Yoga for Back Pain, Cranberry for Cystitis Prevention, Soy Isoflavones for Hot Flashes, Curcumin for Pre-Diabetes, and Breathing Retraining for Asthma

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YOGA IMPROVES CHRONIC LOW BACK PAIN AND ASSOCIATED PSYCHOLOGICAL EFFECTS

Level 1 (likely reliable) evidence

Reference: Complement Ther Med. 2012; 20(3):107–18.

At least 10% of US adults suffer from chronic low back pain (CLBP) lasting over three months.[1] Conventional interventions – consisting primarily of pharmacotherapy, local injections, surgical procedures, and physical therapy (PT) – often fall short. Back pain is the most common reason Americans report using complementary and alternative medicine (CAM) of any kind.[2] Popular CAM choices for CLBP include chiropractic, acupuncture, massage, and the practice of yoga, which researchers investigated in the present study.

Eighty patients admitted to a residential health center in Bangalore, India for CLBP were randomized to one of two seven-day interventions: comprehensive yoga program vs. physical therapy program.[3] Yoga consisted of postures and breathing exercises (*asana* and *pranayama*) specifically designed for patients with CLBP, meditation, along with counseling and lectures based on yoga philosophy. Physical therapy consisted of non-yogic exercise for low back pain plus matched counseling and educational sessions. Comparing yoga to physical therapy, mean scores decreased for pain (visual analog scale) by 49% vs. 17.5%, depression (Beck Depression Inventory) by 47% vs. 19.9%, state (momentary) anxiety by 20.4% vs. 1.2%, and trait (general) anxiety by 15.9% vs. 2.3% ($P \leq .001$ for all comparisons). Spinal mobility was improved by 49.5% in the yoga group vs. 34.6% in the PT group (not statistically significant). There were no worrisome adverse events.

Several outpatient studies on CLBP, all with methodological limitations, have demonstrated the benefits of yoga for pain and/or disability.[4–8] This carefully designed and executed trial was unique in that it involved a short-term, residential intervention and included the added dimension of psychological sequelae. Also unusual was the use of an adequate attention control, which was employed in only one of these other trials.[8] It should be noted that yoga is anything but monolithic, and CLBP patients should be advised to steer clear of certain "westernized" yoga practices (eg, "power" yoga) that may increase the risk of injury. In follow-up studies, researchers may consider the persistence of beneficial effects beyond the study period, degree of incorporation of learned behavior into everyday lifestyle, and generalizability to non-Indian populations.

CRANBERRY PRODUCTS MAY NOT REDUCE RISK OF SYMPTOMATIC URINARY TRACT INFECTION

Level 2 (mid-level) evidence

Reference: Cochrane Database Syst Rev. 2012;(10):CD001321.

Urinary tract infections (UTIs) are a common problem, causing seven million office visits, one million emergency care visits, and 100,000 hospitalizations a year in the United States.[9] Highly susceptible populations include women with recurrent infections, pregnant women, older adults, children, neuropathic bladder patients, and cancer patients undergoing radiation treatment. Cranberry products have been used for decades as a means of preventing UTIs. In vitro, cranberry is capable of inhibiting proanthocyanidin (PAC) A linkages, making it difficult for bacteria, especially *Escherichia coli,* to adhere to the bladder lining. The threshold at which an anti-adherence effect is achieved (known as the PAC equivalent) is 36 mg of cranberry proanthocyanidins. Twice daily dosing is typically recommended.[10]

This Cochrane review evaluated the effectiveness of cranberry products for the prevention of UTI in susceptible populations as defined above. It expands a previous 2008 review from 10 to 24 trials with a total of 4473 participants. All but five trials suffered from at least one inherent limitation including lack of blinding, unclear allocation concealment, or a

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high dropout rate. Eleven studies could not be included in the meta-analyses for lack of relevant data. Of those, two small studies reported significant effects of cranberry compared with placebo. Of the remaining 13 studies with 2462 patients, cranberry products (juice, tablets, or capsules) did not reduce the risk of symptomatic UTI overall as compared to placebo, water, or no treatment (risk ratio [RR] 0.86, 95% confidence interval [CI] 0.71–1.04). Similarly, no significant benefits were found for each susceptible subpopulation. Three studies compared cranberry to antibiotic prophylaxis in women with recurrent UTI or children. These studies used cranberry capsules or syrup instead of juice. The two studies in women ($n = 358$) revealed cranberry product to be equally effective compared to antibiotics in reducing risk of repeat UTI, though with a wide confidence interval (RR 1.31, 95% CI 0.85–2.02). The study in children ($n = 198$) likewise showed cranberry product to be as effective as antibiotics (RR 0.69, 95% CI 0.32–1.51). Two studies with 152 participants compared cranberry to probiotics, one in adults and one in children. These reported a significant reduction in symptomatic UTI with cranberry (RR 0.42, 95% CI 0.24–0.74). Overall, there was a high dropout rate and poor adherence to therapy, most commonly due to poor palatability of the juice.

Wang et al. published a similar meta-analysis in July 2012, again looking at prevention of UTI in susceptible populations based on 13 studies with 1616 participants.[11] In an overall meta-analysis (of 10 trials), the use of cranberry products was not associated with a statistically significant reduction in risk for UTI (RR 0.68, 95% CI 0.47–1.00), though the confidence interval did not exclude a meaningful therapeutic effect. This result became significant with the exclusion of a single high-quality, outlier trial finding no benefit (RR 0.62, 95% CI 0.49–0.8). In subgroup analyses, results favored cranberry products in women with recurrent UTI, females, juice over other products, and more frequent use. Other subgroups showed no significant benefit. The authors noted the same high degree of heterogeneity and bias as in the Cochrane review.

Prior to these reviews, there had been evidence, based mostly on small trials, to support the common perception that cranberry products can help prevent UTI recurrence, particularly in higher risk subpopulations. The addition of larger trials in the Cochrane review now suggests that cranberry's reputation is beginning to get "bogged" down. Part of the problem appears to be compliance, particularly with the long-term palatability of cranberry juice. If future studies are undertaken, researchers would do well to avoid attrition bias by using well-tolerated capsules or tablets standardized to the PAC equivalent.

SOY ISOFLAVONES REDUCE HOT FLASH FREQUENCY AND MAY REDUCE HOT FLASH SEVERITY IN MENOPAUSAL WOMEN

Level 1 (likely reliable) evidence

Reference: Menopause. 2012;19(7):776–790.

Hot flashes are transient vasomotor events that produce symptoms of warmth, sweating, flushing, and occasionally palpitations and anxiety.[12] The most common menopause-related symptom, hot flashes, may last for years and be sufficiently distressing to require medical attention. Until recently, clinicians commonly recommended hormonal replacement therapy (HRT) as treatment. But safety concerns raised by the publication of the Heart and Estrogen/Progestin Replacement Study,[13] the Women's Health Initiative Trial,[14] and the Million Women Study[15] have led to a sharp reduction in the use of HRT for this purpose. Soy isoflavones (genistein and daidzein) with their well-established phytoestrogenic effects have long been considered a promising, if less potent, alternative.[16] Since the first clinical trial almost 20 years ago,[17] more than 50 trials have investigated the effectiveness of soy foods and isoflavone-containing products for hot flashes.[18] While this research has hinted at a clinically relevant benefit, the magnitude of any favorable effects has remained obscure. In the present study,[18] researchers set out to clarify the benefits of soy isoflavone extract (as opposed to soy foods or soy protein) and identical synthesized isoflavones on the frequency and severity of hot flashes in perimenopausal women not taking other estrogenic agents.

In their systematic review of 19 randomized, placebo-controlled trials, isoflavone intake ranged from 30 to 135 mg/day (median 54 mg/day) with treatment durations of six weeks to 12 months.[18] Median hot flash frequency was 8.3 per day. Only five of the trials were rated as high quality. Among 13 trials with 1196 women, mean placebo-subtracted change in hot flash frequency ranged from −3% to −57% (statistically significant in all but three trials). Among nine trials with 988 women, mean placebo-subtracted change in hot flash severity ranged from +9% to −57% (statistically significant in only four trials). Meta-analyses showed a mean placebo-subtracted reduction of 20.6% (95% confidence interval [CI] 12.9%–28.4%) and 26.2% (95% CI 10.2%–42.2%) for hot flash frequency and severity, respectively, but with heterogeneity. Subgroup and meta-regression analyses suggested greater reductions in hot flash frequency with treatment duration >12 weeks vs. ≤ 12 weeks ($P = .004$) and genistein dose >18.8 mg/day vs. ≤ 18.8 mg/day ($P = .065$).

A recent small study found that 70% of women seeking to avoid HRT would be satisfied with a non-hormonal strategy that produced only a 50% reduction in hot flashes.[19] Despite a common perception in the literature that studies examining soy isoflavones for hot flashes have yielded mixed results,[18] this meta-analysis supports their beneficial effect on both symptom frequency and severity. The favorable effect on hot flash frequency was further supported by a dose–response effect for genistein and a greater reduction with longer duration of treatment. Given their pro-estrogenic activity, concerns have been raised regarding the safety of soy isoflavones in women with breast cancer or at increased risk for it. However, there is no convincing clinical evidence that isoflavone exposure from any source adversely affects breast tissue,[20] and recent epidemiologic studies have suggested that it may actually be protective.[21–23]

CURCUMIN EXTRACT MAY REDUCE RISK OF PROGRESSION TO TYPE 2 DIABETES

Level 3 (lacking direct) evidence

Reference: Diabetes Care 2012;35(11): 2121.

Curcumin is a principal constituent of turmeric (*Curcuma longa*), a popular ingredient in Asian cuisine that adds color and flavor to curry. Turmeric has had many

traditional uses in Ayurvedic medicine, an ancient Indian system of healing. More recently, extensive laboratory and animal research has documented its antibacterial, anti-inflammatory, antioxidant, pro-apoptotic, chemopreventive, chemotherapeutic, anti-proliferative, analgesic, wound healing, and anti-diabetic properties.[24–26] Most of these actions, however, have not been adequately testing in clinical trials. In the present study, researchers investigated the capacity of curcumin to delay the onset of diabetes in high-risk patients.[26]

Researchers randomized 237 patients (mean age 57) with pre-diabetes to curcumin extract 750 mg orally vs. placebo twice daily for nine months.[26] All patients met at least one of three pre-diabetes criteria defined by American Diabetes Association (ADA) at baseline: fasting plasma glucose (FPG) between 100 and 124 mg/dL, plasma glucose at two hours after an oral glucose load (oral glucose tolerance test [OGTT]) between 140 and 199 mg/dL, or a glycated hemoglobin (HbA_1C) from 5.7% to 6.4%. The diagnosis of type 2 diabetes was based on the following ADA criteria: FPG level ≥126 mg/dL, OGTT at two hours ≥200 mg/dL, or $HbA_1C \geq 6.5\%$. Eight-five percent of the participants completed the trial, and 99% were included in a modified intention-to-treat analysis. Comparing curcumin extract vs. placebo at nine months, progression to type 2 diabetes occurred in 0% vs. 16.4% ($P < .001$, number needed to treat [NNT] = 6). Other differences occurred for mean values of the following:

- HbA1c 5.6% vs. 6.0% mg/dL ($P < .01$)
- FPG 86.5 mg/dL vs. 108.2 mg/dL ($P < .01$)
- OGTT (at two hours) 123.4 mg/dL vs. 155.1 mg/dL ($P < .01$)
- C-peptide 1.7 ng/mL vs. 2.2 ng/mL ($P < .05$)
- adiponectin 22.46 ng/mL vs. 18.45 ng/mL ($P < .05$).

Higher levels of C-peptide and adiponectin (an anti-inflammatory cytokine) are associated with a reduction in β-cell function[24] and lower risk of type 2 diabetes,[27] respectfully.

In this double-blind placebo-controlled trial, curcumin extract effectively prevented the development of type 2 diabetes in pre-diabetic patients over a nine-month period. A subsequent study will be required to determine whether curcumin is beneficial over the long term. While these results are encouraging, it is important to note that they all represent surrogate, disease-oriented outcomes. Prolonging the onset of ADA-defined type 2 diabetes with curcumin may or may not have an impact on future morbidity, mortality, or quality of life.

BLAST FROM THE PAST

BREATHING RETRAINING MAY BE ASSOCIATED WITH IMPROVED ASTHMA-RELATED QUALITY OF LIFE

Level 2 [mid-level] evidence

Reference: Thorax. 2009;64(1):55–61.

Prior to the advent of pharmacotherapy, breathing exercises were commonly employed for the treatment of asthma.[28] Like all incurable, chronic diseases, asthma is a complex condition that responds suboptimally to medication management alone. For some patients, environmental triggers are either unknown or unavoidable. Mostly due to study heterogeneity, a Cochrane review (2004) of seven controlled trials was unable to arrive at firm conclusions regarding the benefit of breathing exercises for asthma patients.[29] A subsequent small trial ($n = 85$) comparing an integrated breathing and relaxation modification program with a "usual care" control reported improvements in asthma-related health status, symptoms, and mood in adults.[30] To minimize the non-specific effects of professional attention, researchers in the current study compared the effectiveness of breathing retraining vs. an educational intervention for the management of asthma.[31]

Researchers randomized 183 asthma patients with moderate impairment of health status to three sessions of either physiotherapist-supervised breathing training (BT) or nurse-delivered asthma education (CT). Patients in the BT group received explanations of normal vs. "dysfunctional breathing," plus individual sessions on regular diaphragmatic and nasal breathing that they were encouraged to practice at least 10 minutes daily. In the CT group, general information on the nature of asthma was followed by individual sessions explaining atopy concepts and treatment rationale without personalized asthma advice. At six months, the BT intervention was associated with an improvement in an asthma-related quality of life score vs. control (0.38, 95% confidence interval [CI] 0.08–0.68) according to an intention-to-treat analysis (per protocol difference was 0.64 (95% CI [0.28–1.01]). Assuming, as the researchers did, that a change ≥ 0.5 on this scale is clinically relevant,[32] 71.3% vs. 56.2% experienced a clinically meaningful improvement ($P = .03$, number needed to treat [NNT] = 6). Measures of hyperventilation, anxiety, and depression also significantly improved in the BT group at six months ($P < .05$). However, there were no significant differences in airway physiology, inflammation, or hyper-responsiveness.

The results of this trial suggest that a brief breathing retraining program supervised by a physiotherapist can significantly improve asthma-related quality of life, along with other patient-centered outcomes, in cases of moderately severe asthma. The use of an attention control makes it more likely that these benefits are in fact related to the new breathing techniques adopted by the patients. Although the absolute difference in asthma-related quality of life score fell below an acceptable threshold for clinical significance,[32] the within-group change seen with BT retraining was comparable to that seen in some asthma drug trials.[31] The anticipated observation of no change in disease-centered, physiologic measures despite an improvement in patient-centered, quality of life outcomes lends mechanistic support to the presumption that asthma is a complex disease at least partially responsive to non-pharmacologic interventions.

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