

VOTE

- Peter Strube for Nominations Committee
- Region 3

Herbal Medication and Supplements

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Question?

- List three herbal therapies that would cause concern for anemia and warrant a preoperative CBC or hemoglobin/hematocrit?

- Garlic, ginseng, ginkgo. Garlic is associated with increased bleeding diathesis and ginkgo with unexpected spontaneous bleeding. Hint: Remember the "G's" for bleeding and coagulation issues. [Roizen and Fleisher, *Essence of Anesthesia Practice*, 2nd ed., 2002, pp593-595]-02



History

- Herbal medicine is a ancient art. The arrogance of western medicine has forgotten that its foundation is in decoctions and chants of shamans.
- Herbal medicine is first documented in early Chinese texts during the rule of the Emperor Huang Di in 2697 BC.
- Hippocrates used herbals in his practice
- The Greek Dioscorides *Materia Medica* is still one of the worlds greatest references on herbs.

History

- A lot of common drugs have a base in the herbal world
- Morphine from the opium poppy
- Digoxin from foxglove
- Quinine and quinidine from Cinchona tree
- Currently the World Health Organization cites 121 prescription medications are produced directly from plant extracts

Case Study

- 26 year old female in labor presents for elective epidural-----
- Second baby.. Hx of preterm Labor
- On Fish Oil

Randomised clinical trials of fish oil supplementation in high risk pregnancies. Fish Oil Trials In Pregnancy (FOTIP) Team
BJOG. 2000 Mar;107(3):382-95

- **To test the postulated preventive effects of dietary n-3 fatty acids on pre-term delivery, intrauterine growth retardation, and pregnancy induced hypertension**
- 33-21% reduction in Preterm Labor
- WOW... what does this have to do with a epidural..... We will see

Question?

- Identify the 13 best-selling herbal medicines/supplements and also give the scientific name (*Genus species*) for the herbals.

- The 13 best-selling herbal medicines and supplements are: (1) ginseng (*Panax ginseng*); (2) ginkgo (*Ginkgo biloba*); (3) garlic (*Allium sativum*); (4) glucosamine; (5) St. John's wort (*Hypericum perforatum*); (6) Echinacea (*Echinacea angustifolia*, *E. purpurea*, *E. pallida*); (7) lecithin; (8) chondroitin; (9) creatine; (10) saw palmetto (*Serenoa repens*); (11) ephedra (*Ma-huang*); (12) Kava-kava (*Piper methysticum*); and (13) valerian (*Valeriana officinalis*).

There really is little information available

- Lee—Herbal Medicines and Perioperative care
 - JAMA 2001; 286: 208-216
 - Anesth Analg 2001; 93:1062-1068
- Miller
- Text books
- New research
- Chapters in certain books
- Random clinical trials

Herbals

This is the problem.....

The Dietary Supplement Health and Education Act 1994
This means --- NO regulation

Could market products without any proof of safety or efficacy

Not required to prove outcomes

No regulation of processing or manufacturing
This no regulation developed in a lot of trouble
The only compliance is voluntary.....?????

History

Supplements and herbals have seen a 380-400% increase in use and abuse. The wide spread use has become mainstream

In 2002 a estimated 14% of the US population used H/S
That number is estimated closer to 20% now

In 2002 1 in 5 adults on perscription medicaiton also used H/S as a self prescribed treatment... also that number is estimated higher now

BIG Money.... In excess of a \$15 billion dollar industry

Question??

- There are two things that patients usually lie about or do not inform the anesthesia provider about????

- NPO
- Herbals and supplements...
- Why?
- Herbals and supplement must be good-----
-----RIGHT???

Why should they tell us more importantly why should we ask?

- There is a increase in the morbidity and mortality related to use because we don't understand or comprehend the polypharmacy relationships between what they are taking and what we use.....
- Lee concluded that : Complications can include MI, CVA, Stroke, Bleeding, inadequate oral anticoagulation, prolonged or inadequate anesthesia, organ failure, transplant rejection and interference with perscription medication.
- Surveys suggest that a vast majority (excess of 70%) of patients do not inform providers of their use of these supplements and herbals.

Survey Data

- 2560 patients responded to the survey
- 39% admitted using some form of alternative medicine supplements and/or herbals
- Of the 39% that reported use, 44% did so without the knowledge of their provider, 56% did not inform the anesthesia provider prior to surgery.
- 53% of the patients ceased the use of these products before surgery..... what this also say????? 47% kept using them and didn't tell the provider.

Why?

- 1998 study focused on why do they choose alternative.
- The study found that more had a distrust or dissatisfaction with traditional western medicine.
- Most found these alternatives more inline with there values, beliefs, philosophies..
- I suggest many may have tried these remedies related to the cost..

Problems

- With no regulation.... I know regulation...
- There is no requirements or safeguards.
- Consumers are usually informed of all the great benefits of the "natural" products but no the RISKS>>>>
- The advertising is often misleading and causes misinformation. What is natural is not always safe.

The patient should be asking these questions?

- Are they safe?
- Do they have side effects?
- Are they what they say they are?
- Drug interactions? Are there any and if so, what?

History and Physical

- How do we ask questions????
- Do you ask about herbals or supplements?
- We ask, what medications are you taking? The patient responds... I am not taking any medications.
- Why is this? Patients don't consider herbals/supplements medication. It's natural...
- ASK>>>>>>>>

Pre-op

- Make sure you to obtain a adequate history
- This history will help you avoid potential complications. When we talk about specific herbals/supplements you will be able to understand what the complications.
- Examples of complications include; cardiac issues, low blood sugars, bleeding, increased sedation effects, change in metabolism, interactions with medications.

Pre-op

- Ask specifically about Herbal and supplement use
- Document Document Document Document
- Be open to discussing the herbal and supplements and how they can interact with anesthesia and surgery.
- Example; They are on fish oil and ginger,,, they may need a transfusion.
- Remember advertising sells these drugs and people will and do fall victim to false claims.

This is what they see

- A majority (55-60%) of adds claim they treat, cure or prevent a disease
- Nearly all (75%-80%) "information" sites actually sell drugs or link to the companies that sell them... are these sites trust worthy
- Nearly all lay people believe that internet cites are accurate... WOW

Where can WE go?

- www.fda.gov/medwatch for a history of adverse events
- Information at:
 - www.medwatch.com
 - www.consumerlab.com
 - www.naturalherbs.com
 - www.snopes.com
 - www.therb.com
 - www.casme.com
 - www.healthletter.cufts.edu
 - www.dietary-supplements.info.nih.gov
 - www.cfsan.fda.gov

IF the claim sounds false it probably is... becareful....

Current Thoughts

- All Herbals and Supplement should be stopped at least two weeks prior to surgery.
- Should this be part of the preop physical?
- Should be asking if they stopped them when they get the phone call about surgery?

Interactions

- All medications, herbals and supplements still follow certain principles.
- Interactions, reactions, non-compatibility tachyphlaxis
- A single medication can have a cause and effect relationship
- Toxicology....

Question?

- List the herbal medicines and supplements that may alter coagulation homeostasis and/or bleeding time

- The following herbals and supplements may alter coagulation status and/or bleeding time, especially when used concomitantly with warfarin (coumadin): ginkgo, garlic, dong quai, danshen, feverfew, ginger, DHEA (dehydroepiandrosterone), androstenedione, and glucosamine sulfate. Of special note, garlic *in combination with other herbals* may increase the risk of bleeding. [Roizen and Fleisher, Essence of Anesthesia Practice, 2nd ed., 2002, pp577-611]-02

Medication

- There are Thousands and Thousands of Herbals and supplements. We will focus on only the big ones....
- You will encounter things not on this list... please take the time to look them up and learn.

Question?

- The patient presents with hypertension, tachycardia, agitation, and restlessness. Patient history reveals current treatment with fluoxetine (Prozac), and they also report taking "some alternative medicines for depression." What syndrome does this patient exhibit and which herbal medicine has potentiated the syndrome?

- The patient with hypertension, tachycardia, agitation and restlessness has a serotonin-like syndrome. St. John's wort, often used as a "natural remedy" for depression can produce or potentiate the serotonin-like syndrome. [Roizen and Fleisher, Essence of Anesthesia Practice, 2nd ed., 2002, p610]-02

St. Johns Wort

- This is used for mood enhancement. To use for short term therapy for mild depression. (few clinical trials) or other somatoform disorders
- Active compounds are hypericin and hyperforin
- Action: inhibits the reuptake of serotonin (5-HT), NE and Dopamine
- Has a mild MOA-B activity so it may interact with MOA inhibitors or SSI
- Can also get serotonin syndrome with reaction to medication
- Increases metabolism of some agents ---CYP-3A4
 - Some HIV meds, cyclosporin, alfentanil, versed, lidocaine, Calcium Channel blockers, Serotonin blockers,,,i.e. zofran

St John's Wort

- May inhibit additional pathways that affect coumadin and NSAIDS
- The recommendation as with all herbals and supplements is to stop this drug at least two weeks prior surgery...
- If they are using it for mild depression they may need to stop it sooner so they can do a taper.
- Interacts directly with: anticoagulants, oral contraceptives, antidepressants, anti-seizure medications, and transplant and HIV medications.

St John's Wort

- Decreased Digoxin Levels; Enzyme inductions; Prolonged anesthesia
- Case reports of prolonged emergence and cardiovascular toxicity
- Half-Life of the active compounds are 43.1 hours (hypericin) and 9 hours for hyperforin.
- The long half-life makes this a risky drug
- It can also inhibit narcotic to opioid receptors and this may cause excessive sedation when combined with narcotics

Ephedra

- Contains alkaloids including ephedrine, pseudoephedrine, norephedrine, methylephedrine and norpseudoephedrine.
- It has been suggested for weight loss, diet, increased metabolism, bronchodilator, asthma and the common cold.
- It causes a dose dependent increase in blood pressure and heart rate. This is done through a noncatecholamine sympathomimetic agent that shows alpha 1 and alpha 2 and beta effects.
- FDA banned this product recently
- Risks include: MI, CVA, uncontrolled BP, Increased HR
- Do you remember the problem with Halothane?

Ephedra

- Known to cause hypersensitivity myocarditis, tachyphylaxis from long term use that has depleted all catecholamines... This leads perioperative hemodynamic instability,,,,,
- Uncontrolled hypotension; hypertension (moa) stroke and MI
- Stop at least 24 hours prior to surgery. 2 weeks is better
- This drug is trouble.... Removed by FDA ban
- Half life is 5.2 hours and 80% excreted unchanged in the urine

Echinacea

- Most commonly used to treat viral, bacterial or fungal infection
 - Common cold prevention, UTI and URI
- Long term use can cause immunosuppression and thus affect wound healing or allow for opportunistic infections. This usually occurs after 8wks of use
- Hepatotoxicity can occur although there is no evidence
- Inhibits the P450--CYP3A4 enzyme pathway

Echinacea

- Should be avoided in patients that either require or will require immunosuppression
- Stop medication early
- Contraindicated in Autoimmune disorders and cardiac Disease
- If there is hepatic activity can lead to toxicity of some drugs

Garlic

- Used for lipid lowering and hypertension, help decrease the risk of atherosclerosis by lowering the BP and thrombus formation and lipids. Also used as a antibacterial, antiviral and antifungal.... Mouth wash...Yes, Mouth wash
- Few case reports of epidural hematoma from bleeding
- Stop at least 2 weeks prior to surgery
- May augment the effects of coumadin, heparin, NSAIDS and aspirin.
- May cause perioperative bleeding and hypotension

Garlic

- Garlic inhibits platelet aggregation, reduces thromboxane, increases fibrinolytic activity and increases streptokinase activated plasminogen activator 8-9.
- These effects are dose dependent
- These effects appear to be irreversible and may potentiate the effects of other inhibitors. i.e. prostacyclin, indomethacin, dipyridamole and may interact with ticlid, plavix and aspirin
- Can lower blood pressure.
- Irreversible platelet effects dictate that garlic be stopped well in advanced of surgery.

Question?

- Which herbal medicine inhibits thromboxane synthase and thus has synergistic effects with other antiplatelet agents?

- ? Ginger inhibits thromboxane synthase and may potentiate other antiplatelet agents, increasing the risk of bleeding and coagulation disorders. [Roizen and Fleisher, *Essence of Anesthesia Practice*, 2nd ed., 2002, p594]-02

Ginger

- Ginger contains anticoagulant components. It inhibits platelet aggregation by acting as an inhibitor of arachidonic acid, epinephrine and adenosine diphosphate and collagen.
- This is also a dose dependent relationship
- There is a reduction in thromboxane synthetase and prostaglandin synthetase and there was no reduction in bleeding time, platelet count or platelet function.
- Ginger administered prior to induction of anesthesia can be prophylactic for PONV (1 gram) TOXIC is greater than 2mg/kg/day

Ginger

- Used for PONV as we talked about, motion sickness, vertigo, digestive aid for cramps and menstrual relief
- Increases Bile production..... Bad with gallbladder pt
- Some studies look at killing Ovarian cancer cells, Used as a stimulant, antidepressant, gastro issues, constipation, HTN and delaying the onset of DM
- Increases the perioperative bleeding risks
- Stop at least two weeks prior to surgery

Small hint... if its green in can cause bleeding.

Question?

- State four anesthetic concerns for the patient taking ginger as an herbal supplement?

- Four anesthetic concerns for the patient taking ginger are: (1) interaction with antiplatelet agents, possibly leading to coagulation disorders and increased risk of bleeding; (2) potentiation of barbiturates; (3) prolonged asleep time; and, (4) increased gastric motility, *decreasing* the risk of aspiration. [Roizen and Fleisher, *Essence of Anesthesia Practice*, 2nd ed., 2002, p594]-02

Feverfew

- Used to treat headaches, as a fever reducer and pain reliever
- Parthenolide in feverfew inhibits platelet aggregation
- Used for treatment of migraines. With increased duration of use 3.5-8 years there is no difference in ADP or thrombin stimulated platelet aggregation. However serotonin induced platelet aggregation is decreased.
- Some suggestions indicated it may help with chronic inflammation
- This supplement/herbal interacts with antiplatelet and anticoagulants.

Ginkgo

- Ginkgo is used to enhance memory, PVD, macular degeneration, vertigo, tinnitus and erectile dysfunction
- Ginkgo alters vasoregulation, acts as an antioxidant and modulates neurotransmitter. It also inhibits platelet activating factor.
- The active product terpenoids are thought to cause these effects
- Stop 2 weeks prior even though the active half life is 3-10 hours
- This is a circulatory stimulant; some interaction with MAO inhibitors and SSI
- Case reports indicate increased bleeding in patients.

Ginkgo

- Early studies in Alzheimers patients underway
- Case reports show major complications seen were bleeding including intracranial bleeding, hyphema and post operative bleeding
- Hyphema = is a term used to describe bleeding in the anterior chamber (the space between the cornea and the iris) of the eye.
- Stop 2 weeks prior to surgery.

Ginkgo

- Interactions:
- Increased bleeding times
- Avoid with use of anticoagulants and NSAIDS and aspirin
- A point of interest... I said if it is green it can cause increased bleeding... do studies and evaluations... limit neuroaxial blocks.. Watch for the increased risk of hepatotoxicity and interactions with drugs....

Question?

- Identify the two best-selling herbal medicines that may cause hypoglycemia?

- Garlic, especially when taken concomitantly with chlorpropamide, may cause hypoglycemia. Ginseng has potential to cause hypoglycemia also, especially if the patient is taking oral hypoglycemics. [Roizen and Fleisher, Essence of Anesthesia Practice, 2nd ed., 2002, pp593, 569; Ezekiel, Handbook of Anesthesiology, 2002-2003 ed., p21]-02

Ginseng

- Most action is associated with ginsenosides.....not sure of mechanism of action but the current thoughts are that it acts like steroid hormones. Used as a aphrodisiac and the treatment of DM and sexual dysfunction
- Reports to protect the body from stress and help restore homeostatis
- Some action on glucose control and may see hypoglycemia
- Inhibits platelet aggregation and prolong the coagulation times of thrombin and activated partial thromboplastin.

Ginseng

Stop at least 2 weeks prior to surgery.

Drug interactions

Antiplatelet
Anticoagulants
Hypoglycemia
Hypertension
Bleeding

Valerian

- Valerian is a powerful nerve, stimulant, carminative and antispasmodic. It has a remarkable influence on the cerebro-spinal system, and is used as a sedative to the higher nerve centres in conditions of nervous unrest. St. Vitus's dance, hypochondriasis, neuralgic pains and the like. The drug allays pain and promotes sleep. It is of especial use and benefit to those suffering from nervous overstrain, as it possesses none of the after-effects produced by narcotics.
- Sesquiterpene are the primary pharmacological agent. Used as a pain reliever, sedative and sleep aid.
- Dose dependent sedation and hypnosis
- This appears to be mediated through the GABA neurotransmitter and receptor function
- It will potentiate the anesthesia effects and adjuncts through the GABA System

TAPER when this herbal is used chronically

Kava

Widely used as an anxiolytic and sedative. Some information related to ovarian Cancer and used for throat pain.

Kavalatones appear to be the active pharmacological agent

Dose dependent relationship on the central nervous system. Has antiepileptic, neuroprotective and local anesthetic properties.

May work on the GABA system

Peak levels occur in 1.8 hours and half-life is 9 hours.

Stop 2 weeks before surgery. May need to taper---no data to suggest withdrawal... just be careful

Kava

- Some clinical trials indicate that it might be helpful with anxiety
- Because it works on GABA it may increase barbiturate sedation
- Long term use can lead to reversible skin condition called Kava Dermopathy..... scaly cutaneous eruptions
- LIVER TOXIC in high doses
- Used for relaxation, sleep aid, muscle relaxant for cramping
- Can mimic mild narcotic use. In high dose will see muscle weakness, visual impairment, dizziness and dry skin. Long term use can cause hypertension, reduced protein level, blood cell abnormalities

Question?

- Which alternative/herbal medicine may create a syndrome of hyperaldosteronism characterized by hypernatremia, hypertension, hypokalemia, and suppression of the renin-angiotensin system?

- Licorice (*Glycyrrhiza glabra*) ingestion may create hyperaldosteronism syndrome. Glycyrrhetinic acid inhibits 11-beta-hydroxysteroid dehydrogenase leading to excess glucocorticoids which bind to mineralocorticoid receptors, producing a mineralocorticoid response. Discontinue the herbal medicine at least 2 weeks before elective surgery. [Roizen and Fleisher, Essence of Anesthesia Practice, 2nd ed., 2002, p600]-02

Licorice

- Common use is for gastric/duodenal ulcer, gastritis, cough and bronchitis.
- Chronic use can cause hypertension, hypokalemia and edema
- Uncontrolled studies show reductions in ADH, Aldosterone and plasma renin activity.
- Inhibits the P450 CYP3A4 liver enzyme—to what levels is not yet known

Licorice

- Known interactions with ACE inhibitors, Dig, Steroids, Insulin, Diuretics, Laxatives and increasing K loss and oral contraceptives.
- Do not take with CHF, HTN and can alter aldosterone levels
- Several on going studies looking at being used to decrease Body Fat

Wild Cherry

- Inhibits P450 CYP3A4... clinical significance is still unknown

fine expectorant that *loosens and expels phlegm from the lungs* and has helped bronchitis, colds, flu, dry coughs, tuberculosis and many other pulmonary complaints. It also acts as a *mild sedative* that not only may *calm coughs*, but also *nervous irritability and nervous indigestion*

Milk Thistle

- This herbal may be beneficial. It has liver protective properties. It may help prevent liver damage and hepatotoxic drugs such as excessive alcohol, phenothiazines and buterphenones and acetaminophen.
- Used for Steroid Abuse, to decrease Cholesterol and acute mushroom illness.
- You may see this being using in Liver transplant patients and liver failure patients.
- Post 30 days of use there was a improvement in AST and ALT

Vitamin E

- Used as a antiaging agent, to prevent stroke and pulmonary emboli, treatment to prevent athersclerosis and promote wound healing, antioxidant and to decrease cholesterol.
- Complications include increased bleeding and hypertension
- Decreased platelet aggregation
- No clinical evidence of hypertension problems in the OR
- Used in Infant formula to decrease anemia

Question?

- Identify the herbal medicines and supplements that inhibit platelet aggregation?

- Garlic, evening primrose (*Oenothera biennis*), fish oils (omega-3 fatty acids), and DHEA (dehydroepiandrosterone) are known to inhibit platelet aggregation. Request PT, INR, platelet counts, and hemoglobin/hematocrit during preoperative evaluation. [Roizen and Fleisher, *Essence of Anesthesia Practice*, 2nd ed., 2002, pp588, 591-593]-02

Fish Oil

- **Fish oil** is oil derived from the tissues of oily fish. Fish oils contain the omega-3 fatty acids eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA), precursors of eicosanoids that are known to reduce inflammation throughout the body, and are thought to have many health benefits.
- Studies suggest that it is helpful with cardiovascular disease, CAD, Depression, anxiety, Increased new born outcomes and many many more.....
- Some early studies are looking at using it for depression and suicide prevention... also used for aggressive behavior, alzheimers, parkinsons and psoriasis. This is to name a few... It is used for a wide array of conditions
- Bleeding in high doses...greater than 3 grams per day
- Interacts with some anticoagulation medications and oral contraceptives.

Question?

- One herbal medicine may *oppose* heparin or warfarin anticoagulation therapy. Which herbal is this and what perioperative risks are associated with a large does of this herbal medicine?

- Goldenseal (*Hydrastis canadensis*), sold as an antidiarrhetic, an anti-inflammatory, and hemostatic agent, may *oppose* the anticoagulant effects of heparin and warfarin. An unusually large dose of Goldenseal can cause a labile blood pressure, cardiac inotropy, CNS stimulation, muscle spasms, decreased seizure threshold, and respiratory distress. [Roizen and Fleisher, *Essence of Anesthesia Practice*, 2nd ed., 2002, p599]-02

You might want to look into

- Melatonin
- Chondroitin sulfate
- Glucosamine
- Creatine
- Evening primrose

Questions

Vote for Peter Strube Nominations
Committee....

Thank You