University of Jordan
Faculty of Medicine

Medical Committee
The University of Jordan

Introduction to

Microbiology

Title :

Penicillin & Related Drugs

Professor:

Dr. Asem Al-Shehabi

: 11

- ○ Slides
- ○ Handout
- ● Sheet

Done by: **Ali Abualhija**

Price: .....

Designed by:
Waseem Kamal

MD University of Jordan Class of 2018

groups/Doctor2012
http://medstudygroup.weebly.com

Microbiology : antimicrobial drugs

Sheet 11

Ali abualhija

return to our topic antimicrobial drugs, we have finished major group of antimicrobial drugs which associated with inhibition of protein synthesis mainly aminoglycoside ,tetracyclin and chloramphenicol. and we have in addition type of antimicrobial called **macrolides**.

macrolides are special group of antimicrobial drugs with **larger cycle chemical compound** which contain **14-16 member rings** (in relation to carbon) and they usually **attached 50s ribosomal** subunit. in other words, macrolides associated with **inhibtion of protein** synthesis by inhibit either peptide transferase activity or translocation of the growing peptide mRNA. and these drugs are useful in treatment **of gram positive bacteria** ,staph or strep, which are resistant to the penicillin (penicillinase resistant bacteria).

in such case, you can use the most widely used macrolides which is **erythromycin** or **one of its derivatives : clarithromycin or azithromycin**. in addition, these drugs important in treating patients who are allergy of penicillin due to the fact that these drugs not associated with allergic reaction.

these drugs are long acting (12 hours).
relatively non-toxic drugs which often used in treatment of respiratory tract infection, soft tissues(like wound healing), and less in systematic infection associated with blood sepsis. and in might be used in certain lower respiratory tract infection which caused by special type of bacteria like mycoplasma, chlamedia which usually not covered well by other penicillin and cephalosporine which cannot be used against gram +ve bacteria.

we have other type of macrolides called **lincosamide** which is structure similar to large lacton ring or macrolide drugs only with different in presence of more amino group.

clindomycin and lincomycin are useful drugs in treatment of gram +ve bacteria (caused by staph or strep) especially in oral cavity.

lincomycin is less toxic than clindomycin and more used in clinical practice . especially lincomycine can easily penetrate the bones. so in case of infection of bone caused by gram +ve bacteria , licomycine is useful for treatment.

in addition, in relation to this group of antimicrobial drugs ,which is not found in other group drugs , these drugs are highly effective against anaerobic bacteria. they can kill majority of anareobic bacteria in oral cavity as well as in intestine. but there are some type of bacteria which cannot be affected by these two drugs (clindomycin and lincomycin) like *clostridium difficiles* and administration of these drugs may be associated increased relatively of clostridium dificiles which is found normally in intestine of about 30% of population , and 50% in hospitalized patient . this mean that if you use the lincomycin for long time more than week it will favor the growth of closridium difficiles which is normally produce exotoxins related in producing damage to mucosa of large intestine in the form of what we called pseudomembranous colitis which mean patient will suffer from bloody diarrhea which might increase and produce more damage in colon and ultimately death of patient . therefore, any patient reported for physician that he has bloody in his stool following use of these type of drugs then administration of these drugs should be immediately stopped. and must be replaced by another drug like vancomycin or flagyl in order to reduce severity of clostridium difficiles as well as feature of pseudomembranous colitis.

in addition, cephalosporine if used for long time may be also associated with developing of pseudomembranous colitis .

now we move to other group of drugs which inhibit the nucleic acid DNA or RNA and it's important clinically.

first type of these drugs belong to group called **quinolones**.

quinolones structure three cycles associated with side chain with one carbon group like carboxyl or oxy or hydroxyl and flour (F).

quinolones has many types one of them is basic quinolones without presence of flour(F) atom and this type of quinolones represented by a drug called **nalidixic acid.**

nalidixic acid is the first type which was introduced in the fifties for treatment of urinary tract infection due to the fact that this drug excreted normally mainly in the intestine and urinary bladder, it cannot be absorbed from the intestine and reach any target in our host, it cannot be used for sepsis or for urinary tract infection or meningitis ... etc.

it's only related to infection caused by gram negative and less gram positive . this drug inhibit double helix by inhibition of enzyme called DNA gyrase . which mean that no formation of double helix and so will inhibit bacteria chromosome to replicate.

in relation to nalidixic acid drug which called anti-urinary tract drug (because used mainly in urinary tract infection) we have another similar drug in structure but it associated with nitro group called **nitrofurantoin** and this drug inhibit steps in formation of DNA and used mainly in treatment of gram negative bacteria urinary tract infection .

now we move to **floroquinolones**. it's a basic **quinolones associated with flour** and this group exactly like nalidixic acid inhibit DNA gyrase result in bacreiocidal drug. and it's introduced latter in 1980s and there more than 10 types floroquinolons.

floroquinolones can be used as wide spectrum drug affect both gram positive and gram negative so used for urinary tract infection , upper repiratory tract infection and gastrtro intestinal tract infection. But less effective to treat blood sepsis. Floroquinolones has many derevativies such as: norfloxacin, ciprofloxacin, levofloxacin, and ofloxacin. These are widely used especially ciprofloxacin which are used in treatment of gastro intestinal tract infection and urinary tract infection and less upper respiratory tract infection . whereas, levofloxacin used in order to upper respiratory tract infection caused both gram positive and gram negative , in particular, intracellular bacteria so it's excellent drug.

Another drugs are **rifamycin** or **rifampin** that affect RNA synthesis not DNA usually by affecting RNA polymerase which result in developing of formation of double helix. Rifampin used to treat many type of infection especially infection which caused by intracellular bacteria like brucella, also it might affect cell wall of bacteria like Chlamydia and mycoplasma.

Rifampin is an excellent drug which can affect mycobacteria tuberculosis and not for other infection, why? To prevent developing of resistance against this drug.

Concerning **fusidic acid** , this drug is very effective against gram positive bacteria and it's ,to some extent, have function like rifampin affect also tRNA and prevent protein synthesis . fusidic acid only used as topical ointment and not administrated orally or by IV. And it's excellent especially against MRSA (methicillin resistant staphylococcus aureus) .

Sulfa drugs represented in 1935 by sulphonamide and this chemical drug produced by chemical synthesis and not originated from living tissue and this type of drug have many important function.

Bacteria require to complete synthesis of protein which is necessary for growth of to have the end product which is folic acid. Folic acid should be converted from small molecule which available in nutrient like paraamino benzoic acid (PABA)which converted by many chemical step to produce folic acid. PABA, which important in developing of folic acid , has very similar structure to sulfonamide. Sulfonamide is a

competitive inhibitor to enzyme which is important of converting hydrofolic acid to folic acid.

Due to the fact that our human cells cannot produce folic acid then we have to support our body by nutrient which contain folic acid .

In addition, sulfa drugs it's effective against both gram positive and negative and they found if sulfamethoxazole combined with trimethoprim (another chemical drug) then we have synergistic activity means you have double effect. And the combination between these two drugs result in new drug called (contrimoxazole) and this drug is widely used in treatment urinary tract infection and upper respiratory tract infection . despite the fact that the bacteria develop resistant to this drug, but still used at least 20-30% for treating UTI and URTI.

Now another group of drug which have different mechanisms of action which affect more than one target at same time , may affect tRNA , mRNA , cell membrane….etc.

These drug called **anti-tuberculosis** drugs (drugs which used to treat tuberculosis) normally these drug less important to treat another infections. Also, streptomycin may used to treat tuberculosis but may associated with side effect.

These anti-tuberculosis drugs are : isoniazide , ethambutol, cycloserine, refumpicin , streptomycin.

These drugs used mainly in treatment of microbacterial tuberculosis and tubercule bacilli.

all types of drug which we have already mentioned used for 1- 2 weeks. And rarely for more than two weeks except under certain condition . but anti- tuberculosis drugs used for long time between (6-24) month , it depend on microorganism (mycobacteria) if susceptible or resistant . this long period of treatment mean the patient may suffer from side effect but this is the only way to cure . but the problem if mycobacteria tuberculosis become resistant to one of these anti-tuberculosis drugs especially rifampin . if become resistant mean more duration of treatment and more cost.

For example, treatment of tuberculosis caused by sensitive mycobacterium tuberculosis costs 100 JD but if mycobacterium become resistant the cost is 10,000 JD. Due to prolong duration of treatment and using expensive drugs.

Metronidazol is a special drug due to the fact that this drug is not only effective against bacteria especially anaerobes (both gram positive and negative) but also against parasites especially protozoa which cause GI infection.

In order to know how to select type of antibiotic for treatment patient , you should do the following : 1- collect specimen from patient 2- send specimen to the laboratory for culturing and identification of causative agent and doing what we call antimicrobial or antibiotic susceptible disk to know if microorganisms is susceptible or resistant to other type of antibiotic. And it depends on site of infection . for example , if related to urinary tract infection then we have to select drug which is used for treatment of urinary tract infection. ..and so on.

What we do in laboratory?

We collect bacteria then isolate pure colony (not older than 24 hours) then we spread over surface of special medium culture called *maller hinton agar medium* on the surface in confluent growth means to cover all surface of plate and we weight for few minutes and after that we add antibiotic filter disks paper usually (6-8) in number which contain a definite amount of antimicrobial drugs and after incubation of 24 hours because most type of infection caused by facultative rapidly growing which need 24 hours to grow. And in next day we measure inhibition zone then use disk diffusion test because antibiotic on the disk filter paper will be absorbed from medium and it will be effective if it inhibit growth of the bacteria (inhibition measured in cm) . there are guide lines which shows us international prepared guide lines , in case of tetracycline if use disk 30 microgram/ml , inhibition zone must be at least 18 to considered susceptible if inhibition 17=16-15 considered not susceptible but intermediate susceptible and if it's less than 14 considered as resistant . so in short, this test can help us to select proper type of antibiotic . this procedure isn't easy as you imagine but it's difficult.

In summary, you must have pure and fresh culture and proper amount of antimicrobial disk, in addition, we have to use controlled strains which known to be susceptible to this antibiotic or resistant. Mean a lot of work should be done to get good result .

According to WHO , 5 years ago , we have distributed bacterial tests on 75% of laboratories in Arab world countries . less than half of these laboratories have succeeded to have good marks which we called successful to report about susceptibility and resistance of bacteria. Which mean a lot of result can be not accurate and this form problem . why? Because physician depend on these result in order to treat patient . false result lead to false drug and this contribute to misuse of drugs and developing of resistance .

Sorry for any mistake.