

# Insomnia in oncology; an overview

R Koul, A Dubey

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## Abstract

Insomnia is a sleeping disorder characterized by the inability to fall asleep and or the inability to remain asleep for a reasonable amount of time. Insomniacs have been known to complain about being unable to close their eyes or "rest their mind" for more than a few minutes at a time. In oncology more than 50% of patients suffer from sleep disturbances. Insomnia can lead to fatigue and perhaps have a very severe impact on quality of life and disease course. There are various causes of insomnia in cancer patients and goal of treatment should first be to relieve any underlying pathology. Treatment should be multimodal including both non pharmacological and pharmacological approaches. A systematic plan should be laid out so that in addition to disease process, physician or oncology nurses should pay attention to other related psychosocial factors as well which have been found to precipitate lot of symptoms.

## DEFINITION

Insomnia in general is described as a sleeping disorder in which patient has inability to fall asleep and or the inability to remain asleep for a reasonable amount of time.

Insomniacs have been known to complain about being unable to close their eyes or "rest their mind" for more than a few minutes at a time. Both organic and non-organic insomnia constitute a sleep disorder. At least three types of insomnia have been reported in literature such as transient (intermittent) insomnia which lasts from one night to a few weeks. Most people occasionally suffer from transient insomnia due to causes as jet lag or short-term anxiety.

Acute insomnia is the inability to consistently sleep well for a period of between three weeks to six months while as chronic insomnia is regarded as the most serious; persists almost nightly for at least a month<sup>3</sup>. Insomnia in cancer patients is bit confusing due to cluster of symptoms happening in them. Insomnia should be always distinguished from cancer-related fatigue<sup>4</sup>. Although they are two distinct diseases but, insomnia and fatigue are often interrelated.

Insomnia often leads to daytime fatigue that interferes with normal functioning. Conversely, daytime fatigue can lead to napping, which result in insomnia<sup>4</sup>.

## ETIOLOGY

Various causes for insomnia have been found in literatures which are not limited to drugs such as psychoactive

stimulants, herbs, cocaine, ephedrine and amphetamine. Hormones shift naturally during menstruation and menopause causing some degree of insomnia in females. Sometimes due to disturbances of the circadian rhythm such as shift work and jet lag can cause an inability to sleep at some times of the day and excessive sleepiness at other times of the day. Neurological disorders such as brain tumors, trauma can lead to chronic insomnia. Medical diseases such as hyperthyroidism and wilson's disease have been reported to cause insomnia. Some research suggests that certain social factors, such as being unemployed or divorced, is related to poor sleep and increase the risk of insomnia in women. Insomnia is often precipitated by stress and diagnosis of cancer itself is a stressful event so this stress continues throughout the disease process including treatment. A common misperception is that the amount of sleep a person requires decreases as he or she ages. The ability to sleep for long periods, rather than the need for sleep, appears to be lost as people get older. Some elderly insomniacs toss and turn in bed and occasionally fall off the bed at night, diminishing the amount of sleep they receive<sup>5</sup>.

Finding the underlying cause of insomnia is usually necessary to cure it. The primary goal of insomnia treatment should first be to relieve any underlying disorder (e.g., cancer pain, depression, anxiety) that may be causing the sleep disturbance. Because insomnia in oncology patients is due to a variety of causes (Table 1), treatment must be

multimodal and include both pharmacologic and nonpharmacologic therapies.

Table 1 Risk Factors for Insomnia in Oncology patients

Factors related to Malignancy

- Pain
- Nausea and vomiting
- Headaches and seizures
- Shortness of breath
- Tumor impinging on nerves or viscera
- Paraneoplastic syndromes

Factors related to Treatment

- Steroids
- Biological modifiers
- Hormonal therapy
- Radiation therapy
- Chemotherapy
- Fatigue
- Devices for chemotherapy

Factors related to Environment

- Change in routine
- Hospital and health professionals ( white coat syn)
- Hospital lodges and unfamiliar environment.

Medications

- Sedatives
- Hypnotics
- Antiepileptic
- Steroids
- Caffeine

Psychosocial factors

- Depression
- Anxiety
- Effect on relationships
- Financial

Neoplastic factors

- Pain
- Nausea and vomiting
- Headaches and seizures

Treatment factors

- Steroids
- Hormonal therapy

In oncology the prevalence of sleep disturbances vary by tumor type and stage at which they present .In literature so far the incidence of insomnia is highest in breast cancer patients. The reason elucidated by authors are gender, ovarian ablation due to treatment which causes decrease in estrogen level and cause hot flashes which precipitates sleep disturbances<sup>6</sup> . Other malignancies known to cause insomnia are colorectal cancer, ovarian cancer, lung and melanoma<sup>7</sup> . The likely reason may be the treatment modalities used. In early stage disease insomnia id sue to anxiety and distress due to diagnosis and related events such as radiation and chemotherapy. In advanced stages tumor itself may be impinging on nerve or a viscera cause's pain which eventually leads to insomnia. Chemotherapy, hormonal therapy, immunotherapy and radiation as well as some adjuvant medications cause insomnia<sup>8</sup> . We use steroids quite often in oncology practice and it is a common causative agent for insomnia<sup>9</sup> . Biological modifiers such as interferon's and interleukin used for melanoma and renal cell carcinoma can cause disruption of sleep cycle. In literature it has been reported that high cortisol levels in patients of breast cancer patients with sleep disturbances had higher mortality rate due to immune suppression caused by decreased natural killer cell activity. The stress can increase serum cortisol and precipitate insomnia. This is supported by many authors in the literature<sup>10</sup> .

In recent research done at the cellular levels found that the levels of interleukin 6 and tumor necrosis factor  $\uparrow$  peaks

during sleep and in daytime falls down. Interleukin 6 is inversely related to nocturnal sleep. Vgontzas et al found that the levels of interleukin 6 usually are same in healthy population and people with insomnia but in patients themselves these levels change a lot causing shift. In oncology these cytokines have been found to play very significant role in pathogenesis and treatment hence cause insomnia<sup>11</sup>.

### DIAGNOSIS

Recently the diagnosis of the insomnia syndrome has been redefined using a combination of criteria derived from the International Classification of Sleep Disorders and the DSM-IV. The criteria includes) difficulty in initiating and/or maintaining sleep, whereby sleep-onset latency and/or wake after sleep onset is greater than 30 minutes; sleep efficiency (ratio of total sleep time to total time spent in bed) lower than 85%; difficulties occurring at least 3 nights per week; difficulties occurring for at least 6 months; and difficulties causing marked distress or significant impairment in daytime functioning e.g. fatigue, disturbed mood, performance status)<sup>12</sup>. The Pittsburgh Sleep Quality Index has been used widely in oncology patients for assessment of insomnia. It is a 19 item symptom scale and yields a global score (range 0- 21), the higher the score poorer is the sleep<sup>13</sup>. However there is no consensus in oncology community which scale is better and why so each institution has their own protocols.<sup>13</sup>

### TREATMENT

A plan that combines attention to sleep hygiene and cognitive-behavioral therapy with prescription of hypnotic medications can help relieve the symptoms of insomnia in cancer patients and improve their quality of life<sup>14</sup>. Certain classes of sedatives such as benzodiazepines and newer non benzodiazepine drugs can also cause physical dependence which manifests in withdrawal symptoms if the drug is not carefully titrated down. Some antidepressants such as mirtazapine, trazodone and doxepin have a sedative effect, and are prescribed off label to treat insomnia. The major drawback of these drugs is that they have antihistamines, anticholinergics and anti adrenergic properties which can lead to many side effects. Some also alter sleep architecture. Melatonin has proved effective for some insomniacs in regulating the sleep/waking cycle, but lacks definitive data regarding efficacy in the treatment of insomnia<sup>15</sup>. Melatonin agonists, including Ramelteon seem to lack the potential for abuse and dependence. This class of drugs has a relatively mild side effect profile and lower likelihood of causing morning sedation<sup>15</sup>. Some insomniacs use herbs such as

valerian, chamomile, lavender, hops, and passion flower. Valerian has undergone multiple studies and appears to be modestly effective<sup>16</sup>. Cannabis has also been suggested as a very effective treatment for insomnia. Alcohol may have sedative properties, but the REM sleep suppressing effects of the drug prevent restful, quality sleep. Middle-of-the-night awakenings due to polyuria or other effects from alcohol consumption are common, and hangovers can also lead to morning grogginess. Hypnotherapy, self hypnosis and guided imagery can be effective in not only falling asleep and staying asleep; they can also help to develop good sleeping habits over time. Visualizing can be effective in taking the mind away from present day anxieties and towards a more relaxing place. The key often lies in changes to routine during the day or when patient retires to bed. They should be advised to stick to a schedule and limit time in bed as it increases unrestful sleep. Patients should learn to hide clocks as less they see it more relaxed they would be. Avoid caffeine and alcohol at bedtime. A warm bath or light snack before bedtime may help prepare patient for a sleep. A good massage also may help in relaxing cancer patients if they don't have bony metastasis. Valerian is another dietary supplement purported to be a sleep aid. However, a recent government review of studies done on valerian found the evidence was inconclusive<sup>16</sup>. The National Center for Complementary and Alternative Medicine is funding studies on both melatonin and valerian to better assess their safety and whether they are effective sleep aids<sup>17</sup>.

### CONCLUSION

Sleep disturbances are one of the most frequently encountered symptoms in oncology which has been underestimated due to variety of reasons. If untreated, insomnia can lead to severe fatigue, physiological impact and detrimental effect on quality of life. Each oncology patient should have proper assessment and offered focused therapy either non pharmacological or pharmacological whichever is appropriate for that patient keeping his clinical, social and treatment factors under consideration.

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**Author Information**

**Rashmi Koul, FRCPC**

Astt Professor, Department of Radiation Oncology, Allen Blair Cancer Center 4101 Dewdney Ave . Regina SK S5T7T1

**Arbind Dubey, FRCPC**

Astt Professor, Department of Radiation Oncology, Allen Blair Cancer Center 4101 Dewdney Ave . Regina SK S5T7T1