Contents lists available at ScienceDirect



Autoimmunity Reviews



journal homepage: www.elsevier.com/locate/autrev

Review

Evidence for prescribing exercise as treatment in pediatric rheumatic diseases

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ARTICLE INFO

Article history: Received 28 March 2010 Accepted 6 April 2010 Available online 11 April 2010

Keywords: Exercise training Juvenile idiopathic arthritis Juvenile systemic lupus erythematosus Juvenile dermatomyositis

ABSTRACT

There has been an increasing recognition of adverse short-, mid-, or long-term effects associated with the treatment as well as the disease itself that impair the health-related quality of life and functional capacity of children and adolescents with rheumatic diseases. Interestingly, cumulative evidence has suggested that exercise training may benefit patients with juvenile idiopathic arthritis, juvenile systemic lupus erythematosus, juvenile dermatomyositis and juvenile fibromyalgia, attenuating several clinical symptoms related to physical disability. Remarkably, recent evidence also suggests that exercise may have direct effects on the pathogenesis of autoimmune diseases by attenuating chronic low-grade systemic inflammation. It is also important to emphasize that no exercise-related adverse effects have been reported. This short review provides the evidence for physical training as a treatment of pediatric rheumatic diseases, introducing a novel concept that exercise is a treatment for these populations.

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1. Introduction

Over the last few decades, the survival rate and the prognosis of patients with juvenile idiopathic arthritis (JIA), juvenile systemic lupus

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erythematosus (JSLE) and juvenile dermatomyositis (JDM) have substantially improved. However, there has been an increasing recognition of adverse short-, mid-, or long-term effects associated with the treatment as well as the disease itself that impair the healthrelated quality of life (HRQoL) and functional capacity of patients [1–9]. In this regard, it has been speculated exercise training may improve exercise capacity, performance of daily activities, and overall HRQoL [10]. Furthermore, recent evidence also suggests that exercise may have direct effects on the pathogenesis of autoimmune diseases by

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^{1568-9972/\$ –} see front matter 0 2010 Elsevier B.V. All rights reserved. doi:10.1016/j.autrev.2010.04.001

attenuating chronic low-grade systemic inflammation [11]. This review provides the evidence for physical training as an additional and safe treatment for patients with pediatric rheumatic diseases. Special focus was placed on the underlying mechanisms by which exercise can benefit these patients as well as on the research perspectives in this promising field.

2. Is there a role for exercise training in pediatric rheumatic diseases?

The lack of regular exercise or physical inactivity is an "actual" cause of chronic diseases [12]. More importantly, it is currently established that regular exercise offers protection against all-cause mortality, and there is an accumulative body of evidence from randomized intervention studies demonstrating that physical training is effective as a treatment in children, adolescents and adults with various chronic conditions, such as type 2 diabetes and cardiovascular diseases, which are remarkably associated with chronic systemic inflammation [11].

In clear conflict to the aforementioned evidence, the cornerstone of clinical treatment of active rheumatic diseases has been bed rest, and patients have been restrained from active physical exercise on the presumption that exercise has a detrimental effect on disease activity and joint erosiveness [13]. However, the role of physical inactivity as a treatment in rheumatic diseases has been challenged. Buljina et al. [14], for instance, demonstrated that patients with rheumatoid arthritis who underwent an exercise training program had more significant improvements regarding hand pain, joint tenderness, and activities of daily living score when compared to non-exercised patients. Thus, in the near future, one may expect a shift from the paradigm of "the bed-rest treatment" toward the compulsory recommendation of exercise training for rheumatic patients.

Lately, children and adolescents have also become more physically inactive. As a consequence, the incidence of early-onset chronic diseases has impressively increased [15]. Moreover, the lack of physical activity may also aggravate muscle weakness, atrophy, muscle dysfunction, chronic fatigue, motor-control disturbances, mood disorders, bone resorption, dyslipidemia, obesity, arterial hypertension and insulin resistance in pediatric rheumatic diseases patients. On the other hand, the manifestations of rheumatic diseases, such as chronic joint pain and stiffness, synovitis, and deformity, in concert with the exercise proscription, are also thought to aggravate an inactive lifestyle [16]. Therefore, a vicious cycle that ultimately leads to physical deconditioning, symptom aggravation and poor HRQoL is perpetuated. In this context, exercise training emerges as the most evident therapeutic tool for "stalling" such a deleterious cycle (Fig. 1).

3. Exploring the rational underlying exercise programs for pediatric rheumatic diseases

3.1. Juvenile idiopathic arthritis

Van Brussel et al. [17] demonstrated that both aerobic and anaerobic capacities are significantly decreased in children with JIA compared to age- and sex-matched healthy controls. Noticeably, subgroup analyses revealed that the oligoarticular onset patients did not significantly differ from healthy subjects, whereas the polyarticular rheumatoid factor positive-onset patients had the greatest impairment in both aerobic and anaerobic exercise capacities. Moreover, Giannini and Protas [18] reported reduced isometric quadriceps strength in children with JIA when compared to their healthy peers. Apparently, the muscle weakness is a natural consequence of the muscle atrophy, which in turn is caused by the local arthritis, the chronic pharmacological treatment (e.g., glucocorticosteroids) and the disuse. The repercussion of physical deconditioning for JIA

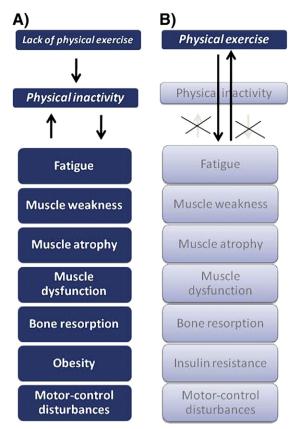


Fig. 1. A) Vicious cycle that leads to symptom aggravation and physical inactivity in pediatric rheumatic patients. Accumulative symptoms that lead to physical incapacity and disability (e.g., muscle weakness and fatigue) may prone the pediatric rheumatic patient to physical inactive lifestyle. The physical inactive lifestyle, in turn, is believed to aggravate several physical symptoms. This cycle may ultimately result in poor quality of life and prognosis. B) Exercise training may "stall" this cycle. The current literature indicates that a well-designed exercise program can at least partially restore muscle, bone and metabolic disturbances caused by both inactive lifestyle and the rheumatic disease itself. The better physical capacity, the higher is the probability to sustain a long-term physical activity lifestyle. Thus, we contend that exercise training is a treatment for pediatric rheumatic patients.

patients has also been examined. Takken et al. [19], for instance, found a positive association between anaerobic exercise capacity and functional ability in patients with JIA. This supports the notion that exercise training may be a valuable strategy for treating JIA patients.

3.2. Juvenile systemic lupus erythematosus

In addition to reduced levels of aerobic fitness, poor exercise tolerance and muscle weakness, JSLE patients also present increased fatigue when compared to healthy subjects [20]. The latter symptom did not correlate significantly with fatigue, disease activity, disease damage, or HRQoL measures. It is also important to note that JSLE patients frequently present dyslipidemia, bone resorption and insulin resistance [4]. Considering the broad spectrum of action of the exercise, it is possible to speculate that a physical training program may systemically benefit patients suffering from JSLE, possibly improving muscle mass, exercise tolerance, bone mineral density, physical capacity, lipid profile and insulin sensitivity, mood, self-esteem, and HRQoL.

3.3. Juvenile dermatomyositis

Patients with JDM often experience strong exercise intolerance [21,22]. Given that cardiac or pulmonary involvement is uncommon in JDM [5], the major contributor to the impaired exercise capacity is

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