

## SLEEP DISTURBANCES IN CANCER PATIENTS

*Terrence Malloy, RPSGT*



My colleague and friend, Susan, wants you to know that she is a cancer survivor. Having been cared for, she is back at work, supervising the care of others, and teaching about the care of others, as the Director of Wellstar Sleep Disorders Services, and adjunct faculty at the Atlanta School of Sleep Medicine & Technology. Her years of work in healthcare did not make her immune to cancer. Her years of learning about sleep, and working as a Sleep Technologist did not make her immune to the sleep disturbances that often plague cancer patients.

45-60% of cancer patients experience significant sleep problems. In a large questionnaire study of more than 900 patients with different types of cancer, the most prevalent complaints were fatigue (44%), leg restlessness (41%), insomnia (31%) and excessive sleepiness (28%). Lung cancer patients had the highest number of problems. Breast cancer patients also reported a high prevalence of insomnia and fatigue. In a study by Ancoli-Israel, 90% reported awakening during the night as the most frequent problem. 85% reported not getting enough sleep, 75% reported difficulty getting back to sleep and 40% reported napping. However, only 17% reported the problems to their physician.

Unreported and unmanaged sleep disturbances not only rob the patient of a desperately needed respite from the pain, discomfort and difficulties of fighting cancer, but they often result in daytime problems. Sleep deprivation may result in irritability, making it difficult to maintain a positive attitude and affecting the relation-

ship with care providers. It may impair concentration and ability to follow a treatment regimen or to make important decisions.

The increased incidence of sleep disorders in patients with cancer may be a direct result of the disease process. Since the brain is the primary site of sleep regulation, other tumors of the brain may impair sleep.

According to Dr. Michael Lacey, a neurologist and Medical Director of Northside Hospital Sleep Medicine Institute, in Atlanta, "Brainstem tumors may cause a disruption in REM cycle or (muscle) atonia. Hemispheric tumors may be relatively asymptomatic if sufficiently small. In these cases, findings on a sleep study predating tumor diagnosis may include consistent focal rhythmic theta or delta slowing, focal epileptiform activity, or asymmetry of K complexes, sleep spindles or even alpha patterns seen in the awake state. Larger tumors may include all the above in addition to focal neurological signs and symptoms correlating with the location of the tumor mass."

Tumors that affect the brainstem and other head and neck tumors have been associated with occurrence of Obstructive Sleep Apnea, (OSA) or Central sleep apnea, (CSA). Tumors that affect lymph nodes, the nose or pharynx may obstruct breathing in sleep. Hypoxemia may be caused by spread of cancer to the lung. Radiation therapy may produce hypotonia of the upper airway muscles. Surgical treatment may alter the upper airway in a way that cause or worsen sleep-disorder breathing. Use of opioid medication may cause periodic breathing or obstructive sleep apnea.

Sleep may also be disrupted by the procedures or drugs used to combat cancer. Patients may develop lung fibrosis in response to chemotherapy or radiation therapy. Patients may experience cough, itching, night sweats, hot flashes, dyspnea, diarrhea, constipation, nocturia, nausea and fatigue. In turn, nausea and diarrhea may lead to metabolic imbalance and hypoxemia, which will disrupt sleep. Corticosteroids, neuroleptics used to treat nausea and vomiting, sympathomimetics used for treating dyspnea and other treatment side-effects can negatively affect sleep patterns.

Restless Legs Syndrome and/or Periodic Limb Movements may also be experienced by cancer patients and significantly delay or disrupt sleep. In one study, Periodic limb movement disorder (PLMD) was found in 53% of patients with breast or lung cancer using Polysomnography. PLMD is marked by repetitive jerks of the leg muscles that can lead to reports of insomnia, daytime sleepiness, or both. Peripheral neuropathy (PN) is a risk factor for PLMD, and therefore any cancer treatment contributing to PN may also predispose to PLMD.

Cancer patients often experience pain, which interferes with their sleep. One study found that, on admission to a cancer institution, 37% of patients reported that pain interfered with the ability to fall asleep. 65% had awakenings and difficulty returning to sleep because of pain. Another study noted that 62% of patients referred to a cancer pain clinic had sleep inter-

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ruption due to pain. The interaction between pain and sleep in cancer patients is complex. Clearly, pain will impair sleep. However, sleep deprivation has an adverse effect on pain threshold and perception. Improving sleep has been shown to be associated with improved pain ratings.

Unfortunately, nocturnal cancer pain is often under-treated, but adequate analgesia, especially with the use of longer-acting or controlled-release medications such as morphine and transdermal fentanyl improves sleep.

Insomnia may pre-exist and worsen at the time of cancer diagnosis or may begin at time of diagnosis. It may continue for years after completion of treatment. Insomnia is an important clinical issue for cancer patients. It has been shown to negatively affect Quality of Life and increase the likelihood of major depression. Depression in patients with cancer has been shown to be associated with increased mortality. There are also data showing impaired immune system function in patients with disturbed sleep.

Edward Stepanski, Ph.D. and D.ABSM (boarded sleep specialist), with the Accelerated Community Oncology Research Network, based in Memphis, TN, reports that, "Chronic insomnia has been linked to increased levels of pain, depression and fatigue." Insomnia may be related to anxiety. Anxiety may begin with the initial diagnosis and may later be related to fear of pain, fear of treatment procedures, work, financial and family concerns and the fear of death.

Drugs commonly used to treat cancer can cause insomnia. Sustained use of CNS stimulants, chemotherapeutic agents (especially anti-metabolites), anti-convulsants can all cause insomnia. Insomnia may also be caused by the withdrawal of medications, during or following treatment. Withdrawal from barbiturates, opioids, benzodiazepines, tricyclic or MAOI anti-depressants and prescription or over-the-counter anti-histamine sedatives may all cause short-term insomnia. As my colleague Susan experienced, withdrawal of hormone therapy, necessitated by her treatment, caused awakenings and insomnia. Although patients with obstructive sleep apnea typically report excessive daytime sleepiness as opposed to insomnia, OSA can be associated with reports of disturbed sleep that present as insomnia.

Like other hospitalized patients, cancer patients may experience frequent interruptions of sleep from treatment schedules, hospital routines, light and noise at night and noise from room-mates. As with other patients who experience chronic insomnia, effective treatment is usually multi-faceted and directed at the various factors involved. As shown above, pain management is an important aspect of the treatment.

We have seen that effective pain management is important. If anxiety is a factor, a study by Battelli and colleagues showed an 80% improvement in patients treated with Lorazepam. Dr. Stepanski also notes that "several studies have shown that Cognitive Behavioral Therapy, (CBT), is effective for patients with cancer.

As noted earlier, fatigue is reported in a high percentage of cancer patients. Fatigue may be caused by physical factors (weight loss, biochemical, hematological and endocrine abnormalities) or psychological factors (depression). Fatigue may also be caused by disruption of the patient's circadian sleep-wake cycle rhythms. This may result from periods of reduced daytime activity and increased nocturnal activity. It is unclear whether daytime napping reduces fatigue or increases it. Whether a patient is hospitalized or at home, reduced exposure to sunlight

may disrupt the circadian rhythms that are essential to normal sleep-wake cycling.

Sleep disorder specialists understand the importance of helping the patient clearly define their symptoms and then considering the differential diagnosis suggested by the symptoms. There is the initial challenge of differentiating a complaint of "being tired", fatigued, or sleepy. Does the patient report muscle weakness, lack of energy, but without sleepiness or does the patient experience episodes of napping or unintended sleep or have an abnormal Epworth score? (The Epworth Scale is used to describe recent history of dozing off.)

If sleepiness is reported, then the range of sleep disorders that may result in sleepiness has to be considered. These may relate to the sleep disruption caused by cancer or its treatment, or may be a co-existing sleep disorder. If fatigue is the problem, it may be caused by a correctable factor, such as electrolyte imbalance, an underlying infection, or undiagnosed metabolic disorder such as thyroid disease or diabetes mellitus.

Ancoli-Israel at UCSD, reports that "Physical activity often improves fatigue. The benefit of a mild exercise program may be successful for a variety of reasons, including that mild exercise synchronizes the rest-activity rhythms."

A fairly new method of administering medications is aimed at minimizing side effects and maximizing therapeutic effects. Chronotherapy is the method of administering medications at different times in the circadian cycle. Recent studies suggest that medications may be more toxic to cancer cells when administered at certain times of the day. This may also diminish the side-effects for the cancer patient. There is also interest in the circadian rhythm of the immune system of cancer patients.

A chronic, life-disrupting, and potentially life-threatening illness often is accompanied by significant sleep problems. These sleep problems may worsen the patient's mental and physical condition and impair much needed rest and care. Sleep problems are significantly under-reported by cancer patients.

Those who work or live with cancer patients or survivors, will benefit from increased awareness of the extent of sleep disruption that is experienced during and after treatment. As health care providers, we should encourage our patients, colleagues and loved ones to communicate sleep problems to their physicians. Better recognition, communication and management will have a positive impact on their quality of life and treatment outcomes.



*Three to five years! When would I find the time?*