

SLEEP

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SLEEP

“Troubled minds have troubled sleep & troubled sleep causes troubled minds.”

It was with these words that Frederic Snyder helped to establish the field of clinical psychiatric sleep disorder in the mid 1960's.

Disturbed sleep is among the most frequent health complaint physicians' encounter. Sleep disorders may either contribute to or result from related medical or psychiatric disorders.

It must be emphasized that insomnia or disturbed sleep is a symptom and a subjective complaint and not an illness. As in any medical specialty area, treating a symptomatic complaint without having first established a specific diagnosis reflects low standards of medical practice.

PHYSIOLOGY OF SLEEP

Most adults sleep 7-8 hrs/night though the duration and internal structure may vary from person to person.

Some patterns of sleep show culturally determined variation e.g. a mid afternoon nap called SIESTA with shortened night sleep as practiced in Italy as against one consolidated sleep episode per night popular in America.

While a mild change of sleep patterns is accepted as normal, less than 4 hr or more than 9 hours is associated with increased mortality.

ORGANIZATION OF SLEEP

There are many stages of sleep varying from very light to very deep.

1. N-REM (Slow wave sleep)
2. REM sleep (Rapid Eye movement sleep)

| N-REM Sleep | REM Sleep |
|---|---|
| Forms 75% of sleep time at night | 25% of sleep time at night |
| Seen in the early part of night | More in early part of morning |
| Deep & restful | The classically described rapid eye movements are present |
| Seen throughout the night and early in the morning | Episodic in nature & present in bouts and they increase in frequency as sleep deepens |
| Associated with decrease in peripheral vascular tone (10-30% decrease in BP, RR & BMR) | Very low muscle tone (atonic) a few irregular peripheral muscle movements may be present with irregular heart rate and respiratory rate |
| Dreams & nightmares do occur but are not recollected (no consolidation of dreams into memory) | Active dreaming present with memory but difficulty in arousing patient is seen |

SLEEP IS AFFECTED BY:

- a) Age
 - Maximum in childhood
 - Decreases in quantity & quality with age.
 - Women sleep more than men do.
- b) Sleep Deprivation
 - NREM is preferentially recovered and it occupies a greater portion of sleep time.
 - Rebound REM seen on 2nd or 3rd day onwards.
- c) Work shift or Jet lag
 - REM sleep may occur at onset of sleep itself instead of later & represents an altered cycle.
- d) Concomitant medication
 - Alcohol, Benzodiazepines & other commonly abused drugs alter the sleep architecture.

NEUROTRANSMITTERS RELATED TO SLEEP

Sleep - Serotonin, GABA, Melatonin

Wakefulness - IL - 1, PG-E₂, catecholamines, adenosine.

AREAS OF BRAIN RELATED TO SLEEP

Sleep

Medullary reticular formation, thalamus & basal forebrain for sleep.

Wakefulness

Brain stem reticular formation, Midbrain, subthalamus, thalamus & basal forebrain for wakefulness pattern.

A free running intrinsic oscillator within brain stem maintains this reciprocal sleep wakefulness.

The sleep is synchronized with external environment by suprachiasmatic nucleus of hypothalamus.

SLEEP DEPRIVATION

Prolonged wakefulness is associated with progressive malfunction of mind and abnormal activities of nervous system.

- # Sluggishness of thought
- # Irritability
- # Psychotic behaviour
- # Nystagmus, tremors, slurred speech
- # Insensitivity to pain
- # Precipitation of a seizure attack
- # Decrease of activity of sympathetic nervous system
- # Impairment of Reproductive function
- # Periodicity of function of endocrine system is lost
- # Thyroid activity is increased to maintain constantly elevated 'Basal Metabolic Rate'.
- # Decrease in immune function noted.

EFFECTS OF SLEEP DEPREVATION

Loss of optimal occupational functioning with poor productivity and increased absenteeism.

1. Increased mishaps and accidents due to poor attention and lack of effective decision making process.
2. Use of illicit drugs, alcohol or over the counter medication for symptoms, which may precipitate an abuse or dependence pattern.
3. Can lead to a secondary increase in stress and depression either directly or secondary to an endocrine abnormality.

MANAGEMENT OF INSOMNIA

- Sleep hygiene
- Chrono therapy
- Light therapy
- Pharmacotherapy
 - Benzodiazepines
 - Zolpidem
 - Zopiclone
 - Zaleplon
 - Trazadone
 - Chloral Hydrate
 - L - Tryptophan
 - Melatonin

Sleep is a complex behaviour and its modification forms the basis for several interventions. Application of behaviour therapy principles to hypnotic drug therapy modulates response and efficacy of treatment.

SLEEP HYGIENE

This required to be used in every patient who comes for treatment. All other forms of therapy are only adjuvant.

Sleep events:

- a) Reassure that the short-term reduction of sleep causes no permanent damage.
- b) Bed must be used primarily for sleep.
- c) Maintain regular sleep/wake scheduling. Sleep and awake at same time irrespective of insomnia.
- d) The area of sleeping should be comfortable and familiar.

Sleep related activities:

1. Reschedule all the leisure or relaxation activities so that they do not interfere with sleep timings.
2. Time for sex, which is one of the best hypnotic, must be separate.
3. Regular exercise schedule helps improve quality of sleep but not to be done at or near bedtime.
4. Yoga, transcendental meditation, biofeedback, muscle relaxation can help, if patients wishes.

5. Regular meals with no heavy meals at bedtime help. A light snack with a glass of warm milk at bedtime helps.
6. Bath in warm water can relax and soothe the person.

Sleep and other drugs:

Caffeine, Nicotine, Alcohol, diet pills, antimetabolites, thyroid preparation, anticonvulsant medication, ACTH like drugs, oral contraceptive pills, α methyl dopa, adrenergic agents, antidepressant drugs all affect sleep & this should be explored if patient has sleep & related complaints when on concomitant medication.

The patient should be told that any change in life or life events can lead to loss of sleep and they spontaneously resolve once the situation is remedied.

CHRONOTHERAPY

In an artificial environment where there is no natural light or any time cues the body has no mode to co-ordinate with exterior. It runs on its internal clock, which is 25-26 hrs, takes about 2 weeks to reset body clock to normal.

LIGHT THERAPY

Full spectrum light for more than 2 hrs is required daily. It is about 200 times brighter than normal. Response seen in 2-4 days but it is not effective for long term. Intermittent glancing at light required.

Side effects: - - headache
 - Eyestrain

BENZODIAZEPINES

Until recently, benzodiazepines were the only hypnotic agents of choice for insomnia. They differ mainly by the speed of absorption and their elimination half-life.

Mechanism of action -

Inhibit the BZ, \otimes on GABA and so opening of Cl^- ion channels.

The following benzodiazepines are approved as hypnotic agents:

Quazepam, flurazepam, -Long half-life

Estazolam, temazepam - Intermediate half-life

Triazolam - Short half-life

Adverse effects -

- Residual daytime effects with tolerance, dependence and withdrawal in the form of discontinuation syndrome are seen
- Cognitive impairment can affect driving or operation of machinery
- Paradoxical aggression
- Drug interactions and cross-tolerance with other drugs and dosage alteration in hepatic and renal compromised patients
- Overdose can cause respiratory impairment (to be treated with flumazenil)

Use -

Longer acting preparations are used for repeated awakenings. Shorter acting are used for difficulty in sleep initiation. Intermittent pharmacotherapy may also be used

1. Close monitoring of drug taking habits essential.
2. Must not be prescribed for more than 7-8 days at a time.
3. Only a qualified professional must make any dose adjustment.
4. Need based self medication must be avoided if possible as it can cause the patient to think sleep without drugs is not possible.
5. Dose must be tapered by 25% every week if drug has been used for more than 3 weeks.
6. Completely stop drugs by 3 weeks of starting it in most of the cases. If the patient requires for longer period reevaluate the patient and rethink the diagnosis.

ZOLPIDEM

Mechanism of action-

Imidazopyridine drug, which acts selective on $\omega 1$ type of BZD receptors. Acts on BZ, \otimes of the GABA - BZD complex. It induces sleep within 20-30 minutes of administration.

Advantages -

- It has selective sedative action.
- No rebound Insomnia on stopping or discontinuation syndrome.
- It increases mean total sleep time and it reduces the number of early awakenings.
- It preserves the stages of normal physiological sleep.
- No tolerance to sleep restoring effects
- No drug interactions

Side effects & Caution -

- Dysphoria
- Emesis
- Watch while driving or use of heavy machinery
- Dose \downarrow in hepatic / renal / elderly

Contraindication -

Pregnancy and children

ZOPICLONE

Partial agonist at GABA - BZD ® complex.

Advantages - Mild action

No residual / carry over of action

No tolerance / dependence even in use of 7-8 weeks.

No withdrawal even with chronic use

Side effects - Dysgeusia, Dry mouth, GI upset,

Palpitation, Dyspnoea, Tremors, Rash, Chills,

Sweating, agitation.

Caution - Respiratory abnormality

Liver disturbances.

Depression

Elderly

Contraindication -Children, pregnancy, and lactation

ZALEPLON

Ultra short acting drug. Acts at GABA - BZD ®.

TRAZODONE

Acts by inhibiting serotonin and alpha-1 adrenergic action

Onset of action is within 1 hrs.

Advantages - Increases sleep time

Decreases awakening

Decreases REM sleep

Drug of choice for fluoxetine induced insomnia

Side effects - Hypotension, gastric irritation, priapism, arrhythmia, relaxation of skeletal muscles.

Caution - Hepatic & renal diseases

Contraindication - Pregnancy, lactation, electro convulsion therapies

CHLORAL HYDRATE

Short acting Hypnotic.

Side effects - Nausea, vomiting, diarrhoea, flatulence, dysguesia, ↑ daytime sedation, in co-ordination, rash, urticaria, purpura, eczema, erythema multiforms,

They increase as the duration of use increases.

Dependence is seen with use more than 2 wks.

Contraindication - Renal, Cardiac, Hepatic DS, Porphyrin, Pregnancy, Lactation.

Drug Interaction - Diuretics, warfarin

L-TRYPTOPHAN

Is converted to serotonin by body.

Advantages - No visual, cognitive, memory deficits, no EEG abnormality.

Side effects - Nausea, muscle pain, dry mouth, ataxia, tremors, eosinophilia, myalgia syndrome (fatigue, myalgia, arthralgia, shortness of breath, rashes, fever, neuropathy, swelling of extremities with CCF)

Contraindication- SSRI's, MAOI (causes the Serotonergic syndrome).

MELATONIN

Useful in shift work & jet lag (Armed forces, pilots).

Latency - 20 mins.

Advantages: - ↑ Sleep time, efficiency of sleep.

Can synchronize daytime sleep/wake cycle for 7-8 hrs of sleep.

CONCLUSION

Sleep is a very important physiological function of the body as it plays a significant role in

- repair mechanism of the body
- helps restore body to the optimum level of functioning.

Insomnia is a distressing complaint not only to the person but other family members especially the bed partner. There needs to be a fine balance maintained between the Behavior therapies and the drugs used for the treatment. Reassurance plays a very important role in the process.

People who have other complaints related to insomnia should be separately evaluated and diagnosed and treated with their disease specific medication.

In all cases our motto must be to provide a wholesome quality of life which is the best gift a doctor can give his patient.

