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Pharmacology

18/MHS07/054

PHA 306 assignment

1. Name of drug?

Answer: Nitrofurantoin (Macrobid)

1. Antibacterial activity;

Macrobid is indicated only for the treatment of acute uncomplicated urinary tract infections( acute cystitis) caused by susceptible strains of Escherichia coli or Staphylococcus saprophyticus. Nitrofurantoin is not indicated for the treatment pyelonephritis or perinephric abscesses.

To reduce the development of drug resistant bacteria and maintain the effectiveness of macrobid and other antibacterial drugs. Macrobid should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available. They should be considered in selecting or modifying anti bacteria therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of the therapy.

Nitrofurantoin lack the boarder tissue distribution of other therapeutic agents approved for urinary tract infections. Consequently, many patients who are treated with macrobid are predisposed to persistence of reappearance of bacteriuria. Urine specimen for culture and susceptibility testing should be obtained before and after completion of therapy. If persistence or reappearance of bacteriuria occurs after treatment with macrobid, other therapeutic agents with boarder tissue distribution should be selected. In considering the use of macrobid, lower eradication rates should be balanced against the increased potential for systemic toxicity and for the development of antimicrobial resistance when agents with boarder tissues distribution are utilized.

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. 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 a urinary tract antibacterial agent whose clinical effectiveness depends on the high urinary drug levels encountered during therapeutic drug dosage. Under these conditions, only low blood drug concentrations are usually found. On the basis of urinary nitrofurantoin excretion determined after oral and intravenous drug administration, orally administered nitrofurantoin in a suitable dosage form is well absorbed. In vitro testing does not accurately reflect nitrofurantoin bioavailability, which is affected by formulation differences, drug particle size, and dosage form. 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.

1. Adverse effects:

The most common side effects with nitrofurantoin are nausea, headache, and flatulence. Less common adverse events (occurring in less than 1% of those taking the drug) include:

Gastrointestinal: diarrhea, dyspepsia, abdominal pain, constipation, emesis

Neurologic: dizziness, drowsiness, amblyopia

Respiratory: acute pulmonary hypersensitivity reaction

Allergic: pruritus, urticaria

Dermatologic: hair loss

Miscellaneous: fever, chills, malaise

Patients should be informed that nitrofurantoin colors urine brown; this is completely harmless.

Some of the more serious but rare side effects of nitrofurantoin have been a cause of concern. These include pulmonary reactions, hepatotoxicity, and neuropathy.