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MATRIC NO. : 17/MHS01/296

DEPARTMENT : HUMAN ANATOMY

COLLEGE : MEDICINE AND HEALTH SCIENCES

COURSE CODE: SYSTEM PHARMACOLOGY

COURSE TITLE : 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.**
2. **Name of the drug**
3. **Antibacterial activity**
4. **Pharmacokinetics**
5. **Adverse effects.**

The predominant cause of urinary tract infections is periurethral colonization of bacteria from a fecal reservoir, which then ascends the urinalysis tract.

The commonly used antibiotics **Nitrofurantoin** and **Metronidazole** can lead to brown urine discoloration. **Chloroquine** and **Primaquine** have also been implicated .

This assignment will be focusing on **Nitrofurantoin** and it’s pharmacological role in urine discoloration.

**NITROFURANTOIN:**

Nitrofurantoin is an antibiotic medication that is used for the treatment of uncomplicated lower urinalysis tract infection. It is effective against most gram-positive and gram-negative organisms. Nitrofurantoin was approved for treatment of lower urinary tract infection . Nitrofurantoin is a sun the tic antimicrobial created from furan and an added nitro group and a side change containing hydantoin.

Several major guild lines have declared Nitrofurantoin as the first-line therapy for treatment of urinary tract infection. It’s primary use has remained the treatment and prophylaxis of urinary tract infections. It’s is advantageous in this role as it concentrates in the lower urinary tract while maintaining a low serum concentration and also does not significantly affect bowel flora.

**ANTIBACTERIAL ACTIVITY:**

Nitrofurantoin is effective against many gram-positive and gram-negative organisms. Nitrofurantoin is bactericidal against most common urinalysis tract pathogens, such as;

1. Escherichia coli
2. Enterococci
3. Klebsiella
4. Staphylococcus
5. Saprophyticus
6. Enterobacter

Its spectrum of susceptibility also includes ***shigella, salmonella, citrobacter, neisseria, bacteroides, group B streptococcus, staphylococcus aureus,*** and ***staphylococcus epidermidis.***

Studies have shown that the effectiveness of Nitrofurantoin does not differ between ESBL-producing E.coli and Non-ESBL-producing E.coli strains. Resistance to Nitrofurantoin remains relatively rare despite several decades of widespread use.

In long-term prophylaxis , numerous studies demonstrated that Nitrofurantoin is an effective prophylactic agent and compares well to other antibiotics in this role.

**MECHANISM OF ACTION:**

Nitrofurantoin is only available as an oral medication. Nitrofurantoin’s optimal dosing remains unknown since its use was approved before modern requirements for rigorous methods for drug development.

Nitrofurantoin’s mechanism of action remains poorly understood since its discovery in the 1940s. Nitrofurantoin uses several mechanisms to achieve an antimicrobial effect. Nitrofurantoin is taken up by bacterial intracellular nitroductases to produce the active form of the drug via reduction of the nitro group. Intermediate metabolites that result from this reduction then bind to bacterial enzymes involved in the synthesis of DNA, RNA, cell wall protein synthesis, and other metabolic enzymes.

Guidelines recommend Nitrofurantoin monohydrate/macrocrystals dosage to be 100mg twice daily for 5 days for the treatment of lower urinary tract infection. A 7-day course is also acceptable.

**PHARMACOKINETICS:**

Nitrofurantoin is readily absorbed and quickly distributed into most body fluids. It is rapidly excreted in large amounts in bile and urine. With the exception of the active drug secretion in the kidney tubule and biliary drug transport, Nitrofurantoin transfer across body membranes occurs by diffusion. Nitrofurantoin has a short elimination half-life in whole blood or plasma. In conjunction with its rapid excretion by the primary routes, there is little evidence for any prolonged binding of Nitrofurantoin to either plasma proteins or tissues. The first-order kinetics involved in Nitrofurantoin absorption and elimination is most appropriately described by a one-compartment open model. Biliary and urinary excretion of unchanged Nitrofurantoin and enzymatic degradation are the primary means of elimination.

**ADVERSE EFFECTS:**

Nitrofurantoin is relatively a safe drug compared to its alternatives.The most common reported side effects include nausea, vomiting, loss of appetite , and diarrhea.

These symptoms usually develop in the first week of therapy. Modern formulations, have less frequency of these effects .

More severe reactions to Nitrofurantoin exist. The most well known severe reaction is pulmonary toxicity. Pulmonary toxicity caused by Nitrofurantoin can be categorized into acute, subacute, and chronic pulmonary reactions.

* The acute syndrome is characterized by sudden onset of;
* fever,
* chills,
* cough,
* myalgia,
* and dyspnea.
* Subacute pulmonary reactions also occur and are characterized by;
* Persistent dry cough
* Dyspnea
* Fever.
* The chronic pulmonary reaction is associated with the insidious onset of persistent dry cough and dyspnea.

Acute, subacute and chronic pulmonary toxicity are reversible with immediate cessation of the drug.

Finally, Nitrofurantoin should not be administered to patients with acute bacterial puelonephritis as it does not reach therapeutic concentrations in the upper urinalysis tract, and bacteremia often accompanies this disease. Also, it is inappropriate and should be avoided by patients 65 years and older due to its potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, particularly when given long term .