Quinolones

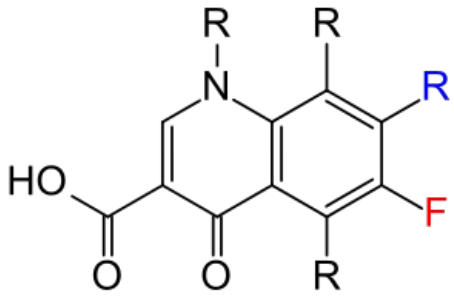
Quinolones belong to the group of **chemotherapeutics**. They are primarily **bactericidal** substances that can be divided into 4 generations according to the antimicrobial spectrum and their properties according to the antibacterial activity, tissue penetration, and the width of the antibacterial spectrum.

Chemically, they are derived from the bicyclic structure - quinolone. Older substances (1st generation) lack a fluorine atom in the molecule. They were designed to treat urinary tract infections and are no longer used today. Newer substances (2nd to 4th generation) have a fluorine atom in the molecule. They have a wider spectrum of action and better system distribution. We also call them fluoroquinolones.

Today we only use fluorinated quinolones in practice. Therefore, the terms "quinolones" and "fluoroquinolones" are interchanged.

Pharmacodynamics

Their effect is concentration-dependent, they have a significant post-antibiotic effect.



Quinolone

Mechanism of action

It is based on the **inhibition of DNA** synthesis. Fluoroquinolones block gyrases (bacterial topoisomerases - the enzymes responsible for the proper entanglement and untangling of bacterial nucleic acid strands during the G phase of the cell cycle). This causes fractures in the bacterial DNA and the death of the bacterial cell.

Mechanisms of resistance

Resistance to fluoroquinolones is relatively common. Resistance arises on the basis of a structural change in the gyrase, a reduction in the permeability of the bacterial membrane, and the expression of efflux pumps. Resistance is often crossed not only with other quinolones but also with other antibiotics (eg tetracyclines, β-lactams).

Side effects

- Allergic skin reactions and phototoxicity (instruct the patient in photoprotection).
- Arthropathy - tendon and cartilage disorders may occur (instruct the patient to rest).
- Dizziness and headache - often in high-risk patients with CNS disease.
- QT interval prolongation.
- GIT difficulties.

Contraindications

- Epilepsy;
- pregnancy and lactation;
- neonates and children under 15-18 years of age (concerns about possible inhibition of articular cartilage growth observed in preclinical studies in young animals).

Pharmacokinetics

Quinolones are well absorbed orally and penetrate well into tissues. They have high concentrations mainly in urine, bile, stool, lungs, kidneys, and prostate.

Interaction

They form non-absorbable complexes with divalent and trivalent ions. When prescribing this antibiotic, it is important to instruct the patient about the unsuitability of concomitant administration of products containing calcium, magnesium, iron, virtually all antacids, and foods rich in these elements.

Fluoroquinolones are inhibitors of the cytochrome system, especially CYP1A2 and CYP3A4 isoforms. They increase the effect of many drugs, especially theophylline, caffeine, digoxin, glibenclamide, rifampicin, cyclosporine.

Glucose tolerance disorders may occur in patients treated with oral diabetics.

Incompatibility

Fluoroquinolones together with β-lactams form complexes. Therefore, it is not possible to administer them together in a single infusion.

Antimicrobial spectrum and indications

Quinolones are effective against G + cocci (Streptococcus pneumoniae), anaerobes, they have very good activity against enterobacteria and G− cocci (Neisseria). They are also used against intracellular pathogens (Legionella, Chlamydia, Mycoplasma,...)

These are reserve drugs. They are indicated only in cases where first-line antibiotics are ineffective or inappropriate. They can be used for intestinal, urinary, biliary, respiratory infections, in combination in the treatment of tuberculosis or leprosy.

Overview of fluoroquinolones

1st generation non-fluorinated quinolones are no longer used in therapy. Fluoroquinolones can be classified into the 2nd to 4th generation. Individual authors differ significantly in the division into generations. In the following text, the division is according to the monograph Pharmacology by Švihovec et al. (2018). For practical use, the division into generations is not crucial, therefore the important characteristics are given directly to the individual representatives. Only substances registered in the Czech Republic are listed in the article.

2nd generation quinolones

Norfloxacin
: The first fluoroquinolone. Norfloxacin does not yet reach sufficient serum concentrations. Indications: urinary tract infections.

Pefloxacin
: In hepatic failure, elimination is delayed. Indications: urinary tract infections.

Ofloxacin
: Decreased renal function slows elimination. Indications: urinary tract infections, pseudomonas infections, cholera, typhoid fever, salmonella and shigella enterocolitis.

Ciprofloxacin
: Elimination is slowed only by significantly reduced renal clearance, no dose adjustment is usually necessary. Interactions: significantly slows down theophylline metabolism (it is always necessary to control the plasma concentrations of theophylline, or to choose another antibiotic). Indications: as wide as of ofloxacin - urinary tract infections, enterocolitis of all kinds, typhoid fever, cholera, pseudomonas infections.

Cifloxinal

3rd generation quinolones

Effective against G + (including pneumococci) and G− microorganisms. Drugs of this generation are usually not registered in the Czech Republic, their typical indication is backup treatment of pneumococcal infections.

Levofloxacin
: The enantiomer of ofloxacin has very similar properties. Indications: pneumonia, pyelonephritis, and urinary tract infections, bacterial prostatitis, or locally as medicine in ophthalmology

4th generation quinolones

Significant effect against Streptococcus pneumoniae, but also against some anaerobes.

Moxifloxacin
: P.o. used in a single daily dose. Indications: only as a backup antibiotic - acute exacerbation of COPD, pneumonia, pelvic infections, or locally as an ophthalmological drug.

Prulifloxacin
: P. o. in one daily dose. Indications: only as a backup antibiotic for the treatment of urinary tract infections, acute exacerbations of chronic bronchitis, bacterial rhinosinusitis.

Links

Related articles

- Antibiotics

- Sulfonamides

Sources

- LINCOVÁ, Dagmar a Hassan FARGHALI, et al. Základní a aplikovaná farmakologie. 2. vydání. Praha : Galén, 2007. ISBN 978-80-7262-373-0. MARTÍNKOVÁ, J, S MIČUDA a J CERMANOVÁ. Antibiotika [online]. [cit. 2010-07-14]. <https://www.lfhk.cuni.cz/farmakol/predn/bak/kapitoly/atb-bak.doc/>. ŠVIHOVEC, Jan, et al. Farmakologie. 1. vydání. Praha : Grada, 2018. ISBN 978-80-271-2150-2. Souhrn údajů o přípravku. Levofloxacin Mylan 500 mg. 2019. Dostupné také z URL <www.sukl.cz>. Souhrn údajů o přípravku. Avelox 400 mg. 2020. Dostupné také z URL <www.sukl.cz>. Souhrn údajů o přípravku. Unidrox 600 mg. 2020. Dostupné také z URL <www.sukl.cz>.