PT 431 Team Pharmacology

Reproductive Block

Lecture 7

Drugs used in treatment of gonorrhoea and syphilis

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Syphilis

Introduction

1-What is Syphilis ?

Sexually transmitted disease caused by bacterium : TreponemaPallidum (spirochete)

2- Classification of Syphilis:

A- Primary	B- Secondary	C- Latent	D- Congenital Syphilis
▪ Single sore (chancre) 	▪ Skin rash & mucous membranes lesions 	▪ 70% of patients may be asymptomatic	▪ If a woman is pregnant and has symptomatic or asymptomatic early syphilis, organisms may pass through the placenta to infect the fetus. ▪ May be prevented if the woman is treated before 16th to 18th weeks of pregnancy. Treatment after that will cure the infection and stop the damage to the baby, but it may not reverse damage already caused by infections.

Therapy of Syphilis

Antibiotics:

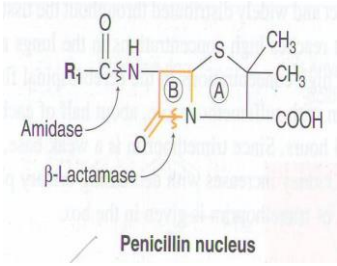
- Amount, route & duration based on the stage of the illness.
  e.g. in neurosyphilis , treatment continue for 10 days up to 2 weeks.
- Antibiotics prevent further complications but may not reverse damage that has already occurred.

Generally, what are the drugs used in treating Syphilis ?

- Penicillins
- Tetracyclines
- Macrolides
- Cephalosporins

Therapy of Syphilis

1- Penicillin (β-lactam antibiotic):



Is the MOST COMMON(BEST) antibiotic that can be used to treat Syphilis in all stages.

A. Mechanism of action:

inhibit bacterial cell wall synthesis **(bactericidal drug)**

B. Preparations:

1- Penicillin G	2- Procaine penicillin	3- Benzathine penicillin
Short acting (4-6 hrs) **I.V**	Long acting (24-48hrs) **I.M**	Long acting (every 3-4 weeks) **I.M**
All are acid unstable (not taken orally because HCL will degrade it) All are penicillinase sensitive (they can be destroyed by B-lactamase- producing organisms)		

C. Adverse effects:

- **Hypersensitivity** (may cause anaphylactic shock, so we have to do sensitivity test before each dose)
- Nephritis (with high doses) NOT common
- Convulsions (with high doses or in renal failure (b/c the penicillin is not metabolized in human body, and it's excreted unchanged through the kidneys.)
- Superinfections.

2- In case of hypersensitivity(Allergic patients)to penicillins, we give alternatives such as :

- **Tetracyclines** such as : **Doxycycline - Tetracycline - Minocycline**
- **Macrolidessuch** such as: **Clarithromycin (in Syphilis) - Azithromycin (used more with gonorrhea)**
- **Cephalosprins** such as: **Ceftriaxone – Cefotaxime - Cefixime**

Tetracyclines (e.g. Doxycycline-Tetracycline-Minocycline)

Kinetics: Well absorbed orally, Long acting(once daily)

MOA: inhibit bacterial protein synthesis, reversibly binds to **30 S** bacterial ribosomal subunit. **(bacteriostatic)**

Adverse effects:

1.gastric upset
(nausea- vomiting- diarrhea) (give with food)
2. Effects on calcified tissues:
(Brown discolouration of teeth –children)
(Deformity or growth inhibition of bones –children)
Should avoid milk and milk products after taking tetracyclines
3- Hepaotoxicity (prolonged therapy with high dose)
4. Phototoxicity
5-vestibular problems (vertigo, nausea, vomiting)
more commom with **Tetracycline - Minocycline**
6. Superinfections.

Contraindications:

1. Pregnancy
2. Nursing mothers
3. Children(below 10 yrs)

Macrolides (e.g. Clarithromycin)

MOA: inhibit protein synthesis, reversibly binds to **50 S** bacterial ribosomal subunit **(bacteriostatic)**

Adverse effects :

1.Gastric upset
(Nausea, vomiting, abdominal pain & diarrhea)
2.Inhibits hepatic microsomal enzyme(P-450system)
(drug-drug interaction!)
3.Allergic reactions- urticaria, mild skin rashes
4.Irregular heart beats(recent) !!!

Cephalosporins

(e.g. Ceftriaxone - Cefotaxime- Cefixime)

MOA : inhibit cell wall synthesis
(beta-lactam just like Penicillin) – **(bactericidal)**
3rd generation: Ceftriaxone - Cefotaxime - Cefixime

Adverse effects :

1. Allergic manifestations(NOT up to anaphylactic shock)
2. Thrombophilibitis (inflammation of veins) at injection site
3. Superinfection(psudeomembranous colitis)
4. Diarrhea(as a result of superinfection)

Syphilis & Pregnancy

- **Penicillin** is the only antibiotic that should be used during pregnancy.
- If the woman is allergic to penicillin, desensitization is done, so it can safely taken or **Ceftriaxone** or **Clarithromycin** as alternative.

Gonorrhea

Introduction

1- What is Gonorrhea ?

An infection Caused by Neisseria gonorrhea, a pus producing bacteria.

Therapy of Gonorrhea

2- What are the drugs used to treat Gonorrhea ?

- **3rd generation Cephalosporins: Ceftriaxone, Cefotaxime, Cefixime**
- **Fluoroquinolones: Ciprofloxacin**
- **Spectinomycin**

..Uncomplicated gonorrheal infections (Localized) ..

A. Recommended regimens (1st line treatment):

1- **3rd generation cephalosporins** (Single –dose):
   - **500mg of Ceftriaxone, IM**
   - **500 mg of Cefotaxime, IM**
   - **400 mg of Cefixime, orally** (recently some gonococcal strains become resistant to oral Cefixime)

2- **Macrolides**
   - **Azithromycin**

3- **Fluoroqionolones –** (Single oral dose):
   - **Ciprofloxacin**
   - **Ofloxacin**
   - **Levofloxacin**

Fluoroqionolones (E.g. **Ciprofloxacin - Ofloxacin – Levofloxacin)**

MOA : Inhibit DNA synthesis by inhibiting DNA gyrase enzyme **(Bactericidal)**

Adverse effects :

1. Nausea , vomiting &diarrhoea
2. Headache & dizziness(CNS)
3. May damage the growing cartilage**(arthropathy)** #pregnancy, breast feeding, and Adolescent under 18y/o
4. Phototoxicity – avoid excessive sunlight

Contraindications:

1. Pregnancy 2. Nursing mothers **3.** Adolescent under (18 years)

B- Alternative treatment to patients who cannot tolerate or treated by the (1st line treatment):

1- **Spectinomycin :** 2gm I.M (once)

Spectinomycin

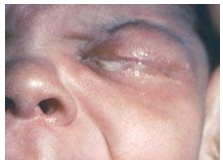
MOA: Inhibits protein synthesis by binding to **30 S** ribosomal subunits **(Bactericidal)**

Adverse effects :

1. Pain at the site of injection
2. Fever , nausea
3. Nephrotoxicity (rare)

.. Complicated gonorrheal infections ..

- Spread through the Blood to:
  -**Eye** -Joints
  -Heart valves -Brain
- Newborn eye infection may lead to **blindness** if not treated.



A. Treatment of Complicated gonorrheal infections with conjunctivitis in Newborn:

1- Silver nitrate:

- MOA: Its germicidal effects are due to precipitation of bacterial proteins by liberated silver ions
- Put into conjunctival sac once immediately after birth (not later 1 h after birth).

2- Erythromycin:

- 0.5% ointement for treatment & prevention of corneal &conjunctival infections.
- Put into conjunctival sac immediately after birth (no later than 1 hr after delivery).

- Adult eye infections, spread on fingers, can lead to **blindness.**

B. Treatment of Complicated gonorrheal infections with conjunctivitis in Adult:

1- **Ceftriaxone** 500mg IMI for 3 days
2- **Spectinomycin** 2g IMI for 3 days

Pregnant or Breast feeding

- **Ceftriaxone** 500 mg IMI (single dose) Plus **Azithromycin** 1g orally (single dose)
- **Spectinomycin** 2g IMI (single dose) plus **Azithromycin** 1g orally (single dose)

Antibiotics that NO longer recommended for gonorrhea treatment

- **Sulfonamides**
- **Tetracycline**(NOT Tetracyclines! **Tetracycline** is one of the Tetracyclines preparations, *we can use Doxycyline in gonorrhea*)
- **Penicillins**
- **Oral cephalosporines** e.g. oral Cefixime

MCQs

1-All of the following antibiotics can be used to treat Syphilis in pregnant women except:

A. Penicillin
B. Macrolides
C. Tetracycline
D. Ceftrixone

2-The drug of choice for treating Syphilis is:

A. Penicillin
B. Macrolides
C. Tetracycline
D. Ceftrixone

3-Which one of the following is true regarding the mechanism of action of Clarithromycin:

A. It inhibits bacterial protein synthesis by reversibly binds to 30 S bacterial ribosomal subunit.
B. It inhibits protein synthesis by reversibly binds to 50 S bacterial ribosomal subunit.
C. It inhibits bacterial cell wall synthesis.
D. It inhibits DNA synthesis by inhibiting DNA gyrase enzyme.

4-Which of the following would you use to treat a newborn with conjunctivitis due to gomorrhea:

A. Silver nitrate
B. Cefixime
C. Erythromycin
D. A+C

5- A 9-year-old female having uncomplicated gonorrheal infection is treated with Ciprofloxacin. Which one of following side effects can be caused by Ciprofloxacin.

A. Brown discoloration of teeth
B. Arthropathy
C. Thrombophilibiti
D. Hypersensitivity

1-C 2-A 3-B 4-D 5-B