

CHAPTER

PHARMACOLOGY

(Autocoid)

Autocoid

- ◆ Substance synthesized, secret and act locally called autocoid
- ◆ Also called local hormone

(1) Amine

- ◆ Histamine (Triple response)
- ◆ 5 HT (Triphasic response)

(2) Lipid (long chain fatty acid)

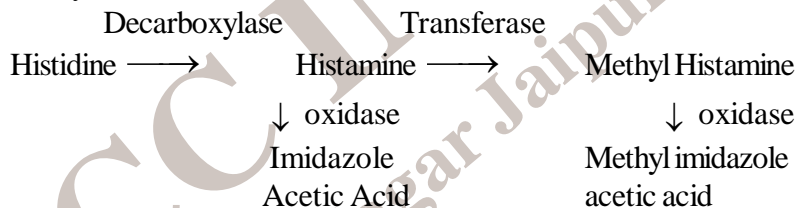
- ◆ Prostaglandin (induce pain, inflammation, pyrexia)
- ◆ Leucotriens (cause Bronchoconstriction)
- ◆ Platelet activating factor (↑ platelet)

(3) Peptide

- ◆ Bradykinin
- ◆ Angiotensin
- ◆ Kallidin

Histamine

- ◆ Histamine synthesized from histidine



- ◆ Histamine majorly act on H_1 and H_2 receptor
- ◆ Histamine cause dilation of small Blood vessels, can result of Hypotension and flushing
- ◆ Increase capillary permeability and causes edema
- ◆ Intradermal injection cause Triple response
 - Red reaction (vasodilation)
 - Wheal (exudation of fluid)
 - Flare (spreading redness due to exon reflex)
- ◆ Histamine cause positive inotropic effect (H_2 stimulation) and Negative dromotropic effect (H_1 stimulation)
- ◆ Histamine is powerful Bronchoconstrictor causes Anaphylactic shock and Abdominal cramp.
- ◆ Histamine ↑ HCl secretion, cause gastric ulcer
- ◆ Histamine causes pruritis and pain
- ◆ Histamine maintain wakefulness and stimulate reticular activating system.

Drug - Beta Histine - orally, used to control vertigo in meniers disease

Histamine Antagonist

H₁ antagonist

1) First generation antihistaminic -

- ◆ cause sedation and psychomotoric impairment
- ◆ These drug also have anti cholinergic, anti vertigo, anti Allergic activity and Anti emetic activity
- ◆ These are contraindicated to attentive person

(a) Highly sedative

- (1) Diphen hydramine
- (2) Dimen hydrinate
- (3) Promethazine
- (4) Hydroxyzine (Atarax)

(b) Moderate sedative

- (1) Pheniramine (Evil)
- (2) Cyproheptadine (Aptizer anti 5HT)
- (3) Cinnerazine (Anti vertigo)
- (4) Meclizine
- (5) Buclizine

(c) Mild sedative

- Chlor pheniramine
- Mepyramine
- Cyclizine
- Doxylamine

- ◆ Anti Histaminic are DOC for Idiopathic pruritis
- ◆ cinnarazine use in vertigo
- ◆ Cyproheptadine increase appetite.
- ◆ Diphen hydramine, promethazine dimenhydrinate also used morning sicknes.
- ◆ Anti Histamine are Prophylactic agent for motion sickness .
- ◆ Doxylamines is most preffered drug for morning sickness.

ADR of first generation anti Histaminics

- ◆ Sedation ,psychomotor impairment
- ◆ Dry mouth, constipation, Blured vision, urinary retention

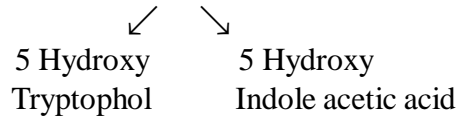
2) Second generation Anti Histamine

- ◆ **Terfinadine** - fastest acting, overdose causes Torsade de point
(polymorphic ventricular Tachycardia)
- ◆ **Fexofenadine** is active metabolite of Terfinadine
- ◆ **Astemizole** - slowest and longest acting
- ◆ **Loratadine** - long acting
- ◆ **Desloratadine** - metabolite of Loratadine
- ◆ **Cetirizine** - metabolite of hydroxyzine
- ◆ **Levocetirizine** - L - isomer of cetirizine (more potent)
- ◆ **Olapatadine** - Nasal spray for seasonal allergic rhinitis

- ◆ **Alcaftadine** - ophthalmic solution for allergic conjunctivitis

Serotonin (5HT)

- ◆ 5HT also called Neurotransmitter of Happiness
- ◆ Biosynthesized by Tryptophan
Tryptophan → 5 Hydroxy tryptophan → 5 HT



- ◆ Serotonin produce Triphasic response on BP by IV injection
- ◆ Serotonin ↑ Platelet aggregation, ↓ Acid secretion and ↑ Mucus secretion

(1) Selective Drug

- ◆ **5HT₁ agonist (Partial)** - Buspirone, gapirone used as antianxiety
- ◆ **5HT₁ agonist** - Sumatryptan (Doc for Acute migraine) Naratryptan
- ◆ **5HT₂ antagonist** - Ketanserin, Retanserin used as anti hypertensive
 - ◆ Clozapine, olanzapine, Risperidone are atypical anti psychotic used in schizophrenia and Bipolar disorder
- ◆ **5HT₃ antagonist** - Ondansetron, granisetron, Tropisetron Most effective anti emetic(DOC in chemotherapy induced vomiting)
- ◆ **5HT₄ agonist** - Cisapride, mozapride, Tagaserod useful in GERD

(2) Non selective drug

- ◆ Cyproheptadine - Anti 5HT increase appetite and weight gain
- ◆ Methy sergide - anti 5HT, used prophylaxis of migraine
- ◆ LSD - Hallucinogen

Ergot Alkaloid

- ◆ Derived from fungus claviceps purpurea on rye plant
- ◆ Drug posses partial agonistic and antagonist effect on 5HT₁ α₁ and dopaminergic receptor
- ◆ **Ergot derivative cause** - Dry gangrene of Hand and feet (Max-Ergotamine)
- ◆ **Ergotamine and dihydro** -ergotamine used in acute attack of migraine(max.ergotamine)
- ◆ **Diphdro Ergotoxine** - used in Dementia
- ◆ **Bromocryptine** - use in parkinson, hyper prolactinemia and Acromegaly
- ◆ **Methy sergide** - prophylaxis of migraine attack
- ◆ Ergot Alkaloid are contraindicated in pregnancy because They cause uterine contraction, and miscarriage
- ◆ Ergometrine used in postpartam heamorrhage

Drug for migraine

- ◆ Migraine is unilateral pulsatile headache due to dilation and inflammation effected cerebral vessels

Drug

- ◆ **Ergotamine** - oral / sublingual
- ◆ **Dihydro ergotamine** - Parentral
- ◆ Caffiene is added to enhance absorption of ergotamine

- ◆ Sumatryptan - DOC for Acute attack of migraine
- ◆ Triptan and ergotamine are contraindicated for patient of CAD (Coronary artery disease) for them Butorphanol (opioids are preferred)

Drug for prophylaxis of migraine

- (i) Propanolol
- (ii) Flunarazine (Ca and Na channel Blocker)
- (iv) Methysergide, TCA, and cyproheptadine
- (v) Clonidine
- (vi) Topiramate

Prostaglandin

- ◆ Prostaglandin and thromboxane are synthesized from Arachadonic Acid
- ◆ PGI₂ called prostacycline
- ◆ NSAID inhibit both prostaglandin and Thromboxane

CNS - Prostaglandin are pyrogenic cause fever

CVS - Prostaglandin are vasodilator (Except PGF₂)

- ◆ Thromboxane is vasoconstrictor

Platelet - Prostacycline (PGI₂) inhibit platelet aggregation while thromboxane is potent platelet aggregator

- ◆ Epoprostenol (prostacycline) used as anti aggregatory drug in dialysis and cardio pulmonary Bypass

Uterus - Misoprostol with mifepristone or methotrexate used for induction of Abortion in first few weak pregnancy

- ◆ Misoprostol and dinoprostone employed in cervical ripening during labour
- ◆ Carboprost (PGF_{2α}) used to control post partum heamorrhage
- ◆ Prostaglandin induce pain during Mensturation (Dysmonorrhoea)

Bronchi - Prostaglandin (except PGF_{2α}) are Bronchodilator while thromboxane is Broncho constrictor

GIT - Prostaglandin ↓ acid secretion and ↑ Mucus secretion and mucosal Blood flow.

- ◆ Misoprostol used in drug induced peptic ulcer

Kidney - PG causes renal vasodilation

- ◆ PG stimulate renin release

Male reproductive system - used in erectile dysfunction system

Eye - Latanoprost and unoprostone used in glucoma

- ◆ Epoprostenol - PGI₂
- ◆ Dinoprostone - PGE₂
- ◆ Mesoprostol - PGE₁
- ◆ Carboprost - PGF_{2α}
- ◆ Latanoprost - PGF_{2α}

Leucotriens

- ◆ First synthesized leucotriens LTA_4
- ◆ Leucotriens also known as slow releasing substance of anaphylaxis (SRS-A)
- ◆ Corticosteroid decrease production of leucotriens by inhibiting phospholipase A_2
- ◆ Zileuton is lipoxygenase inhibitor
- ◆ Montelukast, zafirlucast are LT antagonist platelet activating factor
- ◆ PAF is most potent agent, that increase capillary permeability
- ◆ Apantant and lexipantant are PAF antagonist

Thromboxane(TXA_2)

- ◆ Aspirin inhibit TXA_2
- ◆ Licoferene is Cox-Lox inhibitor

NSAID

(1) Paracetamol

- ◆ Paracetamol not have anti inflammatory activity
- ◆ Paracetamol metabolized into NAPQ (N-acetyl para aminino benzo quinoneimine)
- ◆ NAPQ increase by Alcohol Ingestion
- ◆ NAPQ cause hepatotoxicity
- ◆ Paracetamol is selective cox- 3 inhibitor
- ◆ Paracetamol poisoning - If plasma concⁿ > 300 $\mu\text{g}/\text{ml}$ at 4 hours
plasma concⁿ 45 $\mu\text{g}/\text{ml}$ at 15 hours after ingestion
- ◆ Antidote of PCM Poisoning - N-Acetyl cystiene

(2) Aspirin (Salicylate)

- ◆ Irreversible enzyme inhibitor
- ◆ Rest are reversible enzyme inhibitor
- ◆ It have analgesic and anti inflammatory action.
- ◆ At low dose (40-325 mg) use as antiplatelet.
- ◆ Aspirin use in prophylaxis of MI and stroke.
- ◆ Aspirin is contraindicated during the treatment of Danguie
- ◆ Aspirin used to inhibit Niacin induced flushing.
- ◆ Useful in Dysmenorrhoea and pre Aclampsia
- ◆ At long term therapy - it decrease incidence of colo ractal carcinoma

ADR of Aspirin

- 1) Respiratory Alkalosis - Headache, Vertigo, Tinnitus, Vomiting
- 2) Prolong Bleeding time, use safely with anti coagulant
- 3) Hyper uricemia (Not used in Gout)
- 4) Rey's syndrom in child below 12 year (swelling in Brain and liver)

Classification

(1) Non selective

Salicylate - Aspirin, Diflunisal
Indole - Indomethacin, sulindac
Propionic Acid - Ibuprofen, ketoprofen, Naproxen
Anthranillic acid - Mefenamic acid
Oxicam - Piroxicam, Tenoxicam
Arylacetic Acid - Diclofenac, Aceclofenac
Pyrolo pyrrole - ketorolac
Pyrazolone - Pheny butazone

(2) Preferential cox₂ inhibitor

Nimesulide, Meloxicam, Nebumetone

(3) Analgesic anti pyretic with poor antinflammatory action

Paracetamol (Acetaminophen) - Para-amino phenol
Nefopam - Benzoxazocine

Use and ADR

- (1) **Indomethacin** - Effective in rheumatoid Arthritis
 - ◆ used in Bartter syndrome (Thickening of loop of Henle) low potassium level
 - ADR** - headache and sedation
- (2) **Pheny butazone** - Cause Bone marrow Suppression
- (3) **Naproxen** - is long acting NSAID
- (4) **Mefenamic acid** - useful in dysmenorrhea
- (5) **Phencetin, sulindac and Nebumetone** are prodrug
- (6) **Ketorolac** - can be administered IV
- (7) **Piroxicam and Tinoxicam** - longest acting NSAID
- (8) Nemesulide not use in child below 13 year due to heamorrhage
- (9) Cox-2 inhibitor have rise of M₂ and stroke due to Thrombosis on long term use.
Eterocoxib is long acting cox-2 inhibitor

Anti Rheumatoid drug

- ◆ Rheumatoid arthritis is an autoimmune disorder
- ◆ Rheumatoid arthritis is chronic inflammatory disorder
- ◆ Caused by attack of own immune system
- ◆ RA effect many joint of body
- ◆ NSAID Provide symptomatic relief, Not relief the progression of disorder
- ◆ Drug for Rheumatoid arthritis (Disease modified anti rheumatoid drug DMARD)

CHAPTER

AUTOCOID

(EXERCISE)

- All of following can be used prophylaxis of Migraine except
(A) Sumatriptan (B) Valproate
(C) Propranolol (D) Topiramate
- Which is not second generation anti histaminic
(A) Loratadine (B) Terfenadine
(C) Cyclizine (D) Azalastine
- NSAID inhibit
(A) Cyclooxygenase
(B) Phospholipase-Az
(C) Lipoxy genase
(D) All
- Patient on Aspirin will have increase in.
(A) Clotting time
(B) Bleeding time
(C) Prothrombin time
(D) Thromboplastin time
- Mesoprostol is
(A) Steroid (B) Prostaglandin
(C) NSAID (D) Cholinergic
- Leucotrien inhibitor is
(A) Zeleuton (B) Monteleukast
(C) Salbutamol (D) Indomethacin
- Gout is a
(A) Auto immune disorder
(B) Metabolic disorder
(C) Cytotoxic disorder
(D) Hormonal disorder
- Antidote of PCM Poisoning
(A) Atro pine
(B) N-Acetyl cystiene
(C) Prozosin
(D) Depivefrone
- Prodrug from NSAID
(A) Phenecetin (B) Sulindac
(C) Nebumetone (D) All
- Caffein used with Ergotamine during treatment of migraine
(A) decrease absorption of Ergotamine
(B) Increase absorption of Ergotamine
(C) No Effect on absorption
(D) As Bronchodilator
- Common ADR of NSAID
(A) Peptic ulcer (B) Hepato toxicity
(C) Nephro toxicity (D) All
- Triphasic response shown by
(A) Histamine (B) Dopamine
(C) Serotonin (D) Adrenaline
- Bromo criptine used in
(A) Parkinson
(B) Hyper lacticemia
(C) Acromegaly
(D) All of these
- Cetirizine is metabolite of
(A) Premethazine (B) Hydroxyzine
(C) Terfenadine (D) Levocetirizine
- Aspirin not use in
(A) Platelet aggregation
(B) Gout
(C) Niacin flushing
(D) Myocardial infaction
- Drug used in carbaplatin induced vomiting
(A) Domperidone (B) Promethazine
(C) Ondasetron (D) Metaclopramide

ANSWER KEY

1.A	5.B	9.D	13.D
2.C	6.A	10.B	14.B
3.A	7.B	11.D	15.B
4.B	8.B	12.C	16.C