20 - METABOLIC SYNDROME AND CARDIOVASCULAR DISEASE: THE RELATIONSHIP BETWEEN PHYSICAL EXERCISE AND INTERLEUKIN-6

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INTRODUCTION

Although genetic inheritance be of great importance in determining factor and susceptibility to cardiovascular diseases, environmental factors and modifiable lifestyle, including diet and exercise, have been shown to be crucial in preventing these diseases (GALZARAND et.al., 2012). It is estimated that 75% of new cases of chronic degenerative diseases could be explained by inadequate diet and physical inactivity. Still, low cardiorespiratory fitness, muscular strength and low physical inactivity may increase three to four times the prevalence of Metabolic Syndrome (COELHO et.al., 2009).

Metabolic syndrome consists of alterations in the metabolism of carbohydrates, lipids, abdominal obesity, hypertension, and clotting disorders and is characterized by a proinflammatory state, an increase of circulating levels of cytokines such as, C-Reactive Protein, Tumor Necrosis Factor (TNF-alpha) and interleukin-6 (IL-6) (GOTTLIEB et.al., 2008).

Therefore, the general objective of this study was to review about Metabolic Syndrome and Cardiovascular Diseases and the relationship of these diseases with exercise and Serum Levels of Interleukin-6.

METHODOLOGY

A literature review subject to the description of the study was conducted. Publications in English, Portuguese, Italian and Spanish scientific articles researched in MEDLINE (PUBMED), BIREME (LILACS) and SCIELO 2008-2014 data and books published from 2005 to 2010 studied at the Central Library and Library of Medicine, were used Pontifical Catholic University of Rio Grande do Sul (PUCRS). The subject descriptors used were: Metabolic Syndrome, Cardiovascular Disease, Interleukin-6 and Exercises.

METABOLIC SYNDROME AND ATHEROSCLEROTIC

Several studies have focused on the association between metabolic syndrome and atherosclerosis. The Atherosclerosis is a chronic inflammatory and degenerative process that affects the blood vessels and is characterized by the accumulation of lipids, inflammatory cells and fibrous elements in the sub endothelial space in the intimal layer of the artery (TEODORO et.al., 2010).

Cardiovascular Diseases have clinical manifestations usually in the form of acute myocardial infarction, stroke, angina or sudden death (TEODORO et.al., 2010; LIU et.al., 2011).

A systematic review of progression of atherosclerosis, intravascular ultrasonography combined with 3459 patients, those with Metabolic Syndrome or not, and all with arterial disease, it was found that in individuals with Metabolic Syndrome, the prevalence of disease progression was longer (57.8%). However, in a multivariate analysis, the same study found that the progression of atherosclerotic plaque seemed to be more influenced by individual risk factors in patients with coronary heart disease who have jointly diabetes mellitus and abdominal obesity. So, the question remains equivocal that metabolic syndrome may possess a specific disease entity or, if it simply represents an association of risk factors that describe its definition (OZGUR et.al., 2010).

However, poor diet and physical inactivity are among the major factors that can trigger the metabolic syndrome and, consequently, cardiovascular disease. But when modified, can bring great benefits and ensure quality of life to those who are educated and appropriate for a healthy life (GOTTLIEB et.al., 2008).

CARDIOVASCULAR DISEASE AND INTERLEUKIN-6

Interleukin-6 is a multifunctional cytokine that regulates humoral and cellular response and plays a central role in inflammation and tissue injury. Its effects are mediated through interaction with its receptor complex, IL-6RB, also known as gp130. Also plays a role in the pathogenesis of Coronary Artery Disease and large amounts of IL-6 are found in human atherosclerotic plaques (FISMANN et.al., 2010).

The levels of IL-6 are associated with an increased risk of cardiovascular events in the evolution of patients after acute coronary syndrome, however, the prognostic value of serum titers of IL-6 are not defined in patients with stable chronic coronary artery disease (FAIN et.al., 2010).

Positive levels of interleukin-6 are correlated with increased mortality, such as unstable angina, left ventricular dysfunction, propensity to diabetes and its complications, hypertension, obesity and various cancers (FISMANN et.al., 2010).

However, Interleukin-6 also possesses anti-inflammatory activity, making two aspects are favorable in the body: protection against bacterial infections, inactivating pro-inflammatory mediators, septic shock attenuating and inducing the production of cortisol and in a second aspect influencing insulin sensitivity during regular physical exercise (LAVIE et.al., 2009; DELBIN et.al., 2009).

EXERCISE AND INTERLEUKIN -6

IL-6 was shown to have a controlling stake in metabolic pathways during regular exercise. When combined, balanced diet and regular exercise, were optimal therapies for obesity. In addition, IL-6 is a biologically active substance which is not only secreted by cells of the immune system during inflammatory conditions, but is also released by adipose tissue and muscle contraction in the absence of inflammation (EDER et.al., 2009).

In skeletal muscle, the expression of IL-6 increases after exercise and is expressed by muscle fibers during

contraction, is released in large amounts of muscle to the circulation during this practice. This cytokine may play an important role in glucose homeostasis during prolonged exercise, optimizing the metabolic response during muscle activity (DELBIN et.al., 2009).

Also, a metabolic perspective, IL-6 has lipolytic effects in combination with physical exercise, and the infusion of IL-6 in rats increased the concentrations of fatty acids and triglycerides in a dose-dependent manner. Thus, mice deficient in IL-6 developed obesity in advance, and when treated with IL-6 for 18 days showed significant reduction in body weight (SOUZA et.al., 2008).

Moreover, Interleukin-6 from skeletal muscle may be considered as a "exercise factor" this "miocina" (cytokine produced in skeletal muscle) can contribute to most of the plasma increases observed during exercise and exercises metabolic effects in other tissues, such as liver, adipose tissue and brain (GOMES et.al., 2009; SOUZA et.al., 2008; FISMANN et.al., 2010).

Fismann and Tenenbaum (2010) emphasize that during exercise the IL-6 is synthesized and released by muscles, and insulin action is enhanced immediately at the onset of muscle recovery. Skeletal muscle can then be considered as an endocrine organ, contractile muscles produce IL-6 and the release into the blood exerting their effects on other organs in a similar way with a hormone.

The increase in circulating levels of IL-6 after exercise is a consistent finding, proportional to exercise duration, exercise intensity, muscle mass involved in mechanical work and muscular endurance capacity. Thus, the possibility is that many of the beneficial health effects may be related to regular physical exercise, in a mediated ultimately by interleukin-6 (FISMANN et.al., 2010).

CARDIOVASCULAR DISEASE AND EXERCISE

Regular exercise is associated with a decrease in the incidence of cardiovascular events (TEODORO et.al., 2010) and has been touted as a major non-pharmacological measures, being beneficial, protective, contributing to the maintenance of health and prevention (PORTO, 2005).

Physical exercise can be defined as any physical activity that is planned, structured, performed with a systematic repetition of oriented movements, with the aim to condition, improve physical fitness and health of those who practice (TERRA et.al., 2010).

In the contemporary world the exercise have a greater contribution in the prevention of degenerative diseases and cardiovascular diseases directly influencing the successful treatment of individuals, re-educating them, providing personal satisfaction, social integration, rehabilitation of the habits of everyday life, and, above all, educational teaching strategies for achieving a healthy lifestyle and quality of life (DELBIN et.al., 2009; COELHO et.al., 2009).

The benefits of exercise have also been shown in the prevention and treatment of risk factors such as hypertension, diabetes mellitus, obesity and osteoporosis (DELBIN et.al., 2009).

Thus, we emphasize that exercise training improves exercise capacity, endothelial function and causes the development of collateral blood vessels occurs in patients with Coronary Artery Disease, Chronic Heart Failure improving and peripheral arterial disease, as well as the exercise regular exercise is associated with loss of body weight, blood pressure and improves insulin sensitivity (TEODORO et.al., 2010).

Also, regular aerobic exercises have been used and recommended in the prevention and treatment of atherosclerosis and dyslipidemia. The Brazilian Society of Cardiology recommends regular aerobic exercise on a weekly frequency of three to six times, lasting 30-60 minutes per session, with moderate intensity, 50-60% of maximum heart rate (TEODORO et.al., 2010; DELBIN et.al., 2009).

Already, Delbin (2009) emphasizes that for the improvement of cardiorespiratory fitness, the ideal physical exercise is one that the individual performs moderately, at an intensity between 50% to 75% of maximal oxygen consumption, with weekly frequency of 3 to 5 sessions and also lasting 30 to 60 minutes of continuous activity. Also emphasizes the individuality of physical training proposed concerning the intensity, frequency and duration of activities, considering the need to evaluate the physical and clinical conditions of each individual so that the effects of exercise are actually beneficial to health.

FINAL

The combination of metabolic syndrome and its five components (hypertriglyceridemia, hyperglycemia, hypertension, low levels of cholesterol- HDL and abdominal obesity/adiposity) should not only be useful in the identification of cardiovascular disease, but also to represent symptoms of other underlying diseases or conditions. Furthermore, the diagnosis of metabolic syndrome can improve the treatment of individuals with subclinical cardiovascular disease diagnosis and helping them and motivating them to change lifestyle (OZGUR et.al., 2010).

Inflammatory markers are well established when related to the development of atherosclerotic disease and are useful in predicting high cardiovascular risk. These same mechanisms that promote dysfunction and/or endothelial injury, initiate the inflammatory process and the release of numerous proteins able to accuse the harmful event when researched and quantified in the blood, increasing the chance of treatment, primarily pharmacological, preventing more serious anomalies and, how secondary search, changes in lifestyle, including balanced diet and exercise routine in life (GOMES et.al., 2009; KAUR, 2014).

Interleukin-6 is a cytokine with operations in both the innate immune response as in adaptive (SOUZA et.al., 2008) and constitutes an important inflammatory marker, is involved in many immunological activities, playing an important role in the rupture process atherosclerotic plaque, with its increased serum levels in these events (GOMES et.al., 2009).

However, elevations of interleukin-6 in response to exercise may exert an anti-inflammatory role, and during his practice, an energy crisis that stimulates hepatic glycogenolysis and glucose release, helping to keep blood sugar may occur (GOLBIDI and LAHER, 2014). Also, Interleukin-6 stimulates angiogenesis mediated vascular growth and vascular endothelial growth factor (LAVIE et.al., 2009).

Still, the expression of Interleukin-6, increases after exercise through muscle fibers during muscle contraction, being released in large amounts, the muscle into the bloodstream. It should be noted that these plasma concentrations of interleukin-6 increase with the duration and intensity of exercise, may have influenced the amount of recruited muscle mass and individual aerobic capacity (FISMANN et.al., 2010).

CONCLUSION

Therefore, the muscle tissue is a source of production of interleukin-6 during prolonged exercise, the aerobic exercise and muscle glycogen concentration can be a determining, regulating this cytokine response to physical exercise, benefiting individuals who practice them regularly, preventing the Metabolic Syndrome and Cardiovascular Diseases (EDER et.al., 2009; TERRA et.al., 2010).

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METABOLIC SYNDROME AND CARDIOVASCULAR DISEASE: THE RELATIONSHIP BETWEEN PHYSICAL EXERCISE AND INTERLEUKIN-6.

ABSTRACT

Environmental factors and modifiable lifestyle, including diet and exercise, have been shown to be crucial in the prevention of metabolic syndrome and Cardiovascular Diseases. Metabolic syndrome consists of metabolic disorders, coagulation disorders and is characterized by a proinflammatory state, an increase of circulating levels of cytokines, such as interleukin-6. Methodology: Literature review by subject. Publications in English, Portuguese, Italian and Spanish scientific articles researched in MEDLINE (PUBMED), BIREME (LILACS) and SCIELO 2008-2014 and books published from 2005 to 2010 were used. Objective: Review about the Metabolic Syndrome and Cardiovascular diseases and the relationship of these diseases with exercise and serum levels of Interleukin-6. Conclusion: The muscle tissue is a source of production of interleukin-6 during prolonged exercise and muscle glycogen concentration can be a determining, regulating this cytokine response to physical exercise, benefiting individuals who practice regularly, preventing the Metabolic Syndrome and Cardiovascular Diseases.

KEYWORDS: Metabolic Syndrome; Cardiovascular Diseases; Exercise; Interleukin-6.

SYNDROME METABOLIQUE ET LES MALADIES CARDIOVASCULAIRES: LES RELATIONS ENTRE L'EXERCICE PHYSIQUE ET L'INTERLEUKINE-6.

RÉSUMÉ

Les facteurs environnementaux et le mode de vie modifiables, y compris l'alimentation et l'exercice, ont été montré pour être crucial dans la prévention du syndrome métabolique et des maladies cardiovasculaires. Le syndrome métabolique est constitué de troubles métaboliques, de troubles de la coagulation et est caractérisé par un état pro-inflammatoire, une augmentation des taux circulants de cytokines telles que l'interleukine-6. Méthodologie: Revue de la littérature par sujet. Publications en anglais, des articles scientifiques portugais, italiens et espagnols recherches dans MEDLINE (PUBMED), BIREME (LILACS) et SCIELO 2008-2014 et livres publiés de 2005 à 2010 ont été utilisés. Objectif: examen sur le syndrome métabolique et les maladies cardiovasculaires et la relation de ces maladies avec l'exercice et les taux sériques de l'interleukine-6. Conclusion: Le tissu musculaire est une source de production d'interleukine-6 lors de la concentration de glycogène musculaire exercice prolongé et peut être un déterminant, réglementant cette réponse des cytokines à l'exercice physique, et empêchant bénéficiant aux personnes qui pratiquent régulièrement.

MOTS-CLÉS: Syndrome Métabolique; Maladies Cardio-Vasculaires; Exercices Physiques; Interleukine-6.

SÍNDROME METABÓLICO Y ENFERMEDAD CARDIOVASCULAR: LA RELACIÓN ENTRE EL EJERCICIO FÍSICO Y LA INTERLEUCINA-6.

RESUMEN

Los factores ambientales y estilo de vida modificables, incluyendo la dieta y el ejercicio, han demostrado ser crucial en la prevención del síndrome metabólico y enfermedades cardiovasculares. El síndrome metabólico consiste en trastornos metabólicos, trastornos de la coagulación y se caracteriza por un estado proinflamatorio, un aumento de los niveles circulantes de citoquinas, tales como interleuquina-6. Metodología: Revisión de la literatura por temas. Publicaciones en Inglés, artículos científicos portugueses, italianos y españoles investigados en MEDLINE (PUBMED), BIREME (LILACS) y SCIELO 2008-2014 y libros publicados desde 2005 hasta 2010 fueron utilizados. Objetivo: Revisión sobre el síndrome metabólico y las enfermedades cardiovasculares y la relación de estas enfermedades con el ejercicio y los niveles séricos de interleucina-6. Conclusión: El tejido muscular es una fuente de producción de la interleucina-6 durante el prolongado ejercicio y la concentración de glucógeno muscular puede ser un determinantes, que regulan esta respuesta de citoquinas al ejercicio físico, prevenir beneficiando individuos que practican con regularidad, prevenir y Síndrome metabólico y enfermedades cardiovasculares

PALABRAS CLAVE: Síndrome Metabólico; Enfermedades Cardiovasculares; Ejercicios Físicos; Interleucina-6.

SÍNDROME METABÓLICA E DOENÇAS CARDIOVASCULARES: RELAÇÃO ENTRE EXERCÍCIOS FÍSICOS E INTERLEUCINA-6.

RESUMO

Fatores ambientais e estilo de vida modificáveis, incluindo dieta e exercícios físicos, têm se mostrado primordiais na prevenção de Síndrome Metabólica e Doenças Cardiovasculares. A Síndrome Metabólica consiste em alterações do metabolismo, distúrbios da coagulação e é caracterizada por um estado pró-inflamatório, apresentando aumento de níveis circulantes de citocinas, como a Interleucina-6. Metodologia: Revisão bibliográfica por assunto. Foram utilizadas publicações em inglês, português, italiano e espanhol de artigos científicos pesquisados nas bases de dados MEDLINE (PUBMED), BIREME (LILACS) e SCIELO de 2008 a 2014 e livros publicados de 2005 a 2010. Objetivo: revisar sobre a Síndrome Metabólica e Doenças Cardiovasculares e a relação dessas doenças com exercícios físicos e níveis séricos de Interleucina-6. Conclusão: O tecido muscular é uma fonte de produção de Interleucina-6 durante o exercício físico prolongado e a concentração de glicogênio muscular pode ser um determinante, regulando a resposta desta citocina ao exercício físico, beneficiando os indivíduos que o praticam regularmente, prevenindo a Síndrome Metabólica e as Doenças Cardiovasculares.

PALAVRAS-CHAVE: Síndrome Metabólica; Doenças Cardiovasculares; Exercícios Físicos; Interleucina-6.