

Vasomotor Symptoms: What is the Impact of Physical Exercise?

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ABSTRACT

Vasomotor symptoms (VMS) or hot flushes are the commonest and the most troublesome symptoms during the menopausal transition. Though usually transient, VMS is the leading menopausal symptom presenting for medical attention. Hormone replacement therapy (HRT) is the most effective treatment for VMS, but many women are reluctant to use HRT and wish to pursue alternative therapy.

Physical exercise of different types has been used as a mean of alleviating VMS. The potential for physical exercise to improve VMS can be explained by its effects on the postulated pathophysiological mechanisms of VMS. However, individual studies on the influence of physical exercise on VMS show conflicting results, with positive, negative or no effects being reported, and the review of evidence is inconclusive. The many differences in the study designs may be a reason for the varying outcomes of the studies.

Physical exercise, however, have multiple benefits in postmenopausal women, in reducing cardiovascular risk factors, improving bone density and preventing osteoporosis, enhancing muscle mass and has a positive effect on overall health. Regular physical activity should, therefore, be promoted in all postmenopausal women, though they may not derive a significant improvement of VMS.

Keywords: Hot flushes, Pathophysiology, Physical activity, Physical exercise, Vasomotor symptoms.

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INTRODUCTION

Vasomotor symptoms (VMS), which include hot flushes (or hot flashes) and night sweats, are experienced by up to 80% of women around menopause.^{1,2} Vasomotor

symptoms are caused by increased vascular reactivity where vasodilatation is followed by vasoconstriction.³ Hot flushes are the commonest⁴ and the most troublesome symptoms during the menopausal transition.^{3,5} Most women complain of symptoms lasting for 6 months to 2 years, though approximately 10% have symptoms persisting for a decade or longer.^{3,6} Vasomotor symptoms is the leading menopausal symptom presenting for medical attention.⁶

The prevalence of VMS varies considerably among ethnicities and menopausal status.^{5,7} Postmenopausal women show a higher prevalence than pre- or perimenopausal women, and Afro-Americans report a greater prevalence than other ethnic groups.⁷ Hot flushes increase with older age, smoking, low educational status, anxiety states and depression.^{5,8} Increase in body mass index (BMI) show contrasting associations with VMS, with studies showing both higher^{1,5,9} and lower⁸ incidence.

Estrogen replacement as hormone replacement therapy (HRT) is the most effective treatment for VMS,¹⁰ but lifestyle modifications have the potential to improve VMS. It is necessary to critically appraise the evidence regarding the effect of physical exercise on VMS as many women are reluctant to use HRT for menopausal symptoms but wish to pursue alternative nonpharmacological treatments. To comprehend how regular physical exercise may influence VMS, the pathophysiology of VMS has to be comprehended.

PATHOPHYSIOLOGY OF VASOMOTOR SYMPTOMS

Reduction in circulating estrogen level around menopause leads to many alterations leading to VMS.¹¹ As the pathophysiology of VMS are unclear, several mechanisms have been proposed to explain the possible mechanisms, such as the narrowing of the temperature regulating threshold in the hypothalamus, alterations in hypothalamic neurotransmitters, changes in vascular reactivity, circulating gonadotropin levels and hypothalamic beta-endorphin levels.

Effects on the Hypothalamic Thermoregulatory Center

The normal core body temperature is tightly regulated within a strict thermoneutral zone especially by the preoptic area of the hypothalamus, and higher and

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lower body temperatures lead to sweating and shivering respectively to maintain temperature homeostasis.³ Alterations in the neuroendocrine processes in the thermoregulatory center of the hypothalamus¹²⁻¹⁴ and narrowing of the thermoneutral range, where major temperature regulating mechanisms do not occur, are possible mechanisms in women with hot flashes.^{3,11} Decrease in circulating serotonin, increase in norepinephrine and decrease in estrogen concentrations are implicated in narrowing of the thermoneutral range.^{5,11} This leads to exaggerated heat loss response, where increased peripheral vascular reactivity causes vasodilatation causing sweating and skin flushing which manifests as hot flashes.^{3,15}

Estrogen acts as a potent neuromodulatory agent in the hypothalamic thermoregulatory center, and declining estrogen concentrations lead to alterations in hypothalamic neurotransmitter activity, especially in the serotonergic and noradrenergic pathways.^{3,13,16}

Changes in Vascular Reactivity

Serotonin and noradrenaline also modulate the vasomotor effects that cause peripheral vasoconstriction and vasodilatation.¹⁶ However, it is still unclear the exact mechanisms by which norepinephrine and serotonin cause VMS. The finding that selective serotonin reuptake inhibitor decreases skin blood flow implies that serotonin may play a role in hot flashes.¹⁷

Decreasing estradiol levels during menopausal transition can alter the threshold for cutaneous vasodilatation and low estrogen levels in postmenopausal women can reduce vascular elasticity, contributing to the impaired vascular reactivity.¹⁶

Apart from estrogen levels, the reduction in estradiol, estrone ratio and estrogen function with regard to polymorphisms in sex steroid-metabolizing enzymes and estrogen receptors too are linked to VMS, contributing to ethnic differences in VMS.¹⁸

Role of Beta Endorphin

Reduction in hypothalamic and peripheral beta endorphin levels have also been hypothesized to contributing to VMS¹⁹ though increase in plasma beta endorphin levels with selective estrogen receptor modulator raloxifene hydrochloride has not improved VMS in postmenopausal women.²⁰

Effects of Exercise on VMS

Physical activity and structured exercise is known to be beneficial in reducing VMS²¹ and The Royal College of Obstetricians and Gynaecologists in the UK²² and the North American Menopause Society²³ have suggested regular exercise as a treatment for vasomotor menopausal

symptoms. However, the ACOG practice bulletin (2014) does not recommend exercise as there is insufficient evidence to do so.²⁴

The evidence from studies on the effect of physical exercise is conflicting, with positive, negative or no effect being reported.

In a Cochrane Database Systematic Review by Daley et al, 2011, six randomized controlled trials (RCTs) in which any type of exercise intervention were compared with no treatment/control or other treatments in the management of menopausal VMS in symptomatic perimenopausal/postmenopausal women were reviewed.⁴ There was no significant standardized mean difference between exercise versus control/any treatment groups (three studies), exercise *vs* yoga groups (two studies) and exercise *vs* HRT (three studies).

Effect of Aerobic Exercise

In a prospective study of 121 women, a 3-day acute bout of exercise reduced both objective and subjective hot flashes within 24 hours after exercise. However, less fit women reported an increase in hot flashes which may be attributed to the absence of the blunted sympathetic vasomotor activation expected in women who participated in regular exercise.²⁵ In a RCT where 176 sedentary symptomatic women underwent unsupervised aerobic training for 50 minutes four times per week during 6 months, a decrease in the frequency of night-time hot flashes based on phone-based diary was significantly larger in the intervention group than in the control group. However, no significant improvement was noted in the intervention group in day time hot flashes or hot flashes assessed using the Women's Health Questionnaire.²⁶ Improved sleep and mood in the intervention group could have contributed to the reduced reporting of nocturnal hot flashes. Aiello et al (2004) in a RCT of 173 overweight, postmenopausal women not taking hormone therapy, reported a significant increase in hot flashes in the intervention group who participated in moderate intensity physical exercise for 1 year.²⁷ In a more recent RCT of 248 sedentary women with frequent VMS, 12 weeks of moderate intensity aerobic exercise training three times per week did not improve frequency or bother of VMS.²⁸

In two surveys of the Australian Longitudinal Study on Women's Health in 3300 middle-aged women, physical activity was not associated with VMS.²⁹ In a cross-sectional study of 305 Turkish women, no significant relationship was observed between physical activity and VMS.³⁰ In a cross-sectional study of 151 healthy women, though regular physical exercise significantly improved most climacteric symptoms, there was no association with VMS.³¹



Effect of Yoga

Yoga is another form of physical exercise increasing practiced and thought to improve VMS, though not many studies are published on this topic. However, in a systematic review and meta-analysis of the effectiveness of yoga for menopausal symptoms of five RCTs with 582 participants, there was no significant impact of yoga on VMS.³² Another systematic review on seven studies too was inconclusive in.³³ A recent RCT of 249 women where 12 weeks of yoga class plus home practice, was compared with usual activity there was no significant effect of yoga in alleviating VMS.³⁴ Another recent RCT on 355 women found a significant improvement in VMS with weekly 90-minute yoga classes with daily at-home practice compared to individualized facility-based aerobic exercise training three times/week.³⁵

Mechanisms by Which Exercise may affect VMS

Several plausible mechanisms explain the positive impact of physical exercise on VMS. Physical exercise, whether an acute bout or chronic exercise training influences neuro-endocrine responses of stress hormones and autonomic nervous system. A second potential mechanism is the release of endogenous opioids.³⁶ Another possibility is that physical exercise may distract women from VMS.²⁸ Gold et al (2006) in the Study of Women's Health Across the Nation (SWAN) reported that high BMI was associated with increase in hot flushes, thus, exercise by decreasing BMI could improve VMS.⁷

Increase in Vagal Tone

Increase in vagal tone occurs as a response to aerobic exercise training, shifting the autonomic balance in favor of the parasympathetic nervous system.³⁷ Though in acute exercise brain norepinephrine and its metabolites increase, with exercise training,²⁸ there is a reduction in 24-hour urinary norepinephrine that may be associated with the increased vagal tone.³⁸ The 'stress buffering' effect of parasympathetic activation during exercise training may have an impact on counteracting the effects of stress hormones, such as cortisol and catecholamines that may precipitate hot flushes in postmenopausal women.²⁸

Increase in Endogenous Beta-endorphin Release

A second hypothesis is concerned with the increase in endogenous beta-endorphin release. Decrease in estrogen is thought to decrease hypothalamic endorphin levels leading to increased norepinephrine and serotonin levels. Hypothalamic and peripheral endorphin production is increased during exercise and basal endorphin levels

are lower in active individuals. Higher endorphin levels decrease the frequency and amplitude of luteinising hormone and regulate GnRH levels, stabilizing. Such effects are postulated to stabilise the thermoregulatory center and reduce the incidence of VMS.^{28,36} It is also known that high BMI is, however, in contrast to the fact that increased adipose tissue may also exacerbate VMS by possibly increasing insulation and reducing heat dissipation.¹

Increased Heat Production and Dissipation

Physical exercise causes increased heat production and dissipation and is usually associated with a feeling of well-being. The habituation during exercise to increased heat and sweating and association this with feeling good may contribute to less reporting of hot flushes by women who exercise.²⁸

The Negative Effects of Physical Exercise

The negative effects of physical exercise on VMS could be through increasing the core body temperature, especially at high intensities or when prolonged. In postmenopausal women with narrow thermoneutral zones, physical exercise could, thus, worsen already present hot flushes.²⁵ Furthermore, women who get less regular exercise may have larger amount of adipose tissue, where the conversion of adrenal androgens to estrogens will be increased. Therefore, exercise by reducing adipose tissue content, could actually increase the severity and incidence of VMS by further decreasing estrogen levels.¹⁹ These mechanisms may contribute to the varied effects of physical exercise on VMS observed in studies.

CONCLUSION

Though physical activity and regular physical exercise is commonly thought to improve VMS, reviews on physical exercise on both aerobic exercise and yoga are inconclusive. Available evidence shows conflicting findings, with positive, negative or no effect being reported.

The results of studies may be varied due to many reasons. The differences in study design, study population, inclusion criteria, measure, type, duration and intensity of exercise and different measure of VMS by objective and subjective means are some factors that could contribute to the diverse outcomes. The pathophysiological mechanisms suggested are varied and uncertain, and multiple mechanisms are postulated to explain how VMS may be influenced by exercise. Thus, results of more studies are to be awaited before forming firm conclusions regarding the effects of physical exercise on VMS.

Physical exercise, however, has multiple benefits in postmenopausal women, in reducing cardiovascular risk factors,^{39,40} improving bone density and preventing osteoporosis,⁴¹ enhancing muscle mass⁴² and has a positive effect on overall health. Regular physical activity should, therefore, be promoted in all postmenopausal women, though they may not derive a significant improvement of VMS.

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