



KING SAUD UNIVERSITY
COLLEGE OF MEDICINE
1ST YEAR, 5TH BLOCK

Treatment of Urinary Tract 1 & 2 Infections



RENAL BLOCK

Classification of urinary tract infections:

1- Symptomatic infections:

Uncomplicated UTI (mainly in women)

acute cystitis

Acute urethritis

recurrent cystitis

Acute pyelonephritis

Complicated UTI

Acute and chronic Prostatitis

2- Asymptomatic bacteriuria.

Urinary tract infections (UTI's):

- It is the 2nd most common infection.
- It is often associated with some obstruction of the flow of urine.
- It is more common in women more than men.
- Incidence of UTI increases in old age(10% of men & 20% of women).
- Normally urine is sterile, Bacteria comes from digestive tract to opening of the urethra.

Treatment of uncomplicated and complicated UTI's:

*Antimicrobial agents:

-TMP or TMP/SMX (co-trimoxazole)

-Nitrofurantoin

-Quinolones

-Tetracyclines

-Aminoglycosides

*β-Lactam antibiotics:

-Extended spectrum penicillins

-Cephalosporins (1st & 3rd G.)

Organisms Causing urinary tract infections

Gm negative bacteria (most common):

E.coli (approx. 80% of cases)

Proteus

Klebsiella

Pseudomonas

Gm positive bacteria (less common):

Staphylococcus species

Chlamydia trachomatis ,Mycoplasma & N. gonorrhoea

	Sulfamethoxazole /Sulfonamides (SMX)	Trimethoprim (TMP)
Mechanism of action	1- Co-trimoxazole (Bactrim, Septra). 2- each agent alone is bacteriostatic. 3-Together they are bactericidal (sequential synergism).	
Pharmacokinetics	-given orally. -Rapidly absorbed from stomach and small intestine. -distributed to tissues and body fluids & crossing the placenta. -bind to serum protein. -Metabolized in the liver by the process of acetylation. -Eliminated in the urine.	same as SMX, Well absorbed from the gut More lipid soluble than SMX TMP concentrates in the prostatic fluid.
Clinical uses	1-Acute urinary tract infections. 2-Complicated urinary tract infections. 3-Recurrent urinary tract infections especially in females. 4-Prostatitis (acute/ chronic).	
Adverse effects	-Gastrointestinal (Nausea, vomiting). -Hematologic: 1-Acute hemolytic anemia (SMX) a) hypersensitivity b) G6PD deficiency 2) Megaloblastic anemia due to TMP (Folate deficiency). SMX))-Kernicterus (bilirubin –induced brain dysfunction). SMX))-Crystalluria. SMX))-Hypersensitivity reactions (skin reaction). SMX))-Neonatal jaundice.	
Contra-indications	-Pregnancy (cross placenta). -Nursing mother (secreted in milk). -Newborn Infants (encephalopathy). -Renal or hepatic failure. -Blood disorders.	

Nitrofurantoin

- Effective against E. coli
- Gram positive cocci are susceptible
- Not effective against P- aeruginosa

Mechanism of action	Changed by bacteria to an active agent that inhibits various enzymes and damages bacterial DNA
Pharmacokinetics	<ul style="list-style-type: none">-Absorbed rapidly and completely from GIT-Well concentrated in the urine-Rapidly metabolized by the liver , 40 % is excreted unchanged into the urine.(Antiseptic)- Turns urine to a dark orange- brown-Given with food-The antibacterial activity is higher in an acidic urine
Adverse effects	<ul style="list-style-type: none">- GIT disturbances: nausea, vomiting, diarrhea & gastric bleeding .-Headache and nystagmus (abnormal sensation) .- Hemolytic anemia (glucose-6-phosphate dehydrogenase deficiency)-Pulmonary fibrosis (on chronic use)
Contra-indications	<ul style="list-style-type: none">-Patients with G 6PD deficiency-Neonates (babies up the age of one month)-Pregnant women (after 38 weeks of pregnancy {late pregnancy})-Patients with decreased renal function
Therapeutic Uses	<ul style="list-style-type: none">-Used as urinary antiseptics .-Prophylaxis of recurrent urinary tract infections-Not effective in systemic UTI as pyelonephritis-Dose: 50-100 mg (orally four times daily) for 7 days

Tetracyclines

Broad spectrum antibiotic, Bacteriostatic

Inhibit protein synthesis by binding reversibly to 30 s ribosomal subunit

Doxycycline

Minocycline

Long acting tetracyclines ,Usually given orally once daily

Absorption is 90-100 % in the upper small intestine, and Metabolized in liver

Protein binding 40-80 %

Distributed well, including prostatic tissues, **so they are used in prostatitis (like co-trimoxazole)**

Cross placenta and excreted in milk.

Doxycycline is excreted through non renal route
(Indication: UTI+Renal failure)

minocycline is excreted through kidney

Divalent cations (Ca, Mg, Fe), milk and its products, and antacids (aluminium hydroxide gel, sodium bicarbonate)

❖ Nausea, vomiting, epigastric pain and diarrhea , Vertigo , Superinfections

❖ Thrombophlebitis (i.v route)

❖ Hepatic toxicity (prolonged therapy with high dose) because it is metabolized by the liver.

❖ **Brown discoloration & deformity of teeth (children)***

❖ **Deformity or growth inhibition of bones (children)***

* Because it takes the calcification of the teeth and bones

Treatment of UTI's & chronic prostatitis due to **Mycoplasma & Chlamydia.**

Pregnancy, Breast feeding, Children (up to 12 years)

Aminoglycoside :

(Gentamicin , Tobramycin)

About :

- Bactericidal antibiotics .
- Inhibits **protein synthesis** by binding to 30S ribosomal subunits (irreversibly)
- Active against **gram negative aerobic** organisms .
- **Poorly** absorbed orally .
- Given I.M, I.V. .
- cross placenta .
- Excreted unchanged in urine .

Adverse effects :

- Ototoxicity .
- Nephrotoxicity .
- Neuromuscular blocking effect .

Therapeutic uses :

- **Severe UTIs** which causes by gram negative aerobic organism .
- Gentamicin is effective in treating **pseudomonal infections** .

Contraindications

- Renal dysfunction
- Pregnancy (because they cross placenta)
- Patients with **hearing** problem (Diminished hearing) (Deafness in neonates)
- **Myasthenia gravis**

β-Lactam antibiotics:

we use Amoxicillin with clavulanic acid*, and piperacillin with tazobactam*

	Extended spectrum	Cephalosporins	
e.g	Piperacillin (Penicillinase sensitive)*	1 st generation: Cephalexin	3 rd generation : Ceftriaxone & Ceftazidime
M.O.A	Inhibit bacterial cell wall synthesis, Bactericidal		
Act against	Very Effective against <i>pseudomonas aeruginosa</i> & <i>Enterobacter</i> .	Mainly effective against G -ve bacteria. -given parenterally. -Use in severe or complicated UTIs & acute prostatitis	

- Bacteria often develop resistance to β-lactam antibiotics by synthesizing a β-lactamase , an enzyme that attacks the β-lactam ring. To overcome this resistance, β-lactam antibiotics are often given with β-lactamase inhibitors like (clavulanic acid and tazobactam)

* Penicillinase = β-lactamase.

	Fluroquinolones Ciprofloxacin (levofloxacin,
M.O.A	Inhibits DNA gyrase enzyme
	Used in UTIs caused by multidrug resistance organisms as <u>pseudomonas</u> , and Prostatitis . *Contraindicated <u>in children under 18 year old</u> .

Prostatitis

Acute prostatitis	Chronic prostatitis
Non- catheter- or catheter associated usually due to G – ve bacteria like (E.coli or Klebsiella)	Due to E.coli, Klebsiella & Proteus
TMP/SMX*, Ceftriaxone, Ciprofloxacin, levofloxacin , <u>Doxycycline in chronic prostatitis especially in trachomatis & chlamydia infections</u>	

Antibiotic used for children in UTI	Antibiotic <u>not recommended</u> for children in UTI
Cephalosprins (ceftriaxone, ceftazidime) Penicillins (amoxicillin) Aminoglycosides (with <u>precaution</u>)	Tetracyclines Quinolones

S U M M A R Y

Drug	Indication	Contraindication	ADRs	Note
Trimethoprim , Sulfonamides	-Acute UTI -Complicated UTI -Recurrent UTI (females) -Prostatitis (acute/chronic)	Pregnancy, Nursing mother, Newborn Infants Renal or hepatic failure, Blood disorders	-Gastrointestinal -Acute hemolytic anemia -Megaloblastic anemia -Kernicterus, Crystalluria, Hypersensitivity reactions, Neonatal jaundice	Crystalluria: precipitation of sulfa.
Nitrofurantoin	-urinary antiseptics . -Prophylaxis of recurrent UTI	G 6PD deficiency Neonates Pregnant ↓renal function	-GIT, Headache and nystagmus.v -Hemolytic anemia -Pulmonary fibrosis (on chronic use)*	Effective against E. coli * We should stop the drug immediately .
Tetracyclines	Treatment of UTI's & chronic prostatitis due to Mycoplasma &Chlamydia.	Pregnancy Breast feeding Children (up to 12 years)	GIT, Hepatic toxicity, Thrombophlebitis (I.V) Brown discoloration & teeth deformity. Deformity or growth inhibition of bones Vertigo Superinfections	We use <u>Doxycycline</u> in patients who have renal problems.
Aminoglycosides	Severe UTIs (gram - aerobic organisms , gentamicin is effective in treating pseudomonal infections) .	●Renal dysfunction ●Pregnancy ●hearing problem ●Myasthenia gravis	●Ototoxicity ●Nephrotoxicity ●Neuromuscular blocking effect	During the course the patients should undergo <u>Hearing test.</u>

M C Q S

Q1: Which one of the following organisms is the most problematic bug and has less sensitivity to antibiotics:

- A- E-coli
- B- Klebsiella
- C- Proteus
- D- P.aeruginosa

Q2: A 35 years male came to the urology clinic complaining form dysuria, hematuria and fever for the last three days.

The report from the microbiology lab revealed the presence of pseudomonas aeruginosa in the urine sample.

Which one of the following is the most effective antibiotic in this case?

- A- Ciprofloxacin
- B- Gentamycin
- C- Tetracyclines
- D- Piperacillin

Q3: The enzyme that will be inhibited by trimethoprim in its synergism with Sulfamethoxazole is:

- A- Dihydropteroate synthetase
- B- Dihydrofolate synthase
- C- Dihydrofolate reductase
- D- All the above

Q4: Which one of the following antibiotics is contraindicated in children:

- A- Ceftriaxone
- B- Ceftazidime
- C- Amoxicillin
- D- Quinolones

Q5: The underlying cause for sulfonamides to be contraindicated in pediatric patients with UTI is:

- A- They elevate blood bilirubin levels by displacing it and binding to plasma proteins which cause Kernicterus.
- B- They impair immature hepatic function.
- C- They stimulate the synthesis of bilirubin.
- D- None of them

Q6: What is the most serious adverse effect due to chronic use of nitrofurantoin:

- A- Hematologic toxicities
- B- Interstitial pulmonary fibrosis
- C- Pneumocystis jiroveci
- D- Erectile dysfunction

Q7: A pregnant lady was referred to the hospital with symptoms of UTI.

She is in the last trimester of gestation.

Which one of the following drugs is contraindicated for her:

- A- Cephalosporin
- B- Ceftriaxone
- C- Penicillin
- D- Nitrofurantoin

Q8: The drug that is contraindicated in myasthenia gravis due to its neuromuscular blocking effect is:

- A- Aminoglycosides
- B- Fluroquinolones
- C- Penicillin
- D- Nitrofurantoin

Q9: A 65 male retired teacher was diagnosed with chronic prostatitis. The physician described the most effective antibiotic for his situation, which is bacteriostatic and inhibit protein synthesis. But he told the patient that he has to avoid milk and its products for at least one hour after taking the drug in order to make it absorbed in a high amount.

Which one of the following is most likely the described antibiotic:

- A- Doxycycline
- B- Gentamycin
- C- Nitrofurantoin
- D- Vencomycin

Q10: A patient with a history of G-6PD deficiency had a UTI two days ago. The intern wanted to describe Nitrofurantoin for him, but when consulting the urologist he reminds him to change the therapy to prevent developing of:

- A- Hemolytic anemia
- B- Macrocytic hypochromic anemia
- C- Hearing loss
- D- Deep vein thrombosis

1-D . 2-D . 3-C . 4-D . 5-A
6-B . 7-D . 8-A . 9-A . 10-A

We hope we made this lecture easier for you
Contact us for any questions or comments
Good Luck !

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