J Rehabil Med 2021; 53: jrm0000X

Cochrane Corner

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WHAT ARE THE EFFECTS OF STRENGTH TRAINING AND AEROBIC EXERCISE TRAINING FOR MUSCLE DISEASE? - A COCHRANE REVIEW SUMMARY WITH COMMENTARY

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The aim of this commentary is to discuss from a rehabilitation perspective the published Cochrane Review "Strength training and aerobic exercise training for muscle disease"(1) by Voet NBM et al.[1], under the direct supervision of Cochrane Neuromuscular Group. This Cochrane Corner is produced in agreement with the Journal of Rehabilitation Medicine by Cochrane Rehabilitation.

Key words: Cochrane Review Summary, exercise training, neuromuscular disease, systematic review, exercise prescription

J Rehabil Med 2021; 53: jrm001XX

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BACKGROUND

Muscle disease comprises a large group of disorders mainly affecting skeletal muscles, although other organs can also be involved (1). Many of these conditions have no curative treatment, e.g. Duchenne muscular dystrophy, facio-scapulo-humeral muscular dystrophy (FSHD), and myotonic dystrophy. These disorders cause progressive weakness and patients usually face difficulties participating in sports, work, and hobbies. Fatigue and pain may affect quality of life. In the past patients with muscle diseases have been advised to avoid exercise (3). However, recent reports suggest that different forms of exercise may be safe and beneficial for patients with a variety of muscle diseases (4–6). Forms of exercise potentially available to these patients include physical fitness training, strength training, and aerobic exercise training (cardiorespiratory fitness training). However, there is a need to determine the optimal duration and training regimens for these patients.

STRENGTH TRAINING AND AEROBIC EXERCISE TRAINING FOR MUSCLE DISEASE[a,1]

(Voet NBM, van der Kooi EL, van Engelen BGM, Geurts ACH, 2019)

WHAT IS THE AIM OF THIS COCHRANE REVIEW?

The aim of this Cochrane Review was to evaluate the effects (benefits and harms) of strength and aerobic exercise training in people with a muscle disease.

WHAT WAS STUDIED IN THE COCHRANE REVIEW?

This Cochrane review is an update of a review first published in 2005 and last updated in 2013 (4, 7). The population addressed in this review were people with a diagnosis of a muscle disease, such as an inflammatory myopathy, metabolic myopathy, muscular dystrophy, or muscle disease with myotonia. The interventions studied were all forms of strength training and aerobic exercise training, or a combination of them, lasting at least six weeks, which were compared to no training. Studies looking at strength training or aerobic exercise training for people in whom muscle weakness was not the primary feature, but secondary to, for example, chronic renal insufficiency, chronic heart failure, renal or heart transplantation, or corticosteroid use, were excluded. Primary outcomes were muscle strength (for strength training) and aerobic capacity (for aerobic exercise training). Secondary outcomes were muscle endurance or muscle fatigue, aerobic capacity (expressed in measures of oxygen consump-

[a]This summary is based on a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2019, Issue 12. Art. No.: CD003907. DOI: 10.1002/14651858.CD003907.pub5 (see www.cochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review. The views expressed in the summary with commentary are those of the Cochrane Corner authors and do not represent the Cochrane Library or Journal of Rehabilitation Medicine.

doi: 10.2340/16501977-2871

tion and parameters of cardiac function or parameters of respiratory function), timed-scored functional assessments of muscle performance (six-minute walk test), quality-of-life measures (Short Form 36 - SF-36 - Health Survey), pain (analogue pain scale), experienced fatigue (Checklist Individual Strength - CIS-fatigue). Safety outcomes were parameters of muscle membrane permeability (assessed by serum creatine kinase – CK - level, myoglobin level), and adverse events requiring withdrawal of the participant from the study (acute rhabdomyolysis, increasing muscle pain, injury, etc.). Authors compared data on these outcome measures at baseline with those obtained after at least six weeks of training.

SEARCH METHODOLOGY AND UP-TO-DATENESS OF THE COCHRANE REVIEW

Review authors searched for studies that had been published up to 16 November 2018 from the Cochrane Neuromuscular Specialised Register, CENTRAL, MEDLINE, Embase, and CINAHL. They also searched the World Health Organization International Clinical Trials Registry Platform and US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov on 22 December 2018. The reference lists of relevant studies identified by the above search strategies were further explored to identify other relevant studies. Authors in the field were also contacted to clarify trial eligibility or to identify additional published and unpublished data.

WHAT ARE THE MAIN RESULTS OF THE COCHRANE REVIEW?

This review included 14 studies (randomised controlled trials (RCTs), quasi-RCTs or cross-over RCTs, with 428 participants. Three trials studied strength training; five aerobic exercise training, and six strength training and aerobic exercise training combined. In six studies the dropout rate was high (up to 39%). Seven studies did not perform an intention-to-treat analysis.

The review shows that:

- Strength training versus no training in myotonic dystrophy: Data from two studies with 71 participants could not be pooled. One study with 35 partiicipants found very low-certainty evidence of no effect from strength training on hand grip force, pinch grip force, or isometric wrist flexor force, and a slight improvement in isometric wrist extensor force. There was also very low-certainty evidence of little or no effect of training on time-scored functional assessments of muscle performance. The other study, in 28 people, found no clear effect of training on isometric or isokinetic knee flexion or extension. Both studies showed few or no adverse effects resulting in withdrawal (very low certainty evidence). No data were provided for the outcomes aerobic capacity, quality of life, pain, and experienced fatigue.
- Strength training versus no training in FSHD: A single study with 35 participants reported that strength training may make little or no difference in people with FSHD in terms of isometric and dynamic strength and muscle endurance of elbow flexors and ankle dorsiflexors (low certainty evidence). Eleven participants reported pain, but the number of complaints did not differ between groups at baseline and at the final visit and strength training may make little or no difference in pain experienced (low certainty evidence). There may be no differences in terms of adverse effects requiring withdrawal (low certainty evidence). Time-scored functional assessments of muscle performance, experienced fatigue, and quality of life ($n=35$) were reported and there was no difference between baseline& final reading and between groups. (Low certainty evidence)
- Aerobic exercise training versus no training in dermatomyositis and polymyositis: The evidence from one study with 14 participants that reported on aerobic capacity and time-scored functional assessments of muscle performance and disability was uncertain (very low certainty of evidence). No adverse effects requiring withdrawal were reported (very low certainty of evidence). Muscle strength, quality of life, pain and fatigue were not reported.
- Aerobic exercise compared to no training for Duchenne muscular dystrophy (DMD): The evidence from three studies of aerobic exercise in Duchenne muscular dystrophy was very uncertain. These were a study with 15 participants on the effects of aerobic exercise on muscle strength of hip extensors, knee extensors, ankle dorsi-flexors, shoulder abductors, and elbow extensors; a study involving 23 people aerobic exercise aerobic capacity (reported as the number of arm and leg revolutions); and a study involving 29 people that reported the outcome time-scored functional assessments of muscle performance and adverse effects requiring withdrawal. Data for fatigue, pain and quality of life were not reported.
- Aerobic exercise compared to no training for facioscapulohumeral muscular dystrophy: Three studies with 93 participants were included in this comparison. One trial with 52 participants reported that aerobic exercise may have little or no effect on muscle strength and pain, but may improve time-scored functional assessments of muscle performance, quality of life, and experienced fatigue. No adverse

events leading to withdrawal were described (low certainty evidence). Another trial involving 38 people provided low certainty evidence that aerobic exercise may slightly increase aerobic capacity.

- Aerobic exercise and strength training compared to no training for mitochondrial myopathy: A single study with 18 participants provided very uncertain evidence on the effects of combined training on muscle strength, aerobic capacity, quality of life, and adverse effects requiring withdrawal (very low certainty of evidence). Time-scored functional assessments of muscle performance, pain and experienced fatigue were not reported.
- Aerobic exercise and strength training compared to no training for myotonic dystrophy type 1: One study with 35 participants was included in this comparison. There was very low certainty evidence that combined training may have little or no effect on time-scored functional assessments of muscle performance. No adverse effects requiring withdrawal were described. Muscle strength, aerobic capacity, quality of life, pain and experienced fatigue were not reported.
- Aerobic exercise and strength training compared to no training for dermato-myositis and polymyositis: Two studies with 43 participants were included in this comparison. In one study, muscle strength was assessed with manual muscle testing of 8 muscle groups (MMT-8). After 12 weeks, the results indicated that the combined training may have no clear effect on the MMT-8 score (very low-certainty evidence). There was also very low certainty evidence that aerobic exercise and strength training may slightly increase aerobic capacity assessed with time cycled till exhaustion, slightly improve power performed at VO_2 max and slightly improve quality of life, with few or no adverse effects requiring withdrawal. The effects on aerobic capacity assessed with VO_2 max and time-scored functional assessments of muscle performance were uncertain. Muscle strength, expressed in measures of endurance or fatigue, pain, and experienced fatigue were not reported.
- Aerobic exercise and strength training compared to no training for facioscapulohumeral muscular dystrophy: This comparison was reported by a single study with 16 participants. Effects on muscle strength, maximal aerobic power, VO_2 peak, time-scored functional assessments of muscle performance, quality of life, experienced fatigue and adverse effects requiring withdrawal were uncertain (very low certainty evidence). Pain data was not provided.
- Aerobic exercise and strength training compared to no training for juvenile dermatomyositis: One study with 26 participants was included in this comparison. Combined training may increase muscle strength assessed as maximum force of knee extensors but may have little or no effect on maximum force of hip flexors (low certainty evidence); it may slightly decrease aerobic capacity measured by endurance time and VO_2peak; it may make little or no difference on time-scored functional assessments of muscle performance; it may slightly improve quality of life; it may slightly reduce pain level; and it may slightly increase experienced fatigue (low certainty evidence). No adverse effects requiring withdrawal were described.

HOW DID THE AUTHORS CONCLUDE?

The authors concluded that considering the available evidence effects of strength and aerobic exercise training or their combination in patients with muscle diseases is uncertain. There is low certainty evidence that strength training alone may have little or no effect at all, while aerobic exercise may possibly improve aerobic capacity for people with facioscapulohumeral muscular dystrophy. There is very low certainty evidence that combined strength and aerobic training may slightly increase strength and aerobic capacity of patients with dermatomyositis and polymyositis and low certainty evidence that participants with juvenile dermatomyositis may have slight increase in muscle strength and decrease in aerobic capacity. There were no documented negative effects of any exercise training program.

WHAT ARE THE IMPLICATIONS OF THE COCHRANE EVIDENCE FOR PRACTICE IN REHABILITATION?

Muscle diseases of various origin (Duchenne muscular dystrophy, Becker muscular dystrophy, myotonic dystrophy, limb-girdle muscle dystrophy, dermatomyositis, polymyositis) affect patients in different age groups ranging from children to adults. Currently there is no curative treatment for most of these conditions. Symptom alleviation and rehabilitation are important components of the management of these patients (8). Exercise prescription is an important component of the rehabilitation interventions provided to these patients. Exercises can be provided in many forms and formats. However, evidence for the effectiveness of exercise in these patients is not very robust. This is due to the lack of well-designed controlled training studies on this heterogenic group of disorders. In addition, the effects of strength training in one type of muscle disorder is not directly applicable to another, but is largely dependent on the underlying biological defect (8).

However, there appear to be no major adverse effects associated with exercise in these patients, particularly when performed under supervision. In the absence of clear evidence, a trial of exercise may be undertaken after discussion between a patient and healthcare professionals. Any programme should be designed by a rehabilitation professional considering physical limitations, muscle strength and patient preferences. It is recommended that exercise is started early in the course of the disease when muscle fiber degeneration is minimal and there are still a substantial amount of trainable muscle fibers (3, 8).

It is also important for rehabilitation professionals to generate high quality evidence regarding the role of different forms of exercises in patients with muscle diseases. Evidence should address the type, intensity and duration of exercises along with the long-term effects of these exercises on patient's mobility, participation in the community and quality of life.

ACKNOWLEDGEMENTS

The authors thank Francesca Gimigliano, MD, PhD, University of Campania "Luigi Vanvitelli" and Communication Working Area Chair, Cochrane Rehabilitation and Cochrane Neuromuscular for reviewing the contents of the Cochrane Corner.

The authors have no conflicts of interest to declare.

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