Journal of Crohn's and Colitis (2009) **3**, 225–231

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REVIEW ARTICLE

Prescription of physical exercise in Crohn's disease

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Received 13 July 2009; received in revised form 28 August 2009; accepted 28 August 2009

KEYWORDS
Crohn's disease;
Prescription;
Exercise

Abstract

Background: Physical exercise may be potentially beneficial for recovering physical condition and improving quality of life in populations suffering from chronic conditions, but little is known about its effects on patients suffering from Crohn's disease.
Aims: To provide reasonable and conservative recommendations for exercise regimens that appear clinically safe and feasible in patients suffering from Crohn's disease.
Methods: Relevant clinical studies about the effects of physical exercise on Crohn's disease, written in English language and carried out with human subjects were reviewed.
Results: Few relevant clinical studies have evaluated the effects of an exercise intervention on patients experiencing Crohn's disease. There seem to be two main types of physical interventions that should be recommended: aerobic activity and muscular resistance training.
Conclusions: Some basic guidelines about how to prescribe physical exercise in Crohn's disease can be provided. However, more research is needed as few studies have been carried out so far.

Contents

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doi:10.1016/j.crohns.2009.08.006

1. Introduction

Over the past decades, considerable knowledge has accumulated concerning the significance of exercise in the treatment of a number of diseases and, as a result, physical activity is now being recommended to a large number of people affected by medical disorders.[1] The positive effect that exercise has on chronic conditions, such as multiple sclerosis, fibromyalgia or systemic lupus, derives from its potential for improving the patients' physical condition and quality of life. These benefits can be observed both from the physical, psychological and sociological point of view, which has led to new ways of understanding multidisciplinary rehabilitation of sufferers.[2] Crohn's disease (CD), is a chronic relapsing inflammatory disorder very similar to those mentioned above regarding some basic facts (unknown aetiology, involvement of the immune system)[3] and some common symptoms such as fatigue, unfitness or decreased quality of life (QoL).[4] In spite of all this, few data exist concerning the safety of exercise in CD and whether or not exercise may have beneficial effects on the patients' health. This review aims to identify the reasons for prescribing physical exercise in CD, to describe the main symptoms of the disease that can be attenuated by means of exercising, and to present the main studies that have examined the influence of exercise in CD patients. Additionally, some basic exercise guidelines for this kind of population are presented in order to enable exercise physiologists to prescribe physical exercise and to better manage CD patients.

2. Anti-inflammatory benefits of physical exercise: role in Crohn's disease

Crohn's disease involves an immune system dysfunction. An imbalance in the local mucosal production of pro-inflammatory cytokines over anti-inflammatory cytokines is thought to cause the ulcerative lesions typical of the disease.[3] Research has related the pro-inflammatory cytokines interleukin-6 (IL-6) and tumour necrosis factor-alpha (TNF-α) to the intestinal inflammation inherent to CD.[5] Although physical activity appears to reduce these inflammation markers, recent research showed that the results of several studies involving cycling, running, swimming and resistance exercises are controversial and no clear pattern emerges from them.[6] It has been suggested that during exercise skeletal muscle produces and releases IL-6 (known as myokine), and as a result of the increased levels of IL-6, TNF-α production is inhibited.[7] From a simple physiological point of view, it seems that despite this reduction in TNF-α levels, the increased level of circulating IL-6 would amplify the inflammatory response in CD, suggesting a negative effect of exercise. However, it has been pointed out that in patients suffering from chronic inflammation, the elevated levels of IL-6 might represent a "defence" mechanism against pro-inflammatory actions caused by TNF-α, which in turn may trigger IL-6 release.[8] Furthermore, it has been suggested that IL-6 levels are weakly linked to CD activity and that this cytokine is a poor disease activity marker.[9] Given all this facts and taking into account that the anti-inflammatory activity induced by regular exercise may have some beneficial effect on patients with chronic disease,[8] physical exercise should be prescribed in CD. However, in some autoimmune dysfunctions, while IL-6 levels have been shown to be reduced after 8 weeks of moderate aerobic cycle training, TNF-α levels have shown to be increased, reflecting the need for further studies on this matter.[10] As far as the anti-inflammatory role of exercise is concerned, it has recently been suggested that heat shock proteins can decrease the secretion of pro-inflammatory cytokines and that exercise may be beneficial for ameliorating CD inflammatory symptoms by inducing heat shock protein presence in the intestines.[11] However evidence is scarce and regarding the anti-inflammatory effects of exercise in CD further investigation is needed.

3. On the effect of physical exercise on Crohn's disease symptoms

The underlying mechanisms of the potential benefits of exercise on CD symptoms are not fully understood. However, there is strong evidence of the effects of exercise on some of these symptoms, especially on those shared by people suffering from other chronic conditions (Table 1).

3.1. Pain

Crampy intermittent pain, located in the abdominal area, and produced by the inflammation of the intestines, is the most common symptom of CD.[12] Although only a small number of studies report exercise-induced analgesia in the setting of inflammatory pain, physical activity (mainly stretching exercises) has shown to be effective in reducing

Table 1 Possible effects of physical exercise on Crohn's disease symptoms.

CD symptoms	Effects of physical exercise
Pain	Swimming exercise induced analgesia by reducing inflammatory and peripheral neuropathic pain.
Bone mineral loss	Aerobic and muscular training can enhance bone mineral density.
Fatigue	Lack of physical fitness can be solved through aerobic and muscular resistance training.
Intestinal problems	Light exercise may have protective effects on the gastrointestinal tract.
Body composition	Resistance training has shown to be effective in increasing total body weight and improving body composition.
Sleep disturbances	Aerobics help people with sleep problems.
Anaemia	Aerobic exercise may reduce or prevent declines in erythrocyte levels.

self-perceived pain in other illnesses where this is one of the main symptoms, such as fibromyalgia.[13] In addition, it has been recently shown that extended swimming exercise induced analgesia by reducing inflammatory and peripheral neuropathic pain in rodents, supporting the use of exercise as a non-pharmacological approach to the management of this symptom.[14]

3.2. Bone mineral loss

Reduced bone mineral density has been reported in between 5% and 80% of CD sufferers, although it is generally believed that approximately 40% of them suffer from osteopenia and 15% from osteoporosis.[5] This fact leads CD patients to be 1.4 to 2.5 times more likely than the normal population to sustain a fracture.[15] The aetiology of bone loss in CD is varied and complex, being generally related to disease treatment (use of corticosteroids and other immunosuppressive medications), calcium and vitamin D malabsorption, vitamin K deficiency, malnutrition and lack of exercise.[16] In this regard, it is widely known that physical activity improves skeleton bone mass mainly in two ways: by muscle pull and by gravitational forces from weight wearing activity. For this reason, it is generally assumed that aerobic and muscular training can enhance bone mineral density (especially in postmenopausal women, who usually develop estrogen deficiency).[17] Furthermore, when these two types of training were combined with balance exercises, a reduction in the risk of falls and fractures was observed.[1] Therefore, physical exercise can be a potentially effective way of counteracting bone mineral loss and its effects on CD patients.

3.3. Fatigue

Fatigue is a frequently reported symptom in CD, even when the disease is in remission but, in spite of its high prevalence, it remains poorly understood.[18] A previous study about the fitness level of CD patients revealed that these people experience a reduction in aerobic capacity as well as a decrease in muscle strength,[19] therefore, lack of physical fitness could be hypothesized as a cause for this symptom. However, blood haemoglobin levels have been found not to be related with the impact of fatigue on this kind of patients,[4] revealing the need for further research in this regard. CD patients often complain about energy loss and poor physical function.[20] Since physical activity has a direct effect on a person's feeling of energy,[21] exercise could attenuate perceived fatigue in this kind of patients as it has been shown in populations suffering from chronic fatigue syndrome.[1]

3.4. Intestinal problems

Two of the most common symptoms in CD patients are diarrhea and constipation,[22] both of which can prevent exercise. However, it has been suggested that physical exercise has beneficial effects on the gastrointestinal tract, mainly due to decreased gastrointestinal blood flow, neuroimmuno-endocrine alternations, increased gastrointestinal motility and mechanical bouncing taking place while exercising.[23] Nevertheless, being the existing scientific evidence in this topic scarce, the effects of physical exercise on the gastrointestinal tract in CD patients must be explained from a different point of view. First of all, it must be pointed out that the most significant negative effect of exercise on the gastrointestinal function occurs at high levels of activity ,[24] therefore CD patients should not reach that point in any case. Secondly, although some studies have observed that physical activity can accelerate orocecal transit time in different populations and improve symptoms of constipation in irritable bowel disease patients,[25] there is no evidence that exercise independently benefits patients with chronic constipation.[24] However, given that light and moderate exercise is well tolerated in inflammatory bowel disease[23] and that it may also have protective effects on the gastrointestinal tract, there is no reason why physical activity should not be recommended in the treatment of CD.

3.5. Body composition

It is well known that CD is frequently associated with weight loss and malnutrition.[3] Both symptoms are possibly caused by low dietary intake, changes in metabolism, increased protein loss and nutrient malabsorption, which in turn lead to disturbances in body composition.[26] As a result, lower values of body weight, body mass index and fat mass are usually found in CD patients.[19] Regarding the role of physical exercise in this matter, it is important to note that although it has been suggested that physical activity may improve appetite in patients with gastrointestinal diseases,[23] the evidence to date regarding the effects of exercise in appetite regulation is controversial.[27] In addition to this, fat mass can be reduced, especially if aerobic exercise is performed. Therefore, it is

possible that the prescription of physical activity should not be presented as an accurate solution to this problem. However, resistance training has shown to be effective in increasing total body weight and improving body composition, by means of increasing skeletal muscle mass in patients showing similar body composition abnormalities.[28] Consequently, it can be appropriate to prescribe this type of physical activity to CD populations.

3.6. Sleep disturbances

CD patients encounter some problems that might be unexpected, such as poor sleep pattern.[20] Indeed, they report more sleep problems than the general population. Several reasons have been identified for broken sleep in CD, including feeling too hot or too cold, having bad dreams, concerns about the illness, abdominal pain and breathing problems.[29] Different studies have shown that physical activities such as aerobics help people with sleep problems,[30] therefore, CD patients may also benefit from exercise in this regard.

3.7. Anaemia

According to recent research,[31] anaemia is the most common systemic complication of inflammatory bowel disease (which includes CD). In this regard, it has been observed that aerobic exercise may reduce or prevent declines in erythrocyte levels,[32] which provides another reason for prescribing exercise in CD.

4. On how physical exercise can improve Crohn's patients' quality of life

CD patients' QoL seems to be significantly worse than that of people with other common illnesses such as type-2 diabetes or recent myocardial infarction.[33] The morbidity associated with the disease, alongside with its young age of onset and its important potential for harm, profoundly affect patients, not only physically, but also through limitations in social and emotional activities.[34] In chronic conditions exercise has been regarded as a useful non-pharmacological tool mainly due to its potential for improving patients' QoL. Since QoL has been described as how people perceive their emotional, physical, functional and social states,[35] the benefits of exercising on CD patients' QoL should be explained according to the effects that physical exercise seems to have on these aforementioned states.

4.1. Emotional state

Several psychological issues can influence CD in a complex manner. For instance, in CD patients there are some factors, such as ineffective coping strategies, pessimism, low perceived control and "catastrophizing" thoughts that can lead to major depression, which is the most common psychiatric diagnosis in this illness.[36] In addition to this, some authors have noted that anxiety is commonly found among people suffering from CD,[37] while some others have estimated that 60% of gastrointestinal disorders are somewhat influenced by psychological stress,[38] suggesting an affected mood pattern in CD populations. In this regard it is important to note that meta-analyses findings have demonstrated the anti-depressant effects of exercise.[39] Indeed, there are a number of theories showing that different hormonal changes (such as an increase in β-endorphin levels and in monoamine concentrations) that occur while exercising can affect mood, revealing the usefulness of physical activity in this matter.[1]

4.2. Physical and functional state

CD patients in clinical remission have shown reduced skeletal muscle strength and endurance capacity,[19] which is in agreement with the reported lack of energy commented before. Both factors could be responsible for the poor physical and functional levels observed in this population.[20] In relation to this, it is important to note that patients suffering from a chronic illness commonly find themselves in a vicious circle: fatigue and poor physical fitness caused by the pathology reduce the amount of exercise that patients do, worsening their physical condition and leading to more fatigue and loss of physical function.[2] Physical training can break this circle by means of enhancing fitness, reducing fatigue level and thereby enabling the patient to better manage daily life.

4.3. Social state

Due to the severity of some of the illness symptoms, CD may create a negative impact on self-image, family relationship and friends,[3] which can cause avoidance of social activities. In this regard, physicians, after consulting with exercise physiologists, should encourage patients to engage, along with their partners, friends or other patients, in social and recreational activities focused on recovering their physical fitness, since exercise group programs proposed for other chronic illnesses have shown a significant socializing effect.[2]

5. Studies in Crohn's disease patients

Although different epidemiological investigations have found an inverse relationship between CD development and occupational and recreational physical activity[40,41] very few relevant clinical studies have evaluated the effects of an exercise intervention on patients experiencing CD (Table 2). In this regard, Loudon et al.[42] evaluated the effects of a 12-week mild walking program on 16 CD patients with inactive or mildly active disease. Once the intervention ended, physical health, general well-being, quality of life and perceived stress improved in some patients without disease exacerbation. Although the study presented some methodological flaws that can limit its findings, such as lack of a control group and small sample size (only 12 patients finished the program), a 6-month post-study intervention showed that 50% of the completers were continuing to exercise between 2 and 6 days per week, suggesting that CD patients obtain some benefit from exercising. Separately, D'Inca et al.[43], evaluated the effect of a one-hour exercise program at a maximum of 60% oxygen on six males with ileal Crohn's disease in remission.

Table 2 Long term physical exercise programs carried out with Crohn's disease patients.

Study	Number of patients (control/ intervention)	Program	Intervention	Frequency	Main outcomes
Loudon et al.	16 (no control group)	Group walking program	20 to 35 min; mean distance walked was 3–4 km per session	3 times per week during 12 weeks	12 patients completed the trial. Physical health, general well-being, stress and quality of life improved without disease exacerbation.
Robinson et al.	117 (57/60)	Home based exercise program	12 core floor-based low impact exercises focused on the hip and lumbar regions	2 times per week during 12 months	88% of the patients in the training group finished the program, but only 26% of them completed the exercise regimen as prescribed. Bone mineral density increased in the lumbar spine and the hip.
Ng et al.	32 (16/16)	Independent walking program	30 min at 60% of maximum heart rate	3 times per week during 3 months	All of the patients completed the program. There were improvements on quality of life and reductions on CD related symptoms.

Although a biochemical analysis showed that the patients at rest had primed neutrophils with increased activation after exercise, the proposed physical training did not elicit subjective symptoms or changes in intestinal permeability and lipoperoxidation. Since without symptom correlation the clinical impact of this activation is hard to assess, this study shows that short-term exercise appeared to be well tolerated by CD patients in remission.

In the first randomized controlled trial, Robinson et al.[44] evaluated the effects of a 1-year low-impact exercise program on 107 CD patients. The program was designed to emphasize dynamic loading of the lumbar spine and involved 12 floor-based dynamic muscular core conditioning exercises performed at home. The patients were required to train at least three times per week, with 10 sessions per month necessary for full compliance. Once the intervention finished, all 53 subjects in the training group showed increased bone mineral density (BMD) in both the lumbar spine and the hip. However, compliance was poor, since only 26% of patients in the experimental group completed the exercise plan as prescribed, mainly due to acute relapse of their symptoms during the program. Nevertheless, the study showed that a home-based muscular training program is feasible in CD patients and that it is a potentially effective method of increasing BMD.

Finally, Ng et al.[45] built on the preliminary work done by Loudon et al. by including a control group and proposing and independent walking program. In this study patients were instructed to perform a low-intensity 30-minute walk three times per week during 3 months. All of the 16 subjects included in the exercise group completed the program, without suffering any disease exacerbation. Once the intervention finished, the obtained data showed that a low-intensity exercise program was enough to elicit improvements in quality of life and to decrease Crohn's disease-related symptoms.

In the light of all this, it seems intuitively appealing to promote participation in regular exercise in the management of CD.

6. Prescribing physical exercise in Crohn's disease

In order to safely prescribe physical activity in CD treatment, it is crucial to know the different types of suitable exercises that exist, as well as the determining aspects of duration, intensity, frequency and progression involved in them. However, only three studies have so far been carried out on CD patients and exercise, which may not be enough to make detailed recommendations and to describe how training sessions should be structured. That is the reason why the basic guidelines for carrying out exercise interventions with people suffering from CD presented here, which are based on the findings of the aforementioned studies, only intend to provide reasonable and conservative recommendations for exercise regimens that appear clinically safe and feasible.

According to the findings of the reviewed clinical studies, there seem to be two main types of physical interventions that should be recommended: aerobic activity and muscular resistance training.

6.1. Aerobic activity

According to several physical exercise interventions carried out with people suffering from different inflammatory pathologies, walking is a safe, practical and easy-to-do form or aerobic exercise which should be recommended given its beneficial effects on the QoL of CD patients. Regarding the level of effort, it has been found that aerobic activity performed between 40% and 60% of maximal oxygen consumption does not affect intestinal impermeability.[45] Simultaneously, it has been shown that CD patients can walk and average distance of 3.5 km without experiencing symptoms' exacerbation.[42] Taking these facts into account, it can be reasonable to prescribe 20 to 30 min of low-intensity walking at 60% of the patients' maximal heart rate, 3 days/week to start with. Once the patients get used to this exercise prescription, they should

be encouraged to perform the same schedule during most days of the week. However, aerobic activity must be stopped whenever the patient feels that fatigue or CD-related symptoms show some sign of exacerbation. Moreover, if CD patients cannot follow the proposed exercise regime, they should walk continuously at their own pace during bouts of 4 or 5 min, in order to obtain a minimum of 20 min of activity per day. In order to obtain better control of the activity, it is important to find a flat surface to walk on and to try to speak during the exercise in order to achieve a slow steady pace and an adequate respiratory rate. It is also advisable to adopt an active lifestyle and to choose exercises that are based on what the patient likes to do. It must be taken into consideration that dehydration is a special concern for people with CD who may experience chronic diarrhea, so it is important to drink plenty of water and to avoid extreme heat. Finally, it must be noted that although other aerobic activities such as swimming, pedalling on a recumbent bike or weight-bearing walking could be advisable, currently there is no available information regarding their effects on CD patients. Hence, further research is needed before any advice can be given.

7. Muscular resistance training

The gold standard exercise treatment to prevent bone mineral loss and to improve body composition in CD patients is muscular resistance training. When prescribing this type of activity, patients should exercise using elastic bands or free weights. The training sessions should start with a 5-minute warm-up, consisting of general whole body mobility and finish with a 5-minute cool-down period of muscular stretching. The main part of the session should include 2 sets of 10–12 muscular resistance exercises focused on the major muscle groups of the trunk and legs. In order to avoid symptoms' exacerbation or excessive fatigue, patients should rest for 15–30 s after each exercise and for 2–3 min between sets. The training program should be performed 2–3 times per week. When performing with elastic bands, patients can start by doing 8–12 repetitions of each exercise, and gradually adjust the intensity by increasing the number of repetitions or decreasing the resting time between them. If free weights are used, the training program should begin by performing 5–8 repetitions at 50% of one maximum repetition (1-RM), which is the maximum weight that can be lifted during one complete repetition of the movement. As the training program progresses, patients should be encouraged to perform 8–12 repetitions at 60% of 1-RM. As far as the amount of lifted weight is concerned, loads can be increased 1–2 kg when the patient completes 10 consecutive repetitions for a muscle group without fatigue.

Regarding the prescription of physical exercise on CD patients, it is important to note that its potential efficacy can be limited by poor adherence, therefore some practical advices are needed. In the first place, exercise programs should be individualized and based on age, fitness level, exercise goals and preferences. Secondly, it must be borne in mind that motivation and maintenance of the exercise is enhanced when group camaraderie is developed, when the activity is enjoyable and when there is demonstrable feedback on positive changes in QoL due to participation. Whenever possible, CD patients should exercise in group, and sessions should be supervised by professionals who will provide them with personalized feedback. In this regard, it is highly recommended that physical exercise be prescribed by an exercise physiologist or sport physician, or at least physicians should consult with this kind of professionals before prescribing exercise to CD patients.

Thirdly, if some economic or movement difficulties along with the necessity of an easily accessible lavatory make it difficult for the patient to attend gymnasiums or sport centres, some solutions must be proposed. Hence, if the patients like to walk or cycle outdoors, it is recommended to plan a route that is close to public restrooms. If they prefer to exercise at home, climbing stairs at a normal pace for 10–12 min could be an alternative to the usual aerobic exercises. Another solution, if the patients do not have elastic bands or free-weights, is to use bottles full of sand or water and to perform calisthenics exercises such as abdominal crunches, back extensions, semi-squats, or chair-stands, among others, following the aforementioned recommendations.

Finally, it must be noted that the studies mentioned in this review have included patients in remission or with mild activity disease, so the information presented here might not apply to patients with high activity disease.

8. Conclusion

Given the characteristics of some of the CD symptoms and knowing the potential benefits of physical exercise on this population, it can be concluded that CD patients can take advantage of physical training. Evidence, however, is limited as few studies have so far been carried out, and more research is needed.

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