### **Neurology pharmacology**

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### Neurology pathophysiology review:

- Alzheimer's Disease (AD):
  - Brain cells die over time, leading to memory loss and confusion.
  - Presentation: Memory loss, getting lost easily, difficulty thinking and making decisions.
- Myasthenia Gravis (MG):
  - The body blocks muscle nerve signals, making the muscles weak, especially after activity.
  - o Presentation: Muscle weakness that gets progressively worse
- Parkinson's Disease (PD):
  - The brain loses dopamine, a chemical that helps control movement, causing shaking, stiffness, and slow walking.
  - o Presentation: Resting tremor, slow movements, stiff muscles, shuffling gait.
- Multiple Sclerosis (MS):
  - The body attacks the nerves and damages the protective coating (myelin), causing problems with muscle movement and coordination.
  - o Presentation: Muscle weakness, vision problems, balance issues, numbness or tingling.
- Most of these medications treat the symptoms and sometimes progression of the disease. They
  do not cure the condition!

### **Drug class: Acetylcholinesterase inhibitors**

- Drugs:
  - Donepezil (Aricept)
  - Galantamine (Razadyne)
  - Rivastigmine (Exelon)
  - Neostigmine
  - Pyridostigmine
  - Physostigmine
- MOA: Inhibit acetylcholinesterase from destroying acetylcholine, increasing ach levels
- Indication: Alzheimer's disease
- SE/AE: GI symptoms may present upon initial treatment, bradycardia
- Does not cure Alzheimer's disease. Is used only to slow progression.
  - Neostigmine and pyridostigmine are both in this class and used for neuromuscular blocker reversal and myasthenia gravis
  - Physostigmine is another drug in this class. It is used to treat anticholinergic toxicity and myasthenia gravis, and neuromuscular blocker reversal

# **Drug class: Dopaminergic**

- Drug:
  - Levodopa / carbidopa (Sinemet)
  - o Entacapone\*
- MOA:
  - o Levodopa: Increases dopamine synthesis in the brain, as it's a precursor to dopamine.
  - Carbidopa: Prevents the breakdown of levodopa before it reaches the brain, allowing more levodopa to enter the CNS.
  - Entacapone: COMT inhibitor that prevents the breakdown of levodopa in the peripheral tissues, increasing the duration of action of levodopa and enhancing its effects.
- Indications: Parkinson disease and parkinsonism
- SE/AE: Nausea and vomiting, dyskinesia, orthostatic hypotension, psychosis
- Most effective pharmacotherapy for PD
- Patient education: Take with food to reduce nausea
- This medication may have "wearing off effect", where symptoms return prior to the time for the next dose

### **Drug class: Dopamine agonists**

- Drugs:
  - Pramipexole (Mirapex)
  - Apomorphine (Apokyn)
- MOA: Unknown
- Indication: Parkinson disease
- SE/AE: Constipation, nausea, dizziness, drowsiness, insomnia
- Patient education: Take with food to reduce nausea

#### **Drug class: MAO-B inhibitors**

- Drug:
  - Selegiline
- MOA: Blocks the breakdown of dopamine by blocking MAO-B
- Indication: Parkinson disease
- SE/AE: Insomnia
- Patient education:
  - Should be administered early in the day
  - Avoid foods that contain tyramine
  - o Caution for interactions with TCAs and other related mental health medications

### **Drug class: COMT inhibitor**

- Drug:
  - Entacapone
- MOA: Blocks the inactivation of dopamine by preventing the breakdown of levodopa
- Indications: Parkinson disease

- This is often added to levodopa carbidopa and other Parkinson regimens
  - Serves to reduce the wearing off effect

### **Drug class: Anticholinergics**

- Drug:
  - Benztropine (Cogentin)
- MOA: Blocks cholinergic receptors
- Indications: Parkinson disease, medication-induced EPS
- Primarily used for symptom of tremor
- SE/AE: Anticholinergic effects

### **Drug class: Immunomodulators**

- Drugs:
  - o Interferon beta 1a (Avonex)
  - o Interferon beta 1b (Betaseron)
- MOA: Unknown
- Indications: Multiple sclerosis and viruses
- Parenteral only
- SE/AE: Flu like symptoms, hepatotoxicity
- Patient education: Flu like symptoms can be reduced by premedicating with NSAIDS
- First line treatment

Other drugs used for multiple sclerosis include monoclonal antibodies and immunosuppressants

### **Drug class: Skeletal muscle relaxants**

- Drugs:
  - Baclofen
  - Carisoprodol (Soma)
  - Methocarbamol (Robaxin)
  - Cyclobenzaprine (Flexeril)
- MOA: Varies, generally act as a CNS depressant
- Indications: Spasticity
- SE/AE: CNS depression
  - Cyclobenzaprine can also have anticholinergic effects
- Patient education: Should not be taken with alcohol or other CNS depressants

#### **Drug name: Dantrolene**

- MOA: Suppressing release of calcium
- Indications: Spasticity and symptoms of malignant hyperthermia
- SE/AE: Weakness,
- Black box warning: Hepatoxicity
- Patient education: Should not be taken with alcohol or other CNS depressants

Benzodiazepines are also indicated for use as a muscle relaxant

### Drug class: Botulinum toxin

- Drug:
  - Onabotulinumtoxin A
- MOA: Muscle inactivation
- Indications:
  - Migraines (chronic)
  - Overactive bladder (OAB)
  - Cervical dystonia (neck muscle spasms)
  - Hyperhidrosis (excessive sweating)
  - Spasticity (muscle tightness in conditions like stroke or cerebral palsy)
  - Strabismus (eye misalignment)
  - Aesthetics (reducing wrinkles, facial lines)
- SE/AE: Depends on indication (Common effects include local pain at injection site, headache, flulike symptoms, and muscle weakness.)
- Onset can be days to weeks, duration lasts for several months
- Patient education:
  - o Adverse effects can occur within hours, days or weeks
  - Avoid rubbing the treated area for a few hours after the procedure to prevent the toxin from spreading to unintended muscles.

### **Drug class: Benzodiazepines**

- Drugs:
  - Lorazepam (Ativan)
  - Diazepam (Valium)
  - Midazolam (Versed)
- MOA: GABA agonist. GABA is an inhibitory neurotransmitter
- Indications: Seizure disorder, insomnia, anxiety, sedation, muscle relaxant
- SE/AE: Muscle weakness, hypotension, sedation, respiratory depression
- Black box warning: Do not mix with other CNS depressants. Can cause addiction and dependency
- Controlled substance (Schedule IV)
- First line for cessation of acute generalized seizure
- Patient education:
  - o Do not take with alcohol or other CNS depressants
- Has an approved reversal agent for benzodiazepine overdose called flumazenil

### Antiepileptic therapy notes:

- All antiseizure medications should be tapered off when discontinued
- Folic acid is recommended to reduce risk to fetus from certain antiseizure medications if taken in pregnancy
- Risk-reward decision must be made on risk of medication versus risk of seizures in pregnant patients

 A non-pharmacological intervention for seizures is the ketogenic diet, may used if medication is not effective

### **Drug class: Hydantoins**

- Drugs:
  - Phenytoin (Dilantin)
  - Fosphenytoin (Cerebryx)
    - Fosphenytoin converts to phenytoin
- MOA: Prolong sodium channel inactivation, which stabilizes impulses
- Indication: Seizure disorder
- SE/AE: Dysrhythmias and hypotension
- Black Box warning: Give slow if via IV to avoid AE
- Can reduce vitamin K, causing bleeding. May need to provide vitamin K
- Toxic to local tissue in the event of extravasation
- Patient education:
  - Can decrease effectiveness of oral contraceptives
  - o Teratogenic

### **Drug class: Succinimides**

- Drug:
  - Ethosuximide (Zarontin)
- MOA: Blocks specific calcium channels. Causes an increase in the seizure threshold
- Indication: Absence seizures

#### **Drug class: Barbiturates**

- Drug:
  - Phenobarbital (Luminal)
- MOA: GABA agonist
- Indications: Seizure disorder, sedation
- SE/AE: Respiratory depression, sedation, hypotension
- Less sedating than other barbiturates
- Controlled substance (Schedule IV)
- Can reduce vitamin K, causing bleeding. May need to provide vitamin K
- Patient education:
  - o Do not take with alcohol or other CNS depressants
  - Can decrease effectiveness of oral contraceptives

## **Drug class: Valproate**

- Drug: Valproic acid (Depakote)
- MOA: Prolong sodium channel inactivation and is also a GABA agonist
- Indications: Seizure disorder, migraines, bipolar disorder
- SE/AE: Weight gain, thrombocytopenia
- Black box warning:

- Hepatoxicity
- Highly teratogenic least preferred for females of childbearing age
- Pancreatitis

## Drug class: Iminostilbene

- Drug:
  - o Carbamazepine (Tegretol)
- MOA: Prolong sodium channel inactivation
- Indications: Seizure disorder and bipolar disorder
- SE/AE: Can present with neuro effects upon start of treatment
- Can reduce vitamin K, causing bleeding. May need to provide vitamin K
- Patient education:
  - o Can decrease effectiveness of oral contraceptives
- Black box warnings: SJS/TEN, aplastic anemia, and agranulocytosis

### **Drug name: Lamotrigine (Lamictal)**

- MOA: Prolong sodium channel inactivation, blocks specific calcium channels, and blocks glutamate
- Indications: Seizure disorder and bipolar disorder
- One of the best options for use in pregnancy
- Black box warning: SJS/TEN
- Patient education:
  - o Can decrease effectiveness of oral contraceptives

#### Drug name: Levetiracetam (Keppra)

- MOA: Unknown
- Indication: Seizure disorder
- One of the best options for use in pregnancy
- Patient education:
  - Can decrease effectiveness of oral contraceptives

## **Drug name: Gabapentin (Neurontin)**

- MOA: Unknown
- Indications: Seizure disorder and post-herpetic neuralgia
- Most of its use is off label for migraines, anxiety, other neuropathic pain
- SE/AE: Fatigue, dizziness, peripheral edema
- Must be tapered

### **Drug name: Topiramate (Topomax)**

- MOA: Prolong sodium channel inactivation, blocks specific calcium channels, blocks glutamate, and is a GABA agonist
- Indications: Seizure disorder and migraines
- SE/AE: CNS effects, weight loss, other adverse effects

- Used off-label for bipolar disorder, eating disorder, essential tremor
- Patient education:
  - o Can decrease effectiveness of oral contraceptives

### **Drug name: Pregabalin (Lyrica)**

- MOA: Inhibits multiple neurotransmitters including epinephrine, glutamate, and serotonin
- Indications: Fibromyalgia, seizures, and neuropathic pain
- SE/AE: CNS effects, weight gain, visual disturbances, peripheral edema

### **Sedative agents:**

### **Drug name: Diprivan (Propofol)**

- MOA: Unknown exact mechanism, promotes release of GABA
- Indications: Anesthesia, induction and sedation
- SE/AE: Respiratory depression and hypotension
- IV only
- Propofol infusion syndrome can occur involving acidosis, cardiac and renal failure and rhabdomyolysis
- Most popular sedation medication in the U.S.

### **Drug name: Etomidate**

- MOA: General anesthetic
- Indication: Induction of anesthesia
- IV only

#### **Drug name: Ketamine**

- MOA: NMDA receptor antagonist dissociative anesthetics
- Indication: Anesthesia
- SE/AE: Psychological effects such as delirium and hallucinations
- Controlled substance (Schedule III)
- Unlike other related agents, ketamine is more likely to increase heart rate and blood pressure
- In low doses produce analgesia (off-label use), in high doses produce anesthesia
- Use for sedation is via the IV route

### **Drug name: Dexmedetomidine (Precedex)**

- MOA: Unknown
- Indications: Agitation related to bipolar or schizophrenia and sedation
- SE/AE: Hypotension and bradycardia
- May develop tolerance and/or withdrawal symptoms, especially with prolonged use
- IV only

#### Benzodiazepines are also used for sedation

## Drug class: Neuromuscular blocker (Paralytic) - non depolarizing

- Drugs:
  - Vecuronium
  - o Rocuronium
- MOA: Inhibiting depolarization
- Indication: Neuromuscular blocker for intubation
- Duration is 30-90 minutes
- Requires mechanical ventilation
- Has a reversal agent called Sugammadex
- Does not provide any analgesia or sedation.
  - o All patients receiving paralytics need analgesia and/or sedation medications

### Drug name: Succinylcholine - depolarizing

- MOA: Inducing depolarization
- Indication: Neuromuscular blocker for intubation
- SE/AE: Hyperkalemia and malignant hyperthermia
  - o Malignant hyperthermia presents with muscle rigidity, fever, hypercapnia
- Only depolarizing neuromuscular blocker
- Can produce fasciculations
- Short acting, effects wear off in a few minutes
- Requires mechanical ventilation
- Does not provide any analgesia or sedation.
  - o All patients receiving paralytics need analgesia and/or sedation medications

### References

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