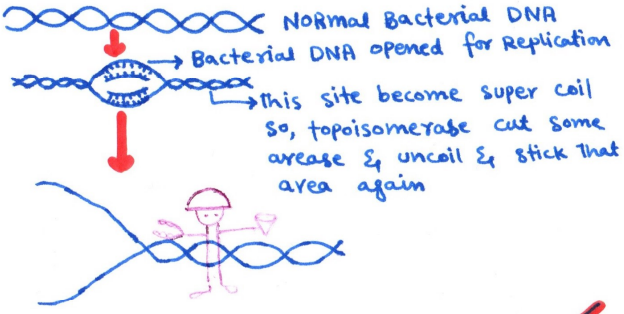
Quinolones & Fluroquinolone

By Zakirullah Yousufzai

* Quinolone = Nalidix Acid
* Fluro Qui--- = Flurinated Nalidix Acid

MECHANISM OF ACTION

* This Drug is Bactericidal
* This Drug act on Topoisomerase Enzyme (DNA GYRASE) & inhibit them:



DNA GYRASE has two Functional Domins:

① Nuclease ⇒ cut the Strand

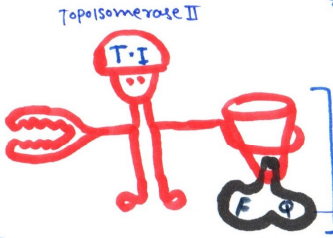
② 2nd domin ⇒ For Resealing Ligase

Topoisomerase II ⇒ in case of G-ve
" IV " " G+ve

Topoisomerase IV cut the Tingling point & reseale it & Separate the DNA from one another

T·IV has two cutter in nuclease domin

These Drugs are widely used b/c



The Ligase Domin is inhibited by Fluroquinolone

The Fluroquinolone Enter to cell by Diffusion & bind to Ligase Domin of Topoisomerase & dysfunction it, so the Endo nuclease unit will work & cut the DNA But doesn't sealed so the DNA destroyed

Classification of Quinolone & Fluroquinolones

1st generation (Quinolone)
- Nalidix Acid
- Gram -ve roads
- But this Drug is rarely used Nowadays (UTI)

2nd generation
- ciprofloxacin
- ofloxacine
- Norfloxacine
- ↑↑↑ G-ve
- G+↑
- ⊕ Atypical like:
  - → mycoplasm
  - → clamydia

3rd generation
- Levofloxacin
- G-ve
- G+ve
- ⊕ Atypical lik
  - → mycoplasm
  - → clamydia
  - → ligeonela
- Streptococcus pneumonia

4rth generation
- Moxifloxacine
- G-ve roads
- G+ve bacil
- G+ve Rod
- O_2 anaerobe
- ⊕ Atypical

as the generation increase the spectrum against G+ve ↑

3rd & 4th generation are called Respiratory Fluro Quinolone

Clinical use of Fluroquinolone

Ciprofloxacine

(Mostly acts on → G-ve, -ve -ve; → G+ve)

1. Acute Diarrhea
2. Traveler's diarrhea (Diarrhea caused by Toxigenic E-coli)
3. cystic Fibrosis (caused by Pseudomonas Auregenosa) ⇒ But not effective on other Respiratory disease
4. Resistant TB ⊕ other drugs
5. Anthrax
6. Typhoid Fever
7. Alternatively of Aminoglycosides (B/c Aminoglycosides are high Toxic)
8. synergisticaly with β-lactam

Difference B/w cipro & Norfloxacine

* Norfloxacine is not well distributed so not used for systemic infection
* norfloxacine is used for:
  - → UTI (e.g cystitis)
  - → Traveler's diarrhea
  - → prostatitis

NOTE:
- Ciprofloxacin is not used ~~in~~ for Respiratory disease except cystic fibrosis
- * ciprofloxacine is contraindicated in children below age 18y. B/c it damage the growing cartilage, But in case of cystic fibrosis we can use cipro, b/c cystic fibrosis cause death.

Levofloxacin

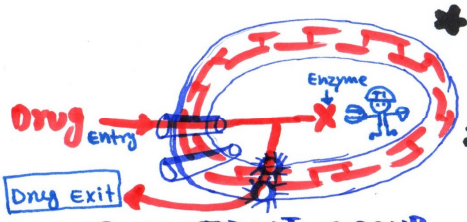
① prostatitis (Note: use for some weeks)
② STDs
③ Skin infection (B/c of broad spectrum)
④ Acute sinusitis
⑤ Acute Exacerbation of Chr. bronchitis
⑥ pneumonia
⑦ osteomyelitis

Moxifloxacin

same like levofloxacin but also used in mixed infection b/c of anaerobe activity.

NOTE: Most of Fluroquinolone are Eleminated by kidney, But Moxifloxacine is Eleminated by liver (so best used in Renal impairment)

Resistant to Flusoquinolone



* **Porin:** are channels through which bacteria gets its nutrients, So the drug also enter to bacteria
* **Efflux:** are active transporters through which the substances comeout of bacteria.

EXTRA

Gram -ve organism have outer & inner membrane, & thin Peptidoglycan, & the G+ve organism have only inner membrane & thick peptidoglycan

⇒ Porin
⇒ Efflux

HOW RESISTANT OCCUR:

① No Entry of Drug to cell (due to narrow porin)
② Exit of Drug by Efflux channels.
③ No Reach of Drug to topoisomerase, b/c destroyed by Enzymes, or altered before reaching to topoisomerase, OR ~~destroyed~~
④ alteration of target:  → so drug can't bind to this site.

3

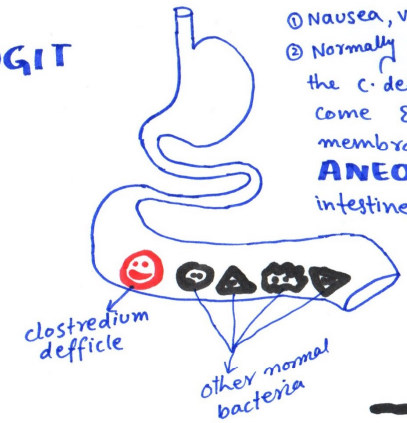
PharmacoKinetic of FluRoquinolone

* Fluroquinolone are well absorbed when orally taken: But Di & Triketines can disturb the absorption like: → sucralfate, → Al^{+}, Mg^{+}, → Fe^{+}, Ca^{+} — these are +ve charged & fluroquinolone are -ve charge so bind, & can't absorb.
* ofloxacine can enter to CNS.
* Injectible form of → ciprofloxacine, → Levofloxacine are availabe

* Except Moxifloxacine all a excreted by Kidney & Moxi are excreted by Liver.
  Livofloxacine & Moxifloxacine are long half life so taken OD.

sideffect of FluRoquinolone

① GIT



① Nausea, vomitting & mid diarrhea
② Normally the clostredium defficile are very low, when the other bacteria died by drug, the C. deffidle increase it's growth, & damage the mucosal membrane, so WBCs come & fight with C. defficile, as a result of inflamatory reaction a membrane are formed & cause srear abdominal pain called **PSEUDOMEMBRANEOUS Colitis**, & in some cases the ganglionic Network destryed in intestine & cause **MEGACOLONE**, & Eventually **DEATH.**

How to avoide PSEUDOMEmbranous Colitis

* Crush the C. defficle by METRO OR VAN:
  its means give METronidazole, & Vancomycine

② CNS ⇒ Headach, dizzness + Epiliptic attack (seizure) b/c

→ inhibit GABA$_a$ Receptor (GABA Keep abnormal discharge of electricle activity)
→ use with theopyline (◻ fluroquinolone inhibit P450), so over accomulation of theopyline
↳ Especilly (ciprofloxacine)
- → warfarine
- → high caffeine

④

③ **SKIN** ⇒ phototoxicity (in this case stop fluroquinolone & use alternative).

④ **CARTILAGE** ⇒ Damage growing cartilage so avoide use in → child ↓18y (except cystic fibrosis); → Pregnant Mother; → Nursing Mother] b/c damage baby growing cartilages.

⑤ RUPTURE of TENdone ⇒ also cause tendenitis,

* cause Rupture specially in persone age ↑60y & using steroids.

⑥ **MOXIFLOXACINE** increase QT interval & case TORSA DEPonthus (twisting of points)

↙ QRS upward than downward 

* So carefully use in Arrythmic patient.

NOTE: the svear sideffects are Rare

⑤