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To exercise, or, not to exercise, during menopause and beyond

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ABSTRACT

Menopausal symptoms in women can be severe and disruptive to overall quality of life. Hormone replacement therapy, is known to be effective in ameliorating symptoms, however, reporting of side effects has resulted in alternative treatment options. Exercise has been assessed as an alternative treatment option for alleviating menopausal symptoms, including, psychological, vasomotor, somatic and sexual symptoms. Here we report the effects of physical activity and exercise on menopause symptoms in menopausal women.

Keywords: Exercise, Physical activity, Menopause, Hot flashes, Vasomotor symptoms, Physiological effects, Endocrine effects

1. Introduction

Menopause, from the Greek word *men-* (month) and *pausis* (cessation), is defined as the end of the woman's fertile life, following loss of ovarian follicular function, usually occurring in the late 40s to early 50s. The transition is not sudden or abrupt and occurs over several years (5-8 years), and is commonly referred to as, change of life or the climacteric. During the transition, a number of signs and symptoms may occur, including, vasomotor symptoms (hot flashes, palpitations), psychological symptoms (mood changes, depression, irritability, anxiety, sleep disturbances), cognitive symptoms (memory problems, concentration) and, atrophic effects (atrophic vaginitis, bladder irritability) [1-4]. Women also report symptoms including night sweats, headaches, fatigue, decreased libido, severe itching, and back and muscle pains [5]. Such symptoms can significantly disrupt a woman's daily activities and overall quality of life [1-4]. Further, during menopause and aging, with changing hormone levels, women are at an increased risk of chronic conditions such as, cancer, type-2 diabetes, autoimmunity, osteoporosis and cardiovascular diseases.

Hormonal replacement therapy (HRT), use of synthetic hormones, estrogen and progestin in women with intact uterus, or estrogen alone for women who have undergone hysterectomy, has been the most effective treatment for the relief of menopause symptoms but is not without risks [6]. A large randomised trial, by the Women's Health Initiative, reported an increased risk of breast cancer and heart disease [7]. In a later study of estrogen alone, there was no association with increased risk of breast cancer, although, the trial was prematurely stopped because of increased risk of stroke [8]. The Million Women Study by Cancer Research UK and the National Health Services, assessed the effects of HRT use in over one million women, and confirmed that HRT was associated with increased breast cancer risks, especially when both estrogen and progestin were used [9-11]. As a consequence of these findings many women have become reluctant to continue or commence

HRT due to fear of adverse risks, which has resulted in a significant decrease in the incidence of breast cancer over the last 10 years [12, 13]. Recently, a global consensus statement on menopausal hormone therapy was published which was aimed for women and health care practitioners to make appropriate decisions on the use of HRT [14]. As a result of the effects of HRT, women seek alternative treatment options, particularly complementary and alternative therapies.

Numerous alternative therapies currently available claim to provide a wide array of benefits to menopausal women, however, scientific support is lacking in most instances. Phytoestrogens, black cohosh, red clover, dong quai, evening primrose oil, ginseng, wild yam and maca (*Lepidium meyenii*) have been studied with conflicting results [15]. Due to breast cancer risks associated with HRT and inconclusive results of alternative treatments, physical activity and exercise has been proposed as an alternative means to improve a women's quality of life during menopausal transition and beyond [16-18].

2. The benefits of exercise for overall wellbeing

Physical activity was recognised by the ancient Greeks for health and wellbeing. Hippocrates (460-370 BC) stated "Eating alone will not keep a man well; he must also take exercise. For food and exercise, while possessing opposite qualities, yet work together to produce health". Physical inactivity is ranked just behind cigarette smoking as a major cause of ill health, placing an enormous economic cost worldwide. In 1996, following the report by the United States Surgeon General's report on the effects of physical activity on health (USDHHS1996), led to an international important component of public health and wellbeing. The short-term benefits of exercise includes, increases in endurance, metabolism and energy, aids in healthier muscles, joints and bones, decreases stress, improved cognitive functioning and promotes better sleeping patterns. Regular exercise participation, either as part of a

lifestyle or as part of a disease intervention program are associated with better quality of life and health outcomes, particularly to cancer [19], heart disease, stroke, blood pressure, type-2 diabetes, obesity, osteoporosis, cognitive functioning and mental health and well-being [20-23].

A 12 week study in obese middle-aged women undertaking 1 hour, 3 days per week resistance and aerobic exercise revealed that metabolic syndrome factors (blood pressure, percent body fat, fasting glucose levels, triglyceride and cholesterol levels) and, visfatin levels, were significantly decreased [24]. Likewise, 3 classes per week, of Bikram yoga improves glucose tolerance in older obese subjects [25], and resistance exercise significantly decreased triglyceride values [26].

An analysis based on 80 studies demonstrated a positive correlation between physical activity and clinical depression, regardless of gender, age or health status [27], and regular exercise by patients after termination of anti-depressants, had lower depression scores than those who were sedentary [28]. On the whole about or regular physical activity participation results in enhanced psychological well-being. This includes improved mood [29], self-esteem [30], and reduced anxiety [31] and stress [32].

Menopause is commonly associated with a range of health complaints, including hot flashes, urinary disorders, joint pain and psychological distress. Women reporting menopausal symptoms are generally of overall poorer health [29]. Serious chronic conditions such as osteoporosis and cardiovascular diseases are more likely to occur after menopause than before [30]. In this respect physical activity has a positive impact on bone density in menopausal women. For example, greater physical activity within 4 life domains, of, sport, active living, home, and work was associated with higher peak femoral neck strength relative to load in 1,919 menopausal women [31]. Moreover, physical activity has a positive effect in the tibial cartilage of the knee during menopause [32].

It is clear that there are many benefits of exercise on bone [33], cardiovascular, metabolic [34, 35], diabetes [36], cancer, longevity [37], psychological well being [38, 39] and overall quality of life [26]. Hence, it is appropriate for women to be physically active throughout the menopausal transition and afterwards.

3. To exercise

It is believed that loss of estrogen levels in women to be the main cause of the symptoms associated with menopause. According to the Centre for Disease Control and Prevention, regular exercise helps relieve stress, enhances overall quality of life, and reduces weight gain and muscle loss, the most frequent side effects of menopause. It is recommended that at least 150 minutes of aerobic activity and 75 minutes of vigorous activity to be undertaken per week for cardiovascular health. In addition, strength training should be included in order to build bone and muscle strength, aid in body fat burn and increase in metabolism, also important factors during menopause.

For example, in a group of menopausal women aged 55-72 who were involved in an exercise program, of 3 hours per week for 12 months, experienced significantly improved physical and mental health and overall quality of life compared to those who were sedentary [40]. More importantly a higher proportion of those who did not participate in the exercise regime reported menopause symptoms (58% reporting symptoms at the beginning of the study compared to 68% at the end of the study), compared to a significant lower reporting in those participating in the exercise study (50% reporting prior to the study compared to 37% at the end of the study). Exercise is therefore considered an important factor to alleviate menopause symptoms. The woman's ability to choose their preferred physical activity increases the likelihood that they will adhere to exercise as a treatment method.

Exercise appears to be a cost-effective alternative with few known side effects. Most importantly, women with greater levels of physical activity report improvements in mental and physical aspects of quality of life [41, 42]. Such improvements can even be achieved with low intensity aerobic activity, such as walking and dancing [43].

3.1. Benefits to vasomotor symptoms

The years leading up to menopause, during menopause and early postmenopause, women experience vasomotor related symptoms such as, hot flashes, night sweats and sleep disturbances. Symptoms could be so severe that the overall quality of life of a woman is severely affected. HRT has been shown to alleviate such symptoms but as indicated can have serious side effects. Lifestyle modification interventions, including structured exercise and physical activity, have the potential to reduce vasomotor menopausal symptoms [18, 44]. In fact, in the longitudinal Melbourne Women's Midlife Health Project, in which 438 women were followed over 8 years, those who exercised every day at baseline were 49% less likely to report hot flashes, and those whose exercise levels decreased were more likely to report hot flashes [45]. Moderate physical activity was associated with decreased objective and subjective hot flashes 24 hours post exercise [46], although worse reported symptoms were reported in women with lower fitness levels. In a randomised controlled trial, 176 symptomatic sedentary women who were given an aerobic exercise regime 50 minutes 4x per week over 6 months, reported a decrease in the frequency of hot flashes [47]. In 3,201 women aged 42-52 years old, monitored yearly for 8 years, hot flashes were associated with higher cholesterol, triglyceride and apolipoprotein A levels [48], and, in 3,075 women, there was a strong correlation between hot flashes and insulin resistance [49]. Physical activity has positive associations in reducing cholesterol, triglycerides, apolipoprotein and glucose levels [24, 25], and, is associated with reducing hot flash symptoms [50].

Finally, sleep quality has also been found to be better in menopausal women who are physically active [51]. For example, physically active women have favourable sleep characteristics with fewer awakenings during the night [52] and improved quality of sleep [53].

3.2. Benefits to psychological symptoms

In the years leading up to, and during menopause, many women report symptoms of, depression (unhappiness, irritability, tearfulness, lack of energy) or anxiety (mood swings, insomnia, heart palpitations, panic attacks, forgetfulness or problems with focus and concentration). Studies have found that exercise participation results in lower perception of symptom severity. These findings add to the evidence suggesting that exercise moderates the psychological symptoms associated with menopause [54, 55]. The effects of exercise in reducing psychological symptoms have been widely reported. A study including Australian midlife women, noted, that exercise was beneficial for somatic and psychological symptoms including depression and anxiety, but not for vasomotor symptoms or sexual function [56]. Likewise, in a group of Korean women, those who were depressed experienced more menopausal symptoms than women who were not depressed, and those who exercised on a regular basis, were less depressed and less symptomatic than those who were not physically active [57].

Exercise as an intervention has also been shown to have a positive impact on menopausal symptoms, depression and quality of life. Providing mental distraction and social interaction [26, 56] are some of the explanations provided for the psychological benefits associated with exercise participation.

Habitual physical activities, those that are part of the participants lifestyle, such as, walking, cycling, gardening and work related physical activities of no more than 60 minutes

per day, have also been found to have a favourable effect on menopause symptoms and quality of life. They improve mood and enhance psychological functioning [58, 59]. In a cross sectional study of 151 regular physically activity women the total Greene score and psychological sub-score were found to be improved [60]. Similarly, in 60 postmenopausal women, those in the exercise group reported improvements in depression and anxiety compared to a control group [61]. Overall, an immediate bout of exercise and regular participation is associated with improved psychological functioning in menopausal women.

3.3. Benefits to somatic symptoms

Somatic symptoms are those related to the body, which includes muscle and joint pains, numbness or tingling in the extremities or elsewhere, dizziness, headaches and shortness of breath. The Health 2000 study in Finnish women reported that physically active women reported significantly fewer somatic symptoms and pain compared to women that were not physically active [62]. Eight years later those that remained physically active exhibited improved quality of life compared to those who were not physically active [63]. Physical activity was also found to improve somatic symptoms in a study of 370 Brazilian women [64]. In addition, in a large cross-sectional study in British women, somatic symptoms were 28% lower among active women [16]. Similarly, in a longitudinal study of 3,300 Australian women, increase in physical activity was associated with fewer somatic symptoms [65]. In the Women's Health Across the Nation (SWAN) study, in over 7 years follow-up, it was noted that physically active women experienced less bodily pain over time during the menopause transition [66]. Likewise, in a 3-year longitudinal study of over 2,400 women from SWAN demonstrated that women who were more physically active at midlife experience less bodily pain over time [67]. This suggests that physical activity positively influences the somatic symptoms in menopausal women and increases overall quality of life.

3.4. Benefits to sexual symptoms

As a result of estrogen deprivation during the menopause transition the woman's sexual drive and functioning decreases. Symptoms of vaginal dryness or thinning of the wall, sexual dysfunction or discomfort are common. In a study of 42 postmenopausal women, divided into 2 groups of aerobic or resistance exercise programs of 3 days per week for 8 weeks, no effects were noted for urogenital complaints and sexual symptoms [65]. However, in a cross sectional study of 151 women who were physical activity, reported improved sexual symptoms [60]. Recently, in 273 Iranian women, a negative significant relation was observed between sexual problems and vaginal dryness and the level of physical activity [68]. The findings with regard to exercise and sexual functioning are equivocal. In addition, this is an area which requires further examination.

4. Or, not to exercise

Not all studies have provided evidence for the moderating effects of exercise participation. The type of exercise intervention was analysed amongst 6 eligible studies in the management of vasomotor menopausal symptoms and was compared to HRT [69]. There was insufficient evidence demonstrating that exercise was effective in treating vasomotor menopausal symptoms, and, it was not clear whether exercise was more beneficial compared to HRT or yoga [69]. In addition, data from the Australian Longitudinal Study on Women's Health including 3,330 women suggested that no improvements in vasomotor or psychological symptoms and only marginal improvements in somatic symptoms were noted when physical activity was introduced as a factor influencing these symptoms [65]. In a study of 280 women, increasing physical activity had no effect on vasomotor and sexual symptoms of menopause [55], and, in 24 women participating in a 3 month physical exercise protocol

there were no improvements in sexual function [70]. In a number of studies including, 16,000 USA women [71], 173 African American and Caucasian women [72], and in 338 overweight women [73], no associations were found between physical activity and vasomotor symptoms. Recently, in a randomised controlled study of 237 women partaking in yoga classes, no improvement to vasomotor symptoms frequency were noted [51]. Likewise, in 164 women partaking moderate physical activity, including walking and yoga, for 4 months, yielded no improvements in sleep quality in menopausal women [74]. In another randomised controlled trial in 3 different sites, which involved 106 women to moderate exercise for 12 weeks and 142 women with no addition of exercise to their daily routine, did not improve vasomotor symptoms, however, small improvements were seen in sleep quality, insomnia and mood including depression [75]. A cross sectional study of 1,071 postmenopausal Turkish women who attended an outpatient clinic from 2005 to 2012, demonstrated no association between regular exercise and urogenital symptoms [76]. Further, in a Norwegian study of 2,002 women there was no relation amongst symptom burden and degree of physical exercise [77]. Likewise, in a Nigerian population of 547 women there was no association with physical activity and menopausal symptoms and overall health related problems [78]. These findings demonstrate that physical exercise has not consistently been shown to be beneficial in ameliorating symptoms associated to menopause.

Important reasons for the equivocal findings on the benefits of exercise on menopausal symptoms are the fact that studies have often assessed physical activity and exercise behaviours by means of self-report rather than objectively. In addition, exercise mode, intensity, frequency and duration has varied across the different studies making generalisations difficult. Finally, some studies have used participants who were already active prior to menopause whereas others include women who started exercise to alleviate

symptoms. Different mechanisms might underlie symptomology in those are active prior to and during menopause versus those who take up exercise during menopause.

5. Exercise beyond menopause

Habitual activity has numerous health benefits, including decreased risk or cardiorespiratory problems, metabolic syndromes, cancer and improved muscle and bone health and psychological symptoms. The risk of having one of these health issues is most prevalent postmenopause [79]. Cardiovascular disease is increased in postmenopausal women, and the risk is lower in physically active women [80], by improving antioxidant capacity and decreasing body iron burden [81]. Blood pressure is lower in physically active postmenopausal women compared to healthy sedentary women [80, 82], and, resistance training with an intensity of 60% of 1 repeat for 12 weeks has beneficial effects on blood pressure, heart rate and cholesterol levels [83]. Likewise, a modified relaxation technique intervention in Thai postmenopausal women had positive effects in lowering blood pressure as soon as 4 weeks after start of treatment [84]. Interestingly, whole body vibration exercise training improves blood pressure, systemic and leg arterial stiffness, and muscle strength, in postmenopausal women [85] although vibration exercise is not without risks. In addition, cardiorespiratory exercise improves metabolic syndrome effects (waist circumference, blood pressure and fasting glucose in postmenopausal women [86]. Further, aerobic exercise and calorie restriction improves insulin sensitivity and reduces the risk of diabetes in postmenopausal women [87]. Decrease in bone mineral density is associated with post menopause, and, walking for more than 6 months improves femoral neck bone mineral density in menopause women as analysed in 10 different trials [88]. Further, skeletal muscle regeneration efficiency declines with age and is related to the decline in sex hormones. Long term resistance training increases muscle strength in postmenopausal women [89]. Clinical

trials are currently being undertaken to determine the effects of exercise on skeletal muscle regeneration and maintenance of muscle mass in postmenopausal women [90]. Physical activity plays a pivotal role in maintaining health and prevent disease beyond menopause, including reduction in cardiovascular disease, breast cancer and diabetes, increasing muscle and bone mass, improving mood and cognitive functioning and overall quality of life [91]. It is important for exercise to play a major role in postmenopausal women, to decrease the risks of disease and improve quality of life.

6. Why bother with exercise during menopause?

Physical activity during the menopause transition and post menopause, offers many benefits such as, weight gain prevention, strengthens bones and increases muscle mass and reduces the risks of other diseases (cancer, diabetes, heart disease). Exercise intervention programs have demonstrated to reduce menopause symptoms, including those of somatic, psychological and to a lesser extent vasomotor and sexual symptoms. Exercise has not been proven to treat menopausal symptoms, however, physically active women during and after menopause are less stressed and have better overall quality of life. Overall, the evidence suggests that exercise is a useful intervention strategy for women during and post menopause to alleviate symptoms. More importantly, exercise has numerous other benefits and is safe with no reported side-effects.

7. Future prospects

Due to inconsistencies associated with effects of exercise to menopause symptoms, in particular those relating to vasomotor symptoms, more well designed and sufficiently powered randomised trials are required to understand the benefits of exercise and menopause symptoms. The inconsistencies reported may be due to varying sample sizes, non randomised

designs, inadequate specified exercise dose (vigorous vs moderate intensity; frequency, duration), mode (aerobic vs resistance exercise), and lack of follow-up. To this effect, a randomised control study over 12 months, is currently being conducted in 261 women to determine physical activity and its effects on hot flashes, night sweats and other menopausal symptoms [92]. Further, the Menopause Strategies: Findings Lasting Awareness for Symptoms and Health (MeFLASH) Network, a collaborative project at 5 clinical sites in USA, is currently undertaking a 3 by 2 factorial design study assessing yoga, exercise and omega-3 supplementation and their effects on menopause symptoms [93, 94]. Interestingly in the MeFLASH trial, 112 previously sedentary women with hot flashes are randomised into moderate to vigorous exercise and are compared to 150 active control women. Findings will help aid in determining whether physical activity has any effects on menopause symptoms, in particular to vasomotor symptoms.

Previous research has shown that weight is associated to menopause symptoms. A study involving 3,330 women in the Australian Longitudinal Study on Women's Health demonstrated a clear relationship with total and vasomotor symptoms and weight loss [65]. In an 8 year follow up study of 1,165 Finnish women, those whose weight remained stable improved their quality of life compared to women who had gained weight [63]. Vasomotor symptoms such as hot flashes and night sweats are more prevalent in women with higher body mass index [95], and in an intensive behavioural weight loss intervention study, which included physical activity, in obese women, resulted in improvement in hot flashes [73]. Conversely, 430 women in a 6 month controlled study demonstrated no associations of weight change with mental and physical quality of life [41]. Future studies should involve weight or weight loss, by means of physical activity, and their effects on menopausal symptoms.

There are many known benefits of exercise on bone, cardiovascular, metabolic, and psychological health. Regular exercise is known to boost the immune system [96, 97], and, decreases inflammation [98] in menopausal women. Studies relating physical activity, to, immunological status, to, menopausal symptoms, during menopause and beyond, hold the key to understanding the underlying mechanisms to menopause symptoms.

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