Sasaran Belajar

Di akhir pembelajaran, mahasiswa mampu memahami mekanisme kerja, indikasi dan efek samping obat:

1. Antikonvulasi
2. Hipnotik sedatif
3. Parkinson
4. Pelemas Otot
5. Anestesi Umum
6. Anestesi Lokal
Status Epilepticus

▶ SE:
  - Continues seizures occurring 30 minutes (epilepsi foundation)
  - More than 30 minutes of continues seizures activity or 2 or more sequential seizures without full recovery of consciousness between seizures (Dodson, 1993).

▶ Systemic and primary brain changes → related to morbidity and mortality rates
  - Decreasing GABA inhibition.
  - Increasing blood pressure (early stage) → decreasing
  - Acidosis (+)
  - Pulmonary edema
  - Hyperthermia
  - Mild leukocytosis
  - GABAergic mechanism fails
► Goal of therapy: to treat the epilepsy and to minimalise the side effects

Principal therapy:
► Monotherapy is better than polypharmacy
► Dosage is increased until the therapeutic effect or toxicity effect are met.
► Polypharmacy is introduced when monotherapy does not work
► Avoiding the sudden withdrawal

**Treatment flowchart for status epilepticus**
Medications

STATUS EPILEPTICUS

Karbamazepin
- Stabilize neural membrane by decreasing Na, Ca and K flows through it.
- Avoid to be given with MAO inhibitor consecutively

Fenitoin
- Difenilhidantoin derivate
- Mechanism of actions are similar to Karbamazepin
- Could be given orally, intra venous and intra muscular

Fenitoin
Karbamazepin
Asam valproat
Gabapentin
Barbiturat
Benzodiazepin
Asam valproat
Gabapentin

Lamotrigin

Na

Glutamate

Ca

GABA
Valproic Acid
► Increasing GABA transmission
► Sedation effect is minimal

Etosuksimid
► Mechanism of action is unknown
► Probably by inhibiting Ca channel

Phenobarbital
► Stimulating GABA receptor
► SE: sedation, nystagmus, ataxia and allergy
► Inducing enzym P450

Primidon
► Mechanism of actions are unknown
► Its active metabolit has long half life
Gabapentin
► GABA agonist
► Adjuvant therapy

Lamotrigin
► Stabilizing neuron and affecting glutamate release
► Adjuvant therapy
► SE: rash (prominent)

Klonazepam
► Stimulating GABA receptor

Felbamat
► Stimulating GABA receptor and inhibiting NMDA receptor
► Used un-frequently
Parkinson disease

- A progressive neurodegenerative disorder associated with loss of dopaminergic nigrostriatal neurons.

- Distinctive features:
  - Resting tremor, rigidity, bradikinetia, and postural instability

Principle therapy

- To facilitate action of dopaminergic
  - Increasing the synthesis and release of dopamine (L-dopa+karbidopa, amantadine)
  - Inhibiting dopamin metabolism (selegilin/deprenil)
  - Activating dopamine receptor (bromocriptine, pergolide)

- To suppress action of cholinergic
  - Blocking muscarinic/cholinergic receptor (trihexphenidyl, benzathopine, diphenhidramine)
L-dova (levodopa)
- Dopamine precursor → inactive form
- Activated by decarboxilase enzyme;
  - Brain
  - Liver & kidneys → cannot pass through BBB → bioavailability → countered by karbidopa/benserazide.

Interaction: piridoxine increases decarboxilated reaction.

On/off phenomenon (+) after 3-5 years application → mechanism ??? Desensitization of dopamine receptor

Not a first line therapy
Selegiline (deprenil)
► Instead of inhibiting metabolism of dopamine:
  ▪ Stimulating dopamine release.
  ▪ Neuro-protective effect
► + MOA inhibitors → crisis of hypertension.

Bromociptine & Pergolide
► Dopamine receptor agonists
► Action: Lesser than L-dopa
► As a single therapy at the early stage
► Combination with L-dopa at the moderate and late stage.
► Tapering dose

Trihexiphenidile & benzotropine
► Action: less than L-dopa
► Adjuvant therapy
► Tapering dose

Diphenhidramine
► Anti cholinergic effect at central level
► Anti histamine
### Amantadine

- **Anti virus**
- **Mechanism:** ??? May be by facilitating dopamine release
- **Action:**
  - Less than L-dopa
  - Better than anti cholinergic

<table>
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<tr>
<th>Early stage:</th>
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<td>- Anti cholinergic or Amantadine</td>
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<td>- When early stage therapy is not effective, L-dopa+karbidopa are started.</td>
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<td>Final stage: dopamine agonists medications and MAO inhibitors.</td>
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### Headache/Cephalgia

- **Migraine**
- **Tension headache**
- **Cluster headache**
Migraine

- **Mechanism:**
  - Genetic
  - Vascular
  - Neural
  - Neurotransmitter serotonin
  - Neurotransmitter dopamine
  - Activation of sympathetic nervous system

- **NSAIDs + caffeine** (aspirin, acetaminophen, salicylic acid, etc)
- **Serotonin receptor agonists** (ergotamine, dihydroergotamine, sumatriptane, naratriptane, rizatriptane, zolmatriptane)
- **Dopamine antagonist** (metoclopramide, CPZ, proCPZ)

Protocol of therapy

- **Mild migraine**
  - NSAIDs, or Serotonin receptor agonist (oral)

- **Moderate migraine**
  - Serotonin receptor agonists (oral/nasal/SC), or Dopamine receptor antagonist (oral)

- **Heavy migraine**
  - Serotonin receptor agonists (SC/IM/IV), or Dopamine receptor antagonist (IM/IV)
NSAIDs
- SE: dispepsia

Stimulator of serotonin (5-HT₁) receptors:
1. ergotamine, dihydroergotamine
   - Non selective 5-HT₁ receptor agonist
   - Contra indication: CHD, pregnancy, peripheral blood vessel constriction, level and kidney disorders.

2. triptan
   - Selective 5-HT₁ receptor agonist
   - Rizatriptan: quickest onset, highest efficacy
   - Naratriptan: in contrast
   - Monotherapy is unadvisable
   - Contra indication: cardiovascular diseases
Dopamine antagonists
► Adjuvant therapy
► Increasing gut motility
► Also could treat: Nausea & vomit

Prevention
► 3 times per month
► Beta blockers (propanolol, timolol)
► Anti convulsive agents (valproic acid)
► MAO inhibitors (phenelzine, isokarbosazide)
► Serotonergic agents (metisergide, siproheptadine)
► Ca antagonist (verapamil)

Tension headache
► Usually bilateral
► Usually following anxiety or depression
► Therapy:
  ▪ NSAIDs + caffeine
  ▪ Muscle relaxant agents
► Prevention: amitriptiline a.n
Cluster headache

- Periorbital pain (temporal bone pain)
- Some signs and symptoms related to eyes
- Mechanism: ??? May be serotonergic transmission disorder

Therapy:
- Prednison
- Lithium
- Metisergid
- Ergotamine
- Na valproic
- Verapamil