Botanicals In Menopause: Clinical Essentials

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Labrix Core Training: Portland
Disclosures

• Scientific Advisory Boards
  - Gaia Herbs Professional Solutions
  - Integrative Therapeutics
  - Nordic Naturals
  - Natural Health International
  - Nutritional Fundamentals for Health
  - Pharmaca Integrative Pharmacies

• Director of Education and Research; Co-owner
  - Vitanica
Fundamental Goals of Intervention

• Symptom relief with minimal impact on increasing risks of other diseases
• Disease prevention and treatment
• Opportunity for changes in life
• Education about health
Categories of Treatment Intervention

- Diet, Exercise, stress management
- Nutritional supplements
- Botanical medicines
- Compounded Bio-Identical hormones
- Pharmaceutical BHRT
- Non bio-identical conventional hormones
- Additional pharmaceuticals
Black Cohosh

(Cimicifuga racemosa)
Clinical Research

Over 125 published scientific papers and presentations on the efficacy and safety of standardized black cohosh extract

In perimenopause/menopause
A 2012 Cochrane review of 16 randomized controlled trials (RCTs) of peri-menopausal or postmenopausal women (n=2,207) using oral mono preparations of black cohosh extract at a median daily dose of 40mg for a mean duration of 23 weeks were reviewed. Comparator interventions included placebo, hormone therapy, red clover, and fluoxetine.

• Authors concluded that there is “currently insufficient evidence to support the use of black cohosh for menopausal symptoms.
• However, there is adequate justification for conducting further studies in this area.”
Black cohosh Meta-analysis 2010

• A systematic review of three data bases (PubMed, Embase and Cochrane library) was conducted to identify relevant literature.

• 288 English language citations screened, 9 RPCT were included.

• 6 demonstrated a significant improvement in the black cohosh group compared with the placebo group. Using date from 7 trials, they calculated a combined estimate for the change in menopausal vasomotor symptoms. preparations containing black cohosh improved these symptoms overall by 26%

Alternative Therapies 2010.16(1):36-44
Black Cohosh 2013

- RDBPCT; n=84 postmenopausal women.
- Black cohosh tablet per day (n=42) or one placebo (n=42) per day for 8 weeks.
- Each tablet contains 6.5 mg of dried extract of black cohosh root, equal to 0.12 to 0.18 mg of 27 deoxyectoine.
- Green climacteric vasomotor scale for both hot flashes and night sweats.
- Results: considerable decline in vasomotor symptom severity and number of hot flashes after 4 weeks and 8 weeks in particular, compared with placebo.

J Caring Sciences 2013;2(2):105-113
Black cohosh- Sleep in Postmenopausal women

- N=48 postmenopausal women aged 45 – 60 years with sleep disturbance
- Results: 76 women were interviewed, of whom 42 women completed the whole trial.
- Black cohosh treatment led to significant polysomnographic changes, including increased sleep efficiency and decreased wake after sleep onset (WASO) duration, and tended to improve PSQI with a medium effect size.
- 15.8% of WASO duration was reduced in the black cohosh group. Vasomotor and physical domains of life quality were improved compared with placebo.
- Conclusions: In early postmenopausal women with a major sleep complaint, black cohosh effectively improved sleep and might be a safe measure in managing menopausal sleep disturbance.
Black Cohosh/St John’s Wort

• Prospective, controlled open-label observational study
• N=6141 women at 1287 outpatient gyn clinics in Germany
• Dose: Remifemin 20 mg tablet bid; Remifemin plus: 3.75 mg iCR extract and 70 mg SJW (frin 245 mg to 350 mg)
• Results: Combination product > black cohosh only for mood symptoms

Briese V, et al. Maturitas 2007;57:405-414
SJW/Black Cohosh

- Peri or postmenopausal Korean women
- Mean Kupperman index scores at 4 and 12 weeks were significantly lower in the treatment group (**P < 0.002**).
- Average decrease in the Kupperman Index was 20 points in the treatment group and only 8.2 points in the placebo group.
- Vaginal dryness and low libido did not improve.
- Average hot flash scores were significantly lower in the black cohosh/St. John’s wort group.

Black Cohosh/SJW 2007

- Herbal/nutrient supplements for mood/anxiety in menopausal women
- Review of clinical trials related to the use of botanicals for depression, anxiety, and mood disturbances. Five of seven trials of SJW for mild to moderate depression showed a significant improvement.
- The one randomized, controlled trial of ginseng in postmenopausal women reported improvements in mood and anxiety.
- All three RCT of ginkgo found no effect on depression.
- In four of eight controlled trials, kava significantly reduced anxiety. Black cohosh significantly reduced depression and anxiety in all studies reviewed.

- Conclusion: SJW and black cohosh were the most useful in alleviating mood and anxiety during menopause.

Menopause 2007; 14(3): 541-549
Safety Studies

Findings:

• Uncontrolled reports, postmarketing surveillance, and human clinical trials of more than 2,800 patients demonstrate a low incidence of adverse events (5.4%).

• Of the reported adverse events, 97% were minor and did not result in discontinuation of therapy, and the only severe events were not attributed to Cimicifuga treatment.

• Confirms the safety of specific Cimicifuga extracts, particularly isopropanolic extract, for use in women experiencing menopausal symptoms.

Black Cohosh
Breast Cancer Safety
Black Cohosh

• Summary:
  - does not have estrogenic action
  - Does not contain phytoestrogens
  - Safe in breast cancer patients
  - Mechanism unclear
  - Most current thinking: acts as an SSRI
  - Good safety profile
New NIH Expert Panel 2008

- Analysis of case reports, adverse event reports, animal data, historical use, regulatory status.
- 30 nonduplicate reports
- All reports of liver damage were assigned possible causality, none were probably or certain causality. Clinical and animal data did not reveal unfavorable information
- NEW: should be labeled to include a cautionary statement
Black Cohosh and Hepatotoxicity

• Nine cases of women with suspected hepatotoxicity due to black cohosh were evaluated to determine if there truly was a causal relationship.

• Only one patient with symptomatic cholelithiasis and fatty liver was suspected of showing some degree of a causal relationship for black cohosh. However, there were uncertainties including no data concerning the daily dose, brand name of the black cohosh, or whether it was in combination with some other herbal product/s. In addition, there may have been some preexisting symptomatic evidence of cholelithiasis.

• A review of these nine cases of initially assumed black cohosh hepatotoxicity revealed a lack of association, with the possible causal association in only one case, for symptomatic cholelithiasis.

SJW in Menopause

- One non placebo controlled, drug monitoring study was conducted in women with menopause symptoms and found that 900 mg of St. Johns wort for 12 weeks significantly improved psychological and psychosomatic symptoms as well as a feeling of sexual well-being.

SJW and Menopause

• 50 women received 20 drops three times daily of St. John’s wort extract (Hyperin) that contained hypericin 0.2 mg/mL and 50 women received a placebo of distilled water. The study duration was two months.

• In women taking St. John’s wort, the frequency began to decline during the 1st and 2nd months, but showed more improvement during the 2nd month. Women who used St. John’s wort showed more improvement in hot flash frequency than placebo. The decline in duration of hot flashes was statistically significant at week 8 and the decline was much more evident in the St. John’s wort group. The severity of hot flashes was relieved in the St. John’s wort group during the 2 months of treatment and was more significant in the second month. Women in the placebo group did not show any significant decrease in severity of hot flashes during the 1st month, but they did have some improvement during the 2nd month, but not as great as those women in the St. John’s wort group.

SJW and perimenopause

• N=47 symptomatic perimenopausal women aged 40 to 65 with three or more hot flashes per day.

• Tx: St. John's wort extract (900 mg three times per day) or placebo. The women used a daily diary to record hot flash severity and frequency during the week before the study group selection process and again for a week before the end of the three month follow-up. The Menopause-Specific Quality of Life questionnaire was also used.

• RESULTS: After 12 weeks of treatment, a nonsignificant difference in favor of the St. John's wort group was observed in the daily hot flash frequency and the hot flash score. After 3 months of treatment, women in the St. John's wort group reported significantly better quality of life scores, and significantly fewer sleep problems compared to placebo.

Menopause. 2009 Mar-Apr;16(2):307-14
Maca phenotypes

- Maca is a cruciferous root growing exclusively in the central Peruvian Andes at 12-14,000 ft.
- Maca - *Lepidium peruvianum* is one of 175 lepidium species
- Within Maca - *Lepidium peruvianum* there are 13 different phenotypes

- Each phenotype is a different color, DNA, analytical profile and even in some cases elicits different physiological effects.
## Maca GO vs Other Maca Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Femmenessence</th>
<th>Raw Maca</th>
<th>Gelatinized Maca</th>
<th>Maca Extracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotype or Color Maca Selection</td>
<td>Specific phenotype combinations for women at each stage of life</td>
<td>Random combination for energy and men’s fertility</td>
<td>Random combination for energy and men’s fertility</td>
<td>For sperm production and energy</td>
</tr>
<tr>
<td>Water Solubility and Bioavailability</td>
<td>99%</td>
<td>68%</td>
<td>87%-97%</td>
<td>?</td>
</tr>
<tr>
<td>Concentration</td>
<td>Full spectrum of active ingredients. Concentrated levels up to 10 times higher than raw maca.</td>
<td>No</td>
<td>Higher than raw but less than extracts - full spectrum</td>
<td>4-10 times one specific active ingredient - generally sub section of glucosinolates</td>
</tr>
<tr>
<td>Peri and Post Menopausal Clinical Trial Success Rates</td>
<td>84%</td>
<td>60%</td>
<td>60%</td>
<td>NA – none designed for women yet</td>
</tr>
<tr>
<td>Reduction in Symptoms</td>
<td>Highly statistically significant*</td>
<td>Statistically significant</td>
<td>Statistically significant</td>
<td>NA</td>
</tr>
<tr>
<td>Impact on Hormones</td>
<td>Increase in estradiol, progesterone, supports adrenals, thyroid, reductions in cortisol and FSH*</td>
<td>None</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Impact on Bone Density</td>
<td>Increased bone density*</td>
<td>None</td>
<td>None</td>
<td>NA</td>
</tr>
<tr>
<td>Impact on Lipids &amp; Cardiovascular Health</td>
<td>Increase in HDL, reduction in LDL, triglycerides, body weight and rebalance blood sugar*</td>
<td>None</td>
<td>None</td>
<td>NA</td>
</tr>
</tbody>
</table>

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure or prevent any disease.
Maca-GO and Postmenopausal women

2 months:
- Non significant decrease in FSH and increase in E2
- Significant increase in LH and increase in Progesterone
- No change in estradiol
Symptom relief: nervous, reduced day VMI, increased libido

8 months:
- Decreased FSH
- Increase LH
- Increased Progesterone
- Increased Estradiol

Int J Biomedical Science 2005;1(1)
Maca-GO and Perimenopause

MACA-GO results:
- reduction in body weight, blood pressure
- increased in HDL, iron
- 74%-87% of women had a reduction in
- reduced VMI, insomnia, nervousness, depression and heart palpitations

dose: 1 gm bid
Maca: effects on anxiety, depression, sexual dysfunction

- RCT: 14 postmenopausal women; 3.5 gm of powdered Maca (Lepidium meyenii) vs placebo for 6 weeks.
- The Greene Climacteric Scale revealed a significant reduction in psychological symptoms including anxiety, depression and sexual dysfunction after Maca consumption compared with baseline and placebo.
- The effects in this study appear to be independent of any measurable influence on sex hormones or SHBG and presumably therefore independent of any action related to the activity of beta-sitosterol, found in Maca.
- It is thought that the flavonoids in Maca inhibit monoamine oxidase activity.

Lepidium (Maca) and sexual dysfunction

• A systematic review was done to assess the clinical evidence for or against the efficacy of Maca for sexual dysfunction.

• Two of these trials suggested a positive effect of Maca on sexual dysfunction or libido in menopausal women or adult. One other RCT did not show effect of Maca in cyclists. The fourth study assessed the effects of Maca in men with erectile dysfunction and did show significant effects.

• While the evidence is limited, there does appear to be some effectiveness of maca in improving sexual function.

Maca and SSRI induced Sexual Dysfunction

• 1.5 g/day vs 3.0 g/day
• N=20 with SSRI induced sexual dysfunction (17 women and 3 men)
• 3.0 g/day had a significant improvement in ASEX and the MGH-SFQ scores
• 1.5 gm/day= no change
• Libido improved significantly but not by dosing
Maca Root and SSRI induced sexual dysfunction in women

N=45 pre and postmenopausal women; tx=1500 mg bid vs placebo

• The mean change in total ASEX and MGHSFQ for maca vs placebo was not statistically significant overall, whether premenopausal or postmenopausal women.

• The remission rates however were higher for the maca group than the placebo group for an ASEX total score of 10 or less (maca = 9.5% and placebo = 4.8%) achieving a MGHSFQ score of 12 or less (30% vs 20%). The higher remission rates occurred in postmenopausal women and the premenopausal women had no significant difference in remission rates between treatment groups on both of the sexual function questionnaires.

• It was only the postmenopausal women who were taking the maca who had an improvement in orgasm compared with placebo and only premenopausal women taking the maca who had an improvement in arousal disorder compared with placebo.

• There was also a significant correlation between the testosterone levels and sexual functioning at the endpoint, on the ASEX questionnaire in women in the maca group, with a trend toward significant on the MGHSFQ in the maca group. No other significant differences were seen in the other hormones that were tested, including estrogen.
Valerian

• Postmenopausal women - aged 50 to 60 years

• 530 mg of concentrated valerian extract twice per day vs. placebo twice per day, for 4 weeks.

• Overall, 30% of the women taking valerian and 4% taking placebo reported an improvement in their sleep quality.
Valerian and Hot Flashes

- DBCT; n= 76 menopausal women; chief symptom of hot flashes; (68 women completed study)
- 225 mg valerian capsule tid vs placebo, for 8 weeks.
- Symptom diary
- At week 4 and week 8 post-treatment:
  - valerian group = significantly less severe hot flashes (9.82 ± 1.87 pre-treatment and 5.23 ± 1.52. 8 weeks compared with the placebo group (9.96 ± 1.84 pre-treatment and 9.86 ± 1.95 after 8 weeks). No significant change in severity in P
  - valerian group = significantly fewer hot flashes (7.91 ± 30.0 and 4.83 ± 0.52 after 8 weeks vs placebo pre-treatment 7.73 ± 2.0 and after 8 weeks 7.75 ± 0.32. No significant change in P group

Siberian Rhubarb (Rheum rhaponticum)

- RCT; 109 perimenopausal women with climacteric complaints.
- Tx: st. ext. ERr 731, from the roots of Rehum rhaponticum, also known as Sibiric Rhubarb. One tablet (250 mg), containing 4 mg of dry extract was given to women (n=54) or placebo given to the other group (n=55) for 12 weeks.

- Menopause Rating Scale II (MRS II). After 12 weeks, the MRS II total score and each MRS II symptom significantly decreased in the rhubarb extract group compared to the placebo group. (P < 0.0001). The overall menopause QOL score was also significantly better in the treatment group compared with placebo. No adverse events were observed.
Siberian Rhubarb (Rheum rhaponticum)

• A standardized extract, ERr 731
• Observational study: three hundred sixty-three menopausal women with menopausal symptoms were given 1 tablet of ERr 731, containing 4 mg, for 6 months.
• The Menopause Rating Scale; 252 women completed the study.
• Significant decrease of the total MRS score from an average of 14.7 points at baseline to 6.9 points at the end of the six months (P < .0001). This was a decrease of 7.8 points.
• Most pronounced improvement, in first 3 months of treatment/most symptomatic at baseline = > 18 points. T
• Hot flashes, irritability, sleep problems, depressive mood, and physical/mental exhaustion.

Siberian Rhubarb (Rheum rhaponticum)

- RCT; n=109 perimenopausal women
- ERr 731; 1 tablet, 4 mg dry extract x 12 wks
- HAMA: from 27.5 points to 9.4 points
- MRS: anxiety decreased 2.2 points in tx group vs 0.3 in placebo
- Wellbeing: improved in tx group but not placebo
- WHQ: 22 point increase in tx group and decreased 7.6 points in placebo
Combination Formula

• Burdock root, Wild yam
  Motherwort, Dong quai, Licorice root

100% had reduction in symptoms
(67% showed reduction with placebo)
71% had reduction in total number of sx.
(17% showed reduction with placebo)

JNM;1997;7(1)
Additional Botanical Considerations

• Hot flashes: Ginseng, Valerian, Red clover, Pinebark, Kava, Kudzu, Hops, Grape seed extract
• Fatigue: Rhodiola, Ginseng, Maca
• DUB: Vitex, Maca
• Cognition: Bacopa, Rhodiola, Vinpocetine, Lion’s mane
• Depression: SJW, Rhodiola, Lavender
• Anxiety: Lavender, Kava
• Heart palpitations: Lemon balm, motherwort
Hot Flashes

- **Mild to Moderate; one or combination**
  - Black cohosh extract 40-80 mg bid
  - Combination products
  - Maca 1,000mg bid
  - Pine bark 100 mg bid
  - Sibiric Rhubarb 250 mg/day
- **Moderate-Severe**
  Consider botanical/nutraceutical + lower dose of HT
  ex/ Black cohosh 40 mg 1-2x/day + E2 0.5 mg/P100 mg
- **Severe**
  - Hormone options
Anxiety + Hot Flashes

Mild to Moderate

• Kava, 70 mg kavalactones tid
or
• Maca - GO+ Kava 70 mg kavalactones tid
or
• Black Cohosh + Kava 70 mg kavalactones tid

Or (consider Black cohosh or Maca-GO or W Phase II + GABA, L-theanine, passionflower, lavender essential oil)
Depression and Hot flashes

Mild - Moderate

1. Black cohosh 20-40 mg bid +++ SJW .3% hypericin 300 mg bid-tid

2. Maca 1 gm bid +++ SJW .3% hypericin 300 mg bid-tid
Perimenopause/PMS

Hot flashes/mood changes + cyclic classic PMS symptoms

• Black cohosh/SJW
  +++

• PMS combo formula
  must haves: SJW, vitex, B6, Ca
Dr. Tori Hudson

• Women’s Encyclopedia of Natural Medicine 2008, second edition
• www.drtorihudson.com
• www.awomanstime.com
• www.instituteofwomenshealth.com
• www.naturopathicresidency.org

THANK YOU!