

“I AM HOT, IRRITABLE AND FEELING LOW; WHAT ALTERNATIVES DO I HAVE BESIDES HORMONE REPLACEMENT THERAPY?”

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ABSTRACT

Women at the end of their reproductive age often complain of climacteric symptoms which can be quite debilitating at times. Physiological changes due to deficient oestrogen have received global attention in the search for an acceptable and safe measure to improve quality of life for women with these complaints. Hormone replacement therapy (HRT) used to be the main treatment for menopausal symptoms. Lately there are concerns about its possible adverse effects of increasing risks of breast malignancy, heart diseases, etc. Complementary Alternative Medicine (CAM) plays a significant role in relieving these climacteric symptoms especially in women with contraindications to hormonal therapy and in those who are worried of its adverse effects. It is important for women to be aware of these CAM to provide them with options to improve their quality of life. This paper explores other pharmacological and non-pharmacological measures as alternatives to hormone replacement therapy (HRT), to assess how useful and reliable they are according to available scientific evidence.

Keywords: Menopausal symptoms, hormone replacement therapy, lifestyle changes, pharmacological therapy, complementary therapy.

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INTRODUCTION

Climacteric symptoms are physiological events caused by failure of ovarian function in many women in their late 40's. 80% of women reaching menopausal age complain of hot flashes – sensation of feeling hot over the chest, neck and face in association with other vasomotor symptoms like palpitation, sweating, irritability, anxiety, etc. Almost 20% of them find it intolerable.^{1,2} Hot flashes usually resolve within a year after the onset of menopause; but about one third of women suffer for longer period of up to three to four years.^{3,4}

For decades, hormone replacement therapy (HRT) has been recognized as the best treatment for problems related to menopause especially hot flashes and vaginal dryness. Recently, there are concerns about its safety when Women Health Initiative (WHI) study reported on a possible association between its use and increased risk of heart disease and breast malignancy even though they are beneficial in reducing risks of osteoporosis and fractures, endometrial and colorectal cancers.⁵ Alternatives to HRT are currently being seen as an attractive option even though there is no substantial evidence of their benefits in relieving vasomotor symptoms due to

menopause. A study conducted in Bologna found that more than 30% of women with menopausal symptoms are taking complementary alternative medicine (CAM) and a quarter of them had used more than one product. It was also reported that 90% of medical practitioners did not seek information about their use on these CAM.⁶

Hormone Replacement Therapy: BENEFITS AND RISKS

Benefits

HRT or oestrogen replacement therapy (ERT) has been shown to improve climacteric symptoms in postmenopausal and perimenopausal women by 60% and 90% respectively. A study conducted by MacLennan *et al.* showed that there was a significant 77% reduction in the frequency of hot flashes for women on HRT as compared to those in the placebo group (weighted mean difference 17.46, 95% confidence interval {CI} 24.72 to 10.21). Symptom severity was also significantly reduced (odds ratio {OR} 0.13, 95% CI 0.08-0.22).^{7,8} About half of postmenopausal women suffer from urogenital atrophy manifested as vaginal dryness, dyspareunia and urinary frequency. Vaginal oestrogen is effective in relieving these

symptoms and can be also used in women with intact uterus.^{9,10} Other associated symptoms such as agitation, anxiety, irritability, low mood, etc. may indirectly be improved with better sleep and less night sweats.¹¹ As sexual function and vaginal atrophy improves, so does their associated complaint of loss of libido.¹²

Risks

There are concerns that HRT could increase the risk of ischaemic stroke in postmenopausal women especially in those with high risks for cardiovascular diseases. There is no evidence that HRT is useful for primary or secondary prevention of stroke or coronary heart disease.^{13,14} Even though the absolute risk of developing breast cancer with use of HRT is small, this risk may increase if HRT is used for longer than five years. WHI investigators reported a significant 26% increase in the relative risk of invasive breast cancer in women aged between 50-79 years who were treated with combined oral conjugated equine oestradiol plus medroxy-progesterone acetate as compared to those on placebo.⁵ Dementia is another age related condition which impairs one's quality of life. A meta-analysis showed that women on HRT have improved verbal memory, motor speed, vigilance and reasoning but were not protected from developing dementia.¹⁵ In fact, HRT enhances the deterioration of cognitive function if it is used above the age of 65 years.¹⁶

WHAT ARE THE AVAILABLE ALTERNATIVES?

1. Non-pharmacological therapy

There is little clinical evidence that behavioural interventions, exercise and acupuncture are beneficial for menopausal symptoms. However acupuncture appears to be safe if sterile disposable needles are used and in some studies it has been shown to be effective in reducing hot flashes though not as effective as oestrogen.¹⁷ Paced respiration technique (slow and deep breathing technique) and trained relaxation technique (e.g. yoga, meditation, etc.) for 20 minutes have shown to be significantly beneficial in a few randomized controlled trials.¹⁸ Maintaining body mass index (BMI) within normal range through regular exercise regimes and healthy balanced diet is also useful.¹⁹ Avoidance of trigger factors such as spicy food, smoking, hot drinks and alcohol would probably help too.

2. Pharmacological therapy: Non-hormonal

Neuroendocrine agents

Neuroendocrine agents interfere with the adrenergic and neurosynaptic pathway to alleviate hot flashes and are scientifically proven to be effective. Drugs like methyl dopa and

veralipride significantly reduce the symptoms but may cause headaches as a side effect.²⁰ Clonidine (α -adrenergic receptor agonist) is also effective but is associated with difficulty in sleeping.²¹

Selective Serotonin Reuptake Inhibitor (SSRI) & Selective Noradrenalin Reuptake Inhibitor (SNRI)

Venlafaxine 75 mg daily was shown to reduce menopausal symptoms (by 61%) compared to placebo (20%). However, follow-up studies showed that its effect wore off after 12 weeks of use. It has side effects to the gastrointestinal and central nervous systems. Other drugs such as paroxetine 25 mg daily or fluoxetine also showed similar effects though for shorter duration of four to six weeks. Side effects include possible sexual dysfunction.^{22, 23}

3. Complementary Alternative Medicine (CAM)

More women are resorting to CAM for treatment of menopausal symptoms even though there is little scientific evidence to support the effectiveness of its use. Many small trials have shown some significant effects of herbal products like black cohosh, ginseng, dong quai, vitamin E, evening primrose oil, isoflavine from red clover or phyto-oestrogen from soy supplements. However, results of these studies especially those on phyto-oestrogen, isoflavine and black cohosh are inconsistent.^{24,25}

In a systematic review by Kronenberg *et al.*, it was found that there was no convincing evidence that herbal products were effective in the treatment for menopausal symptoms. However, black cohosh (also familiarly known as Remifemin) seems to be a popular treatment for hot flashes.²⁶ A number of small controlled clinical trials had shown that use of black cohosh or Remifemin for over two to eight months could alleviate symptoms associated with low level of oestrogen. However, there must be caution for its long term use in human as no data has been collected or established over its possible adverse effects.²⁶ Clinical trials comparing estrogens with black cohosh preparations have shown a low incidence of adverse effects associated with black cohosh; headaches, gastric complaints, heaviness in the legs, and weight problems were the main adverse effects noted.²⁷ American College of Obstetrics and Gynaecology (ACOG) has recommended short term use of black cohosh (six months) for treatment of menopausal symptoms.²⁸

Red clover extract contains isoflavones that was reported to be quite effective in reducing more severe hot flashes in some women. Unfortunately, most clinical studies were not able to elicit significant differences when compared to women treated with a placebo. There was no clear evidence on the best dosage and the type of red clover products to be used as available data was limited.²⁹

Table 1: Alternative therapies for menopausal symptoms

| TYPE | USEFUL | LESS USEFUL | DURATION |
|--|--------|-------------|-------------------|
| Acupuncture | | / | - |
| Relaxation/Paced breathing technique | | / | 20 minutes |
| Antidopaminergic agents e.g. methyl dopa | / | | - |
| Antidepressant e.g. SSRI | / | | - |
| Black cohosh (Remifemin) | / | | 2 to 8 months |
| Red clover (isoflavones) | | / | - |
| Soy supplements (phyto-oestrogen) | / | | More than 6 weeks |
| Ginseng | | / | - |

ACOG has recommended the use of soy supplements over a short term (two years or less) period. It is to be used with caution in women with possible oestrogen dependant diseases due to its oestrogen like effect on the reproductive system.²⁹ In countries like Japan, Korea and China, high dietary intake of soy products which contain natural phyto-oestrogen or products with isoflavones has been proposed as one of the reasons for low prevalence of menopausal symptoms among women in these countries.³⁰ Use of soy products has become more popular in United States even though clinical evidence for its effectiveness is minimal. Comparison of its effectiveness is difficult because of short duration of research studies and wide varieties of soy products experimented. However, many studies have reported that beneficial effects of soy products on menopausal symptoms were seen after at least six weeks of use.

Ginseng was found to improve women's psychological wellbeing though had no significant effect in improving menopause related symptoms.³¹ Prolonged use of ginseng could probably lead to hypertension, oedema, diarrhoea, skin eruptions, insomnia, depression and amenorrhoea.^{31, 32}

CONCLUSION

In spite of strong evidence on the effectiveness of HRT in alleviating menopausal symptoms, many women (more than 90% in some western countries) are seeking alternative therapy. Non-pharmacological measures such as regular exercises, balanced diet, relaxation therapy, yoga, meditation and spiritual guidance, though may be useful to individuals, have not been scientifically proven to be effective. Non-hormonal pharmacological agents such as antidepressants are increasingly used for women with severe climacteric symptoms that interfere with their quality of life. For mild climacteric symptoms, CAM that had been shown to be effective, although without strong evidence, may help. More common and popular CAM in use include black cohosh, soy products (contains phyto-oestrogen) and red clover (contains isoflavones) but it must be noted that they are not without side effects. Choice of treatment has to take into account

individual woman's present and past medical history, concurrent medication, type, severity and duration of climacteric symptoms and impact of symptoms on quality of life. The risks and benefits of various treatment options need to be explained clearly to her. Treatment should be periodically reassessed as menopause-related vasomotor symptoms will abate over time without any intervention in most women.

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Clock drawing test is not useful for screening mild cognitive impairment

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This is a systematic review of nine diagnostic studies.