***Renal pharmacology***

The main function of the kidney is the excretion of waste products such as urea ,uric acid and creatinine . so another important function of renal system in homeostasis ,the regulation of the salt and electrolyte and the volume of the extracellular fluid ,it is also play a part in acid – base balance .

The structures of the urinary system include paired kidneys ,paired uterus, asingle urinary bladder ,and a single urethra .

Inside each kidney are millions of individual structures ,called nephrons that do the actual work of the kidney . a nephron consists of a glomerulus, Bowman's capsule , proximal convoluted tubule , loop of henle , distal convoluted tubule , and a collecting duct .

The most important group of drugs employed for their effect on the kidney are the *diuretics* , these drugs increase the excretion of salt and water.

Substances which affect the water and sats of the body

1-Replacement fluids

2-Diuretics

**Replacement fluids:**

1-Keeping the volume of blood circulation.

2-Preventing fluid losses.

3-Giving solutions for substitutes e.g water and electrolytes

Replacement fluids in vet. Med.

1.Glucose

2.Lactate

3.Electrolytes

4.Giving solutions for substitutes e.g water and electrolytes.

***Diuretics:***

Agents that increase the volume of urine excreted by the kidneys and promote release of water from tissues.

They are therapeutically used to:

1.To remove the water which accumulate inside the body as in case of edema.

 2.Reduce udder edema in cattle.

3. Used to remove the toxin from the body in case of toxicity

4.Used to relief hypertension.

5.Used in case of fever.

Diuretics are include :

***1.Thiazides diuretics:Include***

*1.****Thaizide***

2.***Bendrofluazide****.*

*3.* ***Hydrochlorothiazide****.*

*4.****Cyclopenthiazide and metolazine****.*

This group of drugs has a moderately powerful diuretic action ,they decrease active reabsorption of sodium and chloride by binding to the chloride site of the electroneutronal $Na^{+}$/ $Cl^{-}$ co- transport system and inhibiting it is action.

Clinical use of thiazide diuretics:

1. Hypertension.

 2. Mild heart failure

 3. Sever resistant edema ,

4. Nephrogenic diabetes insipidus , to prevent recurrent stone formation.

Side effects :

 Hypokalemia and Cardiac dysfunction .

***loop diuretics :***

loop diuretics are the most powerful of all diuretics , the loop diuretics drugs act primary on the thick segment of the ascending loop of henle , inhibiting the transport of sodium chloride out of the tubule into the interstitial tissue by inhibiting the $Na^{+}$/$K^{+}$ / $Cl^{-}$ carrier in the luminal membrane .

e.g. 1.**Frusemide(lasix**)

2.**Ethacrynic acid** ,

3.**Torsamide** .

clinical use of loop diuretic :

1-In disease with salt and water over load due to :

Chronic heart failure ,Nephritic syndrome , Renal failure .

2-Hypertension 3- Acute treatment of hypercalcaemia.

Side effects:

 Hypokalemia .

***Potassium – sparing diuretics :***

act on the distal convoluted tubules to promote sodium and water excretion and potassium retention ( interfere with the $Na^{+}$/$K^{+}$ pump that are controlled by aldosteron ).

e.g.1. **Spironolactone**

2. **Triamterene**

3.**Amiloride** .

clinical uses:

To prevent potassium loss.

***Carbonic anhydrous inhibitor :***

These groups of diuretic act through the inhibtion the carbonic anhydrous enzyme which helping the union between water and carbone dioxide to forming carbonic acid ,which play important role in ions exchange

e.g.1. **Acetazolamide** ,

2. **Methazolamide**

3.**Ethozolamide**

These drugs used in disease with symptom of odema and also glaucoma.

***osmotic diuretics :***

increase the osmolality ( concentration ) of the urine filtrate in the renal tubules , resulting in the excretion of chloride , potassium , and water , used to prevent kidney failure and to decrease intracranial and intraocular pressure .

**e.g. 1.Mannitol and glycerin .**

side effect : include fluid and electrolyte imbalance and vomiting .

***Urolith treatment :***

uroliths are abnormal mineral masses in the urinary system .

type of uroliths include : 1.struvite ,

2.calcium oxalate ,

3.calcium phosphate ,

4. cystine and mixed .

each type of urolith may be treated differently and may include dietary management as well as treatment .

drugs used to treat uroliths include :

**Urinary acidifiers**:

are used clinically to produce acid urine , which dissolves and helps prevent formation of struvite uroliths . their use has declined with the use of urinary acidifying diets .

*e.g. 1.****Methionine***

*2.****Ammonium chloride*** *.*

**Urinary alkalinizers** :

Are used clinically to treat calcium

1. oxalate ,

2. cystine , and

3.ammonium urate uroliths .

*e.g.* ***Sodium and potassium citrate***are metabolized and the actions are excreted with bicarbonate to give an alkaline urine .

-this increase the action of some antibacterial drug ( sulphonamide , streptomycin ).

- itself have some antibacterial effects .

-increase excretion of drug ( aspirin , barbiturates ) by alkalinizing the urine .

Xanthine oxidase inhibitors :

-decrease the production of uric acid , which helps decrease the formation of ammonium urate uroliths .

e.g. **Allopurinol**.

***Drug acting on the respiratory system***

The respiratory system includes the upper airway passages , the nasal cavities , pharynx and trachea as well as the bronchi and bronchioles .

Respiration is the exchange of gases between the tissue of the body and to outside environment . it involves breathing in of an air through the respiratory tract ,uptake of oxygen from the lungs , transport of oxygen through the body in the blood stream , utilization of oxygen in the metabolic activities ( cells and removal of carbon dioxide from the body).

Drug therapy of pulmonary disorders is generally directed towards altering a specific physiologic function .

1-***expectorants :***

The drugs that aid in removing thick tenacious mucus from respiratory passages .

a-most of the expectorants are act reflexively by irritating the gastric mucosa ,(Reflex stimulation of vagal nerve endings in the stomach and duodenum ) this in turn stimulates secretions in the respiratory tract , expectorants remove bronchial secretions which are purulent (containing pus ) , viscid ( thick ) or excessive . the loosened material is then moved toward the pharynx through ciliary motion and coughing .

e.g. guanfensin , ammonium salts , lpecacaunna and senega .

b-some types of expectorants act as stimulators of bronchial glands secretion ( diuretics like effect ) by irritation of them like potassium iodide .

c-other type of the expectorants is the inhibitory expectorants , which includes in most the volatile oils like pine oil , turpentine oil and eucalyptus oil .

2-***mucolytics :***

Are agents that liquefy mucous and facilitate expectoration .

e.g. acetylcysteine , bromohexine.

-acetylcysteine :

This drug reacts with mucus resulting in liquefaction of it , this is a mucolytic given by inhalation or nebulization (nebulization is treatment by spry ) .

-bromohexine :

Supports the body's own natural mechanisms for clearing mucus from the respiratory tract , it is secretolytic that is it increase the production of serous mucus in the respiratory tract and makes the phlegm thinner and less sticky .this contributes to a secretomotoric effect ,it helps the cilia –tiny hairs that line the respiratory tract to transport the phlegm out of the lungs .

3-***anti-tussives :***

Cough is a protective reflex , which severs the purpose of expelling sputum and other irritant materials from the respiratory airway.

Types :

-useful productive cough ; effectively expels secretion and exudates.

-useless cough ; non-productive chronic cough , due to local irritant .

anti-tussives are drugs used to suppress the intensity and frequency of coughing .

two types of anti-tussives :

1-central anti-tussives :

Suppress the medullay cough center and may be divided into two groups:

 -opoid anti-tussive e.g. codeine .

 -non opoid anti-tussive e.g. benzonatate , dextromethorphan .

Codeine :

-is considered to be the most useful narcotic anti-tussive agent ,codeine aids in relieving the pain associated with hacking cough .

The main side effects include drowsiness , nausea , vomiting and constipation .

Benzonatate:

Is a non narcotic anti-tussive that produces it is effect through a CNS depressant effect similar to codeine . furthermore it produces a local anesthetic effect on the stretch receptors in the lower respiratory tract ,which control coughing .

This drug has few side effects except that it will numb the mouth , tongue and pharynx .

Dextromethorphan :

Is non narcotic anti-tussive , it is found alone or in combination usually with expectorants .

2-peripheral anti-tussives :

Decrease the input of stimuli from the cough receptor in the respiratory passage .e.g. demulcent like honey and syrup .

3-miscellaneous drugs:

This item of anti-tussive drugs include :

a-histamine receptor blockers :

this group acts by blocking $H^{1}$ receptor in order to get ride from the cough which arises from histamine release .

e.g. promethazine and diphenhydramine .

b-corticosteroids :

they are effective in treating of chronic cough . e.g. prednisolone.

4-***anti – asthmatic drugs:***

Asthma is physiologically characterized by increased responsiveness of the trachea and bronchi to various stimuli and wide spread narrowing of the airways that changes in severity either spontaneously or as a result of therapy .

Impairment of airflow in bronchial asthma is caused by three bronchial abnormalities .

a-contraction of airway smooth muscles.

b-thickening of bronchial mucosa from edema and cellular infiltration .

c-inspiration in the airway lumen of abnormally thick , viscid plugs of excessive mucus .

pathogenesis of asthma :

lgE mediated sensation of mast cells leading to de granulation of histamine in bronchioles consequently causing of bronchoconstriction and increased secretions .

drugs used for treatment of asthma :

drug used in the treatment of bronchial asthma can be grouped in to three main categories :

1-***bronchodilatots :***

Sympathomimetic bronchodilators act by relaxing contractions of the smooth muscle of the bronchioles and they are according to their mechanism of action to :

a -$β$ - adrenergic agonists which include :

 -non selective $β$- agonists e.g. adrenaline ,ephedrine , isoproterenol .

 -selective $β$- agonists e.g. salbutamol , albuterol ,salmetrol .

b- methylxanthines. e.g. theophylline derivatives .

they have long duration of action , making them useful in treatment of nocturnal asthma . they are many mechanisms which explain how the xanthins work on the bronchial smooth muscle , include production of high amount of cAMP and consequently which increase noradrenaline release and production of bronchodilation .

the main side effect of xanthines is the narrow margin of safety .

c-anticholinergic agents . e.g. ipratropium bromide .

they are very useful in case of exercise include asthma .

2-***antiinflammatory agents :***

drugs which prevent or minimize the inflammatory reaction in the bronchi . which include :

-corticosteroids : e.g. dexamethasone , betamethasone , prednisolone .

inhibit all arachidonic acid derivatives ( specially prostaglandins and leukotrienes ) which act as inflammatory mediators . corticosteroids are very useful in treatment of asthma and prevention of recurrent attacks .

corticosteroids have many serious side effects and these side effects appear with long usage . include : primary insufficiency ( Addison's disease) upon withdrawal ,osteoporosis cataracts , growth retardation in children , diabetes , hypokalemia .

3-***mast cell stabilizers :***

e.g. cromolyn sodium .

stabilize the mast cells so that release of histamine and other mediators is inhibited through alteration in the function of delayed chloride channel in cell membrane . it has no role once mediator is released and is used for casual prophylaxis .it is used in treating of the exercise and antigen include asthma , occupational asthma .

5-***respiratoty stimulant :***

These agents which used to treat respiratory failure . they are divided into:

-physiological stimulants:

1-$co\_{2}$ : a direct and potent respiratory stimulant , $co\_{2}$ works by two ways:

 a-directly : by stimulation of respiratory center .

 b-indirectly : by reflex and stimulation of carotid and aortic sinuses .

2-$o\_{2}$ : used by inhibition and it is mixed with 5% with $co\_{2}$ .

 The mechanism of stimulation depend on the sensation of to $co\_{2}$ .

3-analeptics (CNS ) stimulants) : they act indirectly by stimulating of respiratory center in the medulla oblongata .

e.g. leptazole , nickthamide , bemigiride , picrotoxin .

4- local irritants : act by reflex stimulation of respiratory and vasomotor center to improve respiration and ventilation , like ammonia .

6-***decongestants :***

Are the drugs that reduce congestion of nasal passages , which in turn open clogged nasal passages and enhances drainage of the sinuses .

e.g. administered topically :phenylephrine , oxymetazoline .

 orally : ephedrine , naphazoline

mechanism of action : mucous membrane decongestants are $α^{1}$ agonists , which produce localized vasoconstriction on the small blood vessels of the nasal membrane . reduce congestion in nasal passages .

used in congestion associated with rhinitis , hay fever , allergic rhinitis and to a lesser extent common cold .drugs can be administered nasally or orally for long duration of action .