

ALTERNATIVE THERAPIES FOR EPILEPSY

ORRIN DEVINSKY, M.D.
NYU Comprehensive Epilepsy Center

EVALUATING EFFECTIVENESS OF A NEW TREATMENT

- CORRECT DIAGNOSIS
 - Seizure alert dogs - PNES
- NATURAL HISTORY OF THE EPILEPSY SYNDROME
- DOUBLE BLINDING AND CONTROL OF SUBJECTS
- COMPLIANCE

Double Blinding

- Doctors and patients are biased
 - Internal mammary artery bypass
 - Beta blockers vs. ACE inhibitors for hypertension
- Motivated reasoning
- Confirmational bias
 - If you support Obama or McCain, are you really objective in evaluating new data?
- The Myth of Associationism-Causation
 - Vaccines and seizures
 - Mercury and autism

ALTERNATIVE THERAPIES

- ACUPUNCTURE
- HYPNOSIS
- AROMATHERAPY
- BIOFEEDBACK & NEURO-EEG
FEEDBACK
- MEDITATION
- CHIROPRACTIC
- REFLEXOLOGY
- COUNSELING /
PSYCHOTHERAPY
- NUTRITIONAL
- HERBAL REMEDIES
- OSTEOPATHY
- HOMEOPATHY
- YOGA
- MASSAGE

Nutritional Approaches to Epilepsy

- Dietary - ketogenic, modified Atkins/low glycemic
- Avoid excessive (varies!) alcohol
- Supplements
 - Dimethylglycine
 - Taurine
 - Omega fatty acids
 - Vitamins - B6 & E
 - Essential minerals - Magnesium & Manganese
- Elimination diets - may be most helpful for patients with seizures and migraine, abdominal complaints, or hyperactivity
 - No solid data re: aspartame

Herbal Therapies



Herbs for Epilepsy

- *Valerian root*
- *Skullcap*
- *European Mistletoe*
- *Marijuana*
- *Black cohosh*
- *Lobelia*
- *Kava*
- Hyssop
- Blue vervain
- Yarrow
- Geranium
- Kelp
- Bupleurum
- Passion flower
- Carline thistle
- Elderberry
- Mugwort
- Lady's slipper
- Aloe
- Betony
- European Peony
- Ginseng
- Flax seed oil
- Ginger
- Linden
- Chrysanthemum
- Forskolin
- Behen
- Burning bush
- Calotropis
- Gotu Kola
- Groundsel
- Lily of the Valley
- Tree of Heaven
- Yew

How often do people take herbs?

Overall use of complementary and alternative medicines (CAM) in U.S. 1990-1997.

- Herbal product use increased 4x
- In 1997, adults - 33 million office visits regarding herbal products & high-dose vitamins; spent ~\$8 billion
- In 1997, ~15 million adults took prescription medications with herbs and/or high-dose vitamins

How often do people take herbs?

Top 10 selling
herbs and
dietary
supplements:
2002

Herb	U.S. sales (\$ millions)
Ginkgo biloba	150
Echinacea	70
Garlic	50
Ginseng	40
Soy	35
Saw palmetto	30
St. John's wor	30
Valerian	16

How often do persons with epilepsy take herbs?

U.S. and England studies:

- Up to 1 in 3 persons with epilepsy use CAM
- Most do not discuss their CAM use with doctors
- Herbs taken include ginseng, St. John's wort, melatonin, ginkgo biloba, garlic and black cohosh
- Treat seizures (<10%), other symptoms (20%), and general health (>70%)

Peebles et al. Epilepsy Behav 2000;1:74-7

Easterford et al. Epilepsy Behav 2005;6:59-62

Case Presentation

1. 35-year-old woman with epilepsy for 18 years, on carbamazepine and an oral contraceptive.
2. For several months, feeling depressed, though functions well day to day.
3. Hasn't mentioned symptoms to doctor.
4. St. John's wort is an herb for mild depression.

Case Presentation, cont.

You go to a health foods store and look at different bottles of St. John's wort.



Case Presentation, cont.

1. What do the disclaimers on the labels mean?
2. What about the quality of the products
 1. Does the FDA control the manufacturing and testing of St. John's wort, as it does for the testing and manufacturing of prescription drugs?

Federal regulation of herbs

- Herbal products are classified by the government as dietary supplements.
- Dietary supplements are regulated by the 1994 Dietary Supplement and Health Education Act (DSHEA); prescription drugs - much more rigorous requirements of the Federal Food, Drug, and Cosmetic Act.

Federal standards by DSHEA

- Claim -- an effect on bodily structure or function, not against a specific disease.
- Label must include a disclaimer that FDA has not evaluated the product



Federal regulation of herbs, cont.

- Not required to be produced under Good Manufacturing Process standards, like drugs
- No government agency (eg, FDA) independently verifies the quality/production
- Could be contaminated with microbes, pesticides, toxic metals, or adulterated (eg, herbs or drugs)
- Potency and amount per pill/capsule may vary significantly within the same bottle or from batch to batch, or from one branded product to another

Federal regulation of herbs, cont.

Standards set forth by the DSHEA:

- Manufacturers are responsible for the truthfulness of labeling claims
- No government agency independently reviews and verifies the claims and supporting evidence
- Only manufacturers control product quality and verify safety

Case Presentation, cont.

1. What do the disclaimers mean?
2. What about their quality, whether the FDA controls the testing of St. John's wort?, how is it manufactured?
3. What about the amount of active ingredients?

Standardization

- How much of the active ingredient?
- For example, bottle says “carbamazepine 200 mg”
- This is a major problem for herbal products because
 - the active ingredient (s) are usually not known
 - the amount of the assumed active ingredient may vary from pill to pill and product to product
 - it is usually not possible to measure levels in the blood to guide dosage

? The active ingredient

- St. John's wort standardized by its content of hypericin (typically to 0.3% hypericin)
- Hypericin not confirmed as the active ingredient

Case Presentation, cont.

You wonder whether St. John's wort could affect your carbamazepine or birth control pill, and whether it is safe and actually helps depression

Herbal Anticonvulsants: Mechanisms

- Sedative affect/improved sleep: Valerian, Kava, Lobelia, passion flower.
- Increase in brain GABA/GABA receptors (Valerian, Kava)
- Agonist of benzodiazepine receptors (Passion flower).
- Antioxidants (TJ-960)

Herb/AED Interactions

- Don't use Valerian or Kava with alcohol, barbiturates, benzos- sedation/coma.
- Hemorrhagic complications with Ginkgo and St. John's wort.
- St. John's wort can lower carbamazepine levels.
- Shankapulshpi (Ayurvedic formula) decreases 1/2 life of phenytoin and decreases its efficacy.
- Tell your physician about herb use; anticipate potential for interactions.

Herbs and Seizure Medications

- Increase Side effects
 - Valerian Root
 - Kava Kava
 - Passion Flower
 - Chamomile

Herbs that cause Seizures

- **Kava Kava:** GTC from toxicity and withdrawal.
- **Marijuana:** intoxication or withdrawal.
- **Skullcap:** confusion and convulsions with high doses.
- **Ma Huang:** has ephedrine, pseudoephedrine, lowers threshold.
- **Gamolenic acid** lowers seizure threshold: evening primrose oil, borage (starflower).
- **Goldenseal:** hydrastine lowers threshold.
- **Ginseng:** lowers threshold.
- **Ginkgo biloba:** GTCs reported. Neurotoxin 4'-o-methylpyridoxine.
- **Thujone-containing herbs:** wormwood, sage; lower threshold.

Herbs and seizures

- Worsen seizures
 - Ephedra
 - Ma Huang
 - Mate
 - Guarana
 - Borage oil
 - ? Ginkgo
 - ? Ginseng

Side-Effects of Herbs

- Natural doesn't equal safe!
- Herbs and herbal preparations contain many compounds.
- Black cohosh, Valerian, green tea have tannins - can affect absorption of Ca, Cu, Fe, Mg.
- Black cohosh can cause miscarriage via uterine stimulation.
- Lobelia - respiratory paralysis and death.

Herbal Therapies



Traditional Chinese Herbal Medicine (TCHM)

- Epilepsy therapy since 770 B.C.
- Principles of “Yin Yang Wu Xing”
- No well controlled studies
- Numerous laboratory studies show antiepileptic effects for many
- Many preparations are compound

Marijuana

- First used as antiepileptic in 19th century.
- Cannabinoid receptors in brainstem, limbic system, cortex.
- Mixed results
- THC has anti- or proconvulsant effects depending on dose and epilepsy model.
- Many cannabinoids - variable effects
- Epidemiologic study- may be protective against first seizures in men
- Has other potentially negative health consequences (e.g., cardiovascular, pulmonary). ?? withdrawal seizures.
- Illegal and therefore cannot be prescribed except for states with medical marijuana

Melatonin

- Natural hormone
- Promotes sleep
- Used in various neurological conditions
- Antiseizure properties reported clinically in humans (small series, anecdotes) and dogs (nocturnal seizures) and experimentally in rodents

Melatonin's Effects

- Anti-oxidant
- Blocks effects of glutamate (neuroprotective)
- Enhances GABA actions

Clinical Use of Melatonin in Epilepsy Patients

- Given orally 30-60 minutes before bedtime
- Dose ranges from 1-10 mg

Neurofeedback

- Non-invasive
- Utilizes EEG operant conditioning
- Uses light and sound, puzzles
- Animal studies in cat - Science
- Some uncontrolled, small studies show reduction in seizure frequency and/or severity

Neurofeedback

- One hour sessions 1-3 times per week
- 3 months to 1 year
- Cost ~ \$100 per session

Reiter-Andrews Method

- Identification of risk factors for seizures
- Elimination of risk factors for seizures, such as stress and emotional reactions
- Biofeedback
- Self-discovery/education

Relaxation and Epilepsy

- Many patients report stress is a common provocative factor for seizures
- Many patients report that reducing stress can reduce seizure frequency or severity
- Many techniques for relaxation
 - Biofeedback - breathing, heart rate, muscle tension
 - Yoga, pilates exercise
 - Massage, aromatherapy

Exercise and Epilepsy

- Fear of inducing seizures
- 10% of patients report exercise often induced seizures
- 2% of patients report exercise induced seizures in more than 50% of training sessions
- 36% report improved seizure control