



## **Prevalence, Risk factors & Preventive Measures of Drug Induced Insomnia**

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### **ABSTRACT**

*Insomnia is a common complaint. Transient and short-term insomnias usually result from stress or the use of certain pharmaceuticals or drugs. Long-term insomnia is often a symptom of a medical or psychiatric condition or a primary sleep disorder. The purpose of this study is to find out the prevalence, risk factors & preventive measures of drug induced insomnia among the random population. It is survey based study of N=100 conducted on sample population that included patients who are taking Alpha blocker, Beta-Blocker, ACE inhibitors and anti depressant. Data was collected from various public and private scale hospitals of Karachi. The percentages were calculated in which majority of patients who were females taking beta blocker having age more than 50years have insomnia. Study revealed that alpha Blocker, B-blocker, ACE inhibitor and anti depressant can induced insomnia among both genders and effect depends on different individuals at different age group..*

**Keywords:** *Insomnia, Alpha blocker, B-Blocker, ACE inhibitors and anti depressant.*

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### **INTRODUCTION**

Insomnia can influence every aspect of your life. Studies show that difficulties falling or staying asleep may come to the detriment of memory, attention span, and mental well-being.[1][2] Insomnia not only saps your energy and affects your mood, but also can put your health, work performance and quality of life on a downward spiral. Insomnia can be short-term (up to three weeks) or long-term (four weeks or more).[3][4][5] Sleep consists of two distinct states that alternate in cycles and reflect differing levels of brain nerve cell activity. *Non* eye movement (REM) and non-rapid eye movement (NREM). NREM is further subdivided into four stages of progression. Human sleep occurs in periods of approximately 90 minutes.[3][5][6][7][8] Different neurotransmitters are involved in sleep cycle but it has not been cleared that how many neurotransmitters are involved in sleepiness and wakefulness. Basically three mechanisms are responsible for drug induced insomnia.[3][5][9] Firstly the neurotransmitters or receptor sites may affected by the therapeutic effect of drug. [1][3] Secondly the sedative effect of drug used to treat insomnia may carry over into the daytime hours. [1][3] Thirdly the withdrawal effects of drug may also cause sleep disturbances. [1][3] Risk factors associated with drug-induced insomnia are older age, Race and ethnicity, Female sex, Medication use and drug interactions, Co-morbidities [9]. The occurrence of drug induced insomnia is more common in women and in elderly patient. Although the condition is generally associated with chronic diseases like diabetes, obesity, and depression, almost everyone will experience spells of sleeplessness at some point in their life. [1][3][10] Chronic conditions aside, insomnia is also a side effect of a variety of medication. Some of the most commonly prescribed drugs known to disturb sleep patterns. Drugs that may cause insomnia are Alpha-blockers, Beta-blockers, Corticosteroids, SSRI, antidepressants, ACE inhibitors, ARBs, Cholinesterase inhibitors, H1 antagonists, Glucosamine/chondroitin, Statins.[1][9] Beta-blockers are used to treat hypertension and arrhythmias. These drugs slow the heart rate and lower blood pressure by blocking the effect of the hormone adrenaline. Beta-blockers are also used to treat angina, migraines, tremors and in certain kinds of glaucoma. Beta-blockers have long been associated with sleep disturbances, including awakenings at night and nightmares. They are thought to do this by inhibiting the nighttime secretion of melatonin, a hormone involved in regulating both sleep and the body's circadian clock. Low levels of melatonin have

sometimes been observed in chronic insomnia.[1][9][11] Angiotensin-converting enzyme (ACE) inhibitors are used to treat high blood pressure, congestive heart failure and other conditions. These drugs help relax blood vessels by preventing the body from producing angiotensin II. ACE inhibitors boost the body's levels of bradykinin, a peptide that enlarges blood vessels. Bradykinin is thought to be the cause of dry cough. This chronic cough can be severe enough to keep anyone awake. ACE inhibitors can also cause potassium to build up in the body and lead to diarrhea, as well as leg cramps and achy joints, bones and muscles — all of which can disturb normal sleep. [1][8][9] Alpha-blockers are used to treat a variety of conditions, including high blood pressure, benign prostatic hyperplasia and Raynaud's disease. These drugs relax certain muscles and help keep small blood vessels open. Alpha-blockers are linked to decreased REM sleep — the stage of sleep when people dream — and daytime sedation or sleepiness. The proportion of REM sleep drops markedly in old age, and people deprived of REM sleep can experience memory problems.[3][4] Sleep disturbances are generally more prevalent among patients with depression. These disturbances may improve with antidepressant treatment, but there may also be adverse effects due to antidepressant drugs. Some antidepressants adversely affect the physiological structure of sleep, whereas others restore it. Most antidepressants cause REM sleep reduction, generally with increased serotonin function. Intense and prolonged dreams often accompany abrupt withdrawal from antidepressant drugs as a manifestation of REM sleep rebound after drug-induced REM sleep deprivation [1][8][9][12][13] Observance of generally accepted methods of sleep hygiene reduces the probability of development of drug-induced sleep disorders. The term sleep hygiene is used to describe simple behaviors that may help everyone improve their sleep. Establish a regular time for going to bed and getting up in the morning. Avoid naps, especially in the evening. Taking a hot bath about 1.5 - 2 hours before bedtime may help you fall asleep more easily. Do something quiet and relaxing in the 30 minutes before bedtime like Reading, meditating, or a leisurely walk are all appropriate activities. Do not look at the clock. Obsessing over time will just make it more difficult to sleep. Eat light meals, and schedule dinner 4 - 5 hours before bedtime. A light snack before bedtime can help sleep. Spend at least a half hour in daylight every day. The best time is early in the day. Avoid fluids just before bedtime so that sleep is not disturbed by the need to urinate. Strategies that minimize the drug induced insomnia include avoidance of the use of drugs known to produce disturbances of sleep. Long-term use of drugs should be avoided. But if unable to avoid the medication then change the administration time of drug earlier in a day and lower the dose of drug.[1][14][15]

The aim of study is to evaluate the prevalence, risk factor & preventive measures of drug-induced insomnia (Beta blockers, Alpha blockers, ACE inhibitors & Antidepressants) in a random population affected by insomnia.

## **METHODOLOGY**

### **Study plan:**

The study was conducted during time period of Sep 2015-Nov 2016. The study was approved by ethical committee of AL-khidmat hospital.

This retrospective study investigated the medical records of 100 patients of public and private sector of hospitals with co-morbid diseases receiving cardiovascular drugs, especially  $\beta$ -blockers, antihypertensive drugs like ACE inhibitor, Antidepressants and  $\alpha$ -blockers. Consecutive visits over 15 days were performed by retrospective analysis of drug-induced insomnia. On each visit, two of the authors independently recorded the data of patients. The patients were divided into different categories on the basis of: age, sex, drugs consumptions and etiology of insomnia. Clinical records of 100 patients that is 61 female and 38 male with an age range 20 years-more than 5 years who presented themselves with certain disease or co-morbid diseases.

### **INCLUSION CRITERIA**

Only  $\beta$ -blockers, ACE inhibitor, Antidepressants and  $\alpha$ -blockers were included in this study.

### **EXCLUSION CRITERIA**

Other drugs like Corticosteroids, SSRI, antidepressants, ARBs, Cholinesterase inhibitors, H1 antagonists, Glucosamine/chondroitin, Statins were not excluded from the study since they are not used commonly.

### **ANALYSIS**

The study run the data and report the results through Excel.

## **RESULT**

Any statistical analysis of a retrospective study must be approached with caution. It is impossible to determine whether any significant relationships that are found are real or are due to bias in the selection and treatment of patients.

Out of 100 patients only 5% M & 8% F patients (taking Antidepressants); 10% M & 14% F patients (taking  $\alpha$ -blocker); 16% M & 34% F patients (taking  $\beta$ -blocker) & 10% M & 24% F patients (taking ACE inhibitor) have drug induced insomnia. The results found that patients who are taking beta blocker have increased risk of insomnia it is due to reason that it decreases the secretion of melatonin which is involved in sleep cycle.

Table 1: prevalence of drug induce insomnia

Drugs	No. of patients	
	Male	Female
Antidepressants	10%	8%
Alpha blockers	10%	14%
beta blockers	16%	34%
ACE inhibitors	10%	24%

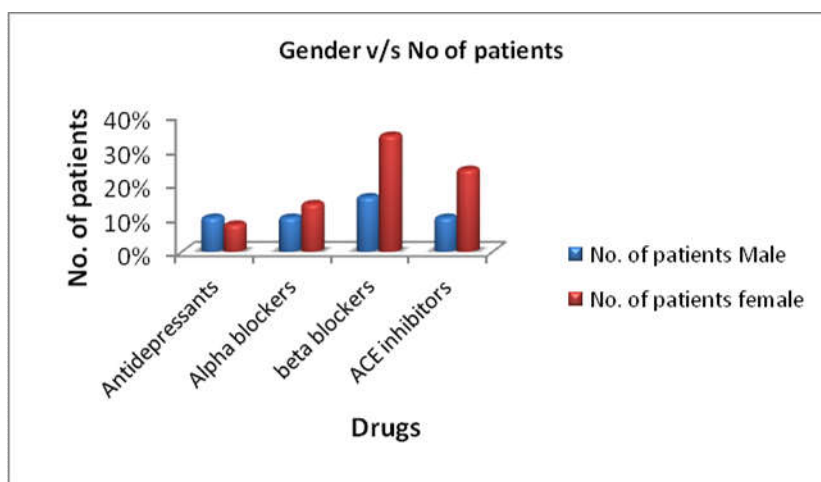


Figure 1 Prevalence of drug induce insomnia

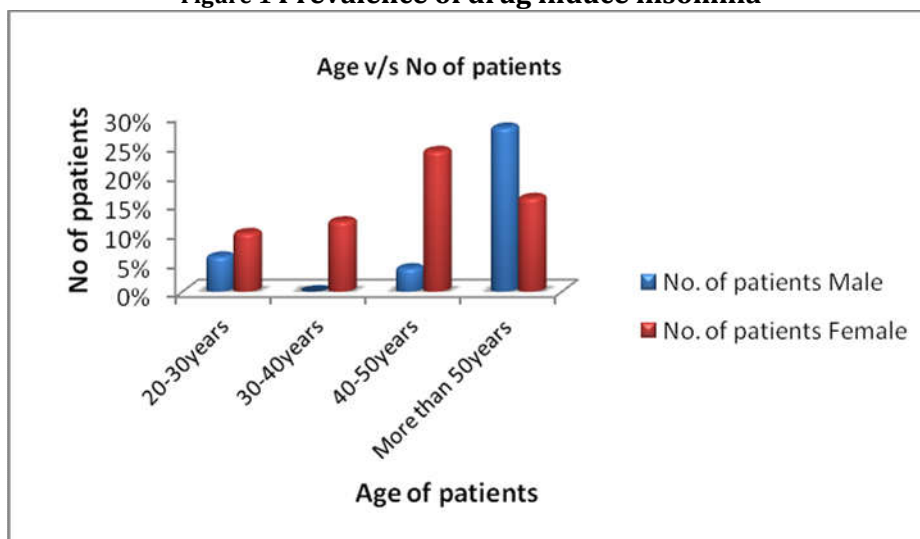


Figure 2: Age V/S no. of patient

While 6% male & 10% female (age range: 20-30years); 0% male & 12% female patients (age range 30-40years); 4% male & 24% female patients (age range 40-50years) & 28% male & 16% female patients (age range more than 50 years) are affected by insomnia. The results shown that older people are more prone to insomnia because of change in circadian rhythm.

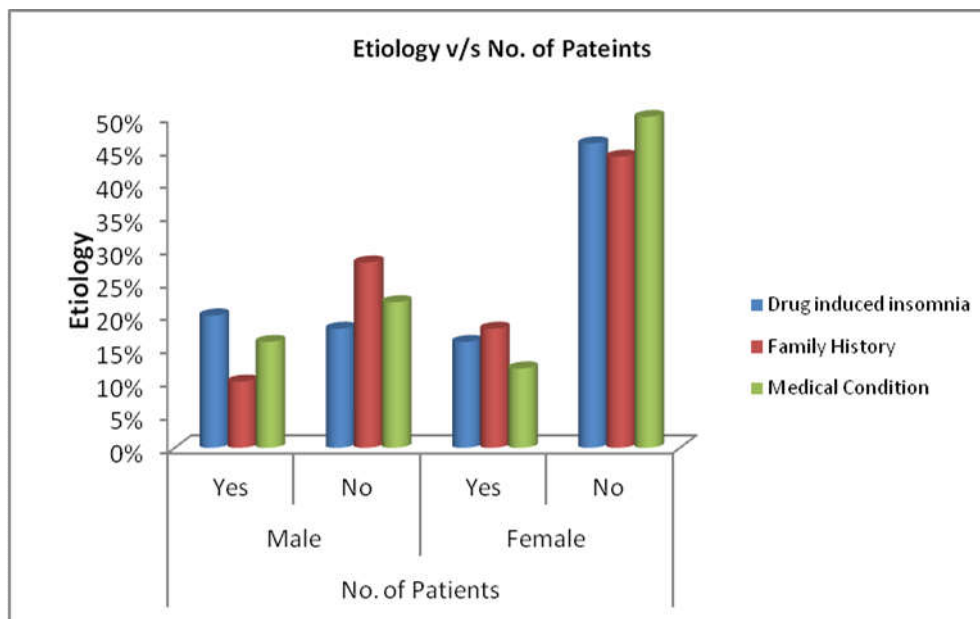


Figure 3 : Prevalence On the basis of Etiology

And etiological result shows that 36% patients (M: 20% & F: 16%) are affected by drug induced insomnia and 34% patients (M: 18% & F: 16%) have no effect. Similarly, 28% (M: 10% & F: 18%) patients have family history of insomnia and 72% patients (M: 18% & F: 44%) have no insomnia in their families. However, 28% patients (M: 16% & F: 12%) have a medical condition and 72% patients (M: 22% & F: 50%) have no medical condition. The result shows that women experienced insomnia more than men it is due to hormonal changes during menstrual cycle and menopause that significantly affect sleep cycle.

## DISCUSSION

Insomnia, also known as trouble sleeping, is a sleep disorder in which there is an inability to fall asleep or to stay asleep as long as desired. Insomnia may be viewed as both a symptom and a syndrome. As a symptom, insomnia may develop secondary to an underlying medical, psychiatric or environmental factor. Patients with insomnia may report trouble falling asleep, difficulty staying asleep, or waking up too early. No matter which sleep phase is impacted, all patients with insomnia report poor quality of sleep overall. Normal sleep architecture consists of non-rapid eye movement (REM) sleep and REM sleep, which cycle throughout the night. Insomnia, a disruption of this sleep architecture, reduces a patient's quality of life, increases the risk of co-morbid medical and psychiatric illness, and poses an increased risk of accidental injury and/or death as a result of reduced ability to perform cognitive tasks. Insomnia affects people of all age groups but people in the following groups have a higher chance of acquiring insomnia: Individuals older than 50, History of mental health disorder including depression & Emotional stress, more prevalent in women and some of the most commonly prescribed drugs known to disturb sleep patterns. Drugs that may cause insomnia are Alpha-blockers, Beta-blockers, Corticosteroids, SSRI, antidepressants, ACE inhibitors, ARBs, Cholinesterase inhibitors, H1 antagonists. Sleep disturbances are generally more prevalent among patients with depression. These disturbances may improve with antidepressant treatment, but there may also be adverse effects due to antidepressant drugs. Some antidepressants adversely affect the physiological structure of sleep, whereas others restore it. Most antidepressants cause REM sleep reduction, generally with increased serotonin function. Sleep disruption and excessive daytime sleepiness caused by beta blockers depend on the lipid solubility of the drugs. Angiotensin-converting enzyme (ACE) inhibitors boost the body's levels of bradykinin which is thought to be the cause of cough which become severe enough to keep anyone awake. ACE inhibitors can also cause potassium to build up in the body and lead to diarrhea, as well as leg cramps and achy joints, bones and muscles — all of which can disturb normal sleep. Alpha-blockers linked to decreased REM (rapid eye movement) sleep — the stage of sleep when people dream — and daytime sedation or sleepiness. The proportion of REM sleep drops markedly in old age, and people deprived of REM sleep can experience memory problems. Previously, it has been reported that up to 50% of patients have insomnia by using specific drugs.

This analysis of drug induced insomnia in 100 patients shows that 50% patients treated with  $\beta$ -blockers are more prone from insomnia while only 34%, 20% & 18% patients suffered from insomnia due to taking ACE inhibitors,  $\alpha$ -blockers & Antidepressants which shows that they have less chances of insomnia. On the basis of age, the results of retrospective studies shows that 16% patients (age range: 20-30years); 12% patients (age range 30-40years); 28% patients (age range 40-50years) & 44% patients (age range more than 50 years) are affected by insomnia. It is concluded that elderly patients are more suffered from drug induced insomnia.

The results of retrospective study on the basis of etiology shows that 36% patients are affected by drug induced insomnia. Similarly, 28% patients have family history of insomnia. However, 28% patients have a medical condition. Therefore, it is concluded that etiology of insomnia in most patients are drug induced insomnia.

Observance of generally accepted methods of sleep hygiene reduces the probability of development of drug-induced sleep disorders. The important preventive measure is avoidance of the use of drugs known to produce disturbances of sleep. Long-term use of sedative-hypnotic drugs should be avoided. Although most withdrawal reactions have been reported with long-acting benzodiazepines, rebound insomnia occurs with greater frequency and severity with short-acting agents. Benzodiazepine therapy should be stopped as early as possible with tapering after moderate dose, prolonged-use therapy, or both. Management usually involves discontinuation of the offending medication. Another possibility to consider is changing the time of administration of the suspected drug.

## CONCLUSION

From this retrospective study, it is concluded that Drug-induced insomnia is prevalent. Many drugs used in the treatment of chronic diseases have the ability to cause insomnia as adverse effects. Any drug with activity in the central nervous system has the potential to affect the sleep-wake cycle; preserving the quality and operation of this cycle can be important for successful treatment of the underlying disease.

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