

Drug Interactions Important in Clinical Dentistry

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DENTAL DRUG	INTERACTING DRUG	RESULT/MANAGEMENT
ANTIBIOTICS		
<u>Penicillins</u>		
All Penicillins	Bacteriostatic antibiotics (clindamycin, erythromycin, tetracyclines)	Static agent may impair action of penicillins. Consult with other prescriber for modification.
Rare decrease in OC effectiveness with >48 hours of antibiotic therapy. Recommend additional barrier contraception for the remainder of the Pill package.	Methotrexate (Rheumatrex, g)	High dose penicillins may decrease MTX secretion. Monitor MTX.
	Oral contraceptives	Rare decrease in estrogen effect. Use barrier contraception for duration of pill cycle.
	Probenecid (Benemid, g)	Tubular secretion of penicillins may be decreased. Usually not problematic.
Ampicillin	Allopurinol (Zyloprim, g)	Doubling in rate of ampicillin rash with concurrent administration (14-22%)
	Atenolol (Tenormin, g)	Atenolol bioavailability may be reduced.
<u>Cephalosporins</u>		
All Agents	Anticoagulants (Coumadin, g)	Risk of bleeding disorders might be increased in anticoagulated patients. Use cautiously.
	Bacteriostatic antibiotics (clindamycin, erythromycin, tetracyclines)	Static agent may impair action of cephalosporins. Consult with other practitioner for modification.
	Probenecid (Benemid, g)	Tubular secretion of penicillins may be decreased. Usually not problematic.
Cefdinir (Omnicef) Cefpodoxime (Vantin) Cefuroxime (Ceftin)	Increased gastric Ph. (Antacids, Acid, Pepcid, Prilosec, Tagamet, Zantac)	Reduced absorption of the cephalosporins. AVOID CONCURRENT USE.
<u>Lincomycins</u>		
Clindamycin (Cleocin, g)	Erythromycin (all macrolides)	Possibility of antagonism. AVOID CONCURRENT USE.
	Kaolin-Pectin	Delay in clindamycin absorption with concurrent use.
	Succinylcholine (Anectine)	Possibility of prolonged respiratory depression. Monitor patient.
<u>Macrolides/Azalides</u>		
<u>Azithromycin (Zithromax, Zpak, g) –only agent that does not inhibit CYP450 3A4 but DOES prolong QT interval so only QT prolongation interactions apply to Azithromycin</u>	Alfentanil	Alfentanil actions increased. Use caution.
	Anticoagulants (Coumadin, g)	Risk of bleeding disorders is increased in anticoagulated patients. Monitor pt.
	Benzodiazepines (alprazolam, diazepam, triazolam)	Increased benzodiazepine levels resulting in CNS depression. Avoid combination in elderly.
dirithromycin (Dynabac) clarithromycin (Biaxin, Biaxin XL, g) erythromycin (base, EC, EES, PCE)	Bromocriptine (Parlodel)	Increase in bromocriptine toxic effects. Consult MD.
	CCBs (diltiazem (Cardizem,g) and verapamil (Isoptin, Calan, Verelan,g)	QT interval prolongation, sudden death, AVOID CONCURRENT USE
	Carbamazepine (Tegretol, g)	Increased carbamazepine levels. Avoid concurrent use. Azithromycin is okay.
	Clindamycin	Possible antagonism. AVOID COMBINATION.
	Cyclosporine (Sandimmune, Neoral)	Increased cyclosporine renal toxicity. Consult MD.
	Digoxin	Increased digoxin levels in 10% of patients. May use cautiously.
	Disopyramide (Norpace, g)	Increased disopyramide levels may cause arrhythmias. Use cautiously.

<p><u>Macrolides(excluding azithromycin)</u></p>	<p>Ergotamine Methylprednisolone</p> <p>Penicillins Pimozide (Orap)</p> <p>SSRIs (citalopram, escitalopram, fluoxetine, Sertraline, vilazodone)</p> <p>“Statins” (except fluva-,pitava-prava)</p> <p>Theophyllines</p> <p>Tolterodine (Detrol)</p>	<p>Acute ergotamine toxicity. Use cautiously Steroid clearance may be decreased. Caution.</p> <p>possible antagonism. Avoid static with cidal Avoid all macrolides-risk of sudden death AVOID CONCURRENT USE MACROLIDES DECREASE METABOLISM OF LISTED SSRIS.MONITOR..</p> <p>Increased statin levels with possible muscle toxicity. AVOID CONCURRENT USE</p> <p>Increased theophylline levels (20-25%). Decreased erythromycin levels may also occur. AVOID CONCURRENT USE if possible. SBE prophylaxis should not cause problems. Increased Detrol effects causing arrhythmias</p>
<p><u>Metronidazole</u> (Flagyl, Flagyl ER, Prostat, g)</p>	<p>Anticoagulants (Coumadin)</p> <p>Barbiturates Cholestyramine (Questran, g) Cimetidine (Tagamet, g)</p> <p>Disulfuram (Antabuse)</p> <p>Ethanol (IV diazepam, IV TMP-SMZ)</p> <p>Lithium</p> <p>Phenytoin (Dilantin) Quinidine Tacrolimus (Prograf)</p>	<p>Risk of bleeding disorders is increased in anticoagulated patients. Consult MD. Decreased metro. Levels. Increase dose. Reduced absorption of metronidazole Metronidazole levels may increase. Not sig.</p> <p>Concurrent use may result in acute psychosis or confusion. Risk of disulfuram-type reaction. AVOID CONCURRENT USE. Increased lithium levels with possible toxicity. Consult MD. Eff. of phenytoin may be incr. Monitor closely. Increased Quinidine levels. Monitor closely. Metronidazole doubles Prograf levels</p>
<p><u>Tetracyclines</u></p> <p>All Agents (doxycycline, minocycline, tetracycline)</p> <p>Doxycycline (Vibramycin, Periostat??)</p> <p>Tetracycline (Sumycin, Panmycin)</p> <p><u>Quinolones: all prolong QT interval</u> All Agents: Ciprofloxacin (Cipro,g) Levofloxacin (Levaquin) Moxifloxacin (Avelox) Ofloxacin (Floxin)</p> <p>Ciprofloxacin</p>	<p>Antacids containing Al, calcium, magnesium</p> <p>Bismuth (Pepto-Bismol)</p> <p>Iron Salts</p> <p>Oral Contraceptives</p> <p>Carbamazepine (Tegretol)</p> <p>Methotrexate (highdose IV)</p> <p>Phenobarbital</p> <p>Phenytoin (Dilantin, g)</p> <p>Colestipol (Colestid)</p> <p>Food (Milk and Dairy)</p> <p>Zinc sulfate</p> <p>Antacids (iron, sucralfate, zinc) Anticoagulants (Coumadin, g)</p> <p>Antineoplastics Cimetidine (Tagamet, g) Cyclosporine (Sandimmune, Neoral) NSAIDs Probenecid (Benemid, g) Theophylline Caffeine</p>	<p>Reduced serum concentrations of tets. Space administration by 1-2 hours.</p> <p>Inhibition of tetracycline absorption. Avoid concomitant administration.</p> <p>Decreased absorption of tets. Space use by 2-3h.Doxy always affected.</p> <p>Slightly increased risk of ovulation. Use additional method during cycle.</p> <p>Metabolism of doxy increased. Monitor response to doxycycline. AVOID DOXYCYCLINE WITH IV METHOTREXATE Decreased serum levels and effect of doxy. Monitor clinical response. Phenytoin stimulates doxy metabolism. Increase doxy dose or use other tet. Colestipol binds tet in intestine. Do not administer concomitantly. Decreased absorption of tet. Space use by 2-3 hours. Tetracycline absorption is decreased. Space use by 2-3 hours.</p> <p>Decreased quinolone absorption. AVOID CONCURRENT USE. Increased risk of bleeding disorders. Monitor INR. Quinolone serum levels may be decreased. Quinolone serum levels may be increased. Cyclosporine renal toxicity may be enhanced. Enhanced CNS stimulation Quinolone serum level may be increased50%. Increased theophylline toxicity possible with Cipro and other. Consult MD Increased caffeine effects are possible.</p>

ANTIFUNGALS

Systemic Azole Agents (fluconazole, itraconazole, ketoconazole): all agents prolong QT interval

	Anticoagulants (Coumadin)	Increased risk of bleeding disorders in anticoagulated patient. Consult MD.
	Benzodiazepines	Alprazolam, triazolam are contraindicated with itraconazole and ketoconazole. AVOID
	Cyclosporine (Sandimmune, Neoral)	Increased cyclosporine levels. Can be used to the patients advantage.
	Rifampin	Decreased levels of the antifungal. AVOID CONCURRENT USE.
	"Statins" (except fluva-,pitava-prava.)	Increased levels and SE of statins.
	Tolterodine (Detrol, Detrol LA)	Increased Detrol-causing arrhythmias.AVOID
fluconazole (Diflucan)	Zolpidem (Ambien)	Increased Ambien effect. Caution.
	Cimetidine (Tagamet, g)	Reduced fluconazole levels. AVOID CONCURRENT USE.
	Citalopram (Celexa,g)	QT interval prolongation.AVOID COMBO.
	Hydrochlorothiazide	Increased fluconazole levels.
	Losartan (Cozaar, Hyzaar)	Increased Losartan hypotension effect
	Oral Contraceptives	Decreased estrogen levels. AVOID CONCURRENT USE.
	Phenytoin (Dilantin, g)	Increased phenytoin levels. Monitor carefully.
	Sulfonylureas	Increased hypoglycemic effect. Monitor blood glucose.
itraconazole (Sporonax)	Digoxin	Increased digoxin levels. AVOID COMBINATION.
	Increased gastric pH	Reduced itraconazole levels
	Isoniazid (INH)	Reduced itraconazole levels
	Losartan (Cozaar)	Increased Losartan hypotension effect
	Sulfonylureas	Increased hypoglycemic effects. Monitor blood glucose.
ketoconazole (Nizoral, g)	Corticosteroids	Possible increase in steroid levels.
	Increased gastric pH	Decreased ketoconazole levels. AVOID CONCURRENT USE.
	Isoniazid (INH)	Decreased ketoconazole levels
	Theophyllines	Decreased theophylline levels. Consult with MD.

NON-NARCOTIC ANALGESICS**NSAIDS**

(including aspirin and COX-2s)

	Anticoagulants (apixaban, dabigatran,edoxaban,,rivaroxaban,warfarin)	Increase risk of bleeding disorders in anticoagulated patient. AVOID COMBO
	Antihypertensives (all <u>but</u> CCBs) (ACEI,B-blockers, diuretics)	Decreased antihypertensive effect. Monitor Blood Pressure.
	Cimetidine (Tagamet, g)	NSAID levels increased/decreased
	Cyclosporine (Neoral, Sandimmune)	Nephrotoxicity of both agents may be increased. Avoid if possible.
	Combo of ACEor ARB & Diuretic	30% increase in risk of kidney injury-called the TRIPLE WHAMMY on the kidney!
	Fluoroquinolones	Increased CNS stimulation
	Lithium	Increased lithium levels. Use sulindac
	Methotrexate (Rheumatrex, Mexate)	Toxicity of methotrexate may be increased. Monitor.
	Phenytoin (Dilantin, g)	Increased phenytoin levels
	Probenecid (Benemid, g)	Increased toxicity of NSAIDs possible.
	Salicylates	Decreased NSAID levels with increased GI effects. AVOID CONCURRENT USE.
	SSRIs	Possible increased risk of bleeding but not thought to be clinically significant
COX-2 SELECTIVE NSAID Celecoxib (Celebrex)	2C ₉ inhibitors (fluconazole)	Increased celecoxib levels

<u>Ibuprofen (Motrin, g)</u> <u>Ketorolac (Toradol, g)</u> <u>Sulindac</u>	Digoxin Salicylates DMSO	Possible increase in digoxin levels. Increased Ketorolac free drug conc. Decreased sulindac effectiveness and severe peripheral neuropathy. Avoid concurrent use.
<u>Sulindac</u> <u>Acetaminophen only</u>	Lithium Barbiturates, Carbamazepine, Phenytoin, Rifampin, Sulfinpyrazone Cholestyramine (Questran, g) Ethanol	Lithium levels remain constant or decrease. The hepatotoxicity of APAP may be increased by high dose or long term administration of these drugs. Decreased APAP absorption. Do not administer within 2 hours of each other. Increased hepatotoxicity of APAP with chronic ethanol ingestion.
<u>Tramadol (Ultram, Ultracet, g)</u>	Any drug that enhances serotonin activity (SSRI antidepressants, "triptans" for acute migraine) Carbamazepine (Tegretol, g) MAOI's (Marplan, Nardil, Parnate) Quinidine	Possible serotonin syndrome. AVOID CONCURRENT USE. Decreased tramadol levels MAOI toxicity enhanced Tramadol increased/metabolite decreased
	Ritonavir (Norvir)	Increased Tramadol effect. AVOID COMBO.
NARCOTIC ANALGESICS		
<u>Opioid analgesics</u>	Alcohol, CNS depressants, local anesthetics, antidepressants, antipsychotics, antihistamines, cimetidine Antimuscarinics and antidiarrheals (e.g. atropine), antihypertensives (e.g. guanadrel) Buprenorphine, nalbuphine, naltrexone	Increased CNS and respiratory depression may occur. Use cautiously. Opioids increase the effects of these drugs. Use cautiously. These drugs block the analgesic effects of opioids. Substitute with NSAIDs.
<u>Codeine (Hydrocodone lesser extent)</u>	2D ₆ Inhibitors, Amiodarone, Cimetidine, Desipramine, Fluoxetine, Paroxetine, Propafenone, Quinidine, Ritonavir	Inhibition of biotransformation of Codeine to active analgesic form. Use different narcotic on 2D ₆ inhibitor patients.
<u>Meperidine (Demerol, g)/Fentanyl/All Fentanyl derivatives</u>	MAOIs (Marplan, Nardil, Parnate, Furoxone) selegiline (Eldepryl) Protease inhibitors Ritonavir (Norvir)	Hypertension/hyperpyrexia or coma and hypotension. AVOID CONCURRENT USE if MAOI taken within 14 days. Increased CNS/resp. depression- AVOID Large increase in meperidine. AVOID COMBO.
LOCAL ANESTHETICS		
<u>Amides (e.g. lidocaine)</u>	Alcohol, CNS depressants, opioids, antidepressants, antipsychotics, antihistamines Antiarrhythmic drugs Beta Blockers, cimetidine	Increased CNS and resp. depression may occur. Use caution. Increased cardiac depression. Metabolism of lidocaine is reduced. Use caution
<u>Esters (e.g. procaine)</u>	Anticholinesterases (Neostigmine) Sulfonamides	Metabolism of esters reduced. Inhibit sulfonamide action.
VASOCONSTRICTORS (epinephrine, levo-nordefrin)		
	Inhalation anesthetics (halothane) Tricyclic antidepressants-high dose (amitriptyline, desipramine, imipramine, nortriptyline, etc) Beta-blockers (nonselective) (e.g. propranolol, nadolol) Phenothiazines (e.g. chlorpromazine) Monoamine Oxidase Inhibitors (MAOIs) Selegiline (Eldepryl, g) COMT Inhibitors (Comtan, Tasmar)	Increased chance of arrhythmia Increased sympathomimetic effects possible. Limit epi to 0.04mg with high dose TCA's. Hypertensive and/or cardiac rx possible. Limit epi to 0.04mg/2hr. visit. Vasoconstrictor action inhibited, leading to possible hypotensive responses. Use cautiously. Slight possibility of hypertensive rx. Slight possibility of hypertensive rx. Slight possibility of hypertensive rx.

AGENTS FOR PARENTERAL ANESTHESIA		
<u>Antihistamines</u>		
diphenhydramine (Benadryl) hydroxyzine (Atarax, Vistaril) Promethazine (Phenergan)	Anticholinergics CNS depressants (alcohol, narcotics)	Increased dry mouth, tachycardia, urinary retention. Monitor. Enhanced duration and intensity of sedation. Reduce dosages.
<u>Barbiturates</u>		
methohexital (Brevital,g)	CNS depressants (alcohol, narcotics) Furosemide (Lasix, g) Sulfisoxazole IV	Additive CNS and resp. depression Orthostatic hypotension Sulfa competes with barb. for binding sites. Smaller and more frequent barb. doses may have to be given.
<u>Benzodiazepines</u>		
diazepam (Valium,G)	CNS depressants (anticonvulsants, alcohol) Cimetidine,OCs,INH,Ketoconazole, Metoprolol, Omeprazole, Propoxyphene, Propranolol,Valproic Acid	Oversedation so may use slower titration. Decreased clearance of diazepam. Can avoid with lorazepam.
midazolam (Versed,g)	Digoxin Calcium Channel Blockers or CCBs (diltiazem-Cardizem, verapamil-Isoptin,Calan, Verelan) CNS depressants (alcohol, barbs) Erythromycin Narcotics (morphine, meperidine, fentanyl) Saquinavir (Fortovase) Thiopental	Increased digoxin levels. CCBs inhibit Cyp3A4 which prolongs the actions of midazolam. Evaluate patient factors to determine clinical significance. Increased risk of underventilation or apnea. May prolong the effect of midazolam. Increased midazolam levels. Monitor. Increased hypnotic effect of midazolam. More hypotension with Versed and Demerol. Increased midazolam levels. AVOID COMBO. After premed with Versed, decrease dose of thiopental for induction by 15%
<u>Narcotics</u>		
fentanyl (Sublimaze,g)	Barbiturate anesthetics Chlorpromazine (Thorazine, g) Cimetidine (Tagamet, g) Citalopram (Celexa,g) Diazepam Droperidol (Inapsine) MAOIs and furazolidone (Furoxone) Nitrous Oxide Ritonavir (Norvir)	Additive CNS and resp. depression. Increased toxicity of both agents. CNS toxicity case reports only. (confusion, apnea, Increased risk of serotonin syndrome With high dose fentanyl gives CV depression. Hypotension < pulmonary arterial pressure. Risk of hypertensive crisis.AVOID COMBO With high dose fentanyl may cause CV depress. Increased fentanyl levels with Norvir
meperidine (Demerol, G)	Barbiturate anesthetics Chlorpromazine (Thorazine, g) Cimetidine (Tagamet, g) MAOIs and furazolidone (Furoxone) Phenytoin (Dilantin, g)	Additive CNS and resp. depression Increased toxicity of both agents. CNS toxicity as with fentanyl. Meperidine has predictable and sometimes fatal reactions with use within 14 days. Type1 :coma,resp dep,cyanosis,low BP Type2:seizures,hyperpyrexia,hypertension,tac hy-cardia. AVOID CONCURRENT USE!!!! Decrease meperidine effects by increased hepatic metabolism
<u>Miscellaneous</u>		
etomidate (Amidate) ketamine (Ketalar,g)	Verapamil Barbiturates Thyroid Hormone Tubocurarine and nondepolarizing muscle relaxants CNS depressants (sedative/hypnotic, inhalation anesthetics, narcotics)	Possibility of prolonged anesthesia Prolonged recovery time. May produce hypertension/tachycardia Ketamine may increase neuromuscular effects and result in prolonged resp. depression. Increase CNS depression of propofol. Premed with narcotics may lead to more pronounced decrease in systolic, diastolic, and mean arterial pressures and cardiac output.
Propofol (Diprivan, G)		