

DRUGS USED IN URINARY TRACT INFECTIONS



URINARY ANTISEPTICS

- Urinary antiseptics are oral agents that
 - exert antibacterial activity in the urine
 - but have little or no systemic antibacterial effects.
- Their usefulness is limited to lower urinary tract infections.
- Why Urinary Antiseptic and not Urinary antibiotics?

DRUGS USED AS URINARY ANTISEPTICS

- Nitrofurantoin
- Methenamine
- Nalidixic acid

NITROFURANTOIN

- ❑ Primarily bacteriostatic
- ❑ Activity limited to *E. coli*
- ❑ **Mechanism of Action:**
 - ❑ Sensitive bacteria reduce the drug to an active agent that inhibits various enzymes → damage bacterial DNA.
- ❑ Antibacterial concentration is not attained in blood or tissues
- ❑ Not to be used with Probenecid, azotemic patients: interferes with tubular secretion of drug.

NITROFURANTOIN

Adverse Effects:

- Gastrointestinal Intolerance: Nausea, epigastric pain, diarrhoea
- Hypersensitivity : fever, chills
- Peripheral neuritis and other neurological effects with long term use
- Hematologic disorders: leukopenia, granulocytopenia, Hemolytic anemia in G6PD deficient patients
- Liver damage, pulmonary reaction with fibrosis on chronic use
- **Contraindicated in renal impairment, pregnancy and neonates.**

NITROFURANTOIN: USES

- ✓ Treatment for uncomplicated lower urinary tract infection
 - ✓ Not associated with prostatitis
- ✓ Supportive long term therapy
- ✓ Long term prophylaxis
 - ✓ Following catheterization, instrumentation, in women with recurrent cystitis

METHENAMINE (HEXAMINE)

- ❖ Prodrug

- ❖ **Mechanism of Action:**

- ❖ Decomposes slowly in acidic urine(Ph 5.5 or less) to release formaldehyde which inhibits all bacteria

- ❖ No antimicrobial activity in blood and tissues.

- ❖ Needs to be administered with mandelic acid or hippuric acid

METHENAMINE

- ❖ Use

- ❖ As Methenamine mandelate in

- ❖ Chronic and resistant UTI not involving kidneys.

- ❖ Not Effective for

- ❖ Acute UTI

- ❖ Catheter prophylaxis

METHENAMINE

❖ Side Effects:

- ❖ Gastritis

- ❖ Chemical cystitis, hematuria

- ❖ Occasional CNS Symptoms

NALIDIXIC ACID

- Nonfluorinated quinolone
- Bactericidal
- Mechanism of Action:
 - Inhibit the replication of bacterial by interfering with the action of DNA gyrase during bacterial growth and development.
- Resistance Develops rather rapidly

NALIDIXIC ACID

➤ Uses:

- Second Line Drugs for UTI
- Recurrent cases
- On the basis of Sensitivity Reports

➤ ADR

- Infrequent: GI upset, rashes
- Headache drowsiness,
vertigo, visual disturbances
- Seizures in children
- Nausea , Vomiting and abdominal pain
- Photosensitivity, urticaria and
Fever

Contraindicated in infants

PHENAZOPYRIDINE

- ↳ Urinary Analgesic
- ↳ Affords symptomatic relief from:
 - ↳ Burning Micturation
 - ↳ Dysuria
 - ↳ Urgency
- ↳ No anti-bacterial property
- ↳ Side Effects:
 - ↳ Nausea, Epigastric Pain

URINARY TRACT INFECTION: TREATMENT

Mostly gram negative organisms

- Acute episode: single organism,
- Chronic/recurrent: mixed infection

Acute Infection: largely self limiting

- High urine flow rate
- Frequent bladder voiding
- Lower UTI: Single Dose Antibiotic or 3 Days Course Suffice
- Upper UTI: Longer Treatment

URINARY TRACT INFECTION: TREATMENT

Bacterial Investigation very important

Smaller than usual doses required for treatment of Lower UTI

Upper UTI requires normal doses as for any other infection

Least Toxic and cheaper drugs should be chosen, for proper duration

Drug should not disrupt normal gut and perineal flora

Frequent recurrences: chronic suppressive treatment with co-trimoxazole, nitrofurantoin, methenamine, cephalixin, norfloxacin

STATUS OF ANTIMICROBIAL AGENTS OTHER THAN URINARY ANTISEPTICS IN UTI

• Sulfonamides:

- Decreased dependability for acute UTI;
- Not used as single drug; employed for suppressive or prophylactic therapy

• Cotrimoxazole:

- Declined responsiveness
- Employed empirically for acute UTI (broad spectrum)
- Prophylaxis for recurrent cystitis in women, catheterized patients

• Quinolones:

- First generation FQs (norfloxacin and ciprofloxacin)

• Ampicillin/Amoxicillin

- Frequently used in the past
- Higher failure and relapse rates: Unreliable for empirical therapy
- Amoxicillin + Clavulanic Acid used these days
- Coamoxiclav+ Gentamycin: initial treatment for acute

STATUS OF ANTIMICROBIAL AGENTS OTHER THAN URINARY ANTISEPTICS IN UTI

• Cephalosporin:

- Increasing use especially in nosocomial *Klebsiella* and *Proteus* infection
- Employed on the basis of sensitivity report, employed for community acquired infections as well
- Cephalexin: alternative for prophylaxis of recurrent UTI, especially women likely to get pregnant

• Gentamycin:

- Sensitive against *Pseudomonas*
- Narrow margin of safety, parenteral administration: bacterial sensitivity awaited

URINARY PH AND ANTI MICROBIAL AGENTS

- Acidic urine required for Methenamine
- Inadequate response, in complicated cases: measurement and correction of urinary pH may be attempted
- Urease positive *Proteus* infections: drugs acting at higher pH should be administered

Favourable urinary pH for antimicrobial action

Acidic	Alkaline	pH immaterial
Nitrofurantion	Cotrimoxazole	Chloramphenicol
Methenamine	Aminoglycosides	Ampicillin
Cloxacillin	Cephalosporin	
	Fluoroquinolone	

URINARY INFECTION IN PATIENTS WITH RENAL IMPAIRMENT

- Difficult to treat
- Drugs Contraindicated:
 - Methamine mandelate,
 - Tetracyclines,
 - Cephalosporin (some)
- Drugs avoided:
 - Nitrofurantion,
 - Nalidixic acid,
 - Aminoglycosides
- Potassium salts and acidifying agents contraindicated