Interactions between medication and food or natural products

Stephen J. Eide R. Ph.
Consultant Pharmacist
Omnicare of Boise

The Nature of Herbal Products

- Herbal products are treated as food supplements
- They cannot say they treat or cure any disease unless they have scientific studies to prove their claims. They can say “has been used to for...” “may help...”
- Quality studies of herbal/drug interactions are rare. Most studies are case studies, the weakest form of medical data
- Most papers just look at the risk for an herbal product decreasing a drug’s effect, but rarely look as a drug’s effect on the herbal product.

Herbal Products Part 2

- Quality control in herbal products has been an issue. The FDA has legal authority for only limited supervision
- There can be questions about which common name fits with which genus and species for the preparation of an herbal product.
- There are potential issues with what parts of the plant are used.
- You do need to consider the excipients along with the herbal product.
- Often with herbal products there is no recognized appropriate dose so strengths can vary widely.
Herbal Product Part 3

- Most of the testing of herbal products for clinical effects are done outside the United States with the best studies done in Germany.
- Many studies are not done to the same standards that the FDA requires for a drug to be released on the market.
- A few herbal products do have data showing they are effective in treating some medical conditions.

The Nature of Case Studies

- A case study has the general format of: The patient took A, then later B happened, perhaps A caused B.
- They are the weakest form of drug or herbal study.
- There is a very high rate of error in any case study.
- Most often they are only useful to decide a larger, more scientific and accurate study should be done.

Most Herbal-Drug Interactions are Based on Case Studies

So it is unclear if any given potential interaction will occur at all.

If it does occur, it is unclear if the interaction will be clinically significant.

It is unclear if an interaction occurs with one manufacturer's herbal product that it will occur with a different manufacturer's product.
Legal Issues with Herbal Products

• The appropriate law is the Dietary Supplement and Health Education Act of 1994 (DSHEA)

• In general the FDA can only take action if the product is mislabeled, adulterated, or makes medical claims they cannot prove.

Topical Herbal Products

• I found no significant interactions between medications and a topically applied herbal product.
• Local reactions are still possible
• It may be difficult to tell the difference between a side effect from either the drug or herbal and an interaction between the drug and herbal.
• If possible, hold a topical herbal product if a topical drug therapy is for a limited duration of time.
• If both will be used chronically, space the administration times as far apart as you can.

Oral Herbal Use

Strategies to Identify and Prevent Problems

• Try to find several reference books or sites you can use to evaluate the risk for a Herbal/Drug interaction. If you have access to Micromedex I found it is a very good reference.
• If the patient has been taking the same drug therapy and herbal products at home with no issues, there is a low risk for any problems. You will still need to consider the possible interactions along with interactions with any added drug.
• Remember to evaluate the quality of the interaction data.
Herbal/Drug Interactions for Select Herbal Products

- **St. John’s Wort**
  - Use with caution with antidepressants or any medication that affects serotonin like Tramadol, Meperidine, or Dextromethorphan.
  - Avoid use with MAOI and partial MAOI like Linezolid, Isoniazid, Selegiline, or Rasagiline
  - Avoid using with decongestants
  - Avoid using with Warfarin, Digoxin, HIV treatment, Estrogen/oral contraceptives, Transplant rejection meds, oral antifungals, benzodiazepines, some antibiotics, some antipsychotics, Omeprazole, and so on.

- **Herbal/Medication Interactions**
  - **Kava (Kava-Kava) (Piper Methysticum)**
    - Avoid use with any CNS active drug
    - Avoid use with any drug that has potential hepatotoxicity
    - Avoid use with Warfarin
    - Avoid use with Parkinson’s medications

- **Ginkoba (Ginkoba biloba)**
  - Avoid use with Warfarin, anticoagulants or any drug that can effect clotting like NSAIDs
  - Avoid use with Calcium Channel Blockers.
Herbal/Medication Interactions

- Black Cohosh (Cimicifuga racemosa)
  - Most of the interactions with Black Cohosh are either theoretical or based on weak case studies.
  - Avoid with fertility treatments
  - Use with caution with antihypertensives
  - Use with caution with estrogen/oral contraceptives
  - Avoid use when treating Ovarian, Uterine, or Breast Cancer
  - Avoid in patients with liver disease.

- Bilberry (Vaccinium myrtillus)
- Goldenseal (Hydrastis canadensis)
- Milk Thistle (Silybum marianum)
- Saw Palmetto (Serenoa repens)
  - No known or suspected drug interactions at this time.

- Chamomile (Matricaria recutita)
  - Limit or avoid use with Warfarin
Herbal/Medication Interactions

• Echinacea
• These recommendations are mostly from the German Commission E
  • Avoid use with any severe chronic progressive disease including cancer, AIDS, or any autoimmune disorder.
  • Use with caution with Warfarin, tricyclic antidepressants, or Clozaril.
  • Avoid use with liver disease.
  • Limit or avoid Caffeine use.

Herbal/Medication Interactions

• Feverfew (Tanacetum parthenium)
  • Avoid use with all anticoagulants or drugs that effect clotting (NSAIDs)
  • Use with caution with migraine treatments

Herbal/Medication Interactions

• Ginseng (Panax ginseng)
  • Avoid use with Warfarin or other anticoagulants
  • Use with caution with loop diuretics
  • Avoid use with Digoxin and Calcium Channel Blockers
Herbal/Medication Interactions

• Green Tea
  • Use with caution with Caffeine and stimulant medications
  • Use with caution with Warfarin and anticoagulants.

Herbal/Medication Interactions

• Hawthorn (Crataegus laevigata)
  • Use with caution with antihypertensive medications, nitrates, and Digoxin.

Herbal/Medication Interactions

• Red Yeast Rice
  • Avoid use with any of the Statins or other lipid lowering drugs
  • Use with caution with Warfarin
  • Avoid use with oral or injectable antifungal medications.
  • Use with caution with Colchicine, Proton pump inhibitors, or medications used to treat AIDS
### Herbal/Medication Interactions

- **Red Clover (Trifolium pratense)**
  - Avoid if pregnant, trying to become pregnant, or breast feeding
  - Avoid with Breast, Ovarian, or Uterine Cancer.
  - Avoid use with Prostate Cancer
  - Avoid use with renal transplant patients.

- **Valerian (Valeriana officinalis)**
  - Use with caution with all sedative medications
  - Use with caution with CNS stimulants.
  - Use with caution with Kava

- **Yohimbine**
  - Use with caution with all blood pressure medications and cardiac medications
  - Use with caution with all antidepressants
  - Use with caution with Parkinson’s medications.
  - Use with caution with drugs that effect MAOI like Linezoid or Isoniazid.
What about the patient who wants their Herbal even though there are possible issues?

- Document the issues involved, that the patient was educated on the issues, and that they want to use the herbal product anyway. Consider obtaining a signed informed consent on the issue.
- Inform the physician of the issues involved. If they approve the herbal product you will need a physician’s note saying why the use is appropriate.
- Consider obtaining a consultant pharmacist note on the issues also.
- Monitor for any potential problems or side effects for an appropriate time period, usually a few weeks to a month.

Thoughts on Food/Drug Interactions

- There are many reference sites that will give you lists of medications that either should be given with food or given on an empty stomach.
- Some food/drug dosing recommendations should always be followed, or the medication use should be avoided.
- With many medications the recommendations are not absolute. Patient issues and the individualization of therapy may be a factor in setting the administration time. However, using a medication outside if the recommended food/drug dosing time will require additional documentation on the part of the Physician and facility.

Thoughts on Food/Drug Interactions

- If therapy needs to be individualized the facility will need to document the reasons why the change is appropriate.
- The physician will need to document these issue in a chart note or progress note.
- I recommend a note from the consultant pharmacist discussing the relevant issues.
- Care plan the change.
- Monitor for effect with any needed follow up.
However

- In general it is best to follow the manufacture’s recommendation about food/drug dosing or the recommendation of the clinical literature.
- There is less chance of a change in the clinical response
- There is less paperwork and monitoring involved.
- There is a lower risk for medication errors.

The Bisphosphonates

- These are medications that are highly reactive and poorly absorbed. Less than 1% of the oral dose is absorbed.
- That is enough to have the desired therapeutic effect.
- Food significantly reduces the amount of drug absorbed as do almost all medications studied.
- Recommendation: Always give these medications on an empty stomach with a full glass of water in the morning at least thirty minutes before any other food, beverage, or medication is given. The patient must remain upright (sitting or standing) for at least thirty minutes. Boniva recommends taking the medication one hour before breakfast and remaining upright for at least one hour.

Ferrous Sulfate or Other Iron Supplements

- The dosing recommendation is to give Iron supplements on an empty stomach for best absorption, however if this results in GI distress then give with food.
- Giving with food will decrease the amount of iron absorbed, however the body will increase the amount of iron absorbed when in an iron deficient state.
- Avoid giving with antacids, calcium, dairy products, or caffeine.
- Iron can be chelated by some compounds making it harder to absorb. Calcium and antacids can precipitate it reducing the absorption.
- For serious deficiency give by injection then use oral therapy for a maintenance dose.
Ferrous Sulfate or Other Iron Supplements

- Document the adverse reactions to Iron therapy on an empty stomach, any resident preference issues, compliance issues, and so on
- You will need a note from the physician documenting the need to give the iron at a non-standard time.
- A note from the consultant pharmacist on the issues involved is useful
- Care plan the change
- Make sure follow up monitoring (iron studies and CBC) are ordered.

Levothyroxine

- Giving Levothyroxine with food can decrease the amount absorbed by 10-20%. Giving with minerals (Calcium, Iron, Aluminum, Zinc) will also reduce the amount absorbed.
- Levothyroxine is best absorbed on an empty stomach given an hour before breakfast.
- There are limited studies that giving the Levothyroxine an hour before lunch or supper results in almost the same effect as giving it before breakfast.

Levothyroxine

- Studies have shown an increase in TSH levels when Levothyroxine is given with Breakfast, after Breakfast, or at bedtime. The TSH, while higher, is often still in the therapeutic range.
- There are also a study showing when Levothyroxine is given with food the absorption, while lower, is consistent and the effect on TSH levels is stable. This study showed that giving Levothyroxine with a meal may require a higher dose to normalize the TSH level but the response was consistent and dependable.
Levothyroxine

- Ideally Levothyroxine should be given one hour prior to a meal
- If there are clinical reasons to give it with a meal then document the clinical reasons
- Obtain a note from the physician noting the reason for the non-standard administration time
- Obtain a note from the consultant pharmacist on the issues involved
- Care plan the new administration time
- Ensure a TSH (and perhaps a Free T4) is ordered to be drawn at least six weeks after the change in the time of administration to monitor for any change in effect.

Proton Pump Inhibitors

- For the maximum effect these drugs should be given 30 to 60 minutes before a meal to allow them time to be absorbed prior to the meal. These drugs work by interacting with the acid pump (proton pump) in the stomach when it tries to start acid production. The acid pump tries to turn on when food arrives in the stomach. So giving them prior to the meal ensures the maximum effect

Proton Pump Inhibitors

- These medications do have some therapeutic effect if given with or after the meal, but not as much. They can still be used if continuous tube feeding is ordered.
- H2 blockers like Ranitidine have a lower maximum effect than the proton pump inhibitors but they can be considered as alternatives if the medication must be given with a meal.
Proton Pump Inhibitors

- If for some clinical reason these medications must be given with a meal then follow the previous steps.
- Educate the patient or POA and document that they want the medication with a meal or that it must be given with a meal (such as with continuous tube feeding).
- Inform the physician and obtain documentation that the use is appropriate.
- Obtain a consultant pharmacist note on the issue.
- Care plan
- Start follow up monitoring.

Summary Herbal

- Most of the data on Herbal/Medication interactions are poor quality case studies. While it is relatively easy to find interaction data, it is hard to know how clinically significant it is.
- You need to act on the information anyway.
- Use of an Herbal when there are contraindications requires documentation and follow up by the facility.

Summary Food/Drug Issues

- When you have a medication that has specific recommendations about dosing in regards to meals, it is best to follow those recommendation if possible.
- If there is a clinical reason to give such a medication at a different time, that is possible but you must follow the appropriate steps with the appropriate documentation.
Questions?