PHARMACOLOGY TEAM

Done by: Eman Alrashidi

Revised by : Prof. OMNIA NAYEL

How to study this lecture :

- First page for general idea of management
- we should memorize the drugs within the tables which are selective in vertigo to treat (emesis + spinning)
  and those Prevent the recurrence
- last three pages differentiate between structural and functional drug inducer then memorize one example for each

THERAPEUTIC MANAGEMENT

Vestibular Suppressants

Intend to dull brain response
(spinning ± emesis)
to vestibular signals from inner ear

- Betahistine
- Benzodiazipines
- H_1 Antagonists / Agonists
- Dopamine Antagonists
- Phenothiazines
- Anticholinergics
- $5HT_3$ antagonists
- TCA

Prevent Recurrence

Intend to suppress acute attacks [tame vertigo episodes]

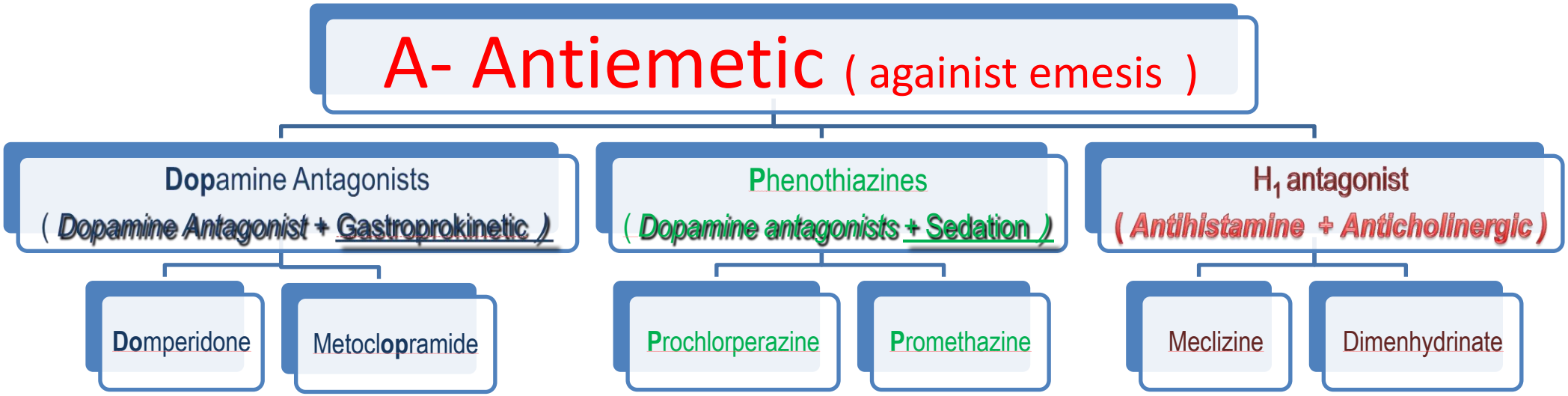
* Diuretics *(thiazides)*
* Vasodilators *[H_1 Agonists]*
* Corticosteroids *(↓inflammation)*
* L-type Ca Channel Blockers
  (cinnarazine, flunnarazine)
  verapamil → constipation

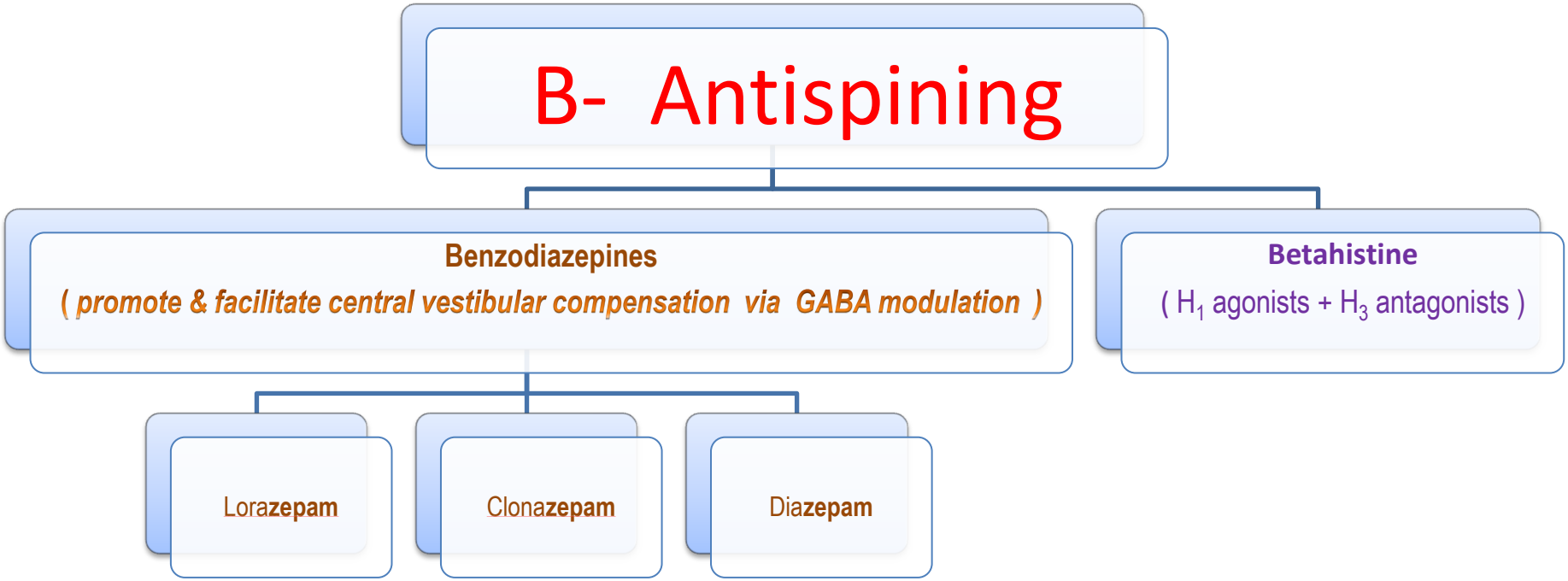
NB. If migraine is too present
→ add on its treatment

THERAPEUTIC MANAGEMENT of VERTIGO

- **Prevent recurrence (see first page)**
- **Vestibular Suppressants (selective drugs):**

Intend to dull brain response (spinning ± emesis) to vestibular signals from inner ear




B- Antispining
Benzodiazepines
(promote & facilitate central vestibular compensation via GABA modulation)
Betahistine
(H_1 agonists + H_3 antagonists)
Lorazepam
Clonazepam
Diazepam

Antiemetic drugs :

drug	action	Mechanism in vertigo	ADRs	contraidication
Dopamine Antagonists **E.g.:** **METOCLOPRAMIDE** **DOMPERIDONE**	**Dopamine Antagonists + gastroprokinetic effect**	- **A potent central antiemetic (METOCLOPRAMIDE)** - **Not cross Brain barrier (DOMPERIDONE)**		
H_1 antagonist **E.g.:** **MECLIZINE -** **DIMENHYDRINATE- (drug of choice in motion sickness)** **مقارنة:** **DIMENHYDRINATE > MECLIZINE as antiemetic** **DIMENHYDRINATE < MECLIZINE As sedation**	**Antihistamines** **Anticholinergics**	**-Block H_1 receptors in CRTZ(chemo receptor trigger zone)** **Sedative effects** **- Weak anticholinergic effects** **Lead to :** **↓ excitability in the labyrinth and blocks conduction in vestibular-cerebellar pathways.**	• **Sedation** • **Dizziness** • **Anticholinergic side effects**	• ***Glucoma*** • ***Prostatic enlargement***
Phenothiazines **E.g.:** **PROCHORPERAZINE(drug of choice in vertigo)** **promethazine**	***Dopamine antagonists*** **+ Antipsychotic,** **+ antiemetic &** **weak sedative activity**	**Block dopamine receptors at CRTZ** **Lead to :** **Antipsychotic, antiemetic & weak sedative activity**		

antispining				
Drug	**action**	**Mechanism in vertigo**	**ADRs**	***contraindication***

BETAHISTINE	**H_1 agonists**
	H_3 antagonists
		• **Weak agonist at H_1 receptors → regulates inner ear fluid homeostasis (labyrinthine circulation) → inducing vaso-dilatation in middle ear → relieves pressure in inner ear**
		• **Strong antagonism of H_3 autoreceptors → ↑ augmenting effects on H_1 receptors in the brain →**
		  ○ **↑ H synthesis in tuberomammillary nuclei of the posterior hypothalamus to promote & facilitate central vestibular compensation**
		  ○ **↑ H release in vestibular nuclei**
		• **↑levels of neurotransmitters such as 5HT in the brainstem, which inhibits the activity of vestibular nuclei.**
			• **Headache**
			• **Nausea**
			• **Gastric effects**
			• **↓ appetite and weight loss**
				• ***Peptic ulcer***
				• ***Pheocromocytoma***
				• ***Bronchial asthma***

Benzodiazepines **Eg:** **Lorazepam** **Clonazepam** **Diazepam**		**Facilitate inhibitory GABA neurotransmission** **Lead to** **↓vestibular response**	**Dependence** **(يدمن المريض عليها)**	

DRUGS INDUCING VERTIGO

- Destructive damaging effects of drugs (or chemicals) on structure or function of labyrinthine hair cells &/ or their neuronal connections

MIXED OTOTOXINS

- Aminoglycoside antibiotics; *gentamycin, kanamycin, neomycin, streptomycin, tobramycin, netlimycin*
- Fluroquinolines, Vancomycin, Polymixin
- Quinine, chloroquine, quinidine
- Nitrogen mustard
- Loop diuretics
- NSAIDs
- Tobacco

STRUCTURAL

FUNCTIONAL

DRUGS INDUCING VERTIGO

VESTIBULOTOXINS

- Drugs altering fluid & electrolyte
  - Diuretics
  - Antihypertensives ….
- Drugs altering vestibular firing
  - Anticonvulsants
  - Antidepressants
  - Sedative hypnotics
  - Alcohol
  - Cocaine

FUNCTIONAL

DRUGS INDUCING VERTIGO

- **Aminoglycoside antibiotics;**
  streptomycin, kanamycin, neomycin, gentamycin, tobramycin, netlimycin

STRUCTURAL

Apoptosis

Neomycin → activate caspases → Death Receptor Pathway

Gentamycin → evoke free radicals → Mitochondrial Pathway

↓local blood flow → biochemical changes → alter electromechanical transduction

- **Quinine, chloroquine, quinidine**
- **Loop diuretics**
- **NSAIDs**

Firing of impulses

FUNCTIONAL


I hope ,, no more confusion about drug in balance