Isoniazid

Isoniazid is a drug used in the treatment of both latent and active tuberculosis. It can be used as a monotherapy for the treatment of latent tuberculosis but is commonly used in a four drug regimen including pyrazinamide, ethambutol, rifampin for active TB. Isoniazid is a pro-drug and requires bacterial catalase peroxidase enzyme to activate it and works by inhibiting the synthesis of mycolic acid. It is metabolized in the liver via acetylation. There are two forms of the acetylating enzyme, a fast acetylator and a slow acetylator. Those with the fast acetylator metabolize the drug more quickly than the slow acetylators. Common side effects include vitamin B6 deficiency, hepatotoxicity and neurotoxicity. Isoniazid is also associated with drug induced lupus erythematosus.

PLAY PICMONIC

Indications

Tuberculosis (TB)

TB-TV

Because isoniazid inhibits the synthesis of mycolic acid, it is used in the treatment of both latent and active tuberculosis. It can be used as a monotherapy for the treatment of latent tuberculosis but is commonly used in a four drug regimen including pyrazinamide, ethambutol, rifampin for active TB.

Mechanism of Action

Requires Catalase Peroxidase

H2O2 Cat

Isoniazid must be initially activated by bacterial catalase peroxidase enzyme because it is a pro-drug.

Decreases Mycolic Acid Synthesis

Down-arrow on Mic made of Acidic-lemon

The mechanism of action is to inhibit the synthesis of mycolic acid, which is necessary for synthesis of the mycobacterial cell wall.

Fast vs Slow Acetylators

Fast vs Slow a-seagull-skater

Isoniazid is metabolized in the liver via process of acetylation. There are two forms of the acetylator enzyme, a fast and slow form. The patients with the fast form metabolize the drug more quickly than the patients with the slow form.

Side Effects

B6 Deficiency

Bee (6) Sax

Use of isoniazid can cause a B6 (pyridoxine) deficiency, which can lead to symptoms such as peripheral neuropathy and sideroblastic anemia.

Neurotoxicity

Neuron with Toxic-green-glow

Peripheral neuropathy and CNS effects are thought to be associated to vitamin B6 (pyridoxine) deficiency.

Hepatotoxicity

Liver with Toxic-green-glow

A well known drug side effect is hepatotoxicity, which can range from abnormal liver function tests to hepatitis.

Drug-induced Lupus

Loopy Pill-butterfly

Isoniazid, along with hydralazine and procainamide are associated with drug-induced lupus erythematosus. These drugs are thought to cause an autoimmune response which causes symptoms similar to lupus erythematosus.