

EXERCISE THERAPY FOR PATIENTS WITH RHEUMATOID ARTHRITIS: SAFETY OF INTENSIVE PROGRAMMES AND EFFECTS UPON BONE MINERAL DENSITY AND DISEASE ACTIVITY: A LITERATURE REVIEW

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ABSTRACT

Rheumatoid arthritis presents many challenges to those involved in its management. Concerns exist over the safety of interventions aimed at increasing aerobic capacity and muscle strength. The objective of this review was to evaluate the outcome of intensive exercise programmes for patients with rheumatoid arthritis on bone mineral density and disease activity. A search of six databases was conducted using relevant search terms. Papers investigating the effect of aerobic and/or strengthening programmes on patients with rheumatoid arthritis were included. Eleven papers out of 30 returned were included; four of these eleven papers had a low risk of bias. Findings from these studies indicated that exercise programmes for patients with rheumatoid arthritis do not increase disease activity, are safe, and slow down the loss of bone mineral in the hip. Results of this review highlight the safety and benefits of aerobic and dynamic strengthening exercise programmes for patients with rheumatoid arthritis.

Keywords: Aerobic, exercise, rheumatoid arthritis, strengthening

INTRODUCTION

As a chronic inflammatory disease, rheumatoid arthritis presents many challenges for effective management. Muscle loss, weakness and joint pain are common consequences of the disease and result in marked reduction in physical activity and aerobic capacity. The causes of the associated disability are many and include behavioural, immunological and metabolic factors.¹

In recent years, it has been recognised that exercise plays a key role in the management of the patient with rheumatoid arthritis: a recent review¹ of the role of exercise for patients with rheumatoid arthritis concluded that exercise reverses the catabolic effects that an inflammatory disease has on muscle, improves function, and decreases disability. Strength training

and aerobic exercise for less than one hour per day is recommended to provide such benefits.¹ Consistent with this view are the results of a previous systematic review,² which concluded that intensive exercise therapy is effective at increasing aerobic capacity and muscle strength in patients with rheumatoid arthritis. The review also highlighted the need for further research to identify the effects of such programmes on functional ability and radiological progression. However, concerns have been expressed by a number of authors as to the safety of such exercise programmes.^{3,4} While there has been previous research in the area of exercise and rheumatoid arthritis, only recently has there been substantive work undertaken focusing on the effects of exercise on radiological progression of the disease and on bone mineral density. Thus, the aim of this literature review is to review current literature

Table 1. Search strategy

<i>Electronic databases searched</i>	
	AMED
	CINAHL
	Medline
	Cochrane Library
	Biomed Reference Collection
	Web of Science
<i>Search terms used</i>	
	Exercise
	Dynamic
	Aerobic
	Strengthening
	Programmes (Programs)

published in the area of the effectiveness and safety of intensive exercise programmes for patients with rheumatoid arthritis, specifically focusing on disease activity, bone mineral density and radiological damage.

PATIENTS AND METHODS

Search strategy

As a Cochrane review² of the literature within the field published prior to 1998 was published in 2000, it was decided to search for literature published since 1999 in order to identify new research in the area. Considerable work has been undertaken since the publication of that Cochrane review, thus expanding the knowledge of the efficacy and safety of the use of such programmes for this patient group. Searches were conducted of six electronic databases of papers published between 1999 and 2004, using key search terms that represented the inclusion criteria (Table 1). The search was extended by secondary searching the reference lists of papers retrieved to identify any additional references for retrieval.

Selection criteria

The following criteria were used in selecting papers for inclusion in the review: randomised trials that

included patients with a definite diagnosis of rheumatoid arthritis using interventions that improved aerobic capacity and muscle strength.

Quality assessment

The quality of the studies was critically appraised in line with the recommendations of the Cochrane Collaboration.⁵ These include rating the validity of a study by using predefined criteria so as to derive an overall assessment of validity. The criteria used in the rating scheme relate to four different types of bias – selection, performance, attrition, and detection bias. An overall assessment of study validity is then achieved consistent with the descriptors outlined in Table 2.

RESULTS

Thirty articles were returned that related to trials of randomised exercise in rheumatoid arthritis. Of these, four were not included in the review as they included patients with osteoarthritis in addition to those with rheumatoid arthritis. A number of papers ($n = 15$) were excluded, as they were review papers only. Thus, eleven papers fulfilled the criteria and were rated with respect to methodological quality. All references were obtained in hard copy.

Methodological quality

The methodological quality of the studies is shown in Table 3. Only four studies (all performed by a single research group) had a low level of bias;⁶⁻⁹ the remaining seven studies¹⁰⁻¹⁶ had high bias. Thus, this review will focus on the results of the four studies with low levels of bias: these studies are summarised in Table 4.

An adequate description of patient selection was provided in all studies.⁶⁻⁹ Methods of allocation used in these studies included permuted block randomisation⁷⁻⁹ and sealed opaque envelopes.⁶ In the four high-quality studies, an independent person generated the allocation sequence, and allocation of patients was by an independent person.

Table 2. Assessment of overall study validity

	Risk of bias	Interpretation	Relationship to individual criteria
A	Low risk of bias	Plausible bias unlikely to seriously alter the results	All of criteria met
B	Moderate risk of bias	Plausible bias that raises some doubt about the results	One or more of the criteria partly met
C	High risk of bias	Plausible bias that seriously weakens confidence in the results	One or more criteria not met

Table 3. Methodological quality of studies accessed (*studies included in review)

	Selection bias	Detection bias	Performance bias	Attrition bias	Risk of bias
Moffett <i>et al.</i> (2000) ¹¹	Not met	Not met	Not met	Not met	High
Westby <i>et al.</i> (2000) ¹⁰	Not met	Met	Not met	Partly met	High
Van den Ende <i>et al.</i> (2000) ^{6*}	Met	Met	Met	Met	Low
Hakkinen <i>et al.</i> (2001) ¹²	Partly met	Not met	Met	Met	High
Bearne <i>et al.</i> (2002) ¹⁶	Partly met	Not met	Partly met	Met	High
Hakkinen <i>et al.</i> (2003) ¹³	Not met	Not met	Met	Met	High
Hakkinen <i>et al.</i> (2003) ¹⁴	Not met	Not met	Met	Met	High
De Jong <i>et al.</i> (2003) ^{7*}	Met	Met	Met	Met	Low
De Jong <i>et al.</i> (2004) ^{8*}	Met	Met	Met	Met	Low
De Jong <i>et al.</i> (2004) ^{9*}	Met	Met	Met	Met	Low
Hakkinen <i>et al.</i> (2004) ¹⁵	Partly met	Not met	Met	Met	High

A randomised study design was used in all four studies⁶⁻⁹ with sample size calculations included in all four studies.

Participants

The profile of participants included in the review was quite diverse: only one study included patients with active rheumatoid arthritis,⁶ while three included participants with a stable DMARD regimen.⁷⁻⁹ Functional classification in rheumatoid arthritis can be measured using a scale from class I to IV with class I representing least amount of functional limitation. With regard to functional classification of participants in these studies, Class I to III participants were included in three studies.⁷⁻⁹

Sample sizes varied markedly between studies: the largest sample consisting of 300 patients.⁷⁻⁹

Outcome measures

A number of different outcome measures were used to evaluate the effectiveness and safety of the programmes. Disease activity was the main focus in two of the studies,^{6,7} and is usually measured by a combination of some or all of the following: number of swollen and tender joints, pain levels, physician and patient global assessment of disease, as well as recording erythrocyte sedimentation rate (ESR), an indirect measure of inflammation. In some cases, the different variables are combined into one unit such as the disease activity score.⁷ Bone mineral density was measured by DEXA scan of the hip region and lumbar spine.⁸ Radiological damage to the small joints of the hands and feet were used as a measure of the safety of these exercise programmes in response to concerns

over the possibility of damage to joints from intensive exercise.⁹ No assessment of economic costs associated with exercise programme delivery were included in any of the studies.

Interventions

The studies reviewed included strengthening and aerobic components in their exercise programmes. Three of the studies⁷⁻⁹ investigated the effectiveness and safety of the RAPIT programme, a one-hourly, biweekly group exercise programme of 1.25 h per session. Each session had three components: bicycle training (20 min), exercise circuit (20 min), and a sporting activity (20 min) Bicycle training was at 70-90% of predicted maximum heart rate (HR; aerobic component) with a rating of perceived exertion of 4-5 on a scale of 0-10. The exercise circuit consisted of 8-10 different exercises to improve muscle strength, muscle endurance, joint mobility and activities of daily living. The proportion of exercise duration/rest duration changed from 90 s/60 s in the first weeks of the programme, to 90 s/30 s after 6 months. Within the exercise circuit, each exercise was repeated 8-15 times. The sporting activity section consisted of impact-delivering sporting activities such as badminton, volleyball, indoor soccer and basketball. The RAPIT programme was compared to a 'usual care group' receiving care from a physiotherapist.

The remaining study⁶ randomly allocated patients to either usual care or to an intensive exercise regimen. The 'usual care group' received a conservative programme of range of motion and isometric exercises; the intensive programme consisted of exercises additional to the conservative programme. These exercises comprised reciprocal isometric and isokinetic

Table 4. Descriptions of studies included in review

Study	van den Ende <i>et al.</i> (2000) ⁶
Gender (female)	20
Sample size	64
Intervention	Isometric and isokinetic muscle strength + bicycling for 15 min, 3 times a week at 60% age-predicted maximum + usual care versus usual care (rom + isometric)
Outcome measures	Disease activity, muscle strength, joint mobility, functional ability
Results	Increased muscle strength and physical function with no increase disease activity in intensive exercise group
Study	de Jong <i>et al.</i> (2003) ⁷
Gender (female)	237
Sample size	309
Intervention	RAPIT programme: 2 weekly: (i) bicycle training (20 min at 70–90% maximum HR; (ii) exercise circuit (20 min); (iii) sport or game (20 min) versus usual care
Outcome measures	Disease activity, functional ability, physical capacity, emotional status, radiographic damage
Results	No detrimental effects on disease activity. Functional ability improved more than 'usual care' group. Emotional status improved in RAPIT group. Patients with baseline joint damage showed more progression of joint damage
Study	de Jong <i>et al.</i> (2004) ⁸
Gender (female)	237
Sample size	309
Intervention	As per de Jong <i>et al.</i> (2003) ⁷
Outcome measures	Disease activity, physical capacity, functional ability, radiological damage of small and large joint X-rays, BMD of hip and lumbar spine
Results	Decrease in BMD in femoral head only both groups, smaller decrease in RAPIT group
Study	de Jong <i>et al.</i> (2004) ⁹
Gender (female)	237
Sample size	309
Intervention	As per de Jong <i>et al.</i> (2003) ⁷
Outcome measures	Rate of radiographic progression of damage in hands and feet (Larsen score)
Results	Significantly less radiological damage in small joints

training of the knee flexors and extensors on an isokinetic dynamometer. Isometric training comprised three series of five contractions at 70% maximum voluntary contraction (MVC) during 6 s with the knee joint at 45° flexion. A recovery time of 30 s between each series was given. Isokinetic strength of both knees was trained by three series of eight reciprocal contractions at 70% MVC at an angular velocity of 60°. Additionally, patients bicycled three times a week for 15 min at 60% of age-predicted maximum.

Study results

Intensive exercise as described in one of the studies⁶ did not exacerbate disease activity. Disease activity decreased over the study period (24 weeks) with a

mean improvement in disease activity score (DAS) of –1.4 and –0.7 in the intensive exercise and usual care group, respectively. The disease activity score is an overall score comprising number of swollen joints, number of tender joints, ESR and patient's global assessment of disease. Similarly, the other study focusing on disease activity⁷ found that there was no detrimental effect in terms of disease activity from the RAPIT programme. Disease activity (as measured by the DAS) showed a gradual, but small, decline over the study period of 2 years.

Bone mineral density (BMD) measurement⁸ showed that the mean rate of decrease of hip BMD was smaller in patients in the RAPIT group than in the usual care group: mean decrease in BMD in the RAPIT group was 1.6% (95% CI, 1.10–2.90) over year 1 and 0.5% (95% CI, 1.1–2.0) over year two.

Finally, results from radiological imaging of participants in the RAPIT programme⁹ indicated significantly less radiological damage than in the 'usual care' participants. Mean increase in radiological damage in the RAPIT group was 3.5 compared to 5.7 in the usual care group, as measured using the Larsen score.

Thus, a number of conclusions can be identified from this review. Exercise programmes for patients with rheumatoid arthritis: (i) do not increase disease activity;^{6,7} (ii) are safe to use in patients with rheumatoid arthritis;⁹ and (iii) slow down the loss of bone mineral in the hip.⁸

DISCUSSION

Traditionally, exercise prescription in the management of patients with rheumatoid arthritis did not include aerobic training or high impact exercises. Concerns existed^{3,4} over the safety of such aerobic exercise programmes, and the use of activities that provided impact to damaged joints. However, the results from this literature review indicate that use of aerobic and strengthening programmes does not increase disease activity, nor cause long-term radiological damage, and may slow down the loss of bone mineral in the hip region. Thus, based on the studies included in this review, exercise programmes for patients with rheumatoid arthritis should include an aerobic component at 50–70% of maximum predicted HR, in addition to strengthening exercises of moderate loads (70% repetition maximum).

While the quality of the studies conducted in this area is improving, more high-quality research needs to be conducted to add to the body of evidence that currently exists for the effectiveness and safety of these programmes. Standardisation of programme content and outcome measurement across studies will allow for meta-analysis of results. Moreover, future research in this area needs to evaluate the effectiveness of these programmes for patients with active rheumatoid arthritis. Only one study⁶ evaluated the effect of these intensive programmes on active disease status; thus, the effectiveness and safety of intensive exercise programmes for active disease has yet to be definitively established. Further research is also needed to identify if differences in outcome occur between patients with early and long-standing rheumatoid arthritis, and differing types of functional classification. Moreover, it is necessary to include an economic analysis of these programmes in order to identify if they represent a cost-effective approach to management of such patients. Savings from these programmes may be considerable if they continue to

provide beneficial effects on bone mineral density, radiological progression, and disease activity in the longer term.

CONCLUSIONS

There is evidence that aerobic and strengthening programmes for patients with rheumatoid arthritis are effective and safe. Longer term benefits of reduced bone mineral loss and reduced joint damage appear to be possible following such programmes; however, there is a need for more longitudinal studies to be undertaken to confirm this for patients with active disease and to identify the economic benefits of these programmes.

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