

The Impact of OTC and Herbal Supplements with Prescription Medications

Michael J. Schuh, BS, PharmD, MBA
Assistant Professor of Pharmacy
Mayo College of Medicine

Objectives

- Review of over-the-counter (OTC), prescription (Rx), and herbal supplement backgrounds
- Discuss common classes of OTC medications as to adverse reactions and drug interactions with Rx medications and herbal supplements
- Discuss common herbals and their properties that can interact with Rx medications

OTC/RX/Herbal Background

- OTC and herbal supplements have their own adverse reactions just like Rx medications
- OTC and herbal supplements interact with Rx medications and with each other
- Herbal supplements are not regulated by the FDA as OTC and Rx medications are

Center for Drug Evaluation and Research (CDER)

- A part of the U.S. Food and Drug Administration (FDA)
- The nation's "watchdog" for consumers regarding OTC, Rx medications and some cosmetics/toiletries that are classified as drugs such toothpaste, antiperspirants, dandruff shampoos, sunscreens

<http://www.fda.gov/fdac/special/testtubetopatient/cder.html>

RX/OTC vs. Herbal Supplements

Center for Drug Evaluation and Research (CDER) Rx/OTC Statement:

- Drug companies seeking to sell a drug in the United States must first test it.... The company then sends CDER the evidence from these tests to prove the drug is safe and effective for its intended use.... **Herbal supplement companies do not!**

<http://www.fda.gov/fdac/special/testtubetopatient/cder.html>

Mechanisms of OTC and Herbal Impact on Rx Medications

- Drug interactions:
 - P-450 hepatic enzyme inhibition or induction (ex. clopidogrel/omeprazole-OTC)
 - Displacement from blood proteins (ex. warfarin/miconazole-vaginal)
 - Receptor site agonist/antagonist (ex. SSRI's/St. John's Wort)

DiPiro, et al. Pharmacotherapy: A physiological Approach
www.thompsonhc.com, accessed 4/7/2010

Mechanisms of OTC and Herbal Impact on Rx Medications

- Aggravation of existing disease state making Rx treatment less effective:
 - NSAID's
 - GERD
 - Peptic ulcer disease
 - Antihistamines
 - Glaucoma
 - BPH
 - Asthma



www.thompsonhc.com, accessed 4/7/2010

Mechanisms of OTC and Herbal Impact on Rx Medications

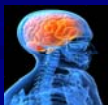
- Direct binding
 - Calcium carbonate/gabapentin
 - OTC fiber and bran/digoxin
- Renal interactions
 - Increased excretion (ascorbic acid/sodium bicarbonate-dependent on weak acid or weak base drug)
 - Decreased excretion (NSAID's)



www.thompsonhc.com, accessed 4/7/2010

Mechanisms of OTC and Herbal Impact on Rx Medications

- Synergism or additive effects
 - Clopidogrel/aspirin
 - Warfarin/aspirin
 - Gingko or garlic or ginger + others/any anticoagulant
 - Antihistamine/CNS depressant medications



www.thompsonhc.com, accessed 4/20/2010

Commonly Used Over-the-Counter (OTC) Medications

Non-steroidal Anti-inflammatory Agents (NSAIDs) and Acetaminophen

Non-steroidal Anti-inflammatory Agents (NSAIDs)

- Used for pain and inflammation
- Peripheral cyclooxygenase (COX 1 & 2) inhibitors
- Most common OTC pain relievers next to acetaminophen (a central COX inhibitor)
- Analgesic, antipyretic, anti-inflammatory, anticoagulant (aspirin)

DiPiro, et al. Pharmacotherapy: A physiological Approach

OTC NSAID Adverse Reactions

- GI Adverse Reactions
 - Nausea and vomiting
 - Heartburn, esophagitis, GI upset
- CV Adverse Reactions
 - Hypertension
 - CHF
 - Edema
- Hematologic Adverse Reactions
 - Anemia
 - Bleeding



www.thompsonhc.com, accessed 4/7/2010

OTC NSAID Drug Interactions with Rx Medications

- Warfarin → Concurrent use of **WARFARIN** and **NAPROXEN** may result in an increased risk of bleeding
- Hydrochlorothiazide → Concurrent use of **NONSTEROIDAL ANTIINFLAMMATORY AGENTS** and **THIAZIDE DIURETICS** may result in decreased diuretic and antihypertensive efficacy
- ARB's, ACEI's, CCB's → Concurrent use of **ANGIOTENSIN CONVERTING ENZYME INHIBITORS** and **NONSTEROIDAL ANTIINFLAMMATORY AGENTS** may result in decreased antihypertensive and natriuretic effects.

www.thompsonhc.com, Accessed 4/6/2010

Acetaminophen

- Most commonly used OTC pain reliever
- Central-acting COX inhibitor
- Hepatotoxic at > 4,000 mg /day chronically
- Synergistic liver damage with RX hepatotoxic medications – (statins, NSAIDS, MTX, amiodarone, and more...)
- Warfarin increased effect at 2,000 mg/day or greater
- Added to many other OTC medications – (Tylenol PM)
- Increased liver damage with ethanol consumption

www.uptodate.com, www.thompsonhc.com, Accessed 4/8/2010

OTC Oral Antihistamines

OTC Oral Antihistamines

- Used for anticholinergic properties:
 - Mucous membrane drying effects for colds - (“pheniramines”)
 - CNS depression → sleep -(diphenhydramine, doxylamine)
 - Motion sickness - (meclizine, dimenhydrinate)
- Some are much less sedating – (loratadine)

DiPiro, et al. Pharmacotherapy: A physiological Approach

OTC Antihistamines Adverse Reactions

- Increased intraocular pressure → aggravation of glaucoma
- Increased urinary retention → aggravation of BPH
- Sedation/CNS depression → drowsiness, confusion/ increased fall risk in elderly
- Thickening of secretions → aggravation of asthma symptoms
- Constipation

DiPiro, et al. Pharmacotherapy: A physiological Approach

OTC Antihistamine Drug Interactions with Rx Medications

- Opiate pain medications (sedation)
- Ambien (sedation)
- Linezolid (anticholinergic effect)
- TCA's (anticholinergic effect)
- MAO inhibitors (anticholinergic effect)
- Metoprolol (metabolism inhibited)

www.thomsonhc.com/ho/hseel/ufi.edu/micromedex2. Accessed 4/09/10
Sharma, A. et al. J Pharmacol Exp Ther. 2005 Jun;313(3)
Hamelin, BA et al. Clin Pharmacol Ther. 2000 May;67(5)

OTC Oral Decongestants

Oral Decongestants

- Act on α – adrenergic receptors of the nasal mucosa \rightarrow vasoconstriction \rightarrow shrinks swollen membranes increases airway patency
- Phenylephrine (“PE” products)
 - 38% dose bio-available - MAO metabolism: gut
- Pseudoephedrine
 - Up to 90% bio-available \rightarrow More effective



Kanfer, I. et al. Pharmacotherapy 1993; 13:116S-128S
Hendeles, L and Hatton R. Journal of Allergy and Clinical Immunology 2006; 118(4):279-280

OTC Oral Decongestant Adverse Reactions

- Dizziness, restlessness, insomnia, Headache, palpitations, dermatitis
- Single dose \rightarrow small increase BP
- Contraindicated: in severe HTN, arrhythmias
- Avoid with cardiac conditions, BPH, hyperthyroidism, Reynaud's syndrome

Clinical Pharmacology, 2010 Gold Standard
Chua, S et al. British Journal of Clinical Pharmacology 1989; 28:369-372

OTC Decongestant Drug Interactions with Rx Medications

- Sympathomimetics (HTN, tachycardia)
- MAO inhibitors (\uparrow sympathetic effect)
- Ergot alkaloids (\uparrow vasoconstriction)
- Atropine (blocks vagal response \rightarrow increased tachycardia)
- TCAs (increase headaches)
- Antihypertensives (oppose HTN control)

Clinical Pharmacology, 2010 Gold standard

Antacids

Antacids

- Aluminum, magnesium and calcium salts
- Use: dyspepsia, stress gastritis, osteoporosis, GERD, peptic ulcer
- Mechanism of action:

Acid neutralization

- $\text{Al}(\text{OH})_3 + 3 \text{HCl} \rightarrow \text{AlCl}_3 + 3 \text{H}_2\text{O}$ [Gaviscon]
- $\text{Mg}(\text{OH})_2 + 2 \text{HCl} \rightarrow \text{MgCl}_2 + 2 \text{H}_2\text{O}$ [Milk of magnesia]
- $\text{CaCO}_3 + 2 \text{HCl} \rightarrow \text{CaCl}_2 + \text{H}_2\text{O} + \text{CO}_2(\text{g})$ [Tums]
- $\text{NaHCO}_3 + \text{HCl} \rightarrow \text{NaCl} + \text{H}_2\text{O} + \text{CO}_2(\text{g})$ [Alka-Seltzer]



Maton, P and Burton, M. Drugs 1999; 57(6) 855-870

Adverse events

- At low doses, sporadic use → few adverse events
- Aluminum containing: constipation
 - 17-30% Aluminum absorbed,
 - with poor renal function, uremic aluminum overload → CNS toxicity dementia
 - High dose, long term use → osteoporosis
- Magnesium containing: diarrhea
 - poor renal function → hypermagnesemia
- Calcium containing: constipation, flatulence
 - poor renal function → hypercalcemia

Maton, P and Burton, M. Drugs 1999; 57(6) 855-870

Drug Interactions

- Bisphosphonates
- Levothyroxine
- Tetracycline antibiotics
- Quinolone antibiotics
- Digoxin
- Sulfonylureas
- Gabapentin

Dipiro, J et al. Pharmacotherapy: a Pathophysiologic Approach 7ed
Clinical Pharmacology, 2010

Interactions cont'd

- Iron supplements (require low gastric pH)
- Ketoconazole, itraconazole (pH)
- Phenytoin
- Rousuvastatin (Crestor®)
- Gabapentin (Neurontin®)
- Delaviridine (Rescriptor®)

Clinical Pharmacology, 2010
Maton, P and Burton, M. Drugs 1999; 57(6) 855-870

Vitamin and Herbal Supplements

Herbals and Vitamins that Impact Coagulation or Clotting

- May increase the risk of bleeding
 - Garlic*
 - Ginger*
 - Ginkgo biloba*
 - Ginseng*
 - Green tea
- May induce coagulation
 - Vitamin K
 - Goldenseal
 - Mistletoe
 - Yarrow



*These agents have multiple adverse reactions

Natural Medicines Database, Accessed April 13, 2010

Herbals that Impact Changes in Blood Pressure

- May lower blood pressure
 - Coenzyme Q-10
- May increase blood pressure
 - Green tea
 - Ephedra/ma huang
 - Bitter orange
 - Licorice
 - Guarana



Natural Medicines Database. Accessed April 13, 2010

Herbals that Impact Blood Glucose Levels

- DHEA- may increase insulin resistance or sensitivity
- Glucosamine- may increase insulin resistance
- Chromium- may increase the risk of hypoglycemia



Natural Medicines Database. Accessed April 13, 2010

Herbals that Impact Blood Glucose Levels

- Cinnamon- may cause hypoglycemia
- Ma huang- may cause hyperglycemia
- Licorice- can cause hyperglycemia
- Ginseng- can cause hypoglycemia



Natural Medicines Database. Accessed April 20, 2010

Selected Herbal/Rx Drug Interactions

- St. John's Wort- may induce psychosis in Alzheimer's, may induce mania in bipolar and depression, may exacerbate ADHD symptoms
- Evening primrose oil- May lower seizure threshold



Natural Medicines Database. Accessed April 13, 2010

Garlic, Ginger, Ginkgo, Ginseng

- Multiple adverse reactions in the body may occur
 - May increase the risk for bleeding
 - Garlic, ginger, ginkgo
 - May increase blood pressure
 - Ginseng
- In addition, garlic and ginger may cause hypoglycemia



Natural Medicines Database. Accessed April 13, 2010

As a Healthcare Practitioner,
What Should I do?

What to Do?

- Respect the patient's right to choose what they want to ingest, BUT....
 - Objectively inform them of the possible consequences of mixing Rx meds with OTC and herbal agents
 - Get a complete med history, including OTC and herbal supplements so potential problems can be discovered and considered with Rx therapy

What to Do?

- Utilize your institutional or local pharmacist to help with possible problems associated with the use of multiple agents
- More pharmacists are delivering medication management services (MTM) who specialize in managing OTC's and herbals interacting with Rx medications

Review Questions

Can OTC medications impact Rx medications?

Can herbal supplements impact Rx medications?

References

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Evaluation

<http://www.surveymonkey.com/s/CURE4>