

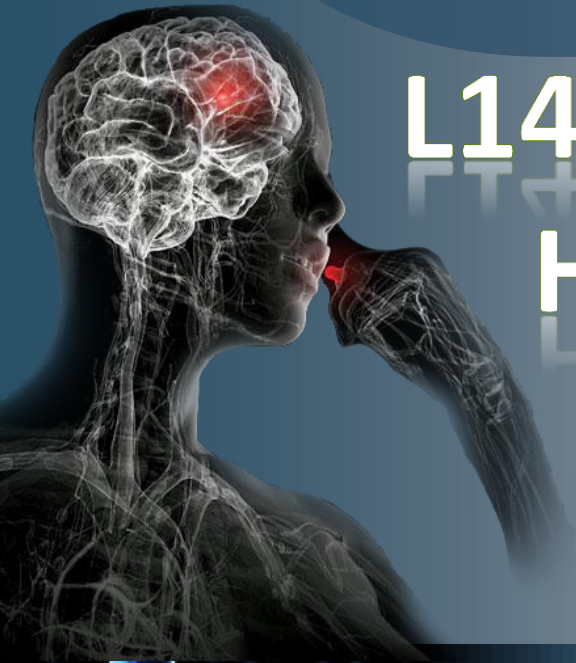
King Saud University
College of Medicine
2nd Year, 1st Block



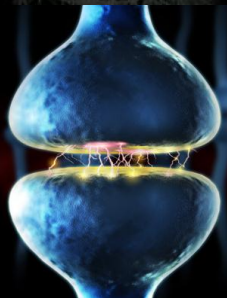
PHARMACOLOGY
433



L14: DRUGS USED IN HEADACHE AND MIGRAINE



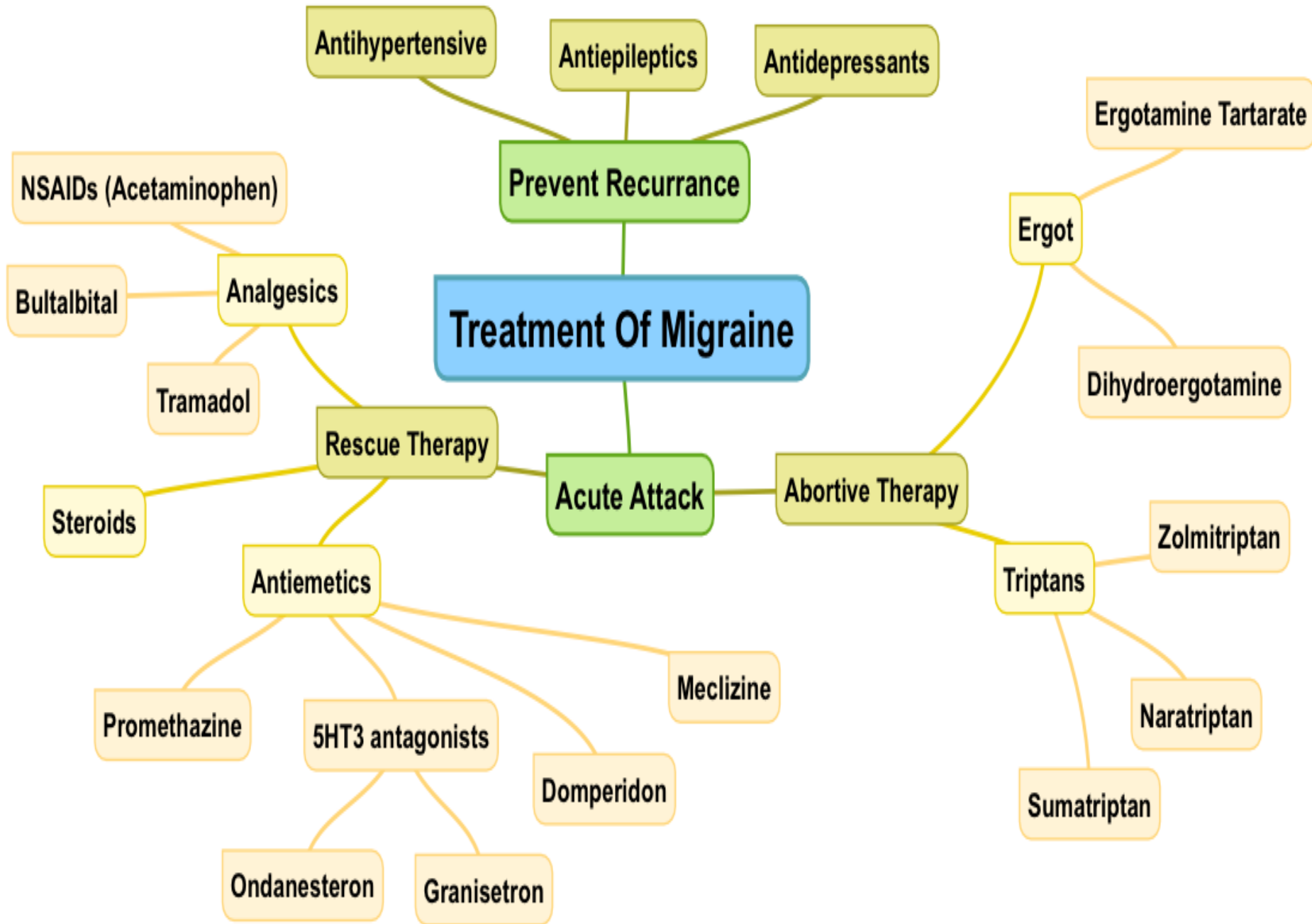
CNS Block





Objectives :

- 1. Differentiate between types of headache regarding their symptoms, signs and pathophysiology.**
- 2. Recognize drugs used to prevent migraine**
- 3. Identify drugs used to rescue and abort migraine**
- 4. Elaborate on the pharmacokinetics, dynamic and toxic profile of some of these drugs.**



Headache

Pain anywhere in the region of the head or neck

Classification

Primary:

Migraine, tension type headache, cluster headache, trigeminal cephalgias and others where cause is unknown
> NSAID

Secondary: Based on the etiology

Trauma, Vascular disorders, Disease, Homeostasis disorders
> Treat the Etiology

Migraine

-Recurrent attacks of throbbing headache

Unilateral / or on both sides.

-Lasting from > 2 up to 72 hrs.

***Preceded (or accompanied) by AURA* (Perceptual disturbance of motor, visual, auditory, and unpleasant smell).**

Triggers

Diet, stress, hormonal changes, climate, disease, therapy, lifestyle

Phases of Migraine

- 1. Prodrom Phase;** a change in mood or behavior that starts hours or days before headache. 60% of migraineurs.
- 2. Aura Phase;** Sensory > motor symptoms starts 5-20 min before the migraine attack. 20% of migraineurs.
- 3. Headache Phase;** moderate to severe pain, increase with activity + anorexia, vomiting, Intolerance to light, sounds, odors
Blurry vision /Blocked nose /Pale face
Sensations of heat or coldness /Sweating /Tenderness of the scalp
- 4. Postdrom Phase:** still not normal, either;
 - * More likely fatigued → irritability /impaired concentration /scalp tenderness /mood changes / GIT symptoms
 - * Less likely refreshed, hyperactive, apprehensive

Treatment of migraine

Treat the acute attacks

Prevent recurrence

Rescue therapy :

- ❖ Non-specific for migraine.
- ❖ For mild to moderate migraine.

Abortive therapy :

- ❖ Specific for migraine i.e.
 - ↓ meningeal dilatation
 - ↓ neural activation via 5HT₁ agonism.
- ❖ Should be taken just before the pain starts because this drug loses effectiveness once the attack has begun

- ❖ ↓ recurrence frequency of the migraine.
- ❖ ↑ The responses of abortive therapy.
- ❖ The effect of therapy needs several weeks to manifest & should continue for **6 months**.

Note: 5HT₁ decreases level of cAMP in the cell so it is **inhibitory**

Treating the acute attacks:

<u>1-Rescue therapy</u>		
Analgesics	Antiemetics <i>Antiemetics = prevent nausea and vomiting</i>	Others
Opioid: NSAIDs Aspirin Acetaminophen (drug of choice)	Dopamine Antagonists (Domperidone) : ✓ Gastro-prokinetic . ✓ ↑ Absorption of <u>abortive therapy</u> . ✓ Drug of choice to avoid sedation and sleeping.	Steroids
Non-opioid: tramadol	5HT₃ antagonists (Ondanseteron, Granisetron) : Note: 5HT3 acts as depolarizing plasma membrane so it is excitatory.	
	Phenothiazines (Promethazine): It is dopamine antagonist but causes sedation	
	H₁ antagonist (Meclizine):	

2- Abortive therapy

A- Ergots :

Non-selective agonists at 5HT1 (it is agonists at α_1 , α_2 and others)

- ↓ release of vasodilating peptides
- ↓ excessive firing of nerve endings
- At blood vessels ↓ vasodilatation

Note: 5HT1 decreases level of cAMP in the cell so it is inhibitory

The duration of each drug is so important the cases which will come are based on that

Ergotamine tartarate

- Better to be given injectable or rectal.
- If taking orally, caffeine increases its absorption (cafergot).
- Short T_{1/2} but the effect remains **for 24 hours**

Dihydroergotamine

- Better to be taken as nasal spray
- Given injectable (if patient is vomiting)

*Indications:

They are only used to abort the attacks [**Exception Dihydroergotamine can be given for severe, recurrent attacks**]

*ADRs:

- **GIT upset**
- **Feeling of cold and numbness of limbs, tingling**
- **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 (tingling or burning sensation**

*Contraindicated:

Pregnancy, Peripheral and coronary vascular diseases, Hypertension, Liver and kidney diseases, prophylaxis of migraine & with β -blocker.

2- Abortive therapy

B- Triptans :

Selective agonists at 5HT₁ receptors

Sumatriptan :

- nasal spray, and injectable
- peaks after 2 min & t_{1/2} nearly 2 hours
(so drug of choice for emergency)

Zolmitriptan

- *nasal spray, and injectable*
- peaks after 2 hrs & t_{1/2} nearly **3 hours**

Naratriptan

- *Oral preparations, nasal spray, and injectable*
- peaks after 2 hrs & t_{1/2} nearly **6 hours**
- For recurrence attacks

Indications:

- ❖ frequent, moderate or infrequent but severe attacks.
- ❖ In cluster headache.

ADRs

- ❖ Mild pain and burning sensation at the site of injection.
- ❖ Vasospasm, Ischemic heart, Angina and Arrhythmias.
- ❖ special ADRs for **Zolmitriptan** (Chest & neck tightness and somnolence).

Contraindicated:

- Peripheral vasospastic diseases
- Uncontrolled hypertension
- History of ischemia
- Cerebrovascular disorders
- with Ergots
- with MAOIs, lithium, SSRIs, → **(5HT increased to toxic level)**
- **Only naratriptan not used with renal and hepatic impairment**

The duration of each drug is so important the cases which will come are based on that

Prevent recurrence

Antiepileptic	Antidepressants	Antihypertensives
<p data-bbox="239 554 587 796">-Topiramate. -Valproic. -Gabapentin.</p> <p data-bbox="239 839 649 1145">Block Na channel & augment GABA at GABA-A receptors</p>	<p data-bbox="736 554 1222 759">-TCA: amitryptylin and nortryptyline. -SSRIs.</p>	<p data-bbox="1263 554 1595 825">-B blockers; propranolol. -Ca Channel Blockers .</p> <p data-bbox="1263 911 1734 1139">Propranolol is commonly used in prophylaxis of migraine attack</p>

SUMMARY

Drug	Uses	S.E
Opioid: NSAIDs, Aspirin Acetaminophen	Analgesics Non-specific for migraine. For mild to moderate migraine <u>Treat the acute attacks</u>	-----
Non-opioid: tramadol		-----
Domperidone, Ondansetron, Granisetron, Meclizine	Non-specific for migraine. For mild to moderate migraine Antiemetics <u>Treat the acute attacks</u>	-----
Ergotamine tartrate, Dihydroergotamine	They are only used to abort the attacks [Exception Dihydroergotamine can be given for severe, recurrent attacks]	-anginal pain due to coronary spasm, and disturbed cardiac rhythm (tachycardia or bradycardia). -Prolong use → rebound headache due to vasodilatation followed by vasoconstriction.
Sumatriptan , Zolmitriptan , Naratriptan	❖ frequent, moderate or infrequent but severe attacks. ❖ In cluster headache.	-Mild pain and burning sensation at the site of injection. -Vasospasm, Ischemic heart, Angina and Arrhythmias. -special ADRs for Zolmitriptan.
Topiramate, Valproic, Gabapentin	Antiepileptic <u>Prevent recurrence</u>	-----
Amitriptylin, nortriptyline, SSRIs.	Antidepressants <u>Prevent recurrence</u>	-----
Propranolol, Ca Channel Blockers	Antihypertensives <u>Prevent recurrence</u>	-----

Quiz yourself

1-A patient suffered an acute migraine attack in the morning, what is the drug of choice to avoid the vomiting?

- A. Meclizine
- B. Domperidone
- C. Promethazine
- D. NSAD's

2-Drug for emergency migraine?

- A. Zolmitriptan
- B. Dihydroergotamine
- C. Sumatriptan
- D. Naratriptan

3- Ergots are agonists for which receptor ?

- A. 5HT1
- B. 5HT3
- C. 6HT1
- D. 1HT5

4-A patient suffered an acute migraine attack which of the following drugs is best used to relieve his pain ?

- A. NSAIDs
- B. Tramadol
- C. Promethazine
- D. Aspirin

5-A Heart patient suffering from migraine which of the following is contraindicated?

- A. NSAIDs
- B. Zolmitriptan
- C. Promethazine
- D. Aspirin

6- after taking migraine treatment a patient developed Chest and neck tightness which of the following drugs was he using?

- A. Zolmitriptan
- B. Sumatriptan
- C. Naratriptan
- D. Dihydroergotamine

7- a depressed patient has an ongoing migraine attacks What is the drug of choice?

- A. Topiramate
- B. Propranolol
- C. Fluoxetine
- D. Valproic

8-a patient has renal impairment, which drug is contraindicated?

- A. Dihydroergotamine
- B. Domperidone
- C. Tramadol
- D. Promethazine

9-A patient has hepatic impairment, which drug is contraindicated?

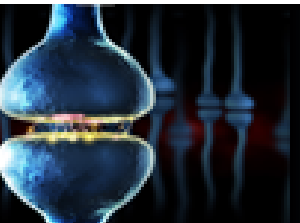
- A. Sumatriptan
- B. Naratriptan
- C. Zolmitriptan
- D. NSAID's

10-A pregnant woman had an migraine attack, what is the drug of choice?

- A. Ergotamine tartarate
- B. Dihydroergotamine
- C. Ergots
- D. NSAID's

Answers:

1-B, 2-C, 3-A, 4-D, 5-B, 6-A, 7-C, 8-A, 9-B, 10-D



CNS Block

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We hope that we made this lecture easier for you
Good Luck !



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