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PHARMACOLOGY

DOCTOR 2019 | MEDICINE | JU

Chloramphenicol

- Broad spectrum (against G+ & G-)
- Very widely distributed throughout the body.

- Very effective (it can reach site of action), no resistance.
- It's a perfect antibiotic without considering side effect.
- With considering side effect: very toxic. (the gray-baby syndrome)
- Disrupt function of 50S ribosomal subunits to reversibly inhibit protein synthesis & prevent growth of the bacterial cell

Gray baby syndrome is a rare but serious side effect that occurs in newborn infants (especially premature babies) following the accumulation of antibiotic chloramphenicol, death is possible.

Chloramphenicol

- Was the drug of choice for Salmonella (Typhoid Fever), but replaced by safer drugs because of side effect.
- Still used for meningitis caused by *H. influenzea.*
- Treatment has to be under monitoring, because it could bind to aplastic anemia.
- Aplastic anemia:
  - Incidence is common 1/40,000.
  - Delayed for a few months after intake. (not instantly)
  - Fatal.

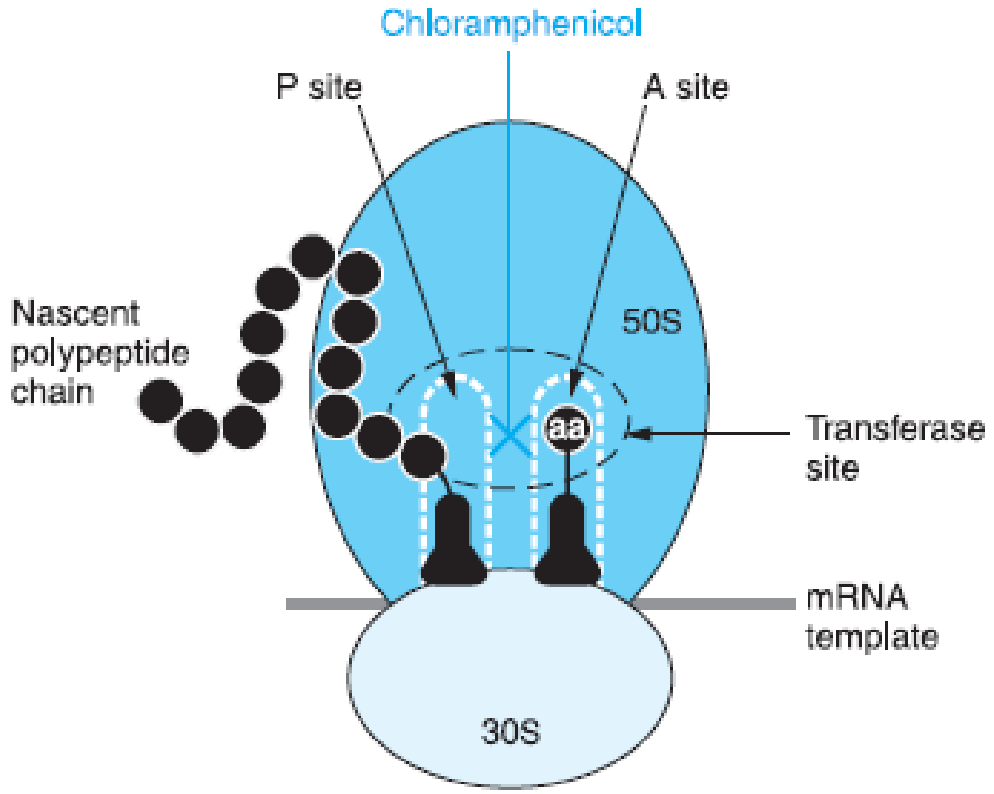

Figure 46–2. Inhibition of bacterial protein synthesis by chloramphenicol. Chloramphenicol binds to the 50S ribosomal subunit at the peptidyltransferase site and inhibits the transpeptidation reaction. Chloramphenicol binds to the 50S ribosomal

– transpeptidation reaction: A reaction involving the transfer of one or more amino acids from one peptide chain to another,

If a bacterial cell make another 50s subunit → continuing protein synthesis.

Mechanism of Action

- Chloramphenicol (Chloromycetin) is a nitrobenzene derivative that affects protein synthesis by binding to the 50S ribosomal subunit preventing peptide bond formation. (transpeptidation)

- It prevents the attachment of the amino acid end of aminoacyl-tRNA to the A site, hence the association of peptidyltransferase with the amino acid substrate.
- Chloramphenicol binds to peptidyltransferase → prevent enzyme to bind to amino acid → prevent amino acid to bind to peptide chain → prevent synthesis.

Mechanism of Action

Resistance could happen after a while and the mechanism is more complex than B-lactamase.

- Resistance due to changes in the ribosome binding site results in:

1- a decreased affinity for the drug to site of action in bacteria,

2- decreased permeability,

3- and plasmids that code for enzymes that degrade the antibiotic.

- The drug-induced inhibition of mitochondrial protein synthesis is probably responsible for the associated toxicity.

Antibacterial Spectrum

- Chloramphenicol is a broad-spectrum antibiotic that is effective against gram-positive and gram-negative bacteria, including Rickettsia, Mycoplasma, and Chlamydia spp.

- Chloramphenicol is also effective against most anaerobic bacteria, including Bacteroides fragilis.

Absorption, Distribution, Metabolism, and Excretion

- Chloramphenicol is rapidly and completely absorbed from the gastrointestinal tract and is not affected by food ingestion or metal ions.
- Parenteral administration is generally reserved for situations in which oral therapy is contraindicated, as in the treatment of meningitis and septicemia or when vomiting prohibits oral administration

Absorption, Distribution, Metabolism, and Excretion

- The biological half-life of chloramphenicol is 1.5 to 3.5 hours (relatively short). Although up to 60% of the drug is bound to serum albumin (bioavailability is low), it penetrates the brain and CSF (reach high concentration therapeutical efficient to meningitis) and crosses the placental barrier. (contradicted with pregnant)
- Chloramphenicol is inactivated in the liver by glucuronosyltransferase and is rapidly excreted (80–90% of dose) in the urine.

Clinical Uses

– The potentially fatal nature of chloramphenicolinduced bone marrow suppression restricts its use to a few life-threatening infections in which the benefits outweigh the risks. There is no justification for its use in treating minor infections.

– Chloramphenicol is no longer recognized as the treatment of choice for any bacterial infection. In almost

all instances, other effective antimicrobial agents are available. (limited to very serious condition)

Since effective CSF levels are obtained, it used to be a choice for treatment of specific bacterial causes of meningitis:

- Haemophilus influenzae,
- Neisseria meningitidis,
- and S. pneumoniae

Additionally, it was effective against H. influenzae–related arthritis, osteomyelitis, and epiglottitis. (when benefits outweigh the risks)

- The development of B-lactamase-producing strains of H. influenzae increased the use of chloramphenicol.

- However, with the advent of third-generation cephalosporins such as ceftriaxone and cefotaxime, chloramphenicol use has significantly decreased.
- If the patient is hypersensitive to B-lactams, chloramphenicol administration is appropriate therapy for meningitis caused by N. meningitidis and S. pneumoniae. (switch between antibiotic depend on patient state and kind of organism)

- Chloramphenicol remains a major treatment of typhoid and paratyphoid fever in developing countries.

- However, with increasing resistance to ampicillin, trimethoprim- sulfamethoxazole we use chloramphenicol and, to some extent, chloramphenicol (if it becomes resistant too), fluoroquinolones and some third-generation cephalosporins (e.g., ceftriaxone) have become the drugs of choice
- Physician should be aware when & what antibiotic use.

- Chloramphenicol also is widely used for the topical treatment of eye infections. (not reach systemic circulation)
- It is a very effective agent because of its extremely broad spectrum of activity and its ability to penetrate ocular tissue.
- The availability of safer, less irritating instilled ophthalmic antibiotics and the increase in fatal aplastic anemia associated with the use of this dosage form suggest that this agent might best be withdrawn, to avoid aplastic anemia which might be happened after stop using chloramphenicol.
- We use it in systemic more than local, also there's a chance to reach high percentage of it because of mistakes in treatment and dose + has a high ability to penetrate.

- Chloramphenicol is an alternative to tetracycline for rickettsial diseases, especially in children younger than 8 years,
- alone or in combination with other antibiotics, it has been used to treat vancomycin-resistant enterococci.

- Another indication for chloramphenicol is in the treatment of serious anaerobic infections caused by penicillin-resistant bacteria, such as B. fragilis
- Chloramphenicol is used for treatment of certain in resistance condition to save patient’s life.

لا عليك يا صاحبي ، لا عليك ...

هذه التي أتعبتك هي نهاية المطاف دُنيا ! هكذا سمّاها خالقها كي لا نغترَّ بها .. فاستجمع قواك إنَّ لك طريقًا عليك أن تمشيه وعلى كاهلك أمانة عليك أن تؤديها ، وقد كان شعارك دومًا :

لا أبرحُ حتى أبلغ ! فلا تبرح ...

أعيذك بكلمات الله التامّات يا صاحبي من أن يكسرك في هذا العالم شيء ومن أن يمسَّك سوء ، ومن أن تنطفئ قبل أوانك ، ومن أن تُؤتى من قِبَل قلبك ... ضع يدك اليُمنى على قلبك يا صاحبي ورتل عليه : " فاللهُ خَيرٌ حَافِظاً " ، واطمئن ما كان لك سيأتيك إلى بابك وما لم يكن لك لن تناله بقوتك ! رغمًا عن اليمّ وعن أنف فرعون عاد موسى إلى أمه ، لأنه من البداية كان لها ، ورغمًا عن كيد النسوة وقضبان السجن عاد يوسف إلى يعقوب لأنه منذ البداية كان له...

فاطمئن يا صاحبي الطمئن .. كل ما فاتك لم يكن لك ، وكل ما لك فلن يَفُوتك سلِّم الأمر لصاحب الأمر ، وسَلْه أن يردَّ غائبك ، ويُرمم قلبك ويجبر خاطرك ... وقبل كل هذا ، سَلْه الرضا عن أقداره ..

فإنك متى رضيتَ استوى عندك المنحُ والمنعُ ...

فاللهمَّ الرضا ، اللهمَّ الرضا ♡

بالتوفيق جميعًا
دمتم بود..