

## Systematic review and meta-analysis proposal

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**Working title:** Hormonal responses to aerobic exercise in woman with fibromyalgia: systematic review and meta-analysis

### INTRODUCTION

*Rationale.* Fibromyalgia is a disorder characterized by chronic widespread pain associated with a wide array of symptoms. It is known that the neuroimmunoendocrine system play a role in the etiology of the disease, with abnormalities in hormones and cytokines [1]. The American College of Rheumatology recommends that people with fibromyalgia participate in a low to moderate aerobic exercise program [2,3]. Beneficial effects of habitual aerobic exercise in fibromyalgia patients seems to be involved with altered levels of some hormones like as growth hormone, insulin like growth factor1(IGF1), resistin, and cortisol [4-6]. Exercise should be also mediated the stimulation of the innate and/or inflammatory response preventing the organism against infection. However, some of the exercise-induced changes in the innate/inflammatory response are mediated by “stress hormones”, which could cause some disturb and exacerbate symptoms of fibromyalgia, especially in women, who are more susceptible to these disease. [8]

*Objectives.* To systematically review the evidence examining effects of physical activity on hormonal response in individuals (woman) with fibromyalgia. The primary outcome measures will be the effect of exercise in hormonal response, but will also consider secondary outcome measures such as pain, quality of life, and fear avoidance behaviors.

*Question.* What is the influence of aerobic exercise on hormonal responses of woman with fibromyalgia?

### METHODS

- *Proposed protocol and registration.* Study inclusion criteria and analysis will adhere to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) (Annals of Internal Medicine, 2009) and the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Collaboration, 2007).
- *Information sources.* Studies for potential inclusion will be found by searching the following electronic databases: MEDLINE, Pubmed, EMBASE, Cochrane Controlled Trials Register, SPORTDISCUS, PsychInfo, PEDro.
- *Electronic search terms/strategies.*

#### 1) EXERCISE

#1. (Exercise [mesh terms] OR (Exercises) OR (Exercise, Physical) OR (Exercises, Physical) OR (Physical Exercise) OR (Physical Exercises) OR (Exercise, Isometric) OR (Exercises, Isometric) OR (Isometric Exercises) OR (Isometric Exercise) OR (Exercise, Aerobic) OR (Aerobic Exercises) OR (Exercises, Aerobic) OR (Aerobic Exercise))

## 2) FIBROMYALGIA

#2) (Fibromyalgia [Mesh terms] OR (Fibromyalgias) OR (Fibromyalgia-Fibromyositis Syndrome) OR (Fibromyalgia Fibromyositis Syndrome) OR (Fibromyalgia-Fibromyositis Syndromes) OR (Syndrome, Fibromyalgia-Fibromyositis) OR (Syndromes, Fibromyalgia-Fibromyositis) OR (Rheumatism, Muscular) OR (Muscular Rheumatism) OR (Fibrositis) OR (Fibrositides) OR (Myofascial Pain Syndrome, Diffuse) OR (Diffuse Myofascial Pain Syndrome) OR (Fibromyositis-Fibromyalgia Syndrome) OR (Fibromyositis Fibromyalgia Syndrome) OR (Fibromyositis-Fibromyalgia Syndromes) OR (Syndrome, Fibromyositis-Fibromyalgia) OR (Syndromes, Fibromyositis-Fibromyalgia) OR (Fibromyalgia, Secondary) OR (Fibromyalgias, Secondary) OR (Secondary Fibromyalgia) OR (Secondary Fibromyalgias) OR (Fibromyalgia, Primary) OR (Fibromyalgias, Primary) OR (Primary Fibromyalgia) OR (Primary Fibromyalgias))

## 3) HORMONES

#3. (Hormones [Mesh terms] OR (Hormone) OR (Hormone Receptor Agonists) OR (Agonists, Hormone Receptor) OR (Receptor Agonists, Hormone))

### *Eligibility criteria*

- ❖ **Types of studies.** Only Randomized Controlled Trials (RCTs) of aerobic exercise in individuals with fibromyalgia will be included. RCTs with greater than five (5) fibromyalgia women per treatment group will be included. Language restrictions, publication date, publication type may or may not be enacted. .
- ❖ **Types of participants.** Women participants age 18-65 with a diagnosis of Fibromyalgia will be considered. Fibromyalgia will be defined in this systematic review and meta-analysis as a syndrome that require tenderness on pressure (tenderpoints) in at least 11 of 18 specified sites and the presence of widespread pain for diagnosis. Widespread pain is defined as axial pain, left- and right-sided pain, and upper and lower segment pain [9]. RCTs that reported data for participants with a medical diagnosis, signs, or symptoms of chronic fatigue syndrome or other chronic musculoskeletal disease will be excluded from the systematic review and meta-analysis.
- ❖ **Types of intervention.** Aerobic exercise (also called aerobic activity, aerobic training, endurance activity or cardio activity) will be assumed in this systematic review as the kind of physical activity or exercise that the body's large muscles (at least one-sixth of the skeletal muscles) move in a rhythmic manner for a sustained period. Brisk walking, running, bicycling, jumping rope, and swimming are all examples. 100% of the training session should consist of AE. Land-based or aquatic aerobic exercise it will be considered. Stretching during warm-up and cool-down periods is not defined as mixed exercise. No restrictions on intensity or frequency or duration of training will be made. We will exclude studies or study arms in case of mixed exercise, defined as a combination of AE with stretching

and/or muscle strength [], or in which AE is part of multicomponent therapy defined as a combination of AE with psychological therapy (structured education or relaxation therapy, cognitive-behavioral therapy) [].

- ❖ **Comparison groups.** Control group (sedentary) or standart care (drugs, treatment as usual)
- ❖ **Types of outcome measures.**
- ❖ Primary outcome:
  - Hormones
  - Global well-being: fibromyalgia impact questionnaire scale (FIQ) total;
  - Pain: VAS, FIQ pain subscale
- ❖ Secondary outcomes:
  - Exercise intensity, exercise duration, exercise frequency, exercise quantity, collateral effects, musculoskeletal fitness? body composition?, cardiorespiratory endurance?
- *Data collection process*
  - ❖ **Inclusion Criteria.**
    - Randomized Controlled Trials (RCTs) and
    - Women aged 18-65 years, and
    - Fibromyalgia and
    - Aerobic physical activity or exercise and
    - Hormones (?)
  - ❖ **Exclusion Criteria.**
    - NOT RCT
    - Children or men
    - Not fibromyalgia
    - Mixed musculoskeletal condition (ex.:fibromyalgia + chronic fatigue)
    - NOT aerobic exercise
    - Mixed exercise (aerobic + resistance or flexibility or other training)
    - Multicomponent therapy (aerobic exercise + psychological therapy)
    - **NOT hormones (inflammatory cytokines or mediators)**
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  - ❖ **Reviewers.** Two reviewers independently will select the trials to be considered in the review, and all selected articles will be retrieved for closer examination. To assess agreement between primary reviewers, we will randomly select 5-10 studies that were selected for inclusion. To ensure accuracy of data extraction or if additional information is needed, reviewers will contact authors of original papers selected for inclusion into the systematic review and/or the meta-analysis. Differences in data extraction will be resolved by reference to original articles and discussion to establish consensus.

- ❖ **Risk of Bias.** All included papers will be subject to an assessment of risk of bias based on guidelines outlined by the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Collaboration, 2007). All review co-authors will be provided materials that standardize reporting of specific domains to identify potential areas of bias as part of their evaluation of study quality.
- *Planned Methods of Analysis.*
  - ❖ **Outcome measures.** We propose to perform a meta-analysis on available data related to hormones release, pain intensity post-exercise. The primary comparisons will be of mean group differences in the primary outcome measures in the actively group versus sedentary group and standard care treatment groups in women with fibromyalgia.

## REFERENCES

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