Pharmacotherapy in Sleep Disorders

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International Classification of Sleep Disorders, Version 3 (ISCD-3)

1) Insomnia
2) Sleep-Related Breathing Disorders
3) Central Disorders of Hypersomnolence
4) Circadian Rhythm Sleep Wake Disorders
5) Parasomnias
6) Sleep-Related Movement Disorders
7) Other Sleep Disorders

Hypnotic medications

- GABA Agonists
  - -Benzodiazepines
  - -Non-Benzodiazepines
- Orexin antagonists
- Antidepressants
- Melatonin Agonists
- Antipsychotics
  - -Typical
  - -Atypical
- Antihistaminics
- Phytotherapy

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OSAHS Treatment;

- Pharmacotherapy;

  -O2

  -Protriptyline

  -Serotonine Reuptake Inhibitors

  -Medication to promote wakefulness

  Stimulants, Modafinil

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Narcolepsy

- Disturbed nighttime sleep (DNS)

  Benzodiazepines, non-benzodiazepines hypnotic

- EDS

  Modafinil, Armodafinil (FDA approved)

- EDS and cataplexy

  Sodium Oxybate: Gamma-hydroxybutric acid (GHB)

- Cataplexy, hypnagogic hallucinations, sleep paralysis

  Antidepressants: SSRIs, SNRIs, TCAs

Table 90-3 Narcolepsy Drugs Currently Available	
Drug	**Usual Dosage* (All Drugs Administered Orally)**
Treatment of EDS	
Stimulants†	
Modafinil	100–400 mg/day
Sodium oxybate	6–9 g/day (divided in two doses)
Methylphenidate	10–60 mg/day
Atomoxetine	10–25 mg/day
Dextroamphetamine	5–60 mg/day
Methamphetamine	20–25 mg/day
Treatment of Auxiliary Effects (e.g., Cataplexy)	
Sodium oxybate (gamma-hydroxybutyrate)	6–9 g/day (divided in two doses)
Antidepressants‡	
Without Atropinic Side Effects	
Venlafaxine XR	75–300 mg/day
Fluoxetine	20–60 mg/day
Viloxazine	50–200 mg/day
Duloxetine	60 mg/day
With Atropinic Side Effects	
Protriptyline	2.5–20 mg/day
Imipramine	25–200 mg/day
Clomipramine	25–200 mg/day
Desipramine	25–200 mg/day

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CRSWPD, Treatment

- Pharmacotherapy
- Melatonin: evening 0.5 – 5mg, 13-14 hour after wake up
- Sedative-Hypnotics
- Stimulants
- Vitamin B12
- Light therapy, timing, duration, intensity
- CBT

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REM Behavior Disorder

-Clonazepam ,

traditional drug of choice for RBD,

0.25 and 2.0 mg at bedtime.

-Melatonin

a slightly more robust effect with fewer adverse effects,

- may be more effective and tolerable in elderly especially with cognitive impairment or parkinsonism.

- 3 - 15 mg at bedtime, with a median dose of 6 mg

-Other drugs:

pramipexole, zopiclone, donepezil, ramelteon, agomelatine, memantine,

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RLS treatment

- Four categories of medications:

-dopaminergic agents,

-alpha-2-delta (a2d) ligands

-opioids,

-benzodiazepines.

RLS treatment

Dopaminergic medications

Long-Term Complications:

1-Augmentation(worsening of the underlying RLS symptoms) develops in most patients, usually insidiously and often longer duration of treatment.

2-Compulsive behaviors and profound sleepiness develop in a few patients,

3- Stopping the medication is difficult for many because of the strong withdrawal symptoms

RLS treatment

- **A2d Ligands (Anticonvulsants)**
- -They are a first-line treatment for RLS when their adverse effects are not a problem.

-marked by the FDA for possible development of suicidal ideation,

-caution is advised for patients with major depression.

- -should be started at low doses

-with a gradual increase in dose about once a week

RLS treatment

- **A2d Ligands (Anticonvulsants)**
- Three a2d agents are currently used to treat RLS.
- Gabapentin enacarbil
- It is approved by the FDA for treatment of RLS at a dose of 600 mg daily.
- Pregabalin

Pregabalin300 mg is as effective as 0.5 mg pramipexole and more effective than 0.25 mg

- Gabapentin

effective for treatment of moderate to severe RLS.

RLS treatment

Opioids

-often prescribed For severe cases of RLS, especially in patients unresponsive to other treatments.

-A prolonged-release oxycodone combined with naloxone (doses of 5 to 40 mg oxycodone and 2.5 to 20 mg naloxone, twice daily) - approved for use in Europe as a second-line treatment.

-Methadone has also been used for treatment of severe RLS in patients with inadequate responses to other medications.

-The dose of methadone for RLS is usually 2.5 to 20 mg a day,

RLS treatment

- **Benzodiazepines**

-benzodiazepines, including clonazepam, nitrazepam, and temazepam,

improve sleep quality and reduce arousals with PLMS in patients with RLS and PLMS.

RLS treatment

- **Iron: oral and Intravenous**
- Oral iron as supplemental treatment when the patient's ferritin level is less than 75 mcg/L.
- Iron deficiency can occur with a normal hemoglobin
- Ferrous sulfate 325 mg, or its equivalent, with vitamin C 100 to 200 mg can be taken twice a day, preferably on an empty stomach,

- In some patients, oral iron can lead to complete remission from the RLS.

RLS treatment

- Step 1: A2 Agents

  Gabapentin enacarbil: 300-600 mg

  Pregabalin: 50 - 450 mg

  Gabapentin: 100 - 1800 mg
- Step2:Dopamine agonists

  Pramipexole: 0.125 - 0.5mg

  Ropinirole: 0.5 - 4 mg
- Step3:Dopamin precursors

  levodopa-benzeserid, levodopa-carbidopa: 100/25, 200/50 mg
- **Benzodiazepines**

  Clonazepam, 0.5-2.0 mg

  Temazepam, 15-30 mg

  Nitrazepam, 5-10 m

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