



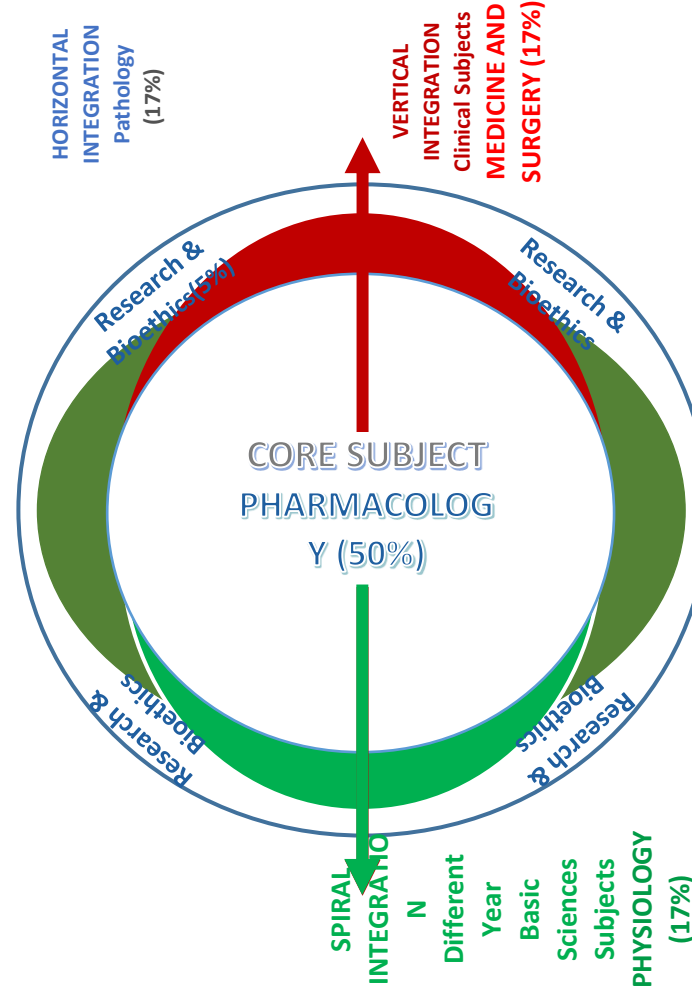
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MOTTO AND VISION



- To impart evidence based research oriented medical education
- To provide best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine



Model 4th Year Pharmacology LGIS (18 slides)

Core Subject –9 slides(50%)

Horizontal Integration
pathology 2 slides–(11%)

Vertical integration
(Clinical Subjects)

- (Medicine and surgery) –3 slides 17%

Spiral Integration (physiology)–
(3 slides) 17%

Research & Bioethics 1
slide(5%)



ERGOT ALKALOIDS & DRUGS USED IN MIGRAINE

4TH YEAR MBBS

LGIS







INTRODUCTION

- Migraine has been ranked among the world's most disabling medical illnesses
- Approximately 15% of people are affected by migraines
- It occurs more often in women(75%)

DIFFERENTIAL DIAGNOSIS

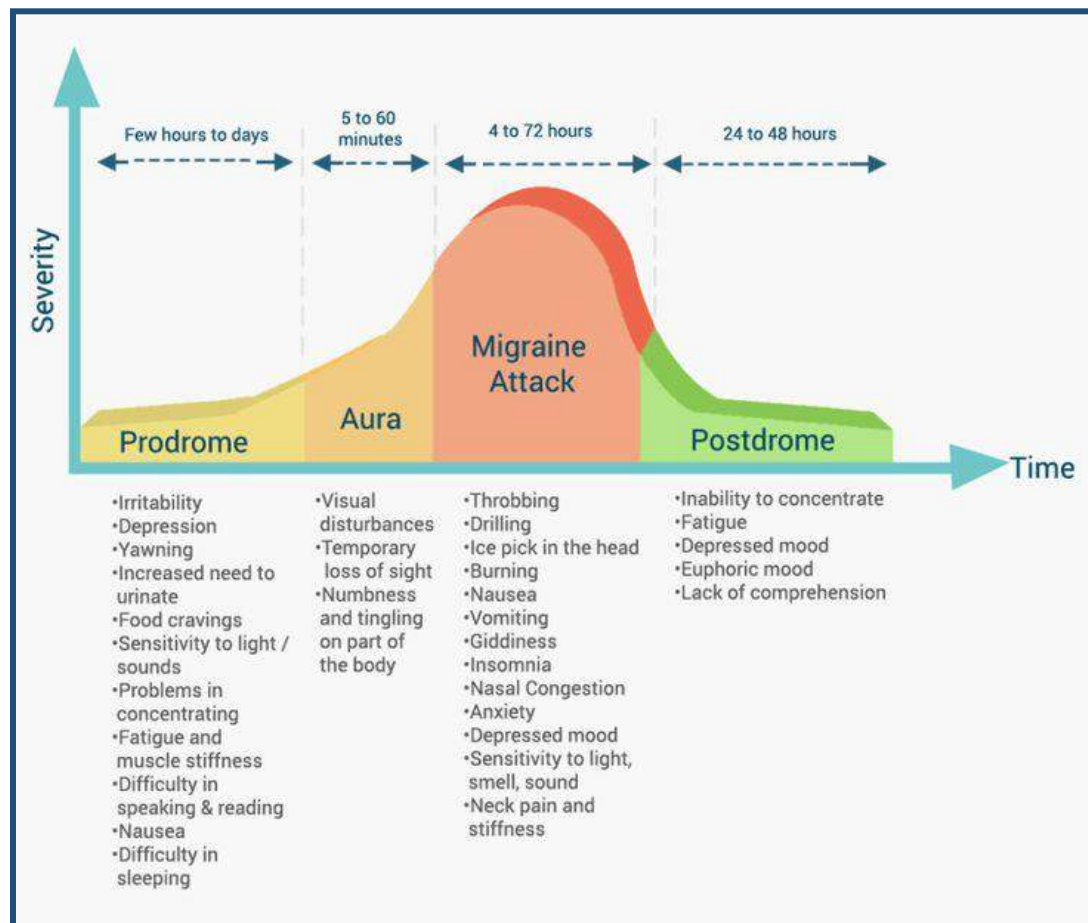
- Episodic attacks
- Moderate to severe intensity
- Throbbing in nature
- Associated with
 - Nausea
 - Vomiting
 - Photophobia
 - Phono phobia
 - Focal neurological symptoms (aura) in 1/3rd patients

Headaches			
Sinus: pain is usually behind the forehead and/or cheekbones	Cluster: pain is in and around one eye	Tension: pain is like a band squeezing the head	Migraine: pain, nausea and visual changes are typical of classic form
			

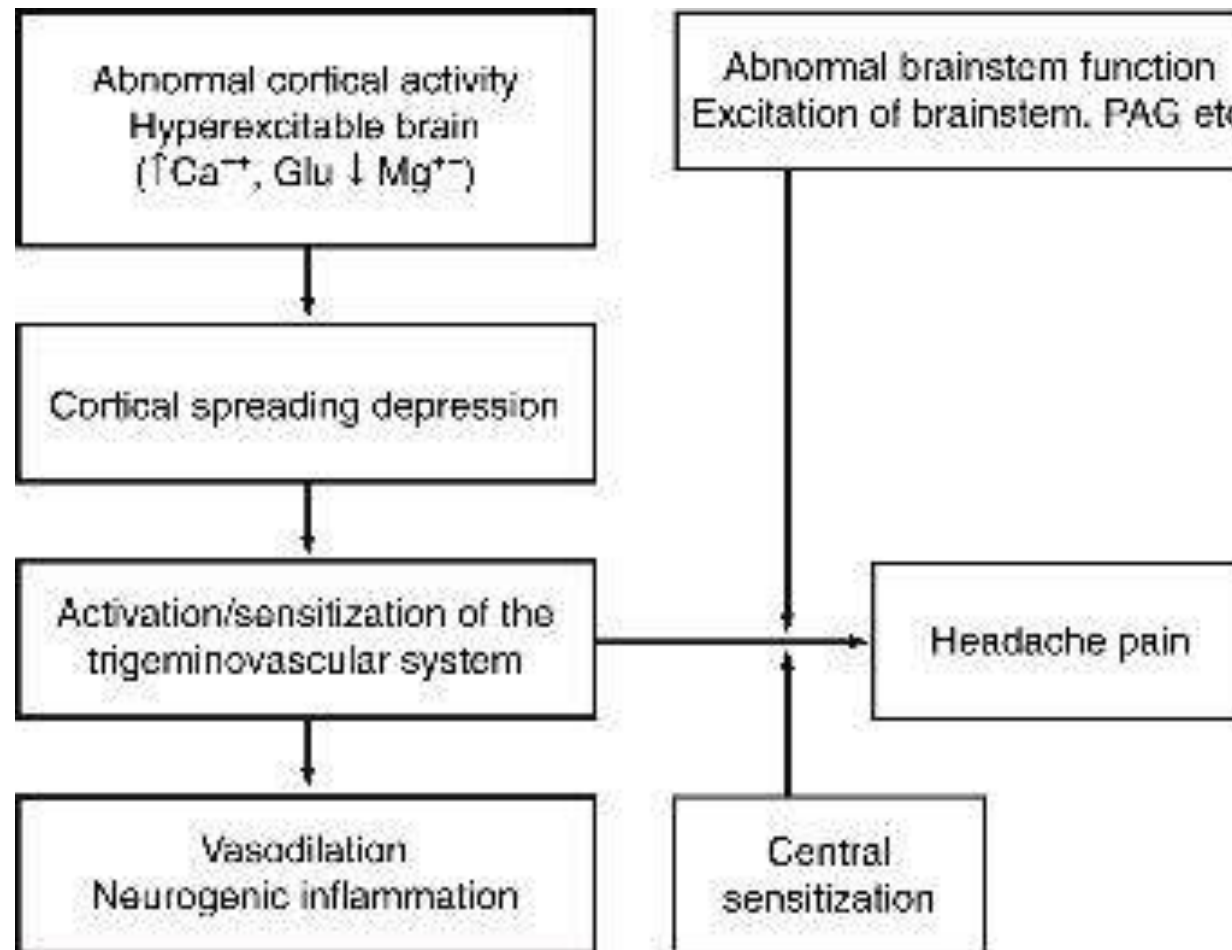
CLINICAL FEATURES OF MIGRAINE

• STAGES OF MIGRAINE

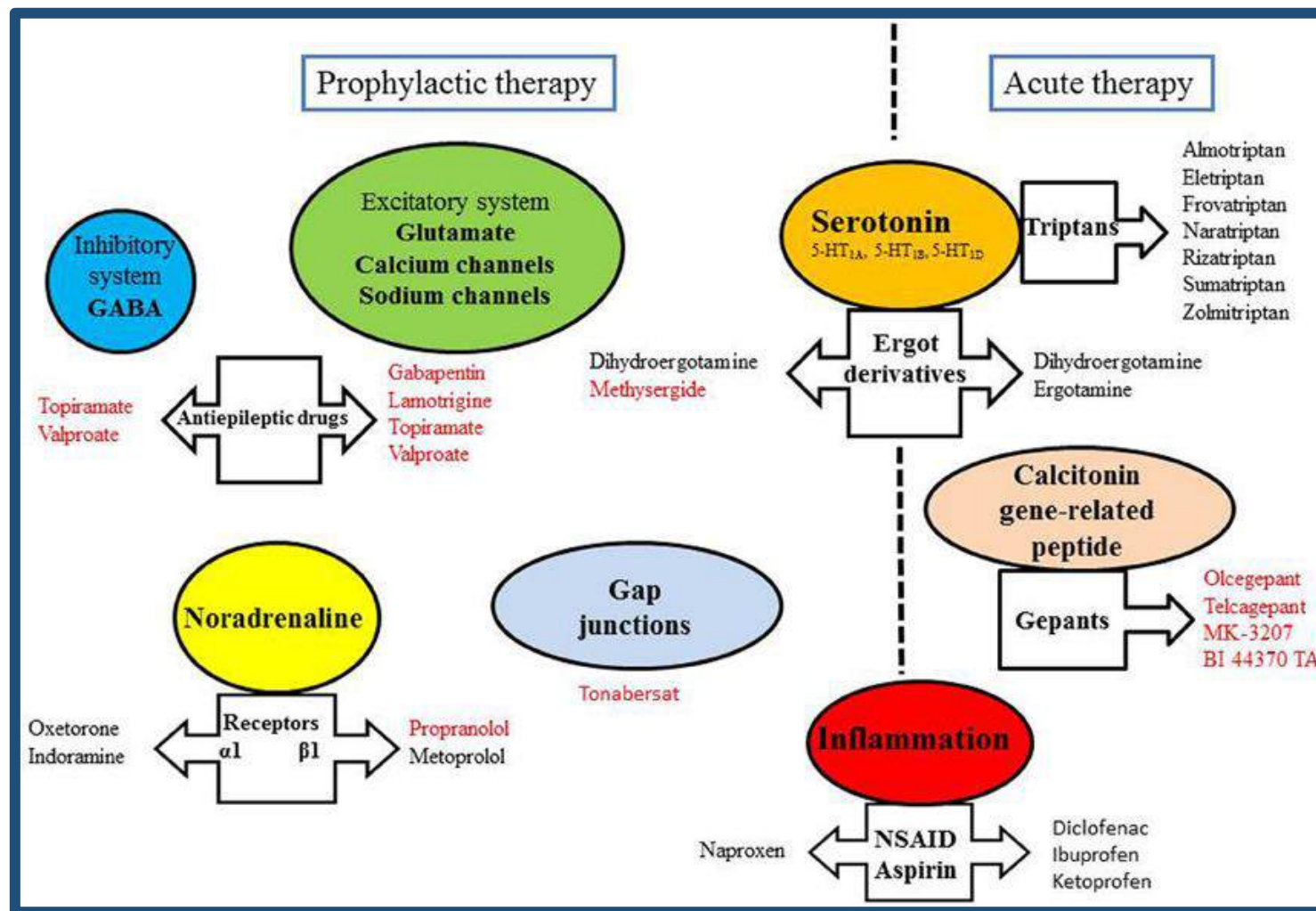
- The prodromal
- The aura
- The pain phase
- The postdrome



PATHOGENESIS OF MIGRAINE



PHARMACOTHERAPY OF MIGRAINE





PHARMACOTHERAPY OF MIGRAINE

- Mild
 - Simple analgesics/NSAIDs (\pm Anti emetic)
- Moderate
 - NSAIDs combinations/Ergot Alkaloids/Sumatriptan(+ Antiemetic)
- Severe
 - Ergot alkaloids/ Sumatriptan/ Rizatriptan(+ Antiemetic)



PROPHYLACTIC TREATMENT

- PHARMACOLOGICAL
 - B-adrenergic blockers(Propranolol, Metoprolol)
 - Non-steroidal anti-inflammatory drugs
 - Ant neuropathic medications such as the antidepressants(Amytryptiline, Venlafaxine)
 - Calcium-channel antagonists
 - Anticonvulsants(Sodium valproate and Topiramate)
 - Pizotifen
 - ACE Inhibitors/ARBs



PHARMACOTHERAPY OF MIGRAINE

- Activation of 5-HT 1D/1B receptors on presynaptic trigeminal nerve endings(triptans, the ergot alkaloids, antidepressants, antiseizure agents inhibit the release of vasodilating peptides & suppress excessive firing of these nerve endings
- Vasoconstriction of dilated vessels ...direct 5-HT agonists (the triptans and ergot)leads to decrease stretching of the pain endings.



5 HT AGONISTS..Triptans

- Sumatriptan
 - Zolmitriptan
 - Almotriptan
 - Eletriptan
 - Frovatriptan
 - Rizatriptan
 - Naratriptan
- Triptans are safe, effective and appropriate first-line treatments for
 - Patients without cardiovascular contraindications
 - Moderate to severe headache and in patients where simple or combination analgesics have failed to provide adequate relief



5 HT AGONISTS..Triptans

- **Serotonin (5-hydroxytryptamine or 5-HT) agonists with high affinity for 5-HT_{1B} or 5-HT_{1D} receptors(receptor types are found in cerebral and meningeal vessels and mediate vasoconstriction)**
- **Action at the 5-HT_{1B} receptors on blood vessels produces cranial vasoconstriction**
- **Action at presynaptic 5-HT_{1D} receptors inhibits the release of vasoactive peptides and nociceptive neurotransmitters**

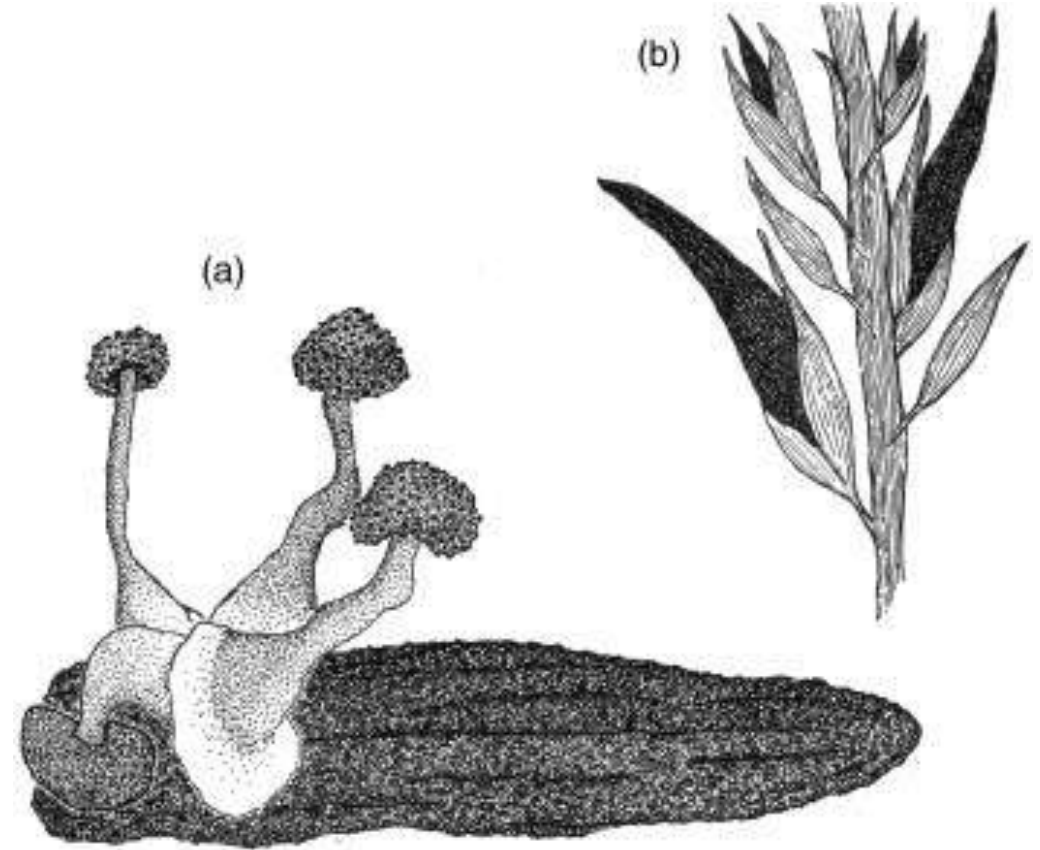
ERGOT ALKALOIDS

SOURCE:

FUNGUS - *Claviceps purpurea*

ERGOTISM:

St. Anthony's fire





CLASSIFICATION

- AMINE ALKALOIDS:
 - 6-Methyl ERGOLINE
 - Lysergic acid
 - Lysergic acid Diethylamide
 - Ergonovine
 - Ergometrine
- PEPTIDE ALKALOIDS:
 - Ergometrine
 - α -Ergocryptine
 - Bromocriptine

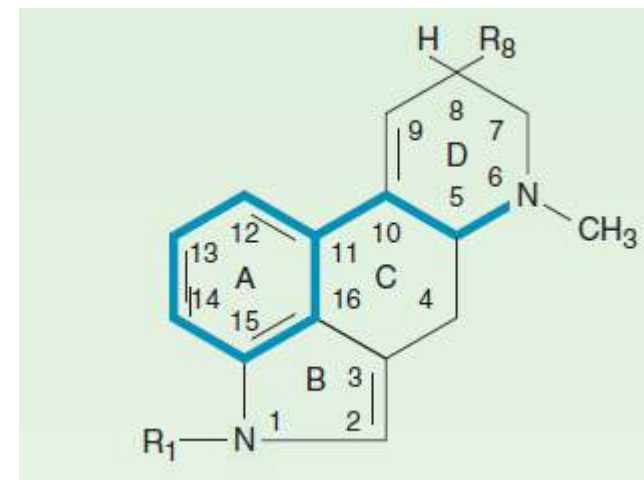
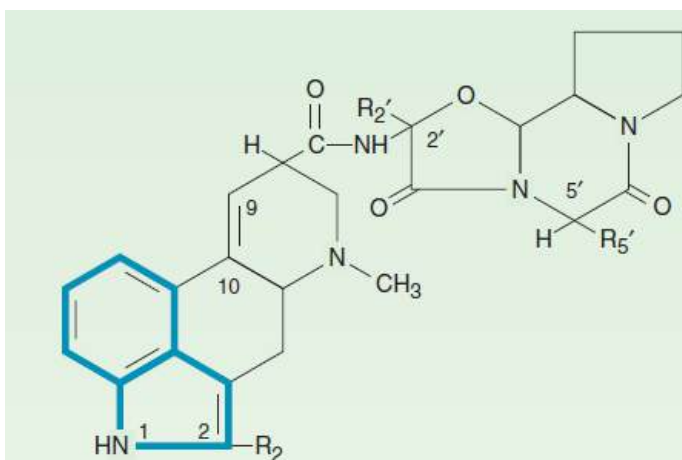


PHARMACOKINETICS

- ROUTES: oral, S/L, I/M, I/V, nasal, rectal
- Amine alkaloids _____rectum, buccal and aerosol inhaler
- Variable absorption from GIT
- Ergometrine & methylergometrine – rapid oral absorption
- Extensive metabolism
- Ergotamine- poor oral BA(Can be increased with Caffeine)

MECHANISM OF ACTION

- Multi-receptor function
 - Agonist, partial agonist, and antagonist at alpha , serotonin
 - Presynaptic 5HT receptor (5HT_{1A/1D})
 - Partial agonist at 5HT₂ – uterus, blood vessels
 - Partial agonist at CNS dopamine
 - Antagonist at blood vessels





PHARMACOLOGICAL EFFECTS OF ERGOT ALKALOIDS

- **CNS:**
 - Hallucinogenic
 - LSD – drug abuse (agonist at $5HT_2$ in CNS both pre & post junctional)
 - Nausea, vomiting – CTZ D_2
 - Decrease extrapyramidal symptoms - striatum D_2
- Inhibition of prolactin secretion – pituitary regulatory D_2
(Bromocriptine, pergolide, Cabergoline....highest selectivity for pituitary dopamine receptors)



PHARMACOLOGICAL EFFECTS OF ERGOT ALKALOIDS

VASCULAR SMOOTH MUSCLE:

- Alpha stimulation – VC – increase TPR & BP
- Also vascular 5HT₂ ...in migraine....Effective due to prejunctional stimulation
- Vasospasm...prolongedSlow dissociation from receptors
- Flow of blood to periphery decreases
- Ergotamine- partial agonist...dihydroergotamine



PHARMACOLOGICAL EFFECTS OF ERGOT ALKALOIDS



UTERUS:

- Stimulation of α_1 & $5HT_2$
- More in uterus at term
- Ergometrine (Ergonovine) more selective
- Rhythmic contractions and relaxation in small doses and prolonged contracture at higher doses



PHARMACOLOGICAL EFFECTS OF ERGOT ALKALOIDS



GIT:

- Stimulation of 5HT₂ receptors
- Increase motility, diarrhea, abdominal cramps
- Dopamine receptors CTZ – anorexia, nausea, vomiting



CLINICAL USES OF ERGOT ALKALOIDS

- ▶ MIGRAINE(Ergotamine)
- ▶ HYPERPROLACTINEMIA(Bromocriptine)
- ▶ POST PARTUM HAEMORRHAGE(Ergometrine)
- ▶ Diagnosis of variant Angina(Ergometrine/Ergonavine)
- ▶ Senile cerebral insufficiency



ADVERSE EFFECTS AND COMPLICATIONS

- CNS: Hallucination, Drowsiness
- GIT: Nausea, vomiting & diarrhoea
- Vasospasm// excessive can lead to gangrene
- Connective tissue proliferation in retroperitoneal space, pleural space & endocardial tissue (Methysergide)



CONTRAINDICATIONS

- Peripheral vascular disease
- Symptomatic coronary artery disease
- Collagen disease
- Pregnancy



BIOETHICS AND RESEARCH

BIOETHICS

- Linde M, May A, Limmroth V, Dahlöf C, Headache Masters Programme. Ethical aspects of placebo in migraine research. Cephalalgia. 2003 Sep;23(7):491-5.

RESEARCH

- Słychan K, Frańczuk A, Makłowicz A, Szpulak A, Kopczyńska E, Głoskowska J, Grzelka M, Kuleta K, Łęska AE, Kejna P. Advances in migraine treatment-a review. Quality in Sport. 2024 Aug 29;21:54055-.



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*Thank
you*

