- Red : important
- Black : in male / female slides
- Pink : in female's slides only
- Blue : in male's slides only
- Green : Dr's notes
- Grey: Extra information, explanation

Editing File

SUMMARY

	Aspirin	Paracetamol	Celecoxib	Diclofenac
Mechanism of action	Non-selective irreversible inhibition of COX	COX3 inhibitor	Selective COX-2 inhibitor	Non selective cox inhibitors
Pharmacokinetics	• Metabolized by Hydrolysis and then Conjugation. • Higher dose= longer plasma half-life	• Metabolized By conjugation • Given orally, well absorbed • t½ =2-4h • Weak anti-inflammatory	• Food decrease its absorption • Highly bound to plasma proteins • Half-life 11 hours	—
Clinical uses	• Acute rheumatic fever • Reduces risk of myocardial infarction • Prevents pre-eclampsia. • Colon cancer incidence is reduced	• Peptic or gastric ulcers • Bleeding tendency • Allergy to aspirin • Viral infections in children • Pregnancy	• Short-term use in postoperative patients • Acute gouty arthritis • Acute musculoskeletal pain • Ankylosing spondylitis	• Acute gouty arthritis • post- operative ophthalmic inflammation(Locally used) • analgesic • Antipyretic • Anti-inflammatory
ADRs	**At normal dose:** • Hypersensitivity, bronchospasm • Reye's syndrome • Impaired hemostasis • GIT side effects: dyspepsia, Nausea, Vomiting. • Mucosal damage • Acute gouty arthritis	**Therapeutic doses** • elevate liver enzymes • Binding of paracetamol to COX is inhibited by peroxides produced in inflammatory sites. **In large doses** • Mainly on liver due to its active metabolite • metabolized into N- acetyl-p-benzoquinone imine, which causes liver damage • Treatment of toxicity of paracetamol is by N-acetylcysteine to neutralize the toxic metabolite.	• Renal toxicity • Dyspepsia & heartburn • Allergy • Cardiovascular (do not offer the cardioprotective effects of non-selective group)	**preparations:** • **Diclofenac + misoprostol (PGE1 analog)** decreases upper gastrointestinal ulceration, but result in diarrhea • **Diclofenac + omeprazole** to prevent recurrent bleeding • 0.1% ophthalmic preparation for postoperative ophthalmic inflammation • A topical gel 3% for solar keratoses • Rectal suppository as analgesic • Oral mouth wash • Intramuscular preparations for pain & fever.
	At overdose: •Salicylism (ringing of ear,vertigo) •Hyperthermia •Gastric And ulceration bleeding	**Chronic abuse:** Nephrotoxicity		
Contraindications	Peptic ulcer, Pregnancy Hemophilic patients, Patients Taking anti-coagulant, Children with viral infections, gout	—	patient with CV disease patients allergic to sulphonamides.	

		Drug	Duration	Mechanism	Metabolism	Uses	Side effects
Spasmolytics	Centrally	**Diazepam**		facilitate GABA action on CNS		**Reduce muscle spasm in:** • Spinal cord injury • Cerebral stroke • Cerebral palsy	
		Baclofen		Act centrally on spinal cord & is GABA Agonist			
	Direct (direct action on skeletal muscles)	**Dantrolene**	t½ = 8-9 h	Interferes with the release of Ca from the sarcoplasmic reticulum. & inhibits excitation-contraction coupling in the muscle fibres.		• Malignant Hyperthermia. • Spastic states.	
Peripherally acting (Neuromuscular blockers)	Depolarizing	**Succinylcholine**	5-10min (short) Fast onset of action	**Phase I** Combines with nicotinic receptors —> contraction open Na channels —> initial stimulation **Phase II** Persistent depolarization leading to paralysis.	By pseudo-cholinesterase in plasma.		• CVS: Arrhythmia (not used in patients with CVS diseases) • Hyperkalemia: cardiac arrest • Eye: intraocular pressure contraindicated in glaucoma (not used in patients with glaucoma) • **succinylcholine apnea** due to deficiency of pseudo-cholinesterase. • **Malignant Hyperthermia**
	Non depolarizing (Competitive)	**Vecuronium (More potent than tubocurarine)**	40min. Short - intermediate	Competitive antagonist for **Ach** at the **nicotinic receptors** present in post-junctional membrane of motor end plate	By **liver**. Excretion in **bile**. (can be used with renal failure patients)		Advantages: • **No** histamine release • **No** tachycardia
		Pancuronium (more potent than curare)	1-2 h (Long)		Excretion by the **kidney** (not used in renal failure patients)		• Hypertension • Tachycardia (Avoid in patient with coronary diseases) • Antimuscarinic action • ↑ NE release
		Mivacurium (as potent as curare)	15min (shortest) Fast onset of action		Pseudo-cholinesterase (not used in patients with Choline esterase deficiency)		• Transient hypotension due to releasing of histamine
		Atracurium (as potent as curare)	30min intermediate		non enzymatic chemical degradation in plasma (Spontaneous hydrolysis)	•in liver failure & •kidney failure (drug of choice).	• Transient hypotension due to releasing of histamine • Bronchospasm (**Should be avoided in asthmatic patients**)
		D-Tubocurarine	1-2 h (Long)		**Kidney** 60% **Liver** 40%	**not** used clinically	• Hypotension • Tachycardia • Bronchospasm *due to releasing of histamine

	Synthetic choline esters (Quaternary ammonium compounds contain N^+(polar))				Naturally occurring alkaloids (tertiary amines)	
Drug	Acetylcholine	Carbachol	Bethanechol	Cevimeline	Pilocarpine	nicotine
Chemistry	Quaternary Polar	Quaternary Polar	Quaternary Polar	Quaternary Polar	Tertiary Non polar= lipophilic (cross BBB= has central effects)	Tertiary Non polar
Absorption	X	Better absorbed than Ach	Better absorbed than Ach		Complete (well absorbed)	
Distribution	Poor	Poor	Poor	Poor	Good distribution	
Metabolism by cholinesterase	✓	X	X		X	
Duration	Very short	Longer (++)	Longer (++)		Longer (++)	
administration	I.V Eye drops	Oral Eye drops S.C	Oral S.C		Oral Eye drops	
Receptors	M,N	M,N	M	M3	M	
Selectivity	X	. Muscarinic actions on Eye,GIT, Urinary bladder .Has nicotinic actions (side effects)	GIT, Urinary bladder	Exocrine glands	More on eye, exocrine glands (secretion)	
Uses	**Not used** cuz: • Not selective • Short action • Rapid metabolism	Glaucoma	• **Paralytic ileus** • **Urinary retention** in cases of post-operative **atony** & neurogenic bladder	. Sjogren's syndrome .Xerostomia (dry mouth)	**.Glaucoma** . Xerostomia (dry mouth)	
Adverse effects					• Profuse sweating • Salivation • Bronchoconstriction • Diarrhea • CNS effects	
Excretion					Enhanced by acidification of urine	

Reversible anticholinesterases

Drug	Action	Kinetics	Pharmacokinetics	Uses
Alcohol (Short acting) (weak H-bond)				
Edrophonium	M,N	Very short 5-15min polar	NOT absorbed orally, given by injection	• **Diagnosis of myasthenia gravis**
Carbamates esters (Intermediate acting) (bind to two sites)				
Neostigmine Quaternary ammonium compound	M,N	Short 0.5-2hr polar	Can be used orally (Polar) prominent on GIT & urinary tract	• Myasthenia gravis treatment • Paralytic ileus • Urinary retention • Curare toxicity
Physostigmine Tertiary ammonium compound	M,N CNS (cross BBB)	Short 0.5-2hr non-polar	Good oral absorption	• **Glaucoma** (Eye) • atropine toxicity
Pyridostigmine	M,N	Short 3-6hr polar	—-	• Myasthenia gravis treatment
Ambenonium "not a stigmine derivative"	M,N	Short 4-8 polar	—-	• Myasthenia gravis treatment
Long acting				
Donepezil	M,N	Long	Given orally	dementia of Alzheimer's disease

Irreversible anticholinesterase

Drug	Action	Kinetics	Mechanism	Uses
Organophosphorous compounds (Long acting) (stable covalent bond)				
Isoflurophate	M,N CNS (lipid soluble)	—-	—	
Ecothiophate	M,N Polar	Long 100hr, polar	Aging make bond extremely stable	• **Glaucoma**
Pralidoxime (PAM) (oximes)	M,N CNS (lipid soluble)	—	reactivates recently inhibited enzymes before aging.	• I.V —> organophosphate intoxication.

Treatment of acute gouty arthritis

Drug	M.O.A	Contraindication, ADR, uses
NSAIDs	most commonly used **first-line treatment** Full doses of NSAID should be initiated immediately and tapered after resolution of symptoms .	**ADRs:** GI ulcer, Bleeding or perforation, Renal insufficiency, Heart failure, Use of oral anticoagulant.
Steroids (corticosteroids)	**P.K:** It can be given orally, IV, IM, or Intra-articularly . Has equal Efficacy with NSAIDs if the steroidal drugs used for a short period.	**used:** good alternative where NSAIDs and colchicine cannot be used or in refractory cases
Colchicine	**Microtubule inhibitor (anti-mitotic)** Binds to microtubules in neutrophils. ● Inhibits cell division by (Mitosis) ● Inhibits chemotactic factors. ● Inhibits inflamosomes & IL-1 production. , not analgesic.	**ADRs:** Diarrhea (sometimes severe and bloody, the patient stops taking the drug) **Contraindication:** renal patients

Prevention of gout recurrent attacks

Drug	Overview, Clinical uses	ADR	P.K
Uricostatic Drugs (increases uric acid synthesis by inhibiting xanthine oxidase)			
Allopurinol	-It is a drug of choice in patients with with both gout & ischemic heart disease. -Inhibit Xanthine oxidase	due to the active metabolite: Acute attacks of gout + toxic epidermal necrolysis +DRESS syndrome +hypersensitivity	it is metabolized by xanthine oxidase into alloxanthin which is pharmacologically active
Febuxostat	-Inhibit Xanthine oxidase -non purine -Can be used in patients with renal disease.	-Increases number of gout attacks the first few months of treatment. -Increases level of liver enzymes.	Given to patients who do not tolerate allopurinol.
Uricosuric Drugs (increases uric acid excretion by blocking tubular reabsorption)			
Clinical use: Control hyperuricemia and prevents tophus formation. **Contraindication:** Patients with renal disease.			
Probenacid	**M.O.A:** Probenecid inhibits Urate Transporters (URAT)	**ADRS:** •Exacerbation of acute attack •Risk of uric acid stone • GIT upset • Allergic rash.	
Sulfinpyrazone	**M.O.A:** Sulfinpyrazone inhibits URAT1 & OAT4	**ADRS:** •Can aggravate peptic ulcer disease. • Aspirin reduces efficacy of sulfinpyrazone. • Enhances the action of certain anti-diabetic drugs	
Recombinant mammalian uricase			
Pegloticase	**used:** for the treatment of chronic gout in adult patients refractory to conventional therapy.	**ADRS:**Infusion reactions. •Anaphylaxis. •Gout flare •Arthralgia •Muscle spasm. •Nephrolithiasis	**P.K:** converts uric acid to allantoin, which is more soluble and readily excreted in the urine

pharmacology
Team 438

GOOD LUCK

Special thanks to Team 435 for their valuable work which inspired us

PHARMACOLOGY
435

A very special thanks to the greatest team members in the world,
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