Part 2: Examining CAM Options in Conventional Biomedical Cancer Care

- Accessing high quality CAM facts and knowledge
- Reviewing clinically relevant interactions involving CAM therapies
- Clarifying the role of oncology nursing in cancer CAM

Sources of CAM Information

- Journals
- Media
- Databases
- Government
- One-on-one communication

Electronic Media

- Central authorities to regulate, control, censor, or approve health related information on the internet do not exist and may not be desirable
- Quality criteria: accuracy, completeness, readability, design, disclosures, and references

References

Internet Evaluation Systems

- Accession
- Use
- Confidentiality of patient data
- Sourcing
- Claims of treatment benefit
- Website support
- Contact information
- Source of funding for advertisements

  - Provider offers information in a standardized, computer readable format using a "Health information disclosure, description and evaluation language (HIDDEL).
  - Develop and promote technologies to guide consumers, establish global web of trusted sites

Full Text Databases

- Natural Medicine Comprehensive Database ©
- Natural Standard ®
- The Cochrane Library
- Cancer Source ™
- HerbMed ®
- International Bibliographic Information on Dietary Supplements
- Micromedex®
- eFacts®

Levels of Evidence

<table>
<thead>
<tr>
<th>Strength of Study Design</th>
<th>Strength of Evidence Measured</th>
<th>Level of Evidence Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Cancer Database</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ONS Priority Symptom Management Project</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural Medicine Database</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Natural Standards Database</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Further inquiry in this area may prove helpful to HCP and patients in accessing the most reliable sites.

Evidence-based practice

- Uses best evidence available and consultation with patients to decide which option best suits the patient

- Evidenced-based Health Care (EBHC)
  - Ability to locate “best evidence”
  - Ability to evaluate evidence to determine what is “best”
  - Ability to disseminate and implement best evidence into practice and policy

**EMPHASIS:** best practices + role of patient participation in clinical decision making
Electronic Resources

- US Food and Drug Administration
- National Institutes of Health
  - National Cancer Institute
    - PDQ Cancer Information Summaries
    - NCI Cancer Patient Education Network
    - Office of Cancer Complementary and Alternative Medicine (OCCAM)
  - Cancer Centers
  - National Center for Complementary and Alternative Medicine (NCCAM)

Electronic Resources

- Community & Professional Organizations
  - American Cancer Society
  - American Society for Clinical Oncology
  - Oncology Nursing Society
CJON Integrated Care 2003-2004

- Clinical Trials in Cancer Part I Biomedical, Complementary, and Alternative Medicine: Finding Active Trials and Results of Closed Trials
- Homeopathy in Cancer Care: Part I & II--Continuing the Practice of “Like Curing Like”
- Translational Research in Cancer Complementary and Alternative Medicine: The National Cancer Institute’s Best Case Series Program
- Part I & II: Expanded Psychosocial Interventions In Cancer Care: An Introduction to Diversional Therapy
- Clinical Aromatherapy Part I & II: Integration Into Clinical Practice

Newsletters

- “Alternative Medicine Alert”
- “Institute of Medicine News”
- “Medline Plus”
- “AMNews”
- “MedWatch”
- “Dietary Supplements/Food Labeling Electronic Newsletter”
Reverse Herbology: Predicting and Preventing Adverse Herb-Drug Interactions

Tuesday, October 26, 2004
Author/Sponsor: Steven A. Kliewer, Ph.D., University of Texas Southwestern Medical Center
Total Running Time: 00:55:58
Bandwidth: 33 Kbps
This is a work of the United States Government. No copyright exists on this material. It may be disseminated freely.

Clinically Relevant Interactions involving CAM Therapies

Which potential interactions between CAM and conventional approaches are clinically relevant?
What are the optimal approaches in communicating clinically relevant potential interactions to providers & patients?


Evaluating CAM Therapies

Ideal: An evidence-based, systematic review including scientific evidence
- Folkloric precedent
- Expert opinion
- History
- Pharmacology
- Kinetics/dynamics
- Interactions
- Adverse effects
- Toxicology
- Dosing

Drug Interactions in Oncology

- Pharmacologic
- Pharmaceutical
- Pharmacokinetic
- Absorption
- Distribution
- Metabolism
- Elimination
- Between cytotoxic and non-cytotoxic drugs
- Pharmaceutically

- Anti-cancer drugs and over-the-counter medications, alternative medicine, or herbs
- Potential interactions between anticancer drugs and over-the-counter or alternative medicines and herbs should not be underestimated.

Fig 1. Common mechanisms for possible interactions between herbs and anticancer drugs

Event Types
- Precautions/warnings/contraindications
- Herb/drug interactions
- Herb/herb/supplement interactions
- Herb/food interactions
- Herb/lab (or diagnostic studies) interactions
  - Liver function, chemistries, CBC, thyroid studies, PFTs, urine studies, nuclear medicine
- Allergies
- Adverse events
  - Dermatologic, neurologic, pulmonary, CV, GI/GU, renal
- Adverse interactions
  - Anticancer agents

Top-Selling Herbal Supplements (2002)

<table>
<thead>
<tr>
<th>2002 Rank</th>
<th>Herb</th>
<th>Indications</th>
<th>Retail Sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Grape</td>
<td>Hypercholesterolemia</td>
<td>3,054,816</td>
</tr>
<tr>
<td>2</td>
<td>Grape</td>
<td>Dementia, intermittent claudication</td>
<td>3,381,351</td>
</tr>
<tr>
<td>3</td>
<td>Evening</td>
<td>Prevention of common cold</td>
<td>4,423,427</td>
</tr>
<tr>
<td>4</td>
<td>Saw</td>
<td>Prostate hyperplasia</td>
<td>6,024,896</td>
</tr>
<tr>
<td>5</td>
<td>Ginseng</td>
<td>Physical and mental fatigue</td>
<td>7,762,350</td>
</tr>
<tr>
<td>6</td>
<td>Milk</td>
<td>Mental depression</td>
<td>8,120,329</td>
</tr>
<tr>
<td>7</td>
<td>Cranberry</td>
<td>Urinary tract infection</td>
<td>10,950,138</td>
</tr>
<tr>
<td>8</td>
<td>St. John's Wort</td>
<td>Depression</td>
<td>11,857,782</td>
</tr>
<tr>
<td>9</td>
<td>Black cohosh</td>
<td>Insomnia, stress</td>
<td>13,331,196</td>
</tr>
<tr>
<td>10</td>
<td>Antibiotics</td>
<td>Allergic rhinitis, sinusitis, asthma, urticaria</td>
<td>15,594,575</td>
</tr>
<tr>
<td>11</td>
<td>Ginkgo</td>
<td>Alzheimer's disease</td>
<td>18,492,145</td>
</tr>
<tr>
<td>12</td>
<td>Ginseng</td>
<td>Anxiety</td>
<td>21,553,518</td>
</tr>
<tr>
<td>13</td>
<td>Ginseng</td>
<td>Tinnitus, tinnitus</td>
<td>23,053,036</td>
</tr>
<tr>
<td>14</td>
<td>Ginseng</td>
<td>Menopause, irritable bowel disease</td>
<td>32,448,366</td>
</tr>
<tr>
<td>15</td>
<td>Ginseng</td>
<td>Urinary tract infection</td>
<td>34,509,288</td>
</tr>
</tbody>
</table>

Gingko
- Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 and CYP2C19 inhibition)
- Discourage with alkylating agents, antitumor antibiotics, and platinum analogues (free-radical scavenging)
- Drug/drug interactions: NSAIDS, anticoagulants (bleeding)
- Either alone or in combination with aspirin or warfarin
- Discourage use prior to surgery

Ginseng
- Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 inhibition)
- Discourage in patients with ER+ breast cancer and endometrial cancer (stimulation of tumor growth)
<table>
<thead>
<tr>
<th>Plant</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Valerian</strong></td>
<td>- Caution with tamoxifen (CYP2C9 inhibition)</td>
</tr>
<tr>
<td></td>
<td>- Caution with cyclophosphamide, and teniposide (CYP2C19 inhibition)</td>
</tr>
<tr>
<td><strong>Grape Seed</strong></td>
<td>- Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 inhibition),</td>
</tr>
<tr>
<td></td>
<td>- Caution with alkylating agents, antitumor antibiotics, and platinum analogues (free radical scavenging)</td>
</tr>
<tr>
<td><strong>Garlic</strong></td>
<td>- Avoid with dacarbazine (CYP2E1 inhibition)</td>
</tr>
<tr>
<td></td>
<td>- Avoid with other concurrent chemotherapy (inconclusive data)</td>
</tr>
<tr>
<td></td>
<td>- Drug/drug interactions: (bleeding)</td>
</tr>
<tr>
<td></td>
<td>- discourage use prior to surgery</td>
</tr>
<tr>
<td><strong>Clinical Trials with Garlic (open)</strong></td>
<td>- Pilot Study to Evaluate the Influence of Garlic on the Pharmacokinetics of Docetaxel in Patients With Locally Advanced or Metastatic Breast Cancer NCI-04-C-0084</td>
</tr>
<tr>
<td></td>
<td>- Objectives</td>
</tr>
<tr>
<td></td>
<td>- Determine the clinical pharmacokinetic behavior of docetaxel with and without garlic tablets in patients with locally advanced or metastatic breast cancer.</td>
</tr>
<tr>
<td></td>
<td>- Determine the toxicity of this regimen in these patients.</td>
</tr>
<tr>
<td></td>
<td>- No concurrent administration of the following:</td>
</tr>
<tr>
<td></td>
<td>- Alprazolam, Cyclosporine, Diltiazem, Dofetilide</td>
</tr>
<tr>
<td></td>
<td>- Erythromycin, Fluvoxamine, Itraconazole, Ketoconazole, Quinine, Hypericum perforatum (St. John’s wort), Tacrolimus, Theophylline, Warfarin, Zolpidem</td>
</tr>
<tr>
<td><strong>Echinacea</strong></td>
<td>- Avoid with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 induction)</td>
</tr>
<tr>
<td><strong>Soy</strong></td>
<td>- Avoid with tamoxifen (antagonism of tumor growth inhibition)</td>
</tr>
<tr>
<td></td>
<td>- Avoid with treatment of patients with ER+ breast cancer and endometrial cancer (stimulation of tumor growth)</td>
</tr>
</tbody>
</table>
Clinical Trials with Soy (open)

- Phase II Randomized Study of Soy Protein in Postmenopausal Women With Breast Disease Taking Tamoxifen and Experiencing Hot Flashes, CALGB-79805, NCI-P02-0206
- Phase II Randomized Study of Dietary Soy in Patients With Elevated PSA Levels, CALGB-79806, NCI-P02-0207
- Phase II Randomized Study of Soy Isoflavones Before Radical Prostatectomy in Patients With Stage I or II Adenocarcinoma of the Prostate, WSU-C-2418
- Randomized Study of Isoflavones in Reducing Risk Factors in Patients With Stage I or II Prostate Cancer, MCC-0002, NCI-P01-0195
- Randomized Pilot Study of Isoflavones Versus Lycopene Prior to Radical Prostatectomy in Patients With Localized Prostate Cancer, MCC-0105, NCI-3811, NCI-P02-0216

St. John’s Wort

- Avoid with all concurrent chemotherapy (CYP2B6, CYP2C9, CYP2C19, CYP2E1, CYP3A4, and P-glycoprotein induction).

Clinical Trials with St. John’s Wort (open)

- Phase III Randomized Study of Sertraline (Zoloft®) Versus Hypericum Perforatum (St. John’s Wort) in Cancer Patients With Mild to Moderate Depression
  - CCCWFU-98101, CCCWFU-BGOI-152
  - Objectives: Compare the change in depression severity in cancer patients with mild to moderate depression treated with sertraline vs Hypericum perforatum.
  - No concurrent administration of any of the following:
    - Theophylline, Protease inhibitors used to treat AIDS, Digoxin, Calcium-channel blockers (e.g., diltiazem or nifedipine), Cyclosporine, Benzodiazepines (e.g., diazepam or alprazolam), Coenzyme A reductase inhibitors (cholesterol-lowering agents), Macrolide antibiotics (e.g., azithromycin, erythromycin, or clarithromycin), Dihydropyridine calcium channel blockers (e.g., nifedipine), Griseofulvin, Phenobarbital, Phenytoin, Rifampin, Rifabutin, Ketoconazole, Fluconazole, Itraconazole, Grapefruit juice, Naturopathic/herbal products that would interfere with Hypericum perforatum.

Kava

- Avoid in all patients with pre-existing liver disease or evidence of hepatic injury (herb-induced hepatotoxicity) or in combination with hepatotoxic chemotherapy.
- Caution with camptothecins, cyclophosphamide, EGFR-TK inhibitors, epipodophyllotoxins, taxanes, and vinca alkaloids (CYP3A4 induction)

Nuclear Medicine Interactions

“Although at this time, little evidence and only hypotheses are available on the effects of CAMs such as vitamins, supplements, and herbal remedies on nuclear medicine diagnostic and therapeutic procedures, one should be aware of the possibilities of radiopharmaceutical interactions.”

Herb or Vitamin Use + Chemotherapy

N=76, chart review

Results
- HV + chemo was common (78%)
- "at risk" profiles of HV + chemo (27%)
- Multivitamin, calcium, vitamin A, C, E, B6, selenium, coenzyme Q10, beta carotene, glutamine, tea (black, green)
- Most patients discussed information with HCPs + friends + naturopathic physicians

Methods to improve communication for HV use between cancer patients receiving chemotherapy and HCP is necessary to identify and minimize the risk of these interactions.


Antioxidant Herbs & Vitamins

- Cancer treatment or prevention
  - Vitamin A
  - Vitamin C
  - Vitamin E
  - Lycopene
  - Green tea
  - Soy
  - Grapeseed extract
  - Melatonin
  - selenium

- Concern about interference with RT or some chemotherapy agents
  - Alkylating agents
  - Anthracyclines
  - Platinum-based
  - Remains area of study and controversy

Mediators of Cytotoxicity

Free Radicals and Reactive Oxygen Series

- AGENTS THAT RELY
  - Anthracyclines
  - Bleomycin
  - Daclinomycin
  - Epipodophyllotoxins
  - Platinum compounds
  - Alkylating agents

- AGENTS THAT DO NOT RELY
  - Antimetabolites
  - Vinca alkaloids
  - Hormonal agents
  - Taxanes
  - Biotherapies

- AGENTS THAT RELY
  - Antimetabolites
  - Vinca alkaloids
  - Hormonal agents
  - Taxanes
  - Biotherapies

- AGENTS THAT DO NOT RELY
  - Anthracyclines
  - Bleomycin
  - Daclinomycin
  - Epipodophyllotoxins
  - Platinum compounds
  - Alkylating agents


Natural Standard Special Report: CAM Therapies

- Drug Interactions
  - Impaired metabolism
  - Clinically significant bleeding
  - Hepatotoxicity
  - Estrogenic or progestational activity
  - Interference with nuclear medicine scanning


Acupuncture

- Contraindications
  - Thrombocytopenia
  - Neutropenia
  - Cardiac pacemaker
Clinically Relevant Interactions involving CAM Therapies

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Clarifying the Role of Oncology Nursing in Cancer CAM

- Evolution Over Time
  - Testimonials
  - Assessing & documenting CAM use
  - Referral to CAM providers
  - Navigators
  - Designing integrative programs
  - CAM Providers
  - CAM Research

Role of Nursing

Oncology nurses must

1. Expand individual knowledge regarding complementary, alternative, and integrative therapies in oncology care through oral, written, and experiential learning modes.

Oncology nurses must

1. Access credible information, resources, and appropriately credentialed practitioners of complementary, alternative, and integrative therapies.

Oncology nurses must

1. Document informed consent procedures, tolerance, and response to therapy for patients receiving complementary, alternative, and integrative therapies in oncology care.

Oncology nurses must

1. Seek proper training, demonstrate competency, and obtain necessary credentials if practicing complementary, alternative, and integrative therapies in oncology care.

Role of Nursing

Oncology nurses must

...develop a working knowledge of cost issues, reimbursement, liability, ethical and legal issues surrounding complementary, alternative, and integrative therapies in oncology care.

The Oncology Nursing Society. The Use of Complementary and Alternative Therapies in Cancer Care. [ONS position]. Pittsburgh: Oncology Nursing Society: 2002

Currently under revision

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...synthesize present knowledge in establishing evidence-based practice involving the use of complementary, alternative, and integrative therapies in oncology care with regards to safety, efficacy, concurrent use with conventional therapy, and long term use.

Mark O. Hartfield Clinical Research Center Medical Wednesday, September 22, 2004

Accessed high quality CAM facts and knowledge

Reviewed clinically relevant interactions involving CAM therapies

Clarified the role of oncology nursing in cancer CAM