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BASIC STUDY

Exercise training and pulmonary arterial hypertension: A review of the cardiac benefits

Entraînement physique et hypertension artérielle pulmonaire : un examen des avantages cardiaques

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Physical activity;
Cardiac remodeling;
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Summary
Aims. — Patients of pulmonary arterial hypertension (PAH) exhibit reduced functional capacity and exercise tolerance. Despite the evidences that exercise training is beneficial to this population, it is still being tested whether regular physical exercise can mitigate the complications of PAH. The aim of this review was to point out the cardiac functional and structural adaptations to exercise training in animal models of PAH, and highlight the cellular and molecular mechanisms underlying the benefits of exercise to individuals with PAH.
News. — A systematic review of original articles published in PubMed and ScienceDirect databases was conducted by two independent researchers. Relevant information on animal model, exercise protocol, cardiac functional and structural adaptations was extracted and discussed. The results show that in rats with monocrotaline-induced PAH (50—60 mg/kg body weight), the predominant model used, aerobic continuous (treadmill running) and intermittent (voluntary wheel running) exercise training of moderate intensity, performed either prior or during the development of PAH, promote benefits to the myocardium. Moreover, the articles reveal that the cardiac function (i.e. restoration of right ventricle systolic and diastolic pressure, AT/ET ratio, TAPSE and cardiomyocyte contractility) and structure (i.e. reduced hypertrophy and fibrosis; improved profile of proteins related to cellular contraction and inflammatory response) are

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enhanced by exercise training. Furthermore, these exercise adaptations result in augmented exercise capacity and survival of animals with PAH.
Conclusion. — Regular aerobic exercise of moderate intensity promotes cellular and molecular adaptations that improve myocardial function and structure along with increased exercise tolerance and survival.

MOTS CLÉS
Activité physique ;
Remodelage cardiaque ;
Circulation pulmonaire ;
Maladies cardiaques

Résumé
Objectifs. — Les patients souffrant d'hypertension artérielle pulmonaire (HAP) présentent une réduction de la capacité fonctionnelle et de la tolérance à l'effort. Malgré les preuves que l'entraînement physique est bénéfique pour cette population, il est encore testé si un exercice physique régulier peut atténuer les complications de l'HAP. Le but de cette revue était d'identifier les adaptations fonctionnelles et structurelles cardiaques en réponse à l'entraînement physique dans des modèles animaux d'HAP et de mettre en évidence les mécanismes cellulaires et moléculaires en soulignant les bienfaits de l'exercice chez les personnes souffrant d'HAP.
Informations. — Une revue systématique des articles originaux publiés dans les bases de données PubMed et ScienceDirect a été réalisée par deux chercheurs indépendants. Des informations pertinentes sur le modèle animal, le protocole d'exercice, les adaptations fonctionnelles et structurelles cardiaques ont été extraites et discutées. Les résultats montrent que chez les rats avec HAP induite par la monocrotaline (50—60 mg/kg de poids corporel), le modèle prédominant utilisé, aérobie continue (course sur tapis roulant) et intermittent (roue volontaire) exercice d'intensité modérée, exécuté avant ou pendant le développement de l'HAP, sont bénéfiques pour le myocarde. En outre, les articles révèlent que la fonction cardiaque (rétablissement de la pression systolique et diastolique du ventricule droit, rapport AT/ET, TAPSE et contractilité des cardiomyocytes) et la structure (réduction de l'hypertrophie et de la fibrose) sont améliorés par l'entraînement physique. De plus, ces adaptations d'exercice entraînent une augmentation de la capacité d'exercice et de la survie des animaux atteints d'HAP.
Conclusion. — L'exercice aérobie régulier d'intensité modérée favorise les adaptations cellulaires et moléculaires qui améliorent la fonction et la structure du myocarde ainsi qu'une tolérance accrue à l'exercice et l'augmentation de la survie chez les animaux.

1. Introduction

Pulmonary arterial hypertension (PAH) is a syndrome caused by restricted blood flow in the pulmonary arterial circulation, resulting in augmented pulmonary vascular resistance, which chronically leads to heart failure [1]. The predominant cause of increased pulmonary vascular resistance is the reduction of vascular luminal cross section due to the adverse remodeling produced by excessive cell proliferation and reduced rates of apoptosis in the arteries and arterioles of the pulmonary circulation [2].

The chronic increase in pulmonary vascular resistance leads to a surge in the right ventricle (RV) afterload [3]. Such overload generates an adverse remodeling of the RV, resulting in hypertrophy associated with increased sarcomeric passive tension (i.e. reduced titin phosphorylation), fibrosis (i.e. increased collagen deposition in the extracellular matrix) and cellular apoptosis leading to a progressive contractile dysfunction [4]. A compensatory RV chamber dilatation allows an enhanced preload, which maintains the volume of blood flow, despite the reduced fraction of shortening. As structural and functional damages progress, RV failure is established. Such insufficiency is characterized by increased filling pressures, diastolic dysfunction and diminishing cardiac output associated with tricuspid regurgitation due to annular dilatation and weak leaflet coaptation [2]. Heart failure is the leading cause of death among patients with PAH [5,6].

Pulmonary arterial hypertension has a poor prognosis, which is evidenced by survival rates that can be less than 3 years in the absence of treatment [7]. At the moment, the survival prognosis for patients with PAH has been determined by the functionality of the RV, and while it maintains its function, the patients remain with few symptoms [3]. Thus, the knowledge of new strategies that contributes to the improvement or maintenance of cardiac function along with the attenuation of the disease progression is paramount for this field of science.

The treatments for PAH have evolved considerably over the last decade due, in part, to advances in the knowledge of the pathobiology of the disease. These treatments aim, given the severe hemodynamic disturbances caused by PAH, to reduce pulmonary arterial pressure and normalize cardiac output. Another important goal is to reverse, or at least prevent, the progression of the disease in order to raise the survival of patients with PAH [1].

Physical exercise has been recognized as a non-pharmacological therapeutic tool in several chronic

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