



Significant Drug Interactions with Tuberculosis Medications

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Rifamycins

- › Rifampin
- › Rifabutin
- › Rifapentine

Rifamycins

- › Need to monitor closely for signs of liver damage
- › Potent hepatic enzyme inducer
- › Induces the cytochrome P450 pathways 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 3A4
- › Induces the metabolism of other medications that use the cytochrome P450 pathways
- › Drugs metabolized on these pathways will have a **decreased drug level**
- › Anything that ends in –nib or –vir





Rifamycins-Rifampin

- › Mainstay of treatment
- › Big concern for drug interactions
- › Used more now in prophylaxis
- › LTBI 600mg once daily for 4 months



Rifamycins-Rifabutin

- › Used as an alternate to rifampin in AIDS patients
- › Enzyme inducer
- › LTBI 300mg once daily for 4 months or in treatment of active TB in HIV

Rifamycins-Rifabutin

- › Rifabutin levels may increase with HIV meds, antifungals, and macrolides because these inhibit the metabolism of rifabutin
- › Dosage decrease to 150mg per day when given with medications to treat HIV: protease inhibitors: nelfinavir, amprenavir, indinavir
- › Dosage increase needed to 450-600mg when given with efavirenz without the protease inhibitor



Rifamycins-Rifapentine

- › Given in prophylaxis with Isoniazid just once a week for 3 months
- › Or used with other meds in treatment of active TB





Rifamycins-Drug Interactions

- › Verapamil (Calan for hypertension and angina)
- › Methadone (for pain or narcotic detoxification)
- › Digoxin (Lanoxin in heart failure or AFib)
- › Cyclosporine (transplants or autoimmune disease)



Rifamycins-Drug Interactions

- › Steroids (prednisone)
- › Anticoagulants (warfarin-Coumadin, enoxaparin-Lovenox)
- › Haloperidol (Haldol)
- › Theophylline (asthma, emphysema, bronchitis)

Rifamycins-Drug Interactions

- › Barbiturates
- › Oral contraceptives (birth control pills)
- › Quinidine (AFib, AFlutter, tachycardia)
- › Chloramphenicol (antibiotic)
- › Ketoconazole (antifungal)



Rifamycins-Drug Interactions

- › Protease Inhibitors inhibit the metabolism of Rifamycins
- › Causes increased blood levels of Rifamycins-increase risk of liver toxicity
- › Rifamycins induce the metabolism of PI and cause decreased effect –dangerous for HIV patient



Rifamycins-Drug Interactions

- › Food may delay and reduce the amount of rifamycins absorbed-most important that they take the medication
- › Administration with food may be useful for those patients with propensity to nausea, vomiting, or other GI upset.





Rifamycins-Case Presentation

- › RD is a 49 yo BM who was started on Rifampin for LTBI. One month into treatment RD called TB clinic to report BP of 180/100 and severe headache. He was on amlodipine(Norvasc) at the time and had controlled HTN before starting Rifampin. What would you recommend?
- › A)Stop Rifampin and start Isoniazid
- › B)Stop his LTBI treatment
- › C)Adjust the dose of amlodipine
- › D) both A and C
- ›

Rifamycins-Case Presentation

- › Answer- A or D is possible
- › His primary care physician increased his amlodipine and asked the patient to contact the nurse in TB clinic to change his LTBI treatment which we did.
- › Patient needs to continue to check blood pressure until pressure returns to normal



Isoniazid

- › Used in Prophylaxis and Treatment of TB
- › Mainstay of treatment regimens
- › May be administered with or without food, it is rapidly absorbed and can be slowed by food
- › Metabolized by the liver and excreted mostly renally (50% to 70%).
- › Need to monitor closely for liver damage or with renal impairment-can develop anytime during treatment regimen



Isoniazid

- › Isoniazid is primarily inactivated by acetylation
- › Slow acetylators- genetic component and may only be significant in poor or intermediate acetylators
- › Approximately 50% of black and white patients are “slow inactivators”
- › Rest are “rapid inactivators”
- › The large majority of Eskimo and Asian patients are “rapid inactivators”
- › Acetylation rate does not significantly alter the effectiveness, but slow acetylation may lead to higher blood levels and possibly an increase in adverse effects





Isoniazid

- › Inhibits P450 metabolism and may increase the blood level and effects of other medications
- › Substrate of CYP2E1 (major)
- › **Inhibits** CYP1A2 (weak), CYP2A6 (moderate), CYP2C19 (moderate), CYP2C9 (weak), CYP2D6 (moderate), CYP2E1 (moderate), CYP3A4 (weak)
- › **Induces** CYP2E1 (weak/moderate)



Isoniazid-Drug Interactions

- › Inhibits metabolism and increases the effects of:
- › acetaminophen (Tylenol)-liver damage possible
- › benzodiazepines (ones that are hepatic metabolized)-increased side effects, drowsiness



Isoniazid-Drug Interactions

- › Citalopram (Celexa) for depression-increase serum concentration-limit dose to 20mg
- › oral anticoagulants such as warfarin (Coumadin)- increase serum concentration-increased effect of warfarin
- › carbamazepine (Tegretol) for seizures-increased concentration

Isoniazid

- › **Histamine-containing food:** skipjack, tuna, saury, tropical fish
- › can cause hypotension
- › Isoniazid may also inhibit diamine oxidase resulting in headache, sweating, palpitations, flushing, diarrhea, itching, wheezing, or dyspnea
- › avoiding histamine-containing foods
- › **Tyramine-containing food:** red wine, aged cheese, cured meats including sausages and salamis; fava or broad bean pods, tap/draft beers, Marmite concentrate, sauerkraut, soy sauce, soybean condiments
- › can cause flushing, palpitations, headache, mild increase in blood pressure, diaphoresis;
- › has a genetic component, poor acetylators, few reports





Isoniazid-Case Presentation

- › CN is a 75yo WF who is taking Coumadin. She is started on Isoniazid at the local health department. When she started therapy, she was told that she needs to have her INR checked regularly. She calls the TB clinic to report that her check up showed her INR had increased out of range after taking the medication for 3 months. What should happen now?
- › A) stop the Isoniazid
- › B) adjust dose of Coumadin
- › C) change to Rifampin for 12 weeks

Isoniazid-Case Presentation

› Answer-B

- › hypoprothrombinemia effect of Warfarin may be increased by Isoniazid
- › dose-dependent
- › Reaction will be delayed
- › Warfarin is metabolized mainly by CYP2C9 and this path is inhibited weakly by isoniazid- could increase the drug level of warfarin
- › Possible but highly unlikely-little reports in literature
- › consider reducing the dose of Warfarin , during treatment with Isoniazid
- › Monitor prothrombin activity and adjust the dose accordingly.



Ethambutol

- › No significant drug interactions
- › Aluminum hydroxide can decrease level of ethambutol
- › Only 20% metabolized by hepatic system so not a big issue



Pyrazinamide

- › No significant drug interactions
- › Cyclosporine drug levels may be increased





Moxifloxacin-Drug Interactions

- › Drugs that prolong the QT interval increase the risk of life-threatening cardiac arrhythmias, torsades de pointes:
- › Geodon used for bipolar or schizophrenia
- › Antiarrhythmic agents
- › Pimozide (Orap) for Tourettes
- › Chlorpromazine for schizophrenia



Moxifloxacin-Drug Interactions

- › Corticosteroid drugs increased risk of tendinitis and tendon rupture
- › Warfarin-increased blood levels-monitor INR

Streptomycin

- › Any reduction of glomerular function results in decreased excretion of the drug and concurrent rise in serum and tissue levels
- › The risk of severe neurotoxic reactions is sharply increased in patients with impaired renal function or pre-renal azotemia
- › drug interactions will occur with medications given in hospital, not in home setting





Streptomycin-Drug Interactions

- › non-depolarizing muscle relaxants given in hospital setting
- › Furosemide-diuretic can increase streptomycin blood level-potentiate ototoxic effects
- › NSAIDS-can increase blood levels of streptomycin and cause renal insufficiency-avoid using together



References

- › Facts and Comparisons
- › Lexicomp
- › Up to Date