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A meta-analysis of the efficacy of exercise in reducing symptom of fatigue in patients with multiple sclerosis

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Meta-analysis

Abstract

Introduction: Multiple sclerosis is chronic disorders of the central nervous system. One of the most common complaints in patients with multiple sclerosis is fatigue. Exercise can improve physical performance. Studies suggests that exercise activity can be beneficial for fatigue in patients with multiple sclerosis.

Objectives: To study influence of exercise activities on fatigue in patients with multiple sclerosis.

Methods: Researchers used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews and meta-analysis. Researchers searched articles on PubMed, Google scholar and by manual search. Searched articles were screened for relevancy. By use of inclusion and exclusion criteria potential articles were selected.

Results: Out of 229 articles, finally 5 studies included in current meta-analysis. Exercise activities has effect on fatigue. Modified Fatigue Impact Scale (MFIS) score: SMD = 0.47, 95% CI = 0.06–0.87.

Conclusion: Exercise activities can provide beneficial effect on fatigue in patients with multiple sclerosis. This can help patients with multiple sclerosis in daily life activities There is wide scope for further studies to evaluate beneficial effects of exercise activities.

Keywords

- exercise activities
- multiple sclerosis
- fatigue
- Modified Fatigue Impact Scale (MFIS)
- efficacy of exercise

Contribution

A – the preparation of the research project
B – the assembly of data for the research undertaken
C – the conducting of statistical analysis
D – interpretation of results
E – manuscript preparation
F – literature review
G – revising the manuscript

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Introduction

Multiple sclerosis is immune-mediated chronic disorders of the central nervous system.1 The myelin sheath is attacked by immune system which results in involvement[1,2] and destruction of the myelin sheath in the brain and spinal cord and ultimately multiple sclerosis.[1,3] One of the most common complaints in patients with multiple sclerosis is fatigue.[4-6] It causes people with multiple sclerosis problems in their routine daily activities,[4,7] job,[4,8] and affects their mental health.[4,9]

Multiple sclerosis patients benefit from structured exercise.[10,11] symptomatic and supportive measures that can improve daily functioning of patients with multiple sclerosis are important.[4,12] Non-pharmacological measures as exercise can be used as a complementary therapy to decrease the symptoms as fatigue and increase the quality of life in patients with multiple sclerosis.[1,13] Studies indicated that exercise training is associated with increased fitness[4,14] and reduced motor fatigue[4,15] in multiple sclerosis patients.[4]

Positive results from exercise in patients of multiple sclerosis for symptom of fatigue may provide a good option with pharmacological therapy. To what extent exercise can provide beneficial effect for fatigue symptom in patients of multiple sclerosis need to be examined. To understand and analyse it, this meta-analysis is conducted to evaluate influence of exercise activities on symptom of fatigue in patients with multiple sclerosis.

Materials and methods

In the meta-analysis, researchers used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews and meta-analysis (Figure 1).[16] As it is meta-analysis, institutional review board approval was not required.

Search strategy

Relevant studies were identified by a literature search with language restriction of 'English' language in electronic database of PubMed Central and Google Scholar. Advance search done with application of filter in PubMed Central and in Google scholar. Words used in search strategy are: effect, exercise, fatigue, and multiple sclerosis. Literature search was also done directly online in google search. Reference list of filtered studies was also searched to get relevant articles.

Studies selection criteria

Studies filtered in primary search assessed for following inclusion and exclusion criteria:
Inclusion criteria:

- Studies including exercise activities.
- Studies having participants with multiple sclerosis.
- Studies assessed fatigue by Modified Fatigue Impact Scale (MFIS).
- Studies includes pre and post exercise effect on fatigue.

Exclusion criteria:

- Not satisfying inclusion criteria.
- Articles not relevant to multiple sclerosis.
- Free full text article not available of studies.
- Type of articles as letters and review articles.

Study quality

Reviewers assessed studies independently for inclusion and exclusion criteria mentioned in study selection criteria. Reviewers analysed selected studies with following headings: Name of first author with initials, year of publication, brief detail of study population, sample size, age, gender, type of exercise activity, brief detail of exercise activity and brief detail of assessment of fatigue. During detail reading of studies queries for inclusion and exclusion of studies was sort out and finally decided by discussion.

Data extraction

We extracted Modified Fatigue Impact Scale (MFIS)[7,17-20] score with standard deviation before and after sessions of exercise activities in individual articles.[1,4,10,21,22] Data were verified by reviewers and any discrepancies were addressed by discussion and resolved by consensus.

Data analysis

Free online meta-analysis calculator[23,24] was used for analysis of all data and to construct forest plot.

The standardized mean differences (SMD) for the Modified Fatigue Impact Scale (MFIS) score before and after exercise sessions of exercise activity were calculated. The principal summary measure was done with a 95% confidence interval with SMDs.

The Tau2, Chi2 and I2 test was used to measure the Statistical heterogeneity across studies.[25-29] Because of

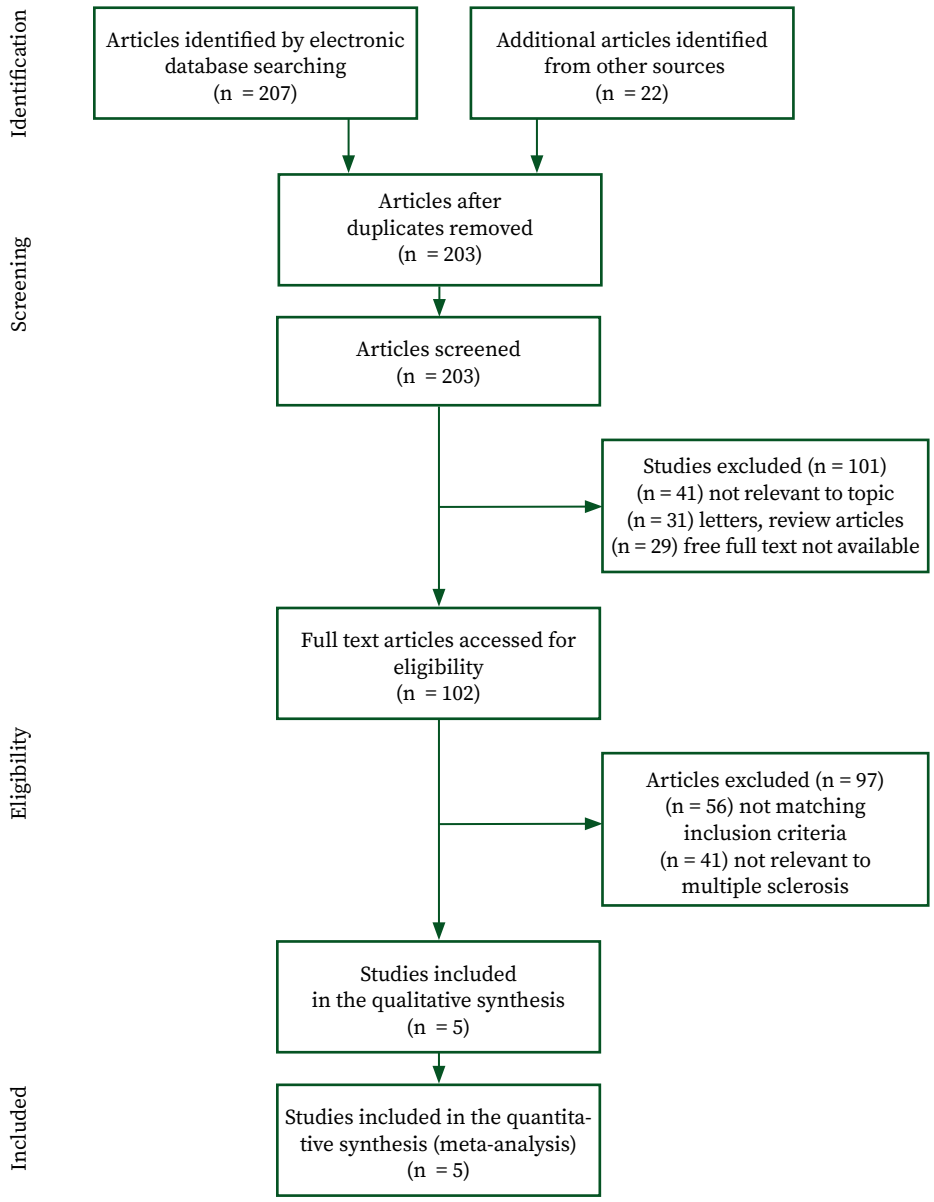

Figure 1. Flow chart article search and study selection

variability in included studies regarding types of exercise activities and among study population, a considerable degree of heterogeneity was expected. So random effects model was used for comparison.[25,30]

Results

Literature search is detailed in Figure 1.[16] Brief description of each included study is detailed in Table 1.

Figure 2 shows Modified Fatigue Impact Scale (MFIS) score for individual studies. Analysis was performed with random effect model. Modified Fatigue Impact Scale (MFIS) score: Tau2= <0.0001, Chi2 =3.30, df = 4, P = 0.51, I2 = 0%. Our results showed that Modified Fatigue Impact Scale (MFIS) score decreased in after exercise activity sessions compared to before exercise activity sessions, according to random effects pooled SMD of Modified Fatigue Impact Scale (MFIS) score before and after exercise activity sessions was : SMD = 0.47, 95% CI = 0.06-0.87 (Figure 2).

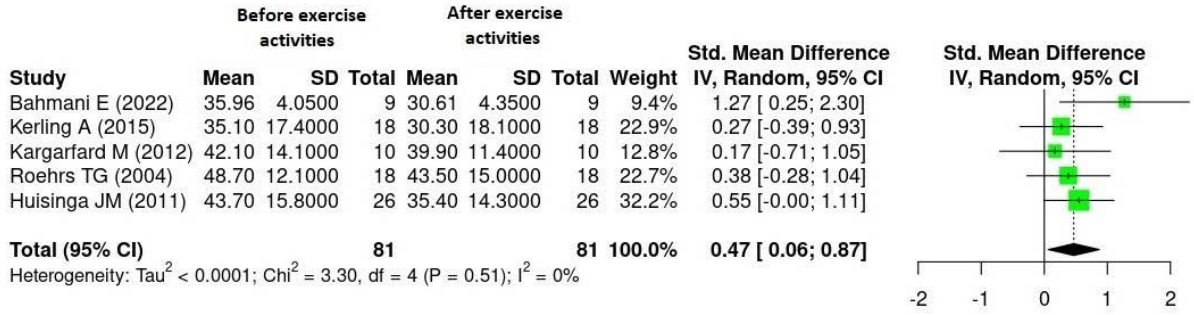

Figure 2. Forest plot of influence of exercise activity on Modified Fatigue Impact Scale (MFIS) score in patients with multiple sclerosis

Table 1. Summary of characteristics of included studies

First author, year	Brief detail of study population	Sample size	Age group (Year)	Gender (male/ female)	Type of exercise activity	Brief detail of exercise activity	Brief detail of assessment of fatigue
Bahmani E. (2022)[1]	Patients with multiple sclerosis selected in study with inclusion and exclusion criteria provided in study.	9	20–40	Female	Aerobic training	Walking aerobics exercise was performed 3 times per week for 2 months as described in the study	Modified Fatigue Impact Scale (MFIS) score recorded before and after intervention program.
Kerling A. (2015)[21]	Patients diagnosed with multiple sclerosis included in the study. Inclusion and exclusion criteria given in the study.	18	18–65	Both	Endurance training	All patients performed a 3-month exercise program consisting of 2 training sessions per week, lasting 40 minutes each.	Modified Fatigue Impact Scale (MFIS) recorded at baseline and after completing the training program.
Kargarfard M. (2012)[4]	Participants included in this study were diagnosed with relapsing-remitting multiple sclerosis. Inclusion and exclusion criteria given in study.	10	—	Female	Aquatic exercise	Participants took part in 8 weeks aquatic exercise in a swimming pool 3 sessions per week, each session lasting 60 minutes.	Modified Fatigue Impact Scale (MFIS) was recorded at the baseline, and at the end of 4 and 8 week of the study.

First author, year	Brief detail of study population	Sample size	Age group (Year)	Gender (male/ female)	Type of exercise activity	Brief detail of exercise activity	Brief detail of assessment of fatigue
Roehrs T.G. (2004)[22]	Patients with progressive multiple sclerosis with inclusion and exclusion criteria given in study were included in study	18	40–65 (Male), 39–71 (Female)	Both	Aquatic exercise	Patients Participated for a 1-hour session 2 times per week for 12 weeks aquatic exercise programme as described in study.	Modified Fatigue Impact Scale (MFIS) was recorded before and after aquatic exercise programme.
Huisinga J.M. (2011)[10]	The study comprised patients with multiple sclerosis with inclusion and exclusion criteria given in the study.	26	19–65	Both	Elliptical exercise training	Participants completed 15 sessions of elliptical exercise training over 6 weeks as described in study.	Modified Fatigue Impact Scale (MFIS) was recorded pre and post training.

Discussion

This meta-analysis was conducted to evaluate effect of exercise activities on symptom of fatigue in patients with multiple sclerosis. Modified Fatigue Impact Scale (MFIS)[7,17-20] used for assessment of fatigue in included studies.[1,4,10,21,22] The meta-analysis examined whether exercise activities decrease Modified Fatigue Impact Scale (MFIS) score. Findings of the study suggests that Modified Fatigue Impact Scale (MFIS) score decreased after exercise activity sessions compared to before exercise activity sessions. These findings suggests that exercise activity has beneficial effect on symptom of fatigue in patients with multiple sclerosis.

Studies in the past performing endurance[21,31,32] or combined training[21,33] showed improvement in fatigue.[21] Increased metabolism induced by aerobic training increases blood flow and reduces weakness of muscle.[1,34] Aerobic training increases oxidation capacity of muscle and increases oxygen delivery to skeletal muscles.[1,4] In patients with multiple sclerosis, aerobic training might reduce fatigue by more blood supply and muscle efficiency.[1,4] Aerobic training could improve fatigue probably by influencing the immune system and by alteration of inflammatory and anti-inflammatory cytokines.[1,35,36]

Kargarfard M et al. (2012), in his article, described possible mechanisms to explain effect of aquatic exercise on fatigue in multiple sclerosis patients.[4] As patients with multiple sclerosis are heat sensitive and warm temperature worsens their symptoms, body temperature can be reduced by pool water which increase exercise tolerance.[4] Water can decrease gravity and resistance against movements of body and help multiple sclerosis patients for long duration of activity with less fatigue.[4]

Participants in studies were from different age group. Participants in the studies were from both genders. Thus, findings of study may be applicable to large population. Studies in meta-analysis has included various types of exercise activity with various exercise protocol. So, it is difficult to isolate effect of individual exercise activity with specific exercise protocol.

Limitation

In search strategy of articles, we selected freely available articles and articles in English language which may have skipped some important articles. In this study effect of exercise activity on Modified Fatigue Impact Scale (MFIS) score in patients of multiple sclerosis is focused. Selected studies measured Modified Fatigue Impact Scale (MFIS) score before and after exercise activity sessions. Studies have various types of exercise activity, different type of exercise protocol, various duration of exercise activity sessions which makes generalization of analysis difficult. Selection of articles done by electronic data base. So, studies of electronic data base which are not screened is likely to be missed. This increase bias in selection process.

Recommendations for future

For more specific evaluation, studies in future should focus on individual exercise activities.

Conclusion

The present meta-analysis study focused on influence of exercise activities on Modified Fatigue Impact Scale (MFIS) score in patients of multiple sclerosis. Overall findings of study suggests that exercise activities decrease Modified Fatigue Impact Scale (MFIS) score. properly designed RCTs are needed to examine this effect in more detail and to implement.

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