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Matric Number: 16/MHS02/026

Department: Physiology

Assignment Title: Drugs used in urinary system disorders

Course Title: URINARY STSTEM PHARMACOLOGY

Course Code: PHA 306

Question

1. A drug used in the treatment of urinary tract infection causes brown coloration of urine. Explain in full detail the pharmacology of the drug under the following headings:

a. Name of the drug

b. Antibacterial activity

c. Mechanism of action

d. Pharmacokinetics

e. Adverse effects

 **ANSWERS**

1. The name of the drug used in the treatment of urinary tract infection and also causes brown coloration of urine is Nitrofurantoin. Nitrofurantoin is a nitrofuran antibiotic used to treat uncomplicated urinary tract infections. Nitrofurantoin is converted by bacterial nitro reductases to electrophilic intermediates which inhibit the citric acid cycle as well as synthesis of DNA, RNA, and protein. This drug is more resistant to the development of bacterial resistance because it acts on many targets at once. Nitrofurantoin is a second line treatment to trimethoprim/sulfamethoxazole. Nitrofurantoin was granted FDA approval on 6 February 1953.

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1. **Antibacterial activity**: Nitrofurantoin is a unique antibiotic, characterized by a hydantoin ring with a nitro-substituted furanyl side chain that is metabolized within the bacteria to produce reactive compounds that are bactericidal. Nitrofurantoin has been shown to have good activity against:
* E. coli
* Staphylococcus saprophyticus
* Coagulase negative staphylococci
* Enterococcus faecalis
* Staphylococcus aureus
* Streptococcus agalactiae
* Citrobacter species
* Klebsiella species
* Bacillus subtilis species

It is used in the treatment of infections caused by these organisms.

Many or all strains of the following genera are resistant to nitrofurantoin

* Enterobacter
* Klebsiella
* Proteus
* Pseudomonas
* Antibiotic susceptibility testing should always be performed to further elucidate the resistance profile of the particular strain of bacteria causing infection.
* Pregnancy
1. **Mechanism of action**: Nitrofurantoin is concentrated in the urine, leading to higher and more effective levels in the urinary tract than in other tissues or compartments. With a 100 mg oral dose, plasma levels are typically less than 1 µg/ml while in the urine it reaches 200 µg/ml.

The mechanism of action is unique and complex. The drug works by damaging bacterial DNA, since its reduced form is highly reactive.[8] This is made possible by the rapid reduction of nitrofurantoin inside the bacterial cell by flavoproteins (nitrofuran reductase) to multiple reactive intermediates that attack ribosomal proteins, DNA, respiration, pyruvate metabolism and other macromolecules within the cell. Nitrofurantoin exerts greater effects on bacterial cells than mammalian cells because bacterial cells activate the drug more rapidly. It is not known which of the actions of nitrofurantoin is primarily responsible for its bactericidal activity. The broad mechanism of action for this drug likely is responsible for the low development of resistance to its effects, as the drug affects many different processes important to the bacterial cell.

1. **Pharmacokinetics**: Nitrofurantoin is administered orally as a microcrystalline or macrocrystalline formulation, of which the latter has a slower absorption rate. Absorption is almost complete, with 2–4% of the dose being recovered from the feces. Serum concentrations are not measurable, except in patients who have severe renal failure. This is because of destruction of nitrofurantoin in the tissues and, in particular, a very rapid renal elimination by glomerular filtration (20%) and tubular secretion, resulting in a serum half-life of only 20 minutes in patients who have normal renal function.18 Excretion is complete within 6 hours after intake and urine concentrations of 200–400 mg/l are achieved after a dose of 100 mg q8h. In patients who have renal failure – who should not be given nitrofurantoin – there are measurable but still very low serum and urine concentrations.

Therapeutic doses of nitrofurantoin are 50–100 mg q8h or q6h for adults and 3 mg/kg/day q12h or q8h for children. Prophylactically, the adult dose is 50–100 mg and the pediatric dose 1–2 mg/kg at bedtime. The duration of treatment when nitrofurantoin is used therapeutically should be 5–7 days. Dosages are not affected by liver function.

1. **Adverse effects**: Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention. Adverse effects include:

**More common**

* Changes in facial skin color
* chest pain
* chills
* cough
* fever
* general feeling of discomfort or illness
* hives
* hoarseness
* itching
* joint or muscle pain
* shortness of breath
* skin rash
* sudden trouble in swallowing or breathing
* swelling of the face, mouth, hands, or feet
* troubled breathing

**Less common**

* Black, tarry stools
* blood in the urine or stools
* burning, numbness, tingling, or painful sensations
* dizziness
* drowsiness
* headache
* pinpoint red spots on the skin
* sore throat
* unsteadiness or awkwardness
* unusual bleeding or bruising
* unusual tiredness or weakness
* weakness in the arms, hands, legs, or feet

**Rare**

* Abdominal or stomach pain
* blindness
* blistering, peeling, or loosening of the skin and mucous membranes
* blue-yellow color blindness
* bluish color of the fingernails, lips, skin, palms, or nail beds
* blurred vision or loss of vision, with or without eye pain
* bulging soft spot on the head of an infant
* change in the ability to see colors, especially blue or yellow
* confusion
* cracks in the skin
* darkening of the urine
* decreased vision
* diarrhea
* diarrhea, watery and severe, which may also be bloody
* eye pain
* general tiredness and weakness
* light-colored stools
* loss of appetite
* loss of heat from the body
* mental depression
* mood or mental changes
* nausea or vomiting
* pale skin
* pale stools
* red skin lesions, often with a purple center
* red, irritated eyes
* red, swollen skin
* red, thickened, or scaly skin
* skin rash
* sores, ulcers, or white spots on the lips or in the mouth
* swollen or painful glands
* tenderness of salivary glands
* unpleasant breath odor
* upper right abdominal pain
* visual changes
* vomiting of blood
* wheezing or tightness in the chest
* yellow eyes or skin