sedative hypnotic drugs 2

Notes about SHD (sedative hypnotic drugs) in general :

1-tolerance is a common features of SHD use

2-compulsive use>>tolerance & physiologic dependence >> withdrawal syndrome>>increase anxiety ,restlessness ,insomnia, CNS excitability may progress to convulsants , weakness and orthostatic hypotension

3-Drugs with long half life >>eliminated slowly enough to accomplish gradual withdrawal with few physical symptoms.

4- triazolam (short half life) >>withdrawal signs even between doses

5 -Withdrawal symptoms of zolpidem, zaleplon, or eszopiclone are less intense than that with BDZs.

6-Lethal dose range is not altered significantly by long-term use.

. Tolerance for specific pharmacological effect>>increase the dose when the lethal range stable >>risk of death

7- cross tolerance :

Patient with history of alcohol >>tolerance to alcohol and SHD >>unsatisfactory therapeutic response

8-The degree of tolerance achieved is not identical for all Pharmacologic effect

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FLUMAZENIL Antagonist

To remember:
BDZ → benzodiazepine

1- competitive antagonist to BDZ

2- Blocks BDZ &zolpidem , zaleplon, eszopiclone

3-used for reversing the CNS effects of BDZ overdose and to hasten recovery following use of these drugs in anesthesia and diagnostic procedures.

4-Antagonism of BDZ-induced respiratory depression is less predictable (may need assessment ventilation)

5- short half life

Adverse effects:

Agitation, confusion, dizziness, and nausea. (2) Important. • Severe abstinence syndrome in patients with physiologic dependence

(3) Important. • May cause seizures and cardiac arrhythmias in patients who have ingested benzodiazepines with tricyclic antidepressants.

Therapeutic uses of sedative hypnotic drugs :

1- ALBRAZOLAM >>panic disorders & agoraphobia

2-MIDAZOLAM>>For sedation and amnesia before and during medical and surgical procedures (in delivery & endoscopy) → Bad for learning

3-termination attake of epilepsy

4- LONG ACTING BDZ >>control of ethanol or other sedative hypnotic withdrawal states

5-PARENTERAL LORAZEPAM>> suppression of delirium tremens (alcohol withdrawal)

Adverse effect

-Hangovereffects:
Include effects such as drowsiness, dysphoria, and mental or motor depression the following day.
Common with long half life & elderly

- exacerbation of breathing problems in patient with chronic pulmonary disease & those with symptomatic sleep apnea

-Extensive clinical use (triazolam) has caused behavioral disinhibition, delirium, aggression, and violence

- Relatively low doses → drowsiness, impaired judgment and diminished motor skills

-Anterograde amnesia, impaired ability to learn new information

- Barbiturates are contraindicated in patients with a history of acute intermittent porphyria.

Drug interaction of sedative hypnotic drugs

1- additive effect with CNS depressants, alcohol, opioids, anticonvulsants, phenothiazines, antihistamines and antidepressant drugs.
2-Interactions at the level of drug metabolizing enzymes. Barbiturates induce drug metabolism.

RAMELTEON

1- Agonist at melatonin receptor MT1,MT2
2- melatonin receptor maintain the circadian rhythms underlying the sleep-wake cycle
3- prescribed for patient who have difficulty in falling asleep
4-No rebound insomnia or withdrawal symptoms (no tolerance)
5- Rapidly absorbed after oral administration and undergoes extensive first-pass metabolism (CYP1A2) , forming an active metabolite with a longer half-life (2-5 hours). CYP2C9 contributes.
• Metabolism induced by rifampin.
6-contraindicated with : inhibitors of CYP1A2 (ciprofloxacin, fluvoxamine, tacrine, zileuton) or CYP2C9 (fluconazole).

Hypnotic only

Adverse effects :

1 -Dizziness, somnolence, fatigue.
2- Endocrine changes (decreases testosterone levels, and increases prolactin levels) >> infertility (important)
3- Use with caution in patients with liver 53dysfunction.

BUSPIRONE

1- selective anxiolytics effect
2- No addiction >>no withdrawal signs
3- no interact with GABA
4- partial agonist activity at brain 5-HT1a receptors
5-Has minimal abuse liability.
6- Anxiolytic effect takes 3-4 weeks to be established>>unsuitable for acute anxiety
7- Used for generalized anxiety but less effective in panic disorders
8- Rapidly absorbed orally but undergo extensive first pass metabolism by CYP enzymes to form several active metabolites
9-half life 2-4 h (Elimination half life)
Erythromycin,grapefruit juice & ketoconazol inhibit CYP3A4 >>>increase half life
Rifampin inducer for CYP3A4>>decrease half life
10- less psychomotor impairment than BDZs
11- elderly patients are not more sensitive to its action
12. Liver dysfunction may slow its clearance
13. Dose not affect driving skills
14. Does not potentate effect of conventional sedative hypnotic, Ethan, tricyclic, antidepressants

Adverse effect :

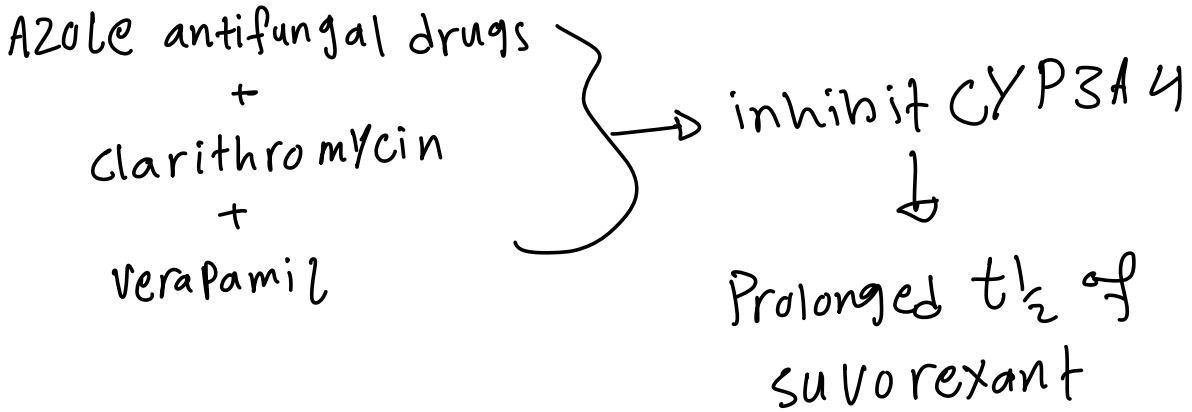
1- nonspecific chest pain ,(tachycardia , palpitation , due to a2 receptor block) , dizziness , nervusness headache , tinnitus
2-Gastrointestinal distress , 3- parasthesia , 4- dose-dependent pupillary constriction

5- high BLOOD PRESSURE significantly in patient receiving monoamine oxidase inhibitors

Orexin receptor antagonists (Almorexant - suvorexant)

- **orexin receptors responsible to keep you wake up**
- **Orexin levels increase in the day and decrease at night.**
- **Loss of orexin neurons is associated with narcolepsy, a disorder characterized by daytime sleepiness and cataplexy.**

↳ Sleep Ending Drugs



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