PHARMACOLOGY TEAM

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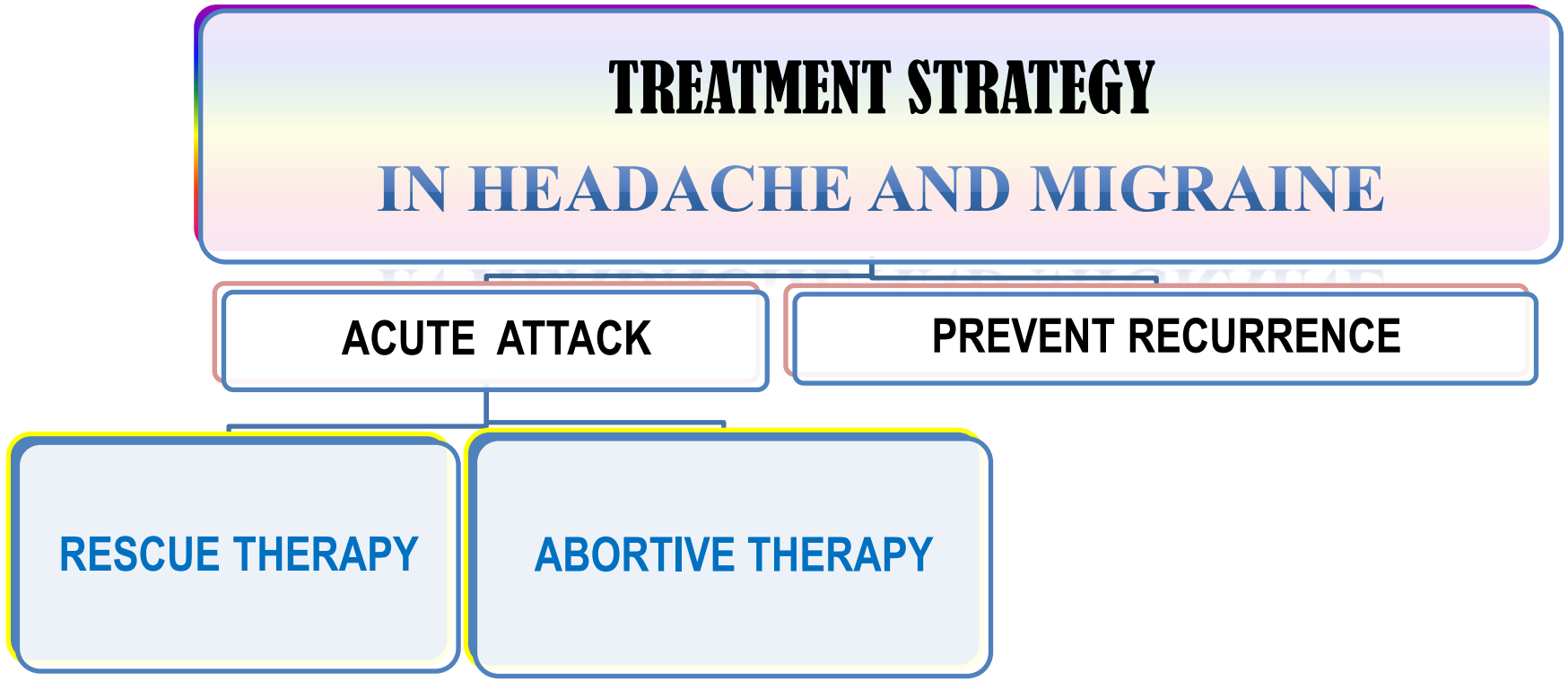
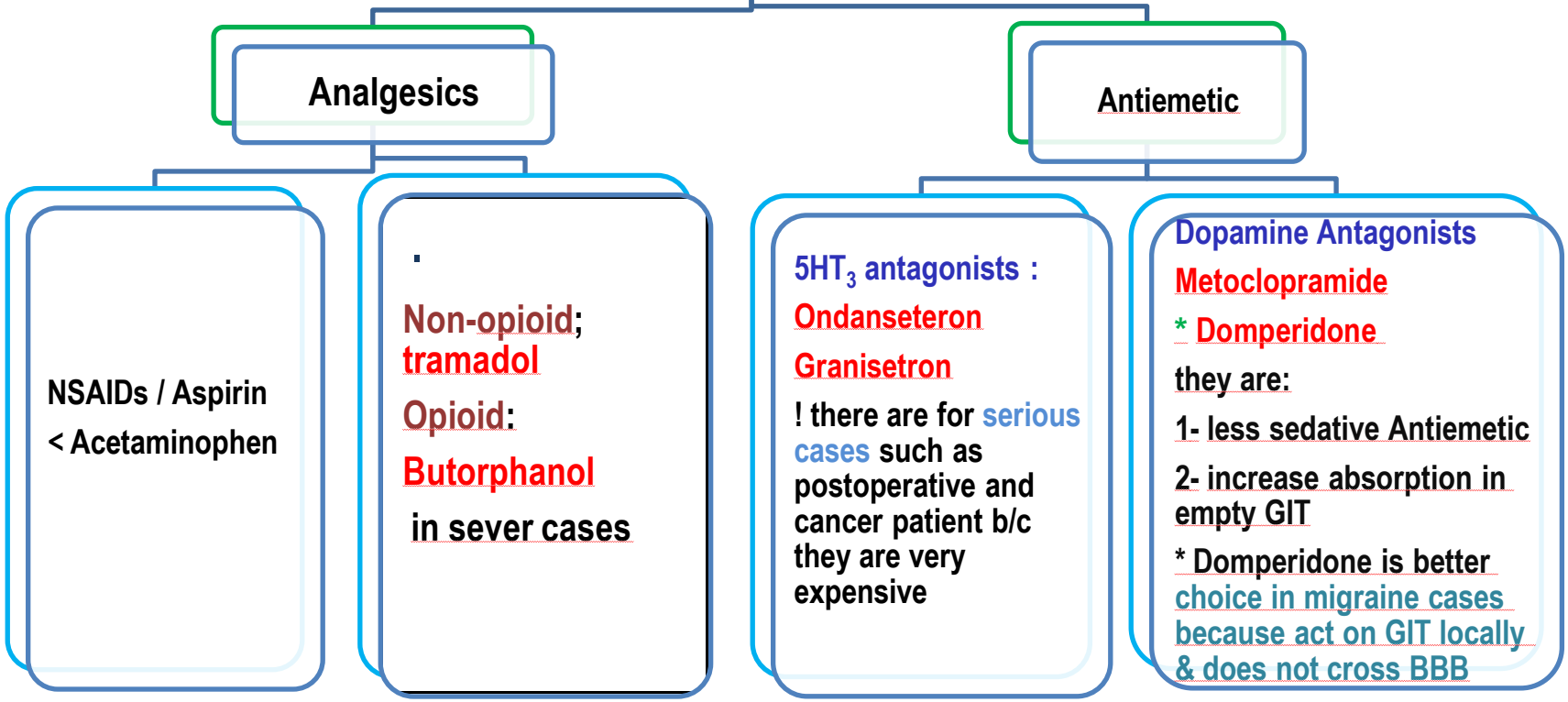
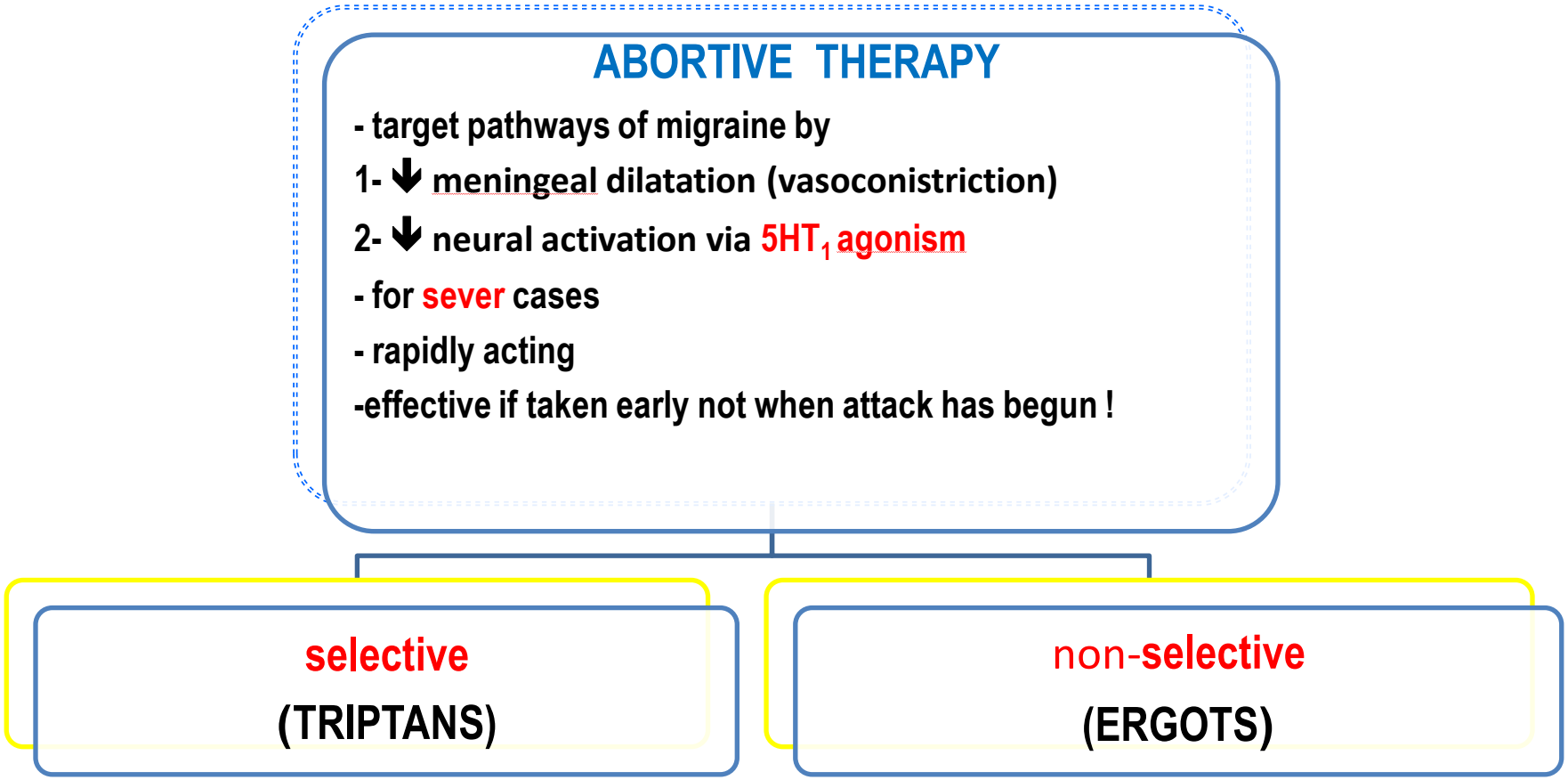

TREATMENT STRATEGY
IN HEADACHE AND MIGRAINE
ACUTE ATTACK
PREVENT RECURRENCE
RESCUE THERAPY
ABORTIVE THERAPY

RESCUE THERAPY

- Target: relieve pain, emesis
- for Mild-Moderate




ABORTIVE THERAPY
- target pathways of migraine by
1- ↓ meningeal dilatation (vasoconistriction)
2- ↓ neural activation via 5HT1 agonism
- for sever cases
- rapidly acting
-effective if taken early not when attack has begun !
selective
(TRIPTANS)
non-selective
(ERGOTS)

	ERGOTS Non-Selective	**TRIPTANES** Selective (sumatriptan, zolmitriptan, naratriptan, rizatriptan)
Mechanism of action	**Agonism at $5HT_1$ receptors** **At presynaptic trigeminal nerve endings→** **↓release of vasodilating peptides** **↓excessive firing of these nerve endings** **At blood vessels → ↓vasodilation & stretching of the pain endings** **↓ transmitter release in the perivascular space.** **Partial agonist effect on α-adrenoceptors → vasoconstriction** **Antagonist to some dopaminergic & serotonergic receptors**	**Agonism at $5HT_1$ receptors** **At presynaptic trigeminal nerve endings→** **↓release of vasodilating peptides** **↓excessive firing of these nerve endings** **At blood vessels →↓vasodilation & stretching of the pain endings** **↓ transmitter release in the perivascular space.** **No α_1, α_2, β –adrenergic , dopamine or muscarinic receptors.**
Indication	**- They are only used to abort the attacks** **- Their use is restricted to patients with frequent, moderate attack or infrequent but severe attacks.**	**- They are only used to abort the attacks** **- Their use is restricted to patients with frequent, moderate attack or infrequent but severe attacks.**
Contraindicaction	**- Pregnancy; fetal distress and miscarriage** **- Peripheral and coronary vascular diseases** **- Hypertension** **- Liver and kidney diseases** **- Fever, sepsis** **- For prophylaxis of migraine.** **- In concurrent use with:** **1- triptans (at least 6 hrs from last dose of tryptans or 24 hrs from stopping ergotamine)** **2- β-blockers** (propranolol)	**- Peripheral vasospastic diseases** **- Uncontrolled hypertension** **- History of ischemia** **- Cerebrovascular disorders** **- Renal or hepatic impairment→ NARA > RIZOTRYPTAN** **- In concurrent use with:** **1- ergots or others inducing vasospasm** **2- MAO Is, lithium, SSRIs, ….→ especially with RIZO & ZOLMITRIPTAN**

Adverse effects	**- Nausea ,vomiting , abdominal pain and diarrhea** **- Feeling of cold and numbness of limbs, tingling** **- Pericardial distress, anginal pain due to coronary spasm, and disturbed cardiac rhythm (tachycardia or bradycardia)** **- Prolong use → rebound headache due to vasodilatation followed by vasoconstriction.** **- Prolong use and high dose → paraesthesia & gangrene** **- Hallucination.**	**- Mild pain and burning sensation at the site of injection.** **- Paraesthesia, tingling ,warmth, heaviness** **- Flushing / Dizziness** **- Vasospasm** **- Ischemic heart; Angina → M.I** **- Hypertension** **- Arrhythmias** **!!!** ZOLMITRIPTAN: **- Chest & neck tightness** **- Somnolence**
Types of drugs	**1- Ergotamine tartarate:** $T_{1/2}$: **nearly 2 hours, but ergotamine produces vasoconstriction 24 hours or longer due to high and long tissue binding ability.** Present in : **oral, sublingual, rectal suppository, inhaler and injectable forms** **Caffeine → increase the absorption of oral preparation** **2- Dihydroergotamine (DHE) :** $T_{1/2}$: **more rapidly than ergotamine** Present in : **nasal spray, inhaler and injectable forms**	**1-SUMATRIPTAN** $T_{1/2}$: **nearly 2 hours** Present in : **nasal spray and injection forms** Peak(T_{max}) : **plasma concentration → 20 min.** **2-ZOLMITRIPTAN** $T_{1/2}$: **nearly 3 hours** Forms : **nasal spray, and injectable forms** Peak(T_{max}) :**after 2 hrs** **3- NARATRIPTAN** $T_{1/2}$: **nearly 6 hours** Forms : **Oral preparations** Peak(T_{max}) :**after 2 hrs** **4- RIZATRIPTANE**

Remember !!!

They are vasoconstrictors → vascular disorders …

DECIDING WHETHER BETTER WITH A TIYPTAN OR WITH DHE.

For patients with headache episodes lasting 2 or 3 days at a time, DHE is often the optimal choice because it has an extremely $t_{1/2}$

For patients with migraines a day or less and need rapid relief of pain, tryptans are often a better choice

- The form of drug preparation could influence the choice :

Injectable sumatriptan reaches T_{max} the fastest followed by DHE nasal spray and rizatriptan

DHE nasal spray, naratriptan, have lower recurrence rates

CHOOSING A TRIPTANS

- Differences in the time to peak blood concentration T_{max}, equates with faster relief of head pain.
- Differences in $t_{1/2}$ → a clinical effect in prevent recurrence of headache

Pharmacokinetics

Medication	T_{max}(h)	$t_{1/2}$(h)
DHE	1	10
Sumatriptan SQ	0.25	2
Rizatriptan	1-1.5	2-3
Zolmitriptan	2.5	3
Naratriptan	2-3	6
Eletriptan	2.8	4
Frovatriptan	2-3	26

CHOOSING A TRIPTANS

! نتكلم عن triptans هنا فقط
اللي قبل بينهم وبين Ergots

For extremely **fast relief** within 15 min. **injectable sumatriptan** is the only choice.

المريض ممكن يتحمل لما يبدأ مفعول الدواء نستخدم :
If onset could start within a couple of hrs, **oral rizatriptan, zolmitriptan**,, or sumatriptan nasal spray are appropriate choices

If expected **re-dosing is needed & / or recurrence** of headache **Naratriptan** , frovatriptan, have slower onset, fewer side effects, and a lower recurrence rate

TREATMENT STRATEGY

PREVENT RECURRENCE

Antidepressants / Antiepileptics / Antihypertensives

Indicated when:

- More than 2 migraine attacks occur per month
- Single attacks that last longer than 24 hours
- Acute symptomatic treatment is needed for > 2-3 times/week
- Headaches impairs the patient's lifestyle
- Abortive therapy fails or is overused

Timing

The full effect of preventive therapy needs several weeks to manifest
Treatment should continue for six months and can be repeated

TREATMENT STRATEGY

PREVENT RECURRENCE

Antiepileptics;

Block Na channel & augment GABA at GABA-A receptors

Topiramate; *weight loss & dysthesia.*

Valproic; *weight gain, hair loss, polycystic ovary → not given to young females*

Antidepressants

Pizotifen; *Like TCA + $5HT_2$ antagonist + mild antimuscarinic & anti-histaminic activity. Drowsiness, ↑appetite → weight gain. Not given with other CNS depressants → sedation Not given with MAO Is*

TCA; *Ami & nortriptyline → Dopamine antagonists*

Antihypertensives

β blockers; *Propranolol, atenolol, metoprolol, Not in young & anxious nor in elderly & depressed, diabetic...etc*

Ca Channel Blockers

Cinnarazine, flunarizine, verapamil.....etc.