Sleep Disorders Pharmacology

UNIVERSITY OF HAWAI‘I HILO PRE-NURSING PROGRAM
NURS 203 – GENERAL PHARMACOLOGY
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Learning Objectives

Understand how circadian rhythms effect sleep

Know the characteristics of the agents used for sleep
Overview

Normal sleep habits and patterns

What happens in insomnia

OTC medications used to promote sleep
- Diphenhydramine
  - Multiple products
- Doxylamine
- Melatonin

RX medication used to promote sleep
- Barbiturates
- Benzodiazepines
- Z-drugs
- Melatonin
What’s the big deal?

Why is sleep so important?
- Stay awake during the day
- Attention and memory function
- Feeling good – emotional health
- Prevent injury (falls)
- Reduce requirement for sleep aids
- Higher quality of life
Under Normal Circumstances

Circadian rhythm

Active Protein

Active Protein
How we feel “awake”
How we feel “sleepy”

Adenosine
How we feel “sleepy”
Insomnia

How do you know if you suffer from insomnia?

- Difficulty falling asleep or staying asleep for 1 month (or non-restful sleep)
- Lack of sleep or quality of sleep causes significant distress or ability to function
- Not due to another condition or sleep disorder
- Not due to mental illness
- Not due to another substance
OTC - Benadryl

MOA – antagonist at the histamine receptor

Dosage forms for sleep
- Oral

Sleep dosage
- 25-50 mg at bedtime (QHS)

ADRs
- Sleep hangover, paradoxical excitation, anticholinergic

Use with caution in elderly
- Paradoxical excitation (children too)
- Falls

Onset – 30-60 minutes

Duration – 4-8 hours

Tolerance may occur with long-term use

Interactions
- CYP2D6 substrates/inhibitors
- Safe in pregnancy
OTC - Doxylamine

MOA – Antagonist at the histamine receptor

Dosage forms for sleep
- Oral

Sleep dosage
- 25mg at bedtime (QHS)

ADRs
- anticholinergic

Not recommended for use in children <12 years

Time to peak – 2-4 hours

Half life – 10-12 hours

Drug-drug interactions
- CNS depressants

Pregnancy category C
- CI in nursing
RX - Barbiturates

Phenobarbital
- MOA – bind to BZD channel and keep it open allowing the continuous influx of GABA
- Use for treatment not recommended
- Sedative uses
  - Mental health patients w/insomnia
  - Psychoses
- Kinetics
  - Onset – 20-60 minutes (oral)
  - Duration – 6-10 hours
  - Half life – long, varies with age
  - Excreted in urine

ADRs
- Bradycardia, hypotension, agitation, drowsiness, confusion, hangover, constipation, N/V, respiratory depression

Interactions - MANY
- Potentially dangerous and fatal, especially when combined with alcohol
- Major CYP3A4, 2D6, 1A2, 2C9 inducer, substrate for 2C19
- Pregnancy B/D
  - Can cause seizures and withdrawal in infant
  - Detected in breast milk
RX - Benzodiazepines

Temazepam (Restoril)

MOA – enhances the inhibitory effect of GABA

Kinetics
  ◦ Half life – 3.5-18.4 hours
  ◦ Time to peak – 1.2-1.6 hours
  ◦ Metabolism – Liver, glucuronidation
  ◦ Excreted – Urine

Considered intermediate acting
  ◦ Not too long – hang over
  ◦ Not too short - addiction

ADRs
  ◦ Increased falls, amnestic effects, respiratory depression, daytime sedation, withdrawal, addiction, tolerance, rebound insomnia, altered sleep patterns

Pregnancy category X
  ◦ Detected in breast milk
RX – Z Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>MOA Description</th>
<th>Advantages</th>
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<tbody>
<tr>
<td>Ambien – Zolpidem</td>
<td>MOA - HYPERPOLARIZES the cell – making the neuron less likely to fire (inhibitory).</td>
<td>Less dependence, tolerance, &amp; abuse</td>
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<td>Lunesta – Eszopiclone</td>
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<tr>
<td>Sonata – Zaleplon</td>
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- Much like benzodiazepines
Ambien

MOA – Selective agonist of the BZD1 receptor – works much like benzodiazepines

Kinetics
+ Onset – 30 minutes
+ Duration – 6-8 hours
+ Metabolized – CYP enzymes (mostly 3A4)
+ Half life – About 2.5 hours, increased in liver disease
+ Excretion – urine & kidney at metabolites

ADRs
+ Headache, drowsiness, dizziness

Interactions
+ Major 3A4 substrate (CYP3A4 inhibitors), alcohol, other CNS depressants

Pregnancy category C
+ Secreted in breast milk
<table>
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<th>Lunesta</th>
<th>Sonata</th>
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<tbody>
<tr>
<td>Half-life – 6 hours – Elderly 9.9 hours</td>
<td>Can be helpful to patient who have trouble</td>
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<tr>
<td>Time to peak – about 1 hour</td>
<td>staying asleep</td>
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<tr>
<td>Excretion – mostly urine as metabolites</td>
<td>Half life – about 1 hour</td>
</tr>
<tr>
<td></td>
<td>Time to peak – about 1 hour</td>
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RX – Melatonin (Ramelteon)

MOA – Potent agonist of melatonin receptors 1&2 which are found in the suprachiasmic nucleus to induce sleep when activated

Kinetics
- Onset 30 minutes
- Half life – 1-2.6 hours, metabolite 2-6 hours
- Metabolism – liver with large 1st pass effect, active metabolite
- Time to peak – 0.5-1.5 hours
- Excretion – Mostly urine as metabolites

ADRs
- Dizziness, somnolence, fatigue, depression, nausea, upper respiratory infection

Interactions
- CYP1A2 substrates & inhibitors, CNS depressants

Pregnancy category C
- Unknown if excreted in breast milk

Studied to be most useful in jet lag related insomnia

OTC available
Questions