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Review

Effects of programmed exercise on depressive symptoms in midlife and older women: A meta-analysis of randomized controlled trials

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ABSTRACT

Objective: To perform a systematic review and meta-analysis to clarify the effect of programmed exercise on depressive symptoms (DSs) in midlife and older women.

Methods: We carried out a structured search of PubMed-Medline, Web of Science, Scopus, Embase, Cochrane Library and Scielo, from database inception through June 29, 2017, without language restriction. The search included the following terms: "depression", "depressive symptoms", "exercise", "physical activity", "menopause", and "randomized controlled trial" (RCTs) in midlife and older women. The US, UK and Australian Clinical Trials databases were also searched. We assessed randomized controlled trials (RCTs) that compared the effect of exercise for at least 6 weeks versus no intervention on DSs as the outcome (as defined by trial authors). Exercise was classified according to duration as "mid-term exercise intervention" (MTEI; lasting for 12 weeks to 4 months), and "long-term exercise intervention" (LTEI; lasting for 6–12 months). Mean changes (± standard deviations) in DSs, as assessed with different questionnaires, were extracted to calculate Hedges' *g* and then used as the effect size for meta-analysis. Standardized mean differences (SMDs) of DSs after intervention were pooled using a random-effects model.

Results: Eleven publications were included for analysis related to 1943 midlife and older women (age range 44–55 years minimum to 65.5 ± 4.0 maximum), none of whom was using a hormone therapy. Seven MTEIs were associated with a significant reduction in DSs (SMD = −0.44; 95% CI −0.69, −0.18; p = 0.0008) compared with controls. The reduction in DSs was also significant in six LTEIs (SMD = − 0.29; 95% CI −0.49; −0.09; p = 0.005). Heterogeneity of effects among studies was moderate to high. Less perceived stress and insomnia (after exercise) were also found as secondary outcomes.

Conclusion: Exercise of low to moderate intensity reduces depressive symptoms in midlife and older women.

1. Introduction

Depressive symptoms are highly prevalent during female midlife, with rates two times higher than those found in men and dependent of the used diagnostic criteria and socio-demographic factors [1–7]. These symptoms are more frequent during the peri- and postmenopause as compared to the premenopause, even after controlling for confounding factors. In addition, women with severe hot flashes are more likely to report depressive symptoms, anxiety, and/or sleep disturbances [5,7–10]. Women experiencing depressive symptoms have worse quality of life, lower work productivity and higher healthcare related costs [11].

Depressive complaints can be managed with pharmacologic or psychological intervention, biofeedback and relaxation techniques. Regular exercise, even just walking, has benefits on female health during midlife and beyond [12]. Physical activity and exercise may improve glucose and insulin metabolism and sleep quality [13–15]. Depression, and mood swings were reduced in postmenopausal sedentary women after 24 months of aerobic exercise irritability [16]. Although physical activity and exercise may improve depressive symptoms, data in the literature is rather conflictive [17]. Hence, we aimed at performing a systematic review and meta-analysis in order to clarify the effect of programmed exercise, for at least 6 weeks, as compared to no intervention over mild to moderate depressive symptoms in mid-aged and older women (> 40 years).

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2. Methods

2.1. Data sources and searches

A comprehensive literature search was performed using PubMed-Medline, Web of Science, Scopus, Embase, Cochrane Library, and Scielo, from database inception through June 29, 2017, without restriction of language or publication status. Database searches were performed independently by two authors (SJMD and HL) using the following combined terms, but not limited to: "depression" OR "depressive symptoms" AND "exercise" OR "physical activity" AND "menopause" AND "randomized controlled trial" (RCTs) OR "randomized clinical trial" in mid-aged and older women. The PubMed search strategy is available as Appendix A. In addition, the US Clinical Trials [18], the UK Clinical Trials Gateway [19] and the Australian Clinical Trials [20] databases were searched for related RCTs (SJMD and PCH).

2.2. Inclusion and exclusion criteria

The following specific inclusion criteria were considered: (1) RCTs in otherwise healthy women aged 40 or more; (2) depressive mood as assessed by specific validated questionnaires or similar tools that include a subscale for the quantitative evaluation of depressive mood or depressive symptoms; (3) available depressive mood baseline data; (4) no significant differences regarding rate of anxiety or severity at baseline between the intervention and control group; (5) studies evaluating the association between depressive symptoms and a program of exercise for at least 6 weeks; (6) controls defined as women who did not participate in the exercise program.

Our exclusion criteria were: (1) the presence of major depression according to DSM-V criteria [21]; (2) studies that included populations with other severe or chronic medical diseases, or psychiatric conditions that may require medical and pharmacologic treatment; (3) the absence of a control group; (4) unclear or no definition of the type of exercise; (5) absence of numerical data generated by specified tools or insufficient information for these to be calculated; (6) non-randomized studies; (7) data published as a review or a conference communication.

2.3. Outcomes

Primary outcome of interest was depressive symptoms as assessed before and after programmed exercise with specific questionnaires, or tools with a subscale or subdomain for depressive symptoms. Planned secondary outcomes of interest were hot flashes and other menopausal symptoms, quality of life, perceived stress, insomnia, body mass index (BMI) changes, and used drugs to manage depressive symptoms.

The following depressive symptom assessing tools were used to select papers to be included in the meta-analysis.

2.3.1. The Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) is a 21-item questionnaire that evaluates behavioral aspects of depression and correlates with its clinical severity (e.g. mild, moderate, severe). The BDI scores for mild, moderate and severe depression correspond, respectively, to 10–18, 19–29, and 30–63 [22].

2.3.2. The Patient Health Questionnaire (PHQ)

The Patient Health Questionnaire (PHQ) is a specific 9-item questionnaire widely used to detect depression in non-psychiatric settings, with a low sensitivity for detecting major depressive disorder. The total score can range from 0 to 27 with higher scores corresponding to greater depressed mood. Scores < 5 are negligible depressive symptoms, 5–14 (inclusive) indicate the presence of depressive symptoms, and 15 or more suggest the presence of major depression [23].

2.3.3. The Women's Health Questionnaire (WHQ)

The Women's Health Questionnaire (WHQ) is a 36-item instrument used to measure physical and emotional well-being. The tool includes 6-items related to depressed mood and 4 items to anxiety. Self-reported symptoms are scored on a 5-point scale (values from 0 to 4) [24]. It has been used to assess quality of life among *peri*- and postmenopausal women.

2.3.4. The Brief Symptom Inventory (BSI)

The Brief Symptom Inventory (BSI) is an 18-item instrument used to screen for psychopathology. It contains 3 six-itemed scales that assess somatization, depression and anxiety with higher scores indicating more intense symptoms [25].

2.3.5. The Geriatric Depressed Scale (GDS)

The Geriatric Depressed Scale (GDS) is a questionnaire that includes 30 items that detect depressive symptoms in the elderly. Each item can be answered *yes* or *no*. The tool is useful for the initial screening, detection and diagnosis of depressive states [26]. A score of 11–14 corresponds to moderate depression, and 15–30 to severe depression.

2.4. Study selection and data extraction

After removing duplicates and articles with no available abstract, manuscripts were screened for eligibility on the basis of their title and abstract. The list of retrieved articles was screened independently by two authors (SJMD and HL) in order to choose potentially relevant papers, who then extracted relevant data (baseline characteristics and outcome variables) from each full-text included article to a previously designed data sheet. Disparities found within the extracted data were discussed by all the authors in order to reach a consensus.

Menopausal status was categorized as premenopausal, perimenopausal and postmenopausal in accordance to the Stages of Reproductive Aging Workshop criteria [27], either by self-reported menstrual bleeding patterns and/or blood follicle stimulating hormone measurement.

Data collection was reported following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [28].

2.5. Risk of bias assessment (study quality)

The methodological quality of the selected RCTs was independently assessed by two authors (SJMD, PCH) using the Cochrane Risk of Bias Tool [29,30]. This instrument assesses the following aspects: random sequence generation (selection bias); allocation concealment (selection bias); blinding of participants and research staff (performance bias); blinding of outcome assessment (detection bias); incomplete outcome data (attrition bias); selective reporting (reporting bias) and any other biases. Each assessed item was described for each RCT as having either a low risk of bias, a high risk of bias, or an unclear risk of bias. RCTs presenting bias for items of randomization or blinding were automatically considered as having an overall high risk of bias.

2.6. Data synthesis and statistical analysis

Effect sizes with 95% confidence interval (CI) were calculated using the Hedges' *g* method. In addition, standardized mean differences (SMDs), for post-intervention depressive outcomes, were pooled using a random-effects model. This model generates a more reliable estimate than the fixed effect analysis; especially when there is substantial heterogeneity. Mean differences (MDs) and their 95% CI, between follow-up and baseline, were calculated for exposed cases and controls and for each study separately. Comparisons were made between intervention and control groups. Hedges' *g* corrects for differences in variances resulting from the inclusion of trials with varying sample sizes. The