Clin-IQ Project

Clinical Question: In peri-menopausal and menopausal women, have nontraditional therapies proven effective at relieving symptoms (hot flashes, irritability, etc.) compared to traditional hormone replacement therapy (HRT)?

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Answer: Yes, there are several effective therapies effective for treating symptoms of menopause. However, no single therapy is more effective than traditional HRT.

Level of Evidence for the Answer: A

Search Terms: Peri-menopausal, Menopausal, treatment, women, hormone replacement therapy

Date Search was Conducted: August 2012

Inclusion Criteria:

Published meta-analysis/randomized controlled trials to determine effective pharmacotherapy in the treatment of menopausal symptoms. Meta-analyses review of randomized controlled trials of non-pharmacotherapy were also included.

Exclusion Criteria: Men and children.

Summary of the Issues:

Many perimenopausal and early postmenopausal women will experience unwanted symptoms of menopause. By far, the most commonly reported symptom is hot flashes/flushes. Hot flashes are characterized by a sensation of intense heat, and are often accompanied by sweating and tachycardia. Collectively, these symptoms are described as the
vasomotor symptoms of menopause. Vasomotor symptoms undoubtedly decrease the quality of life for many menopausal women. Not only do they cause discomfort and embarrassment to women during the day, but vasomotor symptoms can be especially problematic during the night. Severe symptoms may lead to insomnia.¹

Traditionally, symptoms of menopause have been treated with hormone replacement therapy (HRT). The estrogen hormone is known to be a very effective treatment for vasomotor symptoms. However, administration of estrogen to menopausal women may be associated with significant risk. Both primary and secondary prevention trials have concluded that estrogen is not only ineffective in preventing heart disease among older menopausal women; but also, estrogen increases the risk of coronary and thromboembolic events during the first year of treatment. Moreover, evidence links estrogen use to an increased risk of breast cancer and possibly an increased risk of Alzheimer's disease.² Because they fear the potential risks and adverse outcomes associated with HRT use, many women are seeking alternative treatment. As many women are opting not to take HRT, it is increasingly important to identify evidence based lifestyle modification interventions and or alternative medical treatments that have potential to reduce vasomotor menopausal symptoms.³

**Summary of the Evidence:**

Gabapentin is a well known drug used in the treatment of partial seizures, neuropathic pain and post-herpetic neuralgia. It is a gamma-aminobutyric acid (GABA) analog which does not interact with GABA receptors. Gabapentin has antihyperalgesic properties thought to be secondary to binding to, and thus altering, a subunit of voltage-gated calcium channels. However, its exact mechanism remains a mystery. It has recently been studied for its effectiveness in treating vasomotor symptoms of menopause. In comparison with placebo, the
drug gabapentin is effective for the treatment of hot flushes in postmenopausal women. It is found to be just as effective as estrogen in the treatment of postmenopausal hot flushes. In the randomized controlled trial by Reddy et al, dosages of Gabapentin ranging from 400 mg to 2400 mg have been found to reduce hot flashes by 71% (p=.004) over a 12 week period. Estrogen reduced hot flashes by 72% (p = .016). Each was significantly greater than the reduction associated with placebo (54%). The effect of Gabapentin on hot flashes did not differ significantly from that of estrogen (p = .63).2

Escitalopram is a selective serotonin reuptake inhibitor (SSRI) that increases intrasynaptic levels of the neurotransmitter serotonin by blocking the reuptake of the neurotransmitter into the presynaptic neuron. Of the SSRIs currently on the market, escitalopram boasts the highest affinity for the human serotonin transporter. Currently, SSRIs are being studied in their effectiveness in relief of menopausal symptoms and a few studies are promising. The randomized, double-blind study by Freeman, et al shows that Escitalopram has been found to be effective in the treatment of hot flashes. The study determined Ecitalopram’s effectiveness by assessing both primary (objective data) and secondary outcomes (subjective data). The primary outcome measured the reduction in hot flash frequency. The secondary outcomes measured hot flash bother and hot flash severity. The participants received 10 to 20 mg/d of Ecitalopram. In the treatment group, participants reported a 47% reduction in hot flash frequency, compared to a 33% reduction in the placebo group (P<.001). Hot flash severity was decreased by 24% in the treatment group vs 14% in the placebo group. Likewise, the reduction in hot flash bother in the treatment group was 20% vs 18% in the placebo group.4

Physical activity and exercise play a vital role in maintaining a healthy lifestyle. There
is evidence that physical activity benefits many perimenopausal symptoms and associated conditions. However, according to Daley et al., the RCOG studies failed to demonstrate sufficient effectiveness of exercise as a treatment for vasomotor menopausal symptoms, or whether exercise is more effective than HRT or yoga. The meta-analysis demonstrated that the exercise group did not differ significantly from the control group.  

Tibolone is a synthetic steroid hormone (19-nortestosterone derivative) widely used in Europe for menopausal symptoms. It has been found to be more effective than placebo in relieving the frequency of vasomotor symptoms. The odds of vasomotor symptoms for those taking Tibolone are .42 of those taking placebo. Tibolone has proven to be less effective than equipotent doses of combined hormone therapy. The odds of vasomotor symptoms for those taking Tibolone are 4.16 of those taking placebo.  

Soy isoflavones are plant-derived estrogens (phytoestrogens). They have been studied for their effectiveness in combating menopausal symptoms. Actaea racemosa Linnaeus (Black Cohosh) is a supplement derived from the rhizome of the Black Cohosh plant. In a 12-week randomized, placebo controlled, double-blind study, the supplement containing soy isoflavones and A racemosa L. had no statistically significant effect on vasomotor symptoms in perimenopausal women.  

Figure
Conclusion:

Because menopausal symptoms are so prevalent, it is important to determine which treatments are effective. Along with pharmacologic treatments, non-pharmacologic treatments have also been investigated. Because of the diversity of patients and the differences in severity of symptoms, it is important to consider each patient individually when approaching treatment options. A significant benefit from ecitalopram, as well as gabapentin, on the treatment of hot flashes provides effective, well-tolerated, nonhormonal alternatives to perimenopausal and postmenopausal women.

List of Articles Reviewed:

