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REVIEW ARTICLE

Botanical and dietary supplements for mood and anxiety in menopausal women

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Abstract

Objective: This paper reviews the commonly used botanicals for treatment of mood and anxiety disorders in perimenopausal and postmenopausal women and presents information on their safety and efficacy.

Design: The MEDLINE and EMBASE databases were searched for clinical trials related to the use of botanicals for depression, anxiety, and mood disturbances. Papers were excluded if they were in a language other than English, did not include midlife women as study participants, or did not report on changes in mood, depression, or anxiety.

Results: Five of seven trials of St. John's wort 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 randomized, controlled trials 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.

Conclusions: St. John's wort and black cohosh appear to be the most useful in alleviating mood and anxiety changes during menopause. Ginseng may be effective, but more research needs to be done. Kava holds promise for decreasing anxiety in peri- and postmenopausal women; however, women should be careful in the amount and duration of use. Finally, ginkgo and valerian do not appear to be useful in reducing depression or anxiety in this population.

Key Words: Botanical and dietary supplements – Menopause – Depression – Anxiety – Mood.

Although vasomotor symptoms are generally reported as the most common complaint of menopause, many women are bothered by a number of other problems during the menopausal transition. Results of the Study of Women Across the Nation (SWAN) suggest that there are two predominant factors reported among peri- and postmenopausal women: (1) menopausal symptoms, including hot flashes and night sweats, and (2) psychological and psychosomatic symptoms.[1,2] Two of the most common psychological complaints are mood changes: generally increased sadness or depression and increased anxiety.[3,4] Very often these complaints are reported jointly. Both Hispanic and African American women report depressive symptoms more often than white or Asian women.[5]

Anxiety has been strongly associated with hot flashes, especially in the early menopausal transition. In a community-based study of white and African American women, women with high anxiety scores were nearly five times more likely to report vasomotor symptoms than women with normal anxiety scores. In this cohort of women, an anxious state preceded the hot flashes, although there were no differences by racial group.[6]

Epidemiologic data suggest that the risk of depression is greatest when hormonal levels fluctuate, such as during pregnancy, postpartum, and the menopausal transition.[2,7,8] Recent longitudinal research examining predictors of depressed mood in midlife women found that women in the menopausal transition are up to four times more likely to report depressive symptoms than premenopausal women.[9-11] A history of depression was the strongest predictor of current depression. However, new onset of depression was also more likely to occur when a woman was peri- or postmenopausal,

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although perimenopausal depression was more likely to decrease in the postmenopausal period.[9,12] African American women were twice as likely as white women to report depressive symptoms after controlling for other confounders.[9]

As with vasomotor complaints during perimenopause, women are increasingly turning to botanical and dietary supplements (BDSs) to treat psychological and somatic concerns. The use of BDSs among peri- and postmenopausal women has increased in recent years in the United States, with the largest increase in the use of natural hormonal agents.[13-15] Most women report using BDSs because they find alternatives to traditional medicine more congruent with their values, beliefs, and lifestyles.[16,17] Although women report using these therapies to treat symptoms or diseases, very few women can verbalize the health benefits of these supplements. Two thirds of women do not tell their clinicians about use of these products, nor do healthcare providers ask about their use of alternative therapies.[18] Given issues of variability of content, standardization, dose, and purity of botanicals, it is important for health consumers and clinicians to be knowledgeable about the risks and benefits of such treatments.[19] This article reviews the commonly used BDSs for treatment of mood and anxiety disorders for peri- and postmenopausal women and examines the data for safety and efficacy.

METHODS

The MEDLINE and EMBASE databases were searched for clinical trials regarding the use of botanicals for depression, anxiety, and mood disturbances for midlife women. The years searched were 1966 to April 2006. Search terms included women, middle aged, midlife, perimenopause, mood, depression, anxiety, plant extracts, botanicals, dietary supplements, ginkgo, ginseng, black cohosh, St. John's wort (SJW), and kava. Bibliographies of all relevant articles were searched for related references. The Commission E reports and the German Regulatory Health Authority were also examined for botanicals commonly used to treat these conditions. For purposes of this review, only those botanicals tested in clinical trials for efficacy and safety that incorporated midlife women as part of their sample were included.

Articles reviewed for this report were clinical trials (randomized, placebo-controlled trials [RCTs], randomized comparison group trials, or observational studies). The exclusion criteria for articles were (1) language other than English, (2) no midlife women (44-65 y) involved as study participants (men and younger women could be included, but midlife women had to have participated in the study to some extent), and (3) changes in mood, depression, or anxiety were not reported. Studies were reviewed by the authors for their fit with these guidelines.

The studies reviewed used several measures of anxiety and depression as outcome indicators. Most commonly, the Hamilton Depression Rating Scale was used for depression and the Hamilton Anxiety Rating Scale was used for anxiety. The outcome measure used in each study is listed in the tables.

RESULTS

SJW (*Hypericum perforatum)*

SJW is one of the most heavily studied and commonly used botanicals for treatment of mild to moderate depression in the general population. A review of the clinical trials conducted in both men and women published in the late 1990s found that in 37 of 39 trials, the herb was superior to placebo or equivalent to antidepressant medications in improving depression (61% to 75% improvement in mild to moderate depression). This review also found that users of SJW experienced fewer side effects compared to those using antidepressants.[20] Nine years later, the same authors published a meta-analysis that reported that patients with mild to moderate depression had significant beneficial effects from SJW, similar to those of standard antidepressants, although those with major depression showed only minor improvement in symptoms.[21]

Despite all the interest and research on SJW in the past few years, its mechanism of action has not been completely determined. Studies have shown that it inhibits uptake of serotonin, dopamine, and norepinephrine in brain synapses. In other studies, SJW extract was found to bind to adenosine, γ-aminobutyric acid (GABA)A, GABA(B), and glutamate receptors. Finally, in vivo studies in rats have shown a down-regulation of β-adrenergic receptors and an up-regulation of serotonin receptors in the frontal cortex.[22]

Recent trials of SJW for depression in adults are outlined in Table 1.[23-33] Most of these trials were conducted in individuals with mild to moderate depression, although a few studies tested the effects of SJW on those with severe depression. Most studies were not limited to menopausal women but included midlife women as participants. Five of seven trials showed a significant improvement in depressive symptoms for mild to moderate depression compared to placebo,[25-29] and three of these studies demonstrated equivalence to a selective serotonin reuptake inhibitor.[26,28,29] Of the four studies for major depression, three showed no improvement over placebo; however, in two of these trials, the selective serotonin reuptake inhibitor was also ineffective.[30,31] Only one observational study has specifically examined the effect of SJW on psychological complaints during the menopausal transition. This study found that the proportion of women who complained of moderate to severe psychological symptoms decreased from 80% to 20% after 12 weeks of use.[34]

SJW has many known interactions with other pharmaceuticals. It can interact with anticoagulants, cyclosporine, digoxin, and protease inhibitors used for human immunodeficiency virus, specifically decreasing blood concentrations of these drugs.[35] Three published studies of concurrent use of SJW and oral contraceptives reported increased breakthrough bleeding; however, only one of these studies found evidence of follicle growth and increased ovulation.

None of the trials reported unplanned pregnancies as an outcome.[36-38]

Ginseng (*Panax ginseng)*

Ginseng is known as a traditional "tonic" herb that is used to cope with stress and boost immunity; the German Commission E lists its uses as "a tonic for invigoration and fortification in times of fatigue and debility and for declining capacity for work and concentration."[39] Ginsenosides, a type of triterpene glycoside or saponin, are the active compounds in ginseng. They have been demonstrated to have neuroprotective effects in vitro and in vivo.[40] The effects of ginseng seem to be due to its action on the hypothalamus-pituitary-adrenal axis and the immune system.[41]

Ginseng has been studied for peri- and postmenopausal symptoms but has not been found to have estrogenic effects or to improve vasomotor symptoms. Ginseng has been shown to improve somatic complaints such as fatigue, insomnia, and depression and to have a favorable effect on depression and general well-being scales compared with placebo.[42,43] Table 2 outlines the RCTs of ginseng for anxiety and mood.[42,44-47] There have been only two studies of ginseng in menopausal women, and both found improvement in mood and anxiety. One of these studies was observational and did not include a placebo or other comparison group.[48]

Ginseng has an overall positive safety profile with few reported side effects. A recent review paper of ginseng suggests that it may interact with caffeine to cause hypertension, may lower blood alcohol concentrations, decrease the effectiveness of warfarin (Coumadin), and may cause hypoglycemic activity. Because of these theoretical interactions,

TABLE 1. *Studies of botanicals for anxiety and mood (St. John's wort)*

Reference	Study type/ outcome measure	Drug and dose	Participant information	Duration	Results
Studies of mild to moderate depression (all study participants had mild to moderate depression)					
Moreno et al, 2006[23]	RCT/HAM-D	SJW 900 mg/d Fluoxetine 20 mg/d	66 adults; mean age: 40.5 y; 83% female	8 wk	SJW and fluoxetine did not significantly reduce mild to moderate depression compared to placebo
Bjerkenstedt et al, 2005[24]	RCT/HAM-D	SJW 900 mg/d Fluoxetine 20 mg/d	163 adults; mean age: 51.3 y; 80.6% female	4 wk	SJW and fluoxetine did not significantly reduce mild to moderate depression compared to placebo; SJW was better tolerated than fluoxetine
Randlov et al, 2006[25]	RCT/HAM-D, BDI	SJW 270-mg tablet taken TID either 0.12% hypericine or 0.18% hypericine	150 adults; median age: 50.9 y; 75% female	6 wk	SJW groups (0.12% and 0.18% hypericine) showed significant reduction in minor depression compared to placebo in nondysthymic patients only
Gastpar et al, 2005[26]	Randomized comparison group trial[a]/ HAM-D	SJW 612 mg/d Sertraline 50 mg/d	200 adults; mean age: 48.9 y; 74.7% female	12 wk	SJW and sertraline reduced moderate depression; SJW was equivalent to sertraline
Uebelhack et al, 2004[27]	RCT/HAM-D	SJW 900 mg/d	140 adults; mean age: 44.9 y; 67% female	6 wk	SJW significantly reduced moderate depression compared to placebo
Behnke et al, 2002[28]	Randomized comparison group trial[a]/ HAM-D	SJW 300 mg/d Fluoxetine 40 mg/d	70 adults; mean age: 49.7 y; 67% female	6 wk	SJW and fluoxetine reduced mild to moderate depression; SJW was equivalent to fluoxetine
Schrader, 2000[29]	Randomized comparison group trial[a]/ HAM-D	SJW 500 mg/d Fluoxetine 20 mg/d	240 adults; mean age: 46.5 y; 65% female	6 wk	SJW and fluoxetine reduced mild to moderate depression; SJW was equivalent to fluoxetine
Studies of major depression (all study participants had moderate to severe depression)					
Fava et al, 2005[30]	RCT/HAM-D	SJW 900 mg/d Fluoxetine 20 mg/d	135 adults; mean age: 37.3 y; 57% female	12 wk	SJW and fluoxetine did not significantly reduce major depression compared to placebo
Hypericum Depression Trial Study Group, 2002[31]	RCT/HAM-D	SJW 900-1500 mg/d Sertraline 50-100 mg/d	340 adults; mean age: 42.3 y; 65.9% female	8 wk	SJW and sertraline did not significantly reduce major depression compared to placebo
Shelton et al, 2001[32]	RCT/HAM-D	SJW 900 mg/d	200 adults; mean age: 42.4 y; 67% female	8 wk	SJW did not significantly reduce major depression compared to placebo
Szegedi et al, 2005[33]	Randomized comparison group trial[a]/ HAM-D	SJW 900 mg/d Paroxetine 20 mg/d Initial nonresponder dose increased after 2 wk to SJW 1,800 mg/d, paroxetine 40 mg/d	244 adults; mean age: 47.3 y; 69% female	6 wk	SJW and paroxetine reduced moderate to severe depression; SJW equivalent to paroxetine

RCT, randomized, placebo-controlled trial; SJW, St. John's wort; HAM-D, Hamilton Depression Rating Scale; BDI, Beck Depression Inventory.
[a]Randomized comparison group trial = no placebo-only group; all groups take an active compound.

ginseng is not recommended for use in people with high blood pressure or diabetes.[41]

Ginkgo (*Ginkgo biloba)*

Ginkgo biloba is among the most popular and widely available herbal supplements promoted for cognitive enhancement and has mainly been studied for memory and cognition.[49-51] There have been 40 clinical trials conducted examining the effect of ginkgo on cognition, particular difficulty concentrating and memory. Eight were of good quality, seven showed a positive effect, and one positive trial included women with dementia.[52]

Ginkgo is thought to have a positive effect on the vascular system by increasing blood flow to the brain, increasing uptake of glucose by brain cells, and improving transmission of nerve signals.[39,53] It has been approved by the German Commission E for cerebral insufficiency, vertigo, tinnitus, and peripheral vascular disease.[39] Ginkgo is also believed to function as a neuroprotective agent, an antioxidant, a free-radical scavenger, and a membrane stabilizer.[54]

Although one study conducted in young adults found improvement in self-reported mood with ginkgo alone as well as a ginkgo/ginseng combination,[55] the three RCTs of ginkgo (Table 2) for mood in older adults found no significant improvement compared to placebo.[44-46] In a 6-month observational study of older adults, ginkgo users showed significant improvements in mood compared to those not using any treatment, but there was no placebo group.[56] One study in postmenopausal women using a combination ginkgo/ginseng therapy found no effects on mood or anxiety compared to placebo.[47] However, a trial conducted in Germany in older adults showed improvement in resistant depression using ginkgo to augment conventional antidepressants.[57]

Ginkgo has an overall positive safety profile. Reported side effects are rare but include headache and gastrointestinal upset. It has been suggested that ginkgo may potentiate anticoagulants or increase bleeding time, although millions of people take ginkgo regularly, and there have been only two reported cases of bleeding problems.[58]

Kava (*Piper methysticum)*

Kava is a South Pacific herb historically used for both medicinal and social purposes and has been suggested as a treatment for anxiety.[59] The active compounds in kava are thought to be substances known as kavapyrones that have an effect on the limbic system that regulates mood. Studies of kavapyrones have shown that they bind to GABA receptors, inhibit norepinephrine uptake, antagonize dopamine, inhibit monoamine oxidase B, and decrease glutamate release. They do not affect opioid receptors.[60]

Of eight trials of kava for treatment of anxiety (Table 3),[61-68] including two performed in peri- or postmenopausal women, four found significant reductions in anxiety compared to placebo. In one of the studies that found no effect of kava, the pharmaceutical treatments for anxiety were also ineffective. Both studies of peri- or postmenopausal women found that kava reduced anxiety, although there was no placebo group in either trial.

There are serious safety concerns with kava related to its potential hepatotoxicity. The German health authorities have reported 82 case reports of kava use and liver damage. However, all these reports do not represent unique cases; rather, many were duplicate or triplicate accounts. Of the 84 total reports, 20 were found to be unrelated to kava, 21 were most likely connected to other medications taken concurrently with kava, and 31 had insufficient evidence to link kava use to the adverse outcome.[69] Despite the inconclusive evidence, individuals using kava should exercise extreme caution. It is not advised for people taking hepatotoxic medications, consuming excess alcohol, or with

TABLE 2. *Studies of botanicals for anxiety and mood (ginseng and ginkgo)*

Reference	Study type/ outcome measure	Drug and dose	Participant information	Duration	Results
Ginseng only (postmenopausal women only as study participants)					
Wiklund et al, 1999[42]	RCT/PGWB	Ginseng 200 mg/d	384 postmenopausal women; mean age: 53.5 y	16 wk	Ginseng group showed significant improvement over placebo in depression, well-being, and general health
Ginkgo only					
Burns et al, 2006[44]	RCT/POMS	Ginkgo 120 mg/d	93 older adults; ages 55-79 y; 46% female	12 wk	No significant effects of ginkgo on mood compared to placebo
Elsabagh et al, 2005[45]	RCT/HAM-D	Ginkgo 120 mg/d	87 postmenopausal women; ages: 51-67 y	6 wk	No significant effects of ginkgo on mood compared to placebo
Hartley et al, 2003[46]	RCT/visual analogue rating scales	Ginkgo 120 mg/d	31 postmenopausal women; ages: 53-65 y	7 d	No significant effects of ginkgo on mood compared to placebo
Ginseng and ginkgo combination					
Hartley et al, 2004[47]	RCT/visual analogue rating scales	Gingko and ginseng combination: ginkgo 120 mg/d and ginseng 200 mg/d	57 postmenopausal women; ages: 51-66 y	12 wk	No significant effects of ginkgo/ginseng combination on mood and somatic anxiety compared to placebo

RCT, randomized, placebo-controlled trial; PGWB, Psychological General Well-Being Index; POMS, Profile of Mood States; HAM-D, Hamilton Depression Rating Scale.

prior liver conditions. Although the sale of kava has been banned in Canada, Australia, and several European countries, it is still available in the United States.

Other botanicals

Black cohosh has a long history of use, primarily by American Indians and Europeans for a variety of "female complaints," including menstrual problems and childbirth. It is also commonly used for relief of vasomotor symptoms related to menopause, and the vast majority of clinical trials have shown it to be effective for the relief of hot flashes.[70-72] Black cohosh is approved by the German Health Authorities for relief of menopausal symptoms as well as premenstrual syndrome and dysmenorrhea.[39] Recent data from the University of Illinois at Chicago Center for Botanical Dietary Supplements Research in Women's Health have demonstrated that black cohosh does not have an estrogenic mechanism of action as previously thought but acts on serotonin receptors and may relieve hot flashes through a serotonergic effect.[73,74] It is the same serotonergic effect in black cohosh that may improve mood and decrease depression.

There have been four clinical studies of black cohosh for mood or anxiety,[71,75-77] three using black cohosh alone and one using a black cohosh-SJW combination (Table 4). All four studies found that symptoms of anxiety and depression significantly decreased over the treatment period compared to placebo, and one study showed equivalence to hormone therapy.

Black cohosh has a positive safety profile and does not have any documented drug interactions.[78] Recently, there have been several case reports of liver failure in women using black cohosh, although the contribution of black cohosh to liver failure in these cases remain unclear.[79-81] In fact, a National Institutes of Health scientific panel recently reviewed safety data related to these cases as well as general use and concluded that at this time there is no known mechanism with biological plausibility that explains any hepatotoxic activity of black cohosh.[82]

Valerian has been used for centuries by Greeks, Romans, Chinese, Europeans, and American Indians for anxiety and unrest. In the 20th century, it was approved by the German Commission E for "states of unrest and nervous sleep disturbances."[39] Valerian extracts have been shown to increase GABA production and increase the amount of GABA available in the synapses between neurons. One in vitro study demonstrated a high affinity of valerian extracts to

TABLE 3. *Studies of botanicals for anxiety and mood (kava)*

Reference	Study type/ outcome measure	Drug and dose	Participant information	Duration	Results
Studies of kava for anxiety (all participants had anxiety disorders)					
Jacobs et al, 2005[61]	RCT, Internet based/STAI	2 treatments and a placebo group: kava extract 300 mg/d; valerian extract 6.4 mg/d	391 adults; mean age: 41.4 y; 79% women	28 d	No significant effects kava on anxiety compared to placebo
Gastpar and Klimm, 2003[62]	RCT/ASI	Kava extract 150 mg/d	141 adults; mean age: 48.5 y; 74% female	4 wk	No significant effects of kava on mood compared to placebo
Boerner et al, 2003[63]	Randomized comparison group trial[a]/ HAM-A	3 groups: kava extract 400 mg/d; buspirone 10 mg/d[b]; opipramol 100 mg/d[b]	129 adults, ages: 26-65 y; 84% female	8 wk	No significant differences between baseline and follow up in anxiety in kava, buspirone, or opipramol groups
Connor and Davidson, 2002[64]	RCT/HAM-A	Kava extract 140 mg/d	38 adults; mean age: 51.7 y; 82% female	4 wk	No significant effects of kava on anxiety compared to placebo
Geier and Kontantinowicz, 2004[65]	RCT/HAM-A	Kava extract 150 mg/d	50 adults; ages: 51-90 y; 39 total women	4 wk	Kava group showed a significant reduction in anxiety compared to placebo
Volz and Kieser, 1997[66]	RCT/HAM-A	Kava extract 210 mg/d	100 adults; mean age: 53.9 y; 73% female	24 wk	Kava significantly reduced anxiety compared to placebo
Studies of kava with postmenopausal women only as study participants					
Cagnacci et al, 2003[67]	Randomized comparison group trial[a]/ STAI	3 groups: calcium 1,000 mg/d; calcium + 100 mg/d kava; calcium + 200 mg/d kava	68 perimenopausal women; mean age: 50.7 y	3 mo	Calcium + kava groups significantly decreased anxiety compared to calcium-only group; depression significantly decreased between baseline and 3 mo in all groups; no significant differences between groups
DeLeo et al, 2001[68]	Randomized comparison group trial[a]/ HAM-A	4 groups: physiological menopause: HT (estrogen and progestin) + kava (100 mg/d), HT (estrogen and progestin) + placebo; surgical menopause: estrogen + kava (100 mg/d), estrogen + placebo	40 postmenopausal women with anxiety; mean age: 55.5 y	6 mo	Anxiety was significantly reduced in all groups between baseline and 6 mo; reduction was greater in groups taking kava compared to hormones only

RCT, randomized, placebo-controlled trial; HT, hormone therapy; STAI, State-Trait Anxiety Inventory; ASI, Anxiety Status Inventory; HAM-A = Hamilton Anxiety Rating Scale.

[a]Randomized comparison group trial = no placebo-only group; all groups take an active compound.

[b]Buspirone and opipramol are pharmaceuticals used to treat anxiety.

TABLE 4. *Studies of botanicals for anxiety and mood (other botanicals)*

Reference	Study type/outcome measure	Drug and dose	Participant information	Duration	Results
Black cohosh or black cohosh combination (postmenopausal women only as participants)					
Uebelhack et al, 2006[75]	RCT/HAM-D	Combination of black cohosh 15 mg/d, SJW 280 mg/d	301 postmenopausal women; mean age: 52.2 y	16 wk	Black cohosh/SJW group showed significant reduction of psychological complaints compared to placebo
Nappi et al, 2005[76]	Randomized comparison group trial/symptom rating test	Black cohosh: 40 mg/d; transdermal estradiol: 25 μg/7 d + 10 mg/d dihydrosterone for last 12 d of treatment	64 postmenopausal women; mean age: 50.7 y	3 mo	Black cohosh and HT significantly decreased symptoms of depression and anxiety; no significant difference between the two treatments
Osmers et al, 2005[71]	RCT/MRS-I	Black cohosh 40 mg/d	304 postmenopausal women; mean age: 54.5 y	12 wk	Black cohosh showed significant improvement in depressed mood, anxiety, and impaired performance compared to placebo
Wuttke et al, 2003[77]	RCT/MRS-I	Black cohosh 40 mg/d; conjugated estrogens 0.6 mg/d	62 postmenopausal women; ages: 40-60 y	3 mo	Black cohosh showed significant improvement in depressed mood, anxiety, and impaired performance compared to placebo
Valerian or valerian combination					
Andreatini et al, 2002[83]	RCT/HAM-A, STAI	Valerian extract 81.3 mg/d; diazepam 6.5 mg/d	36 participants with generalized anxiety disorder; mean age: 41.1 y; 52.7% female	4 wk	Valerian and diazepam did not significantly reduce anxiety compared to placebo
Soy					
Casini et al, 2006[84]	Crossover RCT/ visual analogue scale	60 mg/d isoflavones in tablet form	78 postmenopausal women; mean age: 49 y	6 mo	7 of the 8 visual analogue scales for mood improved significantly after treatment with isoflavones compared to placebo

RCT, randomized, placebo-controlled trial; HAM-D, Hamilton Depression Rating Scale; MRS-I, Menopause Rating Scale I; HAM-A = Hamilton Anxiety Rating Scale; STAI = State-Trait Anxiety Inventory; SJW, St. John's wort; HT, hormone therapy.

serotonin receptors,[60] suggesting that it could activate serotonin receptors in vivo, although this has not been studied.

Two recent studies that included midlife women examined the effect of valerian supplementation on mood and anxiety (Table 4).[83,84] One study examining the effects of valerian, diazepam, and placebo on adults with generalized anxiety disorder found that neither valerian or diazepam, common antianxiety treatments, had any effect beyond that of placebo on the reduction of anxiety.[83] An observational study of more than 2,000 patients with mild to moderate depression found that a valerian/SJW combination decreased symptoms of depression and anxiety over a 6-week period.[85] There have been no reported drug interactions; side effects such as nausea, headache, dizziness, and upset stomach have been reported in less than 10% of participants in RCTs.[86]

A number of studies have suggested that soy isoflavones may help to enhance cognitive performance for midlife women.[84,87,88] A recent crossover RCT that examined the effects of a soy isoflavone tablet on cognitive performance in postmenopausal women also examined its effect on mood and anxiety. There was a significant improvement in mood with phytoestrogen treatment on two depression inventories and a visual analogue scale. No difference in anxiety was reported.[84]

Some other botanicals recommended for mood and anxiety by the German Commission E, primarily hops and lemon balm, had no clinical trial data in English examining efficacy and safety in midlife women. Many of the herbs recommended by the commission are based on their use in systems of traditional medicine. Hops has been approved by the German Commission E for mood disturbances such as anxiety and restlessness and sleep disturbance.[39] Hops extracts bind to the estrogen receptor in molecular assays, and animal models have shown hops to have an estrogenic effect on the uterus.[89,90] Hops is untested as a treatment for mood and anxiety, and because it does not seem to exert selective estrogen–like selectivity, it may have negative effects on the breast and endometrium of peri- and postmenopausal women.[91] More research on the effect of hops on menopause is needed to determine whether it is safe and effective.

Lemon balm has been traditionally used for centuries for complaints of the "nervous system." It is approved by the German Commission E as a central nervous system sedative for mild sleep disorders and is often used in conjunction with valerian.[39] Lemon balm is also reported to have choline receptor activity in the central nervous system, which may enable it to modulate mood and cognitive performance. Two clinical trials in college-age volunteers to test the efficacy of lemon balm for cognitive performance also showed positive effects on mood and calmness.[92,93] No studies have been conducted in midlife women.

DISCUSSION

This article reviews the safety and efficacy data for botanicals that have been studied for mood and anxiety disorders in peri- and postmenopausal women. No single

botanical or dietary supplement has been shown to have highly reliable effects on depression and anxiety in this population. There is clearly a need for more rigorous clinical trials of botanicals to objectively evaluate their effectiveness and safety.

Of all the botanicals reviewed, there is strong evidence that SJW is the most useful in alleviating depression among both men and women. There has been only one non-placebo-controlled study focused specifically on perimenopausal women for improvement of psychological symptoms, and more RCTs should be conducted to verify the efficacy of SJW in this particular population.

Black cohosh, a heavily studied botanical for relief of hot flashes, also shows very promising evidence of positive mood changes in peri- and postmenopause. As future trials are done on black cohosh for menopausal symptoms, changes in mood, anxiety, and depression should be assessed for a more complete picture of its usefulness. The positive safety profile of black cohosh and its use for decades in Europe make it a good option for women experiencing mood disorders during the menopausal transition. Future clinical trials should also assess the efficacy and safety of the combination of black cohosh and SJW because each individually shows efficacy.

There have been two positive studies on the effects of ginseng for mood and anxiety in peri- and postmenopausal women, suggesting that ginseng might be a useful therapy for mood-related changes. Although there has been increased interest in ginkgo use for mood problems, none of the trials reviewed found it to be effective for improving mood. There have been too few studies on valerian to assess its usefulness for anxiety. Because of the positive safety profile for these herbs, more research should be done in midlife and aging women. Finally, kava does hold promise for decreasing anxiety, especially in peri- and postmenopausal women. However, due to the potential hepatoxicity, its use should be avoided or closely supervised by a healthcare provider with limited duration of use. In future clinical trials, assays of hepatotoxicity should be reported.

CONCLUSIONS

Recent evidence suggests that depression and anxiety are significant complaints during the menopausal transition and many women are turning to botanicals and dietary supplements for relief.[9] Whatever decision women make related to treatment options and use of botanicals for relief of menopausal symptoms, it is critical that healthcare providers discuss these issues with patients to assist them in managing these alternative therapies through an evidence-based approach.

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