Tikrit University
College of Veterinary Medicine

Autacoids

Subject name: Autacoids

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Lecturer name: **Dr. Buthinah Abulhameed**

Email:buthinahamee@tu.du.iq

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Lecturers link

Autacoids

Autacoids :-are substances that are synthesized and function in a localized area they participate in response to injury. Autacoids 'antagonist inhibit autacoids' synthesis ,release or effects on tissue receptor.

Major classes:-

1-Biogenic amines :-histamin,serotonin(5HT)

2-phosophlipid;- derived autacoids include:-

a-Eicosanoides-----PG, Lekotrien(LTs) ,Thrombaxane (TXs).

b-Platelete activity factor (PAF)

3-Polypeptides includes:-angiotensin,kinin.

Eicosanoids :-

Are derived from polyunsaturated acids

Arachidonic acid:-is the primary substrated, it is released from membrane phospholipids, primarily by phospholipase A2 in response to physical,chemical ,hormonal,neurotransmitter stimulates.

Metabolism of Arachidonic acid can take place:-

1-cyclooxygenase pathway----- produce PGs (PGI2.TAX2, PGE).

2- 5-Lipooxygenase pathway -------syntheses LTs.

3-Cytochrom p-450-----epoxides

PGs& TAXs

-PGs are divided into 10 specific molecular groups

-PGFs series PGs ---the subscript (α,β)

-PGE1, PGE2, PGE3,TAXs PGIs.

Degrading PG by enzyme are located in lung, kidney, spleen, adipose tissue, intestine, TAXs in blood fluid.

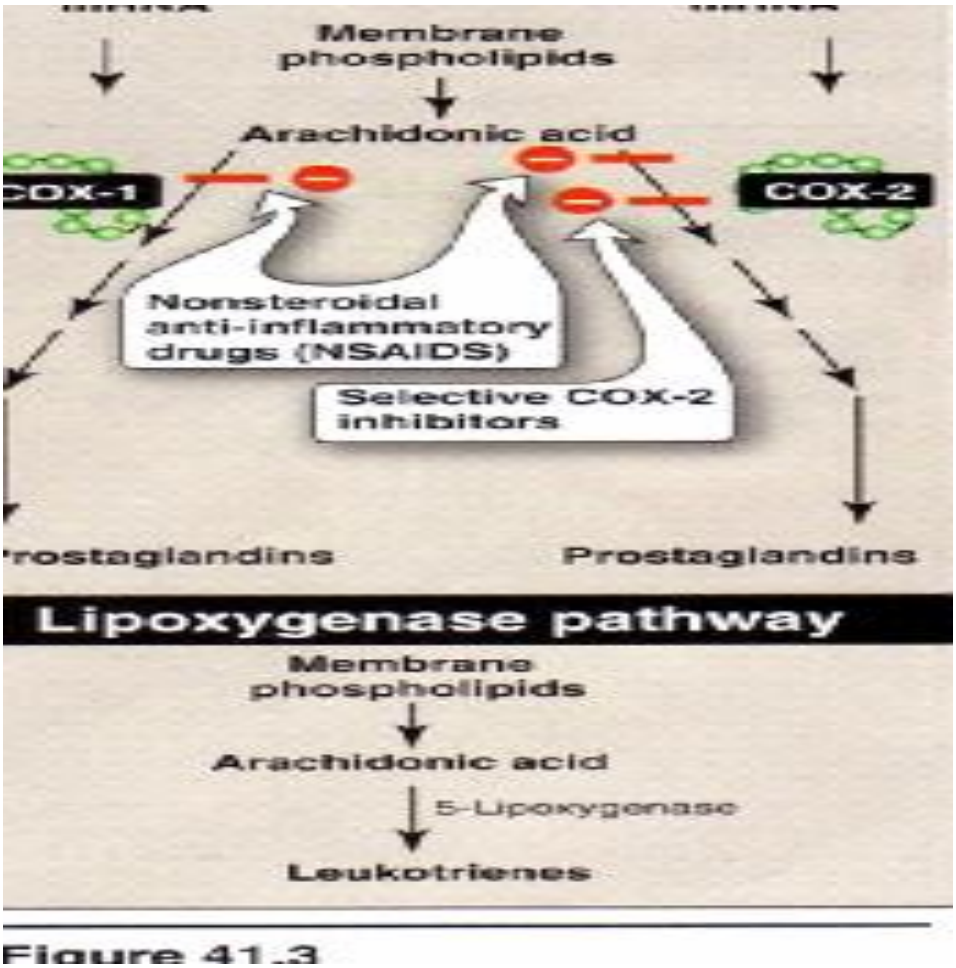

Figure 41.3

Pharmacological effects:- PGs&TAXs

Affect smooth M. platelet aggregation, reproduction system, peripheral and central N.S.

1-Smooth muscle:-PGs &TAXs (in blood v, G.I.T, Lung)

2-platelate aggragation : PGIs(prostcycline & TAXs inhibit and promote platelate aggragation ,PGIs is ynthesizes by vascular endothelium cells and AXTs is synthesized by platelate.

3-Reproduction system effects :-uterus produce PGF2X ,luteolytic hormone.

4-central peripheral N.S. effects:-

A-fever :- PGE1 or PGE2------INCREASE BODY TEMPERTURE

B-Sleep :-infusion of PGE2 into cerebral ventricle include sleep.

C-Nueurotransmission;- PGE type----inhibit the release of (NE)from sympathetic neuron.

5-endocrine effects:- PGE type ----enhance the release of growth hormone(GH),PROLACTIN,thyroid, TSH, ACTH,FSH.LH.

Therapeutic uses;-

PGF2α (cloprstenol, PGF2α ,Fenprostalen, fluprostened)uses in veterinary medicine therapeutic uses:-

1-induction of luteolytisis and synchronization of estrus.

2-treatment of pyometra or chronic endometritis.

3-explusion of mummified fetuses.

4-induction of abortion.

5-scheduling of estrus and ovulation.

6-induction of parturition.

Adverse effects:-parturition unintended, bronochconstration, GIT STIMULATION,.

Several products of PGS series are of current clinical importance. In humane

1-Alprostadil (PGE_1) may be used for its smooth muscle relaxing effects to maintain the ductus arterosus patent in some neonates awaiting cardiac surgery and in the treatment of impotence.

2-Misoprostol, a PGE_1 derivative, is a cytoprotective prostaglandin used in preventing peptic ulcer and in combination with mifepristone (RU486) for terminating early pregnancies. **PGE_2** and **PGF_{2a}** are used in obstetrics to induce labor.

3-Latanoprost and several similar compounds are topically active PGF_{2a} derivatives used in ophthalmology to treat open angle glaucoma.

4-Prostacyclin (**PGI_2, epoprostenol)** is synthesized mainly by the vascular endothelium and is a powerful vasodilator and inhibitor of platelet aggregation. It is used clinically to treat pulmonary hypertension and portopulmonary hypertension. In contrast

,5- **thromboxane (TXA_2)** has undesirable properties (aggregation of platelets, vasoconstriction).

Antagonist:-

PG antagonist ----------aspirin, on steroidal anti-inflammation, corticosteroid.

LTS leukotriene

Are synthesized by the enzyme lipooxgynase in neutrophils,monocytes,macrophage,mast cell,lung,spleen,brain heart.

LTA4------LTB4------LTC4-----LTD4

Stimulai for production include:-

-phagocytsis and the presence of immune complex in macrophages .

-mast cell anti-IgE antibodies .

-release of PAF by basophile and mast cell.

Physiological effects:-

1-slow-reacting substance of anaphylaxis (SRS-A)

-Smooth M. contraction

-increase capillary permeability.

-increase mucous secretion .

-LTB4 is potent its promtes nutrophil adhesion to and migration through the vascular endothelium.

In humane use leukotrienes antagonist for in asthma

-zileuton (inhibitor of lipoxygenase

-zafirlukast, montelukast (receptor antagonists)

-LT-antagonist -----no-clinical in veterinary.

Histamine

Histamine is widely distributed in tissues ,

The strong granules of mast cells and basophils contain histamine, most histamine is stored in the lung ,skin,intestinal mucosa .

-allergic responses in the skin and lung are due part to histamine release .

-food vagall stimulation can release histamine from the stomach mucosal cells the release histamine in imitation gastric acid secretion.

-free histamine the hypothalamus contain histamine that acts as a nurotransmeter in the endocrine system.

Release mechanism of histamine:-

1-Physical injury:-heat, cold,truma can disrupt the mast cells, -1
insect animals venum(erythema,pain,itching).
2-immune-mediated release :-sensitized mast cell or basophils or -2
(IgE)
3-drugs-induce release:-morphin. Tubercurarin… -3

Receptors:-

-H1-Receptor:- contain of bronchiolar ,intestine smooth M., vasodilatation in small arteries and vein ,capillary pereampility ,purities.

H2 Receptors:-mediate gastric acid secretion and vasodilation.

H3 Receptor are located presynaptically on neuron and modulate transmitter release (no –clinical).

Pharmacological effects:-

1-**C.V.S.**

-decrease blood pressure (dilate arterioles,capillaries,venule,increase cardiac contraction, increase heart rat) H1,H2

-Edema, increase capillary pereampillity,fluids,protein cross the basement membrane,producing edema

2-**respirtory system:**

-H1 Receptor activation cause smooth muscle contraction

-stimulation secretion and formation PG

3-**glandular**;-H2 Receptor increase gastric acid and pepsin secretion .

-increase catecholamine from adrenalin.

4-interdermal tissue 1- (**triple respons**e)

---Redding , dilate small arteriolesat injection

-flare ---dilate of the arteriol (flare is thought to involve an axon reflex because cutting the nerve abolisher the reflex)

-wheal----increase capillary pereampi cause separation of the endothelium cell, edema.

2-pain and itching sensory nerve ending.

Therapeutic uses:-

-used diagnosis

-betazole: is an along of histamine for stimulation gastric acid production

Histamine antagonist:-

H1receptor blocker can be divided into:-first –generation drugs are widely used because they are effective and inexpensive most of these drugs penetrate the CNS and cause sedation

Second –generation drugs do not penetrate the blood brain barrier they less CNS toxicity

1-H1 Receptor Antagonist: therapeutic uses

-treatment Allergy -----include urticria, ,allergic reaction of drugs,anaphylaxyis.

-prevention motion sickness.(diphenhydramin,dimenhydrine)

-sedation:promthazine,diphenhydraminare most potent induce –sleep

Adverse effects;-

-C.NS. Depression.

-antimascarinic effects

-C.N.S. stimulation with high doses

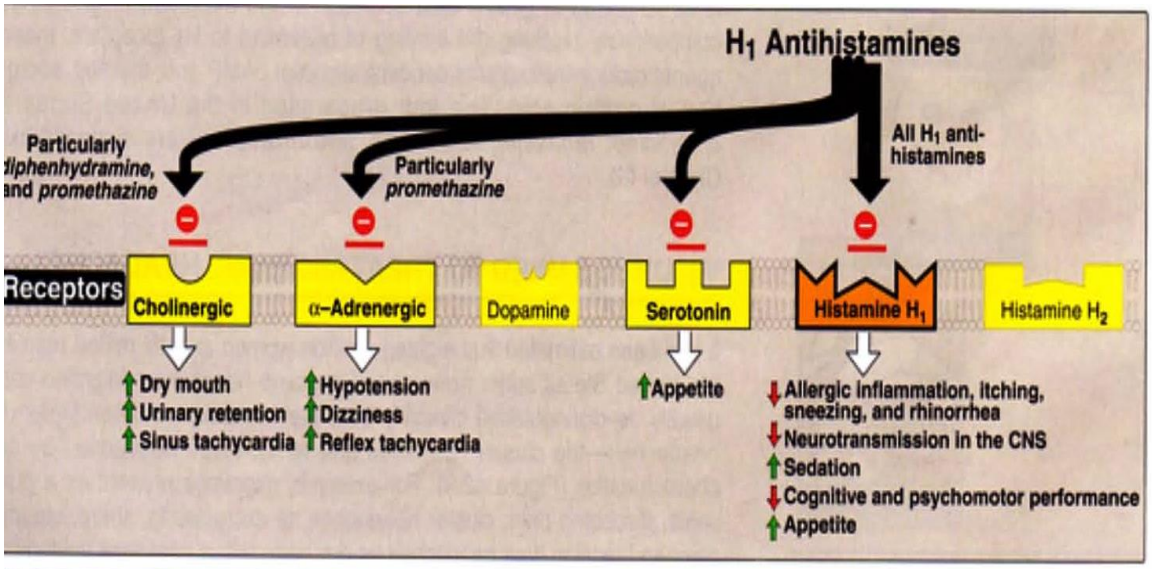

Figure 42.7
Effects of H_1 antihistamines at histamine, adrenergic, cholinergic, and serotonin-binding receptors. Many second generation antihistamines do not enter the brain and, therefore, show minimal CNS effects.

Some H_1 antihistaminic drugs in clinical use.

2-H2 ReceptorAntagonist:

-cimitdin used treatment gastric abomasal. Ulcer , drug induce erosion gastritis,esophigal reflax.

Interaction use reduce metabolism.

-ranitdin: in dog oral

Inhibitors histamine release:-

1-cromolyn sodium : action inhibit the release of histamine and other autocoids from mast cells

Not \ give orally because not absorbed from GIT.

Uses for horse(prevent pulmonary allergic reaction)

2-epinephrine and phedrine:-

Opposing physiologic system uses anaphylaxis.

Drugs	Usual Adult Dose	Anticholinergic Activity	Comments
FIRST-GENERATION ANTIHISTAMINES			
Ethanolamines			
Carbinoxamine (Clistin)	4-8 mg	+++	light to moderate sedation
Dimenhydrinate (salt of diphenhydramine) (Dramamine)	50 mg	+++	Marked sedation; anti-motion sickness activity
Diphenhydramine (Benadryl, etc)	25-50 mg	+++	Marked sedation; anti-motion sickness activity
Ethylaminediamine			
Tripelennamine (PBZ, etc)	25-50 mg	+	Moderate sedation
Piperazine derivatives			
Hydroxyzine (Atarax, etc)	15-100 mg	nd	Marked sedation
Cyclizine (Marezine)	25-50 mg	-	light sedation; anti-motion sickness activity
Meclizine (Bonine, etc)	25-50 mg	-	light sedation; anti-motion sickness activity
Alkylamines			
Prompheniramine (Dimetane, etc)	4-8 mg	+	light sedation
Chlorpheniramine (Chlor-Trimeton, etc)	4-8 mg	+	light sedation; common component of OTC "cold" medication
Phenothiazine derivative			
Promethazine (Phenergan, etc)	10-25 mg	+++	Marked sedation; antiemetic; α block
Miscellaneous			
Cyproheptadine (Periactin, etc)	4 mg	+	Moderate sedation; also has antiserotonin activity
SECOND-GENERATION ANTIHISTAMINES			
Piperidine			
Fexofenadine (Allegra)	60 mg	-	
Miscellaneous			
Loratadine (Claritin)	10 mg	-	Longer action
Cetirizine (Zyrtec)	5-10 mg	-	

d, no data found.