep disorder or depression.

Definitive assessment of primary sleep disorders is best performed in a clinical sleep laboratory. Often, polysomnography and overnight monitoring and observation of sleep are required to establish a firm diagnosis. That said, clues are often evident in patients who report insomnia from common sleep disorders.<sup>1</sup> Patients with restless legs syndrome often complain of ‘crawling feelings’ in the lower extremities as they try to fall asleep. Bed partners of those with periodic limb movement disorder often report that sufferers make jerky movements or inadvertently kick their partners while asleep. Partners typically report loud snoring punctuated by halting apnea spells when the diagnosis is sleep apnea.

Patients who complain of insomnia may benefit from a discussion clarifying the nature of the problem. The high degree of variability among individuals in the ‘normal’ amount of sleep needed to feel rested makes judging insomnia based on hours spent sleeping very difficult. Often, people become concerned if their usual sleep pattern becomes disturbed – if they do not sleep as many hours as they have become accustomed to sleeping or if their sleep becomes more fragmented in the setting of an illness such as cancer. As adults age, total sleep time and the percentage of time spent in REM sleep naturally decrease. Patients with cancer, especially if the tumor or its treatments induce fatigue that necessitates daytime naps, often spend fewer hours asleep at night than usual. As long as sleep is of sufficient quality and duration to be satisfying and restful, the number of hours per day spent asleep or the frequency of sleep periods required is inconsequential. Of course, if most of the day must be devoted to rest and sleep when the patient would otherwise choose to participate in waking activities, then this sleep pattern is a problem. Additionally, it is best for patients to try to establish some regular cycle of sleep with consistent times to go to bed and arise, even if a regular nap needs to be incorporated into this schedule.

As illness progresses and death approaches, wakefulness is commonly punctuated by periods of sleep, and vice versa. Day-night reversal is common. Any disruption of the sleep-wake cycle in a patient with advanced illness should prompt an assessment for the presence of delirium.

## Management

The overall goals of insomnia management in the cancer patient are restoration of adequate restful and satisfying sleep and optimization of perceived quality of life. Once complicating disorders, eg, sleep disorder, depression, symptoms (pain, cough, etc.) and other factors, (caffeine overuse, situational factors, etc.) have been ruled out or treated appropriately, three general approaches to managing insomnia remain: 1) improving sleep hygiene, 2) behavioral interventions to improve sleep quality, and 3) pharmacologic treatments to promote sleep.

### Sleep hygiene

The simplest and best understood of these approaches is promoting the practice of good sleep hygiene.<sup>1,14</sup> Though these pointers are fairly intuitive and may be limited in how much benefit they yield for patients with complicated insomnia problems, they are often neglected and can provide help toward better sleep without cost, adverse effects, or need for refills. Patients should be encouraged to adhere to as much of the following advice about good sleep habits as is practical given their situation, their cancer, and their treatments:

- Try to go to sleep and wake up at the same time of day.
- Minimize use of caffeine and nicotine (especially late in the day, though use at any time can interfere with sleep).
- Avoid alcohol use at night.
- Avoid heavy meals late at night (a light snack at bedtime may help induce sleep, especially if hunger pangs keep someone awake).
- Avoid excessive fluids before bedtime.
- Consider moderate regular exercise, but not just prior to retiring.
- Minimize noise, light, and temperature extremes in the bedroom.
- Consider a bedtime ritual, eg, ‘winding down’ with a warm bath or some light reading, before attempting to fall asleep.

### Behavioral interventions

Behavioral measures, including relaxation techniques, sleep restriction, stimulus control, and cognitive therapy interventions are underutilized and likely to be more effective for chronic insomnia problems than hypnotic medications.<sup>15</sup> Relaxation techniques range from simple maneuvers that can be easily taught and practiced, e.g., simple abdominal breathing, progressive muscle relaxation, to techniques such as hypnosis or biofeedback which are administered by trained professionals. Relaxation tapes, mediation, or contemplative prayer can also be sufficiently relaxing to promote sleep. All relaxation

techniques require a commitment to practicing the technique so that the patient can gain enough facility with the technique to use it to their benefit when needed. Relaxation techniques are most helpful in promoting sleep onset.

Sleep restriction is a technique aimed at reducing fragmentation of sleep by improving sleep efficiency, ie, the percentage of the total time spent in bed that one spends asleep.<sup>15</sup> This technique is initiated by strictly limiting the time one spends in bed to the estimated number of hours one spends asleep, eg, if one estimates sleeping only four hours total of ten hours spent in bed at night, bedtime is adjusted to spend only four hours in bed. The wake time is kept constant and bedtime is adjusted to limit time spent in bed. Although a brief daytime nap may be needed in the first few days of the trial, effort should be made to limit sleep to nighttime as much as possible. The goal is to induce enough sleep deprivation to improve sleep efficiency for the restricted time in bed as close to 100% as possible. Once this is achieved, bedtimes can be moved back (in 30-minute increments every few days) until a fully restful night of sleep is achieved, as long as high sleep efficiency is maintained.

The theory behind stimulus control emerges from a conditioned learning view of insomnia. The goal of this intervention is for the patient to ‘unlearn’ associations between being in bed and doing anything other than sleeping.<sup>15</sup> Patients are instructed to go to bed only when they feel sleepy, and not to stay in bed making futile attempts to sleep if sleep does not come. After twenty minutes without sleep, patients should get out of bed and not return until feeling sleepy again. Other activities such as reading, eating, or sexual activity, must be undertaken in other parts of the home during a stimulus control intervention. Sleeping is prohibited anywhere other than the bed, and patients must maintain a regular wake up time. For motivated patients, stimulus control can be very helpful in promoting sleep onset and improving sleep hygiene.

Interventions incorporating cognitive therapy approaches also show potential to relieve insomnia. In a series that included cancer survivors, sleep was improved after a brief series of cognitive intervention sessions aimed at reducing dysfunctional, self-critical, or counterproductive thoughts that can lead to dysphoria, worry, and distress.<sup>16,17</sup>

## **Pharmacological management**

Pharmacologic interventions have an important role in the management of insomnia in cancer patients.<sup>18</sup> Their use in clinical practice, however, probably exceeds their proper role, especially over the course of chronic insomnia.

Most prescription hypnotics are indicated for brief periods of use (usually less than 14 days), because the rapid development of tolerance can lead to loss of effectiveness, dependence on medication for sleep onset, and changes in sleep architecture that paradoxically worsen the quality and restfulness of sleep.<sup>12,19</sup> Although newer agents may hold promise for prolonged efficacy and tolerability, a sleeping pill alone is not the answer for most patients with sleep problems over the long term.<sup>20</sup>

**Benzodiazepines** are the most commonly used prescription hypnotics, because of their reliable short-term efficacy and favorable safety profile relative to other medication classes, eg, barbiturates. Use benzodiazepines, eg, lorazepam (0.5-2 mg PO nightly as needed), temazepam (15-30 mg PO nightly as needed), and triazolam, at the lowest effective dose for short periods of time. Titrate the dose to give good sleep without residual sedation the following day. Longer-acting benzodiazepines, eg, diazepam, clonazepam, are more likely to have carryover sedation.

**Other newer GABA-receptor agonists**, eg, eszopiclone, zaleplon, and zolpidem (5-10 mg PO nightly as needed), may have some modest advantages relative to benzodiazepines such as less alteration of normal sleep architecture and less risk of amnesia. Whether such differences translate into clinically relevant advantages for these more expensive medications is unclear.<sup>21</sup>

**Antidepressant medications** are clearly indicated when sleep disturbance is judged to be a consequence of clinical depression. Sedating antidepressants, while commonly used to promote sleep even in the absence of a clinical depression, are not formally indicated for management of insomnia and are not well studied as off-label treatments for this indication. Tricyclic antidepressants, most commonly amitriptyline (10-25 mg PO nightly) and doxepin (10-25 mg PO nightly), are sometimes used as hypnotics. Low doses are commonly employed for this purpose. Fortunately, most of the troublesome adverse effects of tricyclics, eg, constipation, dry mouth, orthostasis, are dose related. Note, however, that effects on heart rate and cardiac conduction are not as clearly dose related.<sup>22</sup> Tricyclics may be particularly helpful when insomnia is comorbid with neuropathic pain or anorexia. Mirtazapine (15 mg PO nightly) also has the advantage of promoting appetite as well as sleep onset, and has a milder adverse effect profile than tricyclics, though it is more expensive.<sup>23</sup>

**Trazodone** in doses well below the antidepressant dose range, is commonly used to help promote sleep, though orthostasis and priapism are potential adverse effects.<sup>24,25</sup> Start with 50 mg PO nightly and titrate up every 7 days to effect (400 mg maximum).

**Antihistamines**, as contained in common over-the-counter sleep aids, and alternative agents, such as melatonin and L-tryptophan, are also used by patients suffering from insomnia, though available data are not sufficient to recommend their routine use.

## Day-night reversal

When delirium is present, efforts to reverse the underlying cause and/or cautious treatment with low doses of neuroleptic agents can relieve this circadian disruption.

- Chlorpromazine, 10 – 30 mg PO nightly
- Seroquel, 100 – 400 mg PO nightly

In the absence of delirium, a patient's fragmented sleep can still be distressing to caregivers whose sleep cycles are not synchronous with those of their medically ill loved



ones. Careful consideration must be given and clinical judgment exercised to determine whether this fragmentation of sleep meets the definition of insomnia proposed above, and whether therapy is worth the risk of oversedating the patient during periods of wakefulness.

## Summary

Insomnia is a common problem that complicates and compounds the suffering of patients with cancer. Although it is a subjective symptom and requires a clinical diagnosis, the practical rule of thumb - that insomnia results when the quality or restfulness of sleep is disturbed to the extent that it causes consequences - can be helpful in detecting problems of clinical significance. Effective management requires recognition of remediable problems that cause or complicate insomnia. Once other treatable conditions are recognized and adequately managed, management of remaining insomnia in the cancer patient should attend to good sleep hygiene. While hypnotic medications have a role, particularly in the short-term management of insomnia, behavioral interventions are underutilized and can be effective in promoting sleep over the long term.

## Key take-home points

1. Patients and families may be disturbed by insomnia, particularly day-night reversal.
2. Assess and recommend good sleep hygiene.
3. Antihistamines or benzodiazepines frequently manage insomnia effectively.
4. Trazodone may be particularly useful in the frail and elderly.
5. Low doses of a sedating neuroleptic may be required to manage day-night reversal.

## Pearl

1. High doses of trazodone may be needed to be effective.

## Pitfalls

1. Forgetting that withdrawal from alcohol, other drugs may present as insomnia.
2. Anticholinergic effects of antihistamines and amnestic effects of benzodiazepines may cause frail elderly patients to fall.

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