Community Service

Unit

College of Pharmacy

TOPIC: Awareness on Drug interactions among the Pharmacists

DRUGS		PROBABLE MECHANISMS	RECOMMENDATIONS
1	**Fluoxetine and Phenelzine**	The interaction can result in a central serotonin syndrome. This condition is characterized by mental status changes, agitation, diaphoresis, tachycardia, and death. These symptoms can develop quickly with only 1 or 2 doses of fluoxetine when combined with phenelzine. Serotonin syndrome is possible with any monoamine oxidase inhibitor (MAOI), such as phenelzine or tranylcypromine sulfate, in combination with any drug that increases serotonin levels, such as dextromethorphan, meperidine, and other selective serotonin reuptake inhibitors (SSRIs).	It is recommended that fluoxetine be stopped for at least 5 weeks before an MAOI is prescribed because of the long half-life of fluoxetine and its primary metabolite, norfluoxetine. Also, 2 weeks should be allowed after discontinuation of an MAOI before starting SSRI treatment.
2	**Digoxin and Quinidine**	The interaction can lead to a marked increase in plasma concentration levels of digoxin in more than 90% of patients. Significant changes in serum digoxin are noticed within 24h. The effects from this interaction range from nausea and vomiting to death. The primary mechanism for this interaction is a decreased volume of distribution of digoxin, secondary to its displacement from binding sites in body tissues. Quinidine also decreases renal and non-renal excretion rates of digoxin, which leads to increased steady-state concentrations of the cardiac glycoside.	Ideally, patients taking digoxin should avoid the use of quinidine; however, if the combination is necessary, the patient should be closely watched. Pharmacists should anticipate the need to reduce the digoxin dose by one half.
3	**Sildenafil and Isosorbide Mononitrate**	Sildenafil may markedly increase the hypotensive effects of isosorbide mononitrate (ISMN). Sildenafil was developed as a phosphodiesterase-5 (PDE-5) inhibitor. In the presence of PDE-5 inhibitors, nitrates can cause intense increases in cGMP and dramatic drops in blood pressure.	Patients taking ISMN or any nitrate, including nitroglycerin, should be advised not to take sildenafil.
4	**Potassium Chloride and Spironolactone**	The combination may result in hyperkalemia. The resulting hyperkalemia can be serious and may lead to cardiac failure and death. Spironolactone is a competitive antagonist of mineral corticoids, of which aldosterone is a potent example. This mechanism occurs in the kidney at the distal portion of the nephron and leads to the excretion of Na^+ ions while saving K^+ ions.	Severe hyperkalemia is dangerous, and thus patients who are prescribed spironolactone must undergo an evaluation of serum potassium levels.
5	**Clonidine and Propranolol**	Clonidine is a central α-2 adrenergic agonist that suppresses the sympathetic nervous system from the brain. When clonidine is suddenly withdrawn, the result is a large increase in norepinephrine in the synaptic cleft of the adrenergic neuron. The sensitized α-1 receptors are stimulated, leading to an exaggerated vasoconstriction. The body cannot compensate for this response because the β-2 receptors are blocked when a patient is concurrently taking propranolol. Within 24-72h, a dramatic rebound hypertension is noticed.	The combination may produce a mysterious hypertension that is unrelated to the pharmacology of either agent when administered independently. A sudden withdrawal of clonidine from adjunctive therapy with propranolol may cause fatal rebound hypertension

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6	**Warfarin and Diflunisal**	Nonsteroidal anti-inflammatory drugs (NSAIDs), such as diflunisal, have been shown to increase the risk for gastrointestinal bleeding and the anticoagulant response of warfarin. Other NSAIDs such as ketoprofen, piroxicam, sulindac, diclofenac, and ketorolac have been shown to have similar interactions with warfarin.	Acetaminophen is the alternative of choice. Yet, if an NSAID is needed, non-acetylated salicylates such as magnesium salicylate or salsalate are safer.
7	**Theophylline and Ciprofloxacin**	Concurrent administration may lead to toxic increases in theophylline. This problem occurs because the hepatic metabolism of theophylline is inhibited by ciprofloxacin via the CYP450 enzyme system. Signs of theophylline toxicity include headache, dizziness, hypotension, hallucinations, tachycardia, and seizures.	Levofloxacin or ofloxacin should be considered as an alternative to ciprofloxacin.
8	**Pimozide and Ketoconazole**	Pimozide alone can prolong the QT interval, and it has been linked with ventricular arrhythmias. When pimozide is combined with ketoconazole, the combination can be deadly. Pimozide is a CYP3A4 enzyme substrate, and ketoconazole is a potent inhibitor of CYP3A4. Other drugs such as itraconazole, clarithromycin, erythromycin, diltiazem, and nefazodone are also potent inhibitors of CYP3A4 and should not be administered with pimozide. Fluconazole is weaker, but in larger doses it also inhibits CYP3A4.	Terbinafine is a safer choice because it does not affect CYP3A4.
9	**Methotrexate and Probenecid**	When probenecid is administered with antineoplastic doses of methotrexate, the result can be a 2-3-fold increase in methotrexate levels. Probenecid acts as an active tubular secretion inhibitor and prevents methotrexate from being excreted, thus potentially causing toxicity. This interaction with methotrexate also occurs with penicillins (eg, amoxicillin, carbenicillin) and salicylates.	Adjusting the dose of the drugs could be an alternative.
10	**Bromocriptine and Pseudoephedrine**	The interaction can lead to severe peripheral vasoconstriction, ventricular tachycardia, seizures, and possibly death. Bromocriptine is an ergot-derived dopamine agonist with several uses, including antiparkinsonian therapy. Notable side effects of bromocriptine include thickening of bronchial secretions and nasal congestion. This is significant because it increases the likelihood of a patient	Patients receiving bromocriptine should be advised to avoid all sympathomimetics.

		taking bromocriptine to self-medicate with an OTC decongestant such as pseudoephedrine.	