Clinical Pearls

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Wisconsin Ginseng (Panax quinquefolius) to Improve Cancer-Related Fatigue: A Randomized, Double-Blind Trial, N07C2

Background: Safe, effective interventions to improve cancer-related fatigue (CRF) are needed because it remains a prevalent, distressing, and activity-limiting symptom. Based on pilot data, a phase III trial was developed to evaluate the efficacy of American ginseng on CRF.

Methods: A multisite, double-blind trial randomized fatigued cancer survivors to 2000mg of American ginseng vs a placebo for 8 weeks. The primary endpoint was the general subscale of the Multidimensional Fatigue Symptom Inventory-Short Form (MFSI-SF) at 4 weeks. Changes from baseline at 4 and 8 weeks were evaluated between arms by a two-sided, two-sample t test. Toxicities were evaluated by self-report and the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE) provider grading.

Results: Three hundred sixty-four participants were enrolled from 40 institutions. Changes from baseline in the general subscale of the MFSI-SF were 14.4 (standard deviation [SD] = 27.1) in the ginseng arm vs 8.2 (SD = 24.8) in the placebo arm at 4 weeks (P = .07). A statistically significant difference was seen at 8 weeks with a change score of 20 (SD = 27) for the ginseng group and 10.3 (SD = 26.1) for the placebo group (P = .003). Greater benefit was reported in patients receiving active cancer treatment vs those who had completed treatment. Toxicities per self-report and CTCAE grading did not differ statistically significantly between arms.

Conclusions: Data support the benefit of American ginseng, 2000mg daily, on CRF over an 8-week period. There were no discernible toxicities associated with the treatment. Studies to increase knowledge to guide the role of ginseng to improve CRF are needed.

J. Natl. Cancer Inst. 2013 Aug 21;105(16)1230-1238, DL Barton, H Liu, SR Dakhil, B Linquist, JA Sloan, CR Nichols, TW McGinn, PJ Stella, GR Seeger, A Sood, CL Loprinzi

From Warren Ross, MD, Ellicott City, MD

Soyfood Intake and Breast Cancer

The impact of soyfood intake on breast cancer risk has been intensely investigated. This focus can be attributed to soyfoods being uniquely rich dietary sources of isoflavones. Isoflavones are classified as both phytoestrogens and selective estrogen receptor (ER) modulators. The finding that dietary genistein, the primary soybean isoflavone, stimulates the growth of existing mammary tumors in ovariectomized athymic mice implanted with ER-positive breast cancer cells has led many oncologists to advise their patients against the use of soyfoods. However, the clinical evidence indicates that isoflavone exposure has little effect on markers of breast cancer risk. Furthermore, a pooled analysis that involved 9,514 breast cancer survivors found higher isoflavone intake was associated with a statistically significant 25% reduction in recurrence over the average 7.4-year follow-up period. Given the clinical and epidemiologic data, our position is that clinicians should allow soyfood use by patients for whom soyfoods already represent a normal part of their diet, and should not discourage other breast cancer survivors from moderate consumption.

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From Mark Bricca, ND, LAc, Ashland, OR

TCM Formula for Multiple Myeloma

I have used the combination of a classic TCM formula; Huang Lian Jie Du Tang along with several of the isolates from the main ingredients for multiple myeloma. I use this as an oral protocol and combine with I.M. Artesunate. I have had good results in several cases over the last 3 years. Below are some references.

Artesunate

Artesunate (Art) could act as an anti-tumor agent by way of inducing cell apoptosis, antagonizing angiogenesis, reversing immunosuppression of tumor cells. [1]

Artesunate is a potential drug for treatment of multiple myeloma (MM) and DLBCL at doses of the same order as currently in use for treatment of malaria without serious adverse effects.[2]

ART can block ERK1/2 activation, downregulate VEGF and Ang-1 expression and inhibit angiogenesis induced by human multiple myeloma RPMI8226 cells. [3]

Artesunate treatment decreased the level of NFkappaB p65 protein in the nucleus, while increased the level of IkappaBalpha protein in the cytoplasm. The present result is the first report to show that artesunate may be useful in the treatment of multiple myeloma. [4]

Scutellaria

Huang-Lian-Jie-Du-Tang (HLJDT) and Scutellaria radix have an antiproliferative effect on myeloma cells, especially MPC-1-immature myeloma cells, and baicalein may be responsible for the suppressive effect of Scutellaria radix by blocking IkB-alpha degradation. [5]

Formula:

Huang Lian (Rhizoma Coptidis Recens)
Huang Qin (Radix Scutellariae Baicalensis)
Huang Bai (Cortex Phellodendri)
Zhi Zi (Fructus Gardeniae Jasminoidis)

Scutellaria baicalensis (S.B.) inhibited the growth of ALL, lymphoma and myeloma cell lines by inducing apoptosis and cell cycle arrest at clinically achievable concentrations. The antiproliferative effect was associated with mitochondrial damage, modulation of the Bcl family of genes, increased level of the CDK inhibitor p27KIP1 and decreased level of c-myc oncogene. [6]

Isolates

Wogonin was effective in vitro in promotion of apoptosis of myeloma cell by Akt-modulated, Bax and Bcl-2 related intrinsic apoptotic pathway, wogonin may be a potential therapeutic agent against multiple myeloma. [7]

Baicalein is a potent inhibitor of protein phosphorylation in-

duced by IL-6, and thus may be a useful agent for the treatment of MM. [8]

Baicalin, a flavone present in Scutellaria baicalensis, inhibits the growth of human leukemia and myeloma cells through induction of apoptosis. The observed growth-inhibitory and apoptosis-inducing actions of baicalin in these cells are mediated by down-regulation of anti-apoptotic and up-regulate apoptotic components of the phosphatidylinositide-3-kinase (PI3K)/serine/threonine kinase (Akt) signaling pathway. [9]

In multiple myeloma cell line U266, berberine suppresses NF-kB nuclear translocation via Set9-mediated lysine methylation, leads to decrease in the levels miR21 and Bcl-2, which induces ROS generation and apoptosis. [10]

The effects of berberine, an isoquinoline alkaloid, were investigated in human myeloma cells. The cytotoxic effect of berberine in cancer cells may be partially explained by its direct blockade of these K+ channels. [11]

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From Daniel A. Weber, PhD, MSc, Sydney, Australia

Developing a Botanical Protocol

When putting together a botanical protocol, I first consider the primary, secondary, and companion adaptogens that are appropriate for the patient, and I then layer those with targeted endocrine system regulators or insulintrophic acting agents (for more in-depth information on my approach, see my recent book, *Adaptogens in Medical Herbalism: Elite Herbs and Natural Compounds for Mastering Stress, Aging and Chronic Disease*, Healing Arts Press, 2013).

Some of my favorite primary foundational adaptogens include:

• Panax ginseng: I recommend ginseng to all of my patients, as well as Eleutherococcus senticosus. Eleutheroside B is a very potent insulintrophic compound, it improves oxygen uptake by the cells, glucose uptake, fatty acid uptake, and it is an anabolic nutrient, meaning that it activates protein synthesis.

• Oplopanax horridus: A native northwest botanical (commonly called Devil's club), opolopanax is an excellent adaptogen with significant insulin trophic actions and cancer suppressing actions.

• Aralia manchurica: Also called spikenard, the plant contains araliasides, which are profoundly insulin trophic, insulin-sensitizing compounds. It lowers blood sugar, has anti-diabetic effects, is immune enhancing and has anti-cancer effects.

Additional botanicals and botanical compounds that are beneficial for insulin resistance and diabetes include:

• Berberine: Extracted from Coptis spp., it is a very potent suppressor of cancer, and is also an insulin sensitizer.

• Forskolin: Extracted from Coleus forskolii, it re-sensitizes cell receptors by activating the enzyme adenylyl cyclase and increasing the intracellular levels of cAMP. cAMP is an important signal carrier necessary for the proper biological response of cells to hormones and other extracellular signals.

• Fucoxanthin: A carotenoid found in the seaweed wakame; improves lipid metabolism, lowers blood glucose and insulin levels and has cancer preventive effects.

• Ursolic acid: A compound found in sage, basil, rosemary, and Holy basil (Tulsi); comparable to metformin as an insulin sensitizer, and has a pleotrophic effect that suppresses cancer and is a very potent down-regulator of aromatase.

• Nigella sativa: Commonly known as black cumin seed; has profound insulintrophic and cancer suppressing activity and anti-obesity effects.

• Camellia sinensis: Green tea contains a compound called epigallocatechin gallate (EGCG) that helps to stabilize blood sugar levels. I recommend an extract containing 95% phenolic compounds, 60% catechins with 40% EGCG.

• Salacia reticulata: An Ayurvedic herb used for diabetes; salacia contains mangiferin, a polyphenol that enhances the body's sensitivity to insulin. It also contains inhibitors of sugar digestion and absorption. Salacia's polyphenols inhibit fat metabolizing enzymes and enhance lipolysis (the breakdown of fat stored in fat cells).

• Cinnamomum aromaticum: A familiar kitchen spice, cinnamon has well-known insulintrophic effects and re-dox antioxidant effects. I recommend cinnamon medicinally in formulas and also in medicinal smoothies.

• Trigonella foenum-graecum: More commonly known as fenugreek, this East Indian herb contains saponin compounds with anabolic properties. It also has cancer suppressing and glucose and insulin regulating properties.

I am not opposed to using metformin, and in severe cases of IR (especially if cancer is involved) I recommend it to stabilize a patient. But I usually recommend only one per day, not 2 to 4 a day, which is the amount commonly prescribed. When the patient is stabilized, I wean them off of the medication because of the downsides. Metformin is a potent inducer of lactic acidosis, and can interfere with utilization of B-12 and folate. There are benefits and drawbacks to most pharmaceuticals. Our goal is to maximize the benefits while minimizing potential negative side effects, and this is where the wholistic approach of the Eclectic Triphasic Medical System excels.

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