44 - EVALUATION OF SERUM INTERLEUKIN-6 IN PATIENTS WITH METABOLIC SYNDROME ASSOCIATED WITH CARDIOVASCULAR DISEASE AND ITS RELATION TO PHYSICAL ACTIVITY.

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INTRODUCTION

In recent decades, Cardiovascular Diseases became the leading cause of death worldwide (PORTO, 2005). In Brazil, it is the first cause of death, constituting a serious public health problem (Ross, 1999). Cardiovascular Disease-related metabolic syndrome (MS) has increased overall mortality and cardiovascular mortality 1.5 times about 2.5 times the world's population (Lakka et al.,2002).

Metabolic syndrome is characterized by a complex disorder represented by a set of cardiovascular risk factors, related to central fat and insulin resistance (Liu et al., 2011). It was first described by Reaven in 1988, is characterized by a combination of insulin resistance with hyperinsulinemia, dyslipidemia (atherogenic plasma lipid profile), increased blood pressure, abdominal obesity (visceral) and glucose intolerance (Reaven et al., 1988).

Inflammation seems to be a key factor in the development of diabetes and atherosclerosis (Barzilay et al., 2003). The connection between adipose tissue and systemic levels of adipokines is not clearly understood, although there is some evidence hormonal interaction between adipose tissue and other tissues, such as skeletal muscle (Tomas et al. 2004).

All these manifestations of SM lead to an increased risk of coronary artery disease (CAD), which appears prematurely in these patients. The connection between insulin resistance and an increased risk for developing CAD seems to be complex and multifactorial (Wozniak et al. 2009).

This disorder occurs more frequently among overweight or obese , being more prevalent in women (James et.al. , 2004) , but showing stronger growth in men , as evidenced in the analysis of two subsequent periods , developed by the United States Heath and Evaluation National Nutrition Survey (NHANES) (York et al. 2004).

Moreover, patients with coronary artery disease, both in its acute forms as chronic, have high levels of inflammatory adipokine interleukin-6 (IL-6) compared with patients from the general population, presumably healthy. It is known that increased levels of IL-6 in patients with CAD is significantly more pronounced among patients with Acute Coronary Syndrome (ACS) than in patients with stable CAD (Nijm et al. 2005; Yamashita et al., 2003).

Interleukin -6 is a multifunctional cytokine that regulates body's immune response, hematopoiesis, acute phase response and inflammation. Furthermore, it can be said that IL- 6 has been shown to inhibit insulin action in muscle, liver and adipocytes in vitro and in vivo, and contribute to hepatic insulin resistance in obese subjects (Espinola – Klein et al., 2011). It is a biologically active substance that is not only secreted by immune cells during inflammatory conditions, but is also released in adipose tissue and muscle contraction in the absence of inflammation (Prestes et al., 2006).

In skeletal muscle, the expression of IL-6 increases after physical exercise and is expressed by the muscle fibers during contraction being released in large quantities into the circulation of the muscle during the practice. This cytokine may play an important role in glucose homeostasis during prolonged exercise, optimizing the metabolic response during muscle activity (Prestes et al., 2006). Also, IL-6 was shown to have a controlling stake in metabolic pathways during exercise (Prestes et.al., 2006). When combined diet and exercise are great therapies for obesity (Eder et al., 2009).

The IL- 6 has been proposed as a marker of metabolic syndrome, since it implies many changes related to excessive weight gain and may represent a hormonal factor inducer of resistance at muscle mediated by adiposity. In the obesity produces an accumulation of adipose tissue associated with insulin resistance and cardiovascular diseases (Goyenechea et al., 2005).

Therefore, the treatment of Metabolic Syndrome consists essentially in detecting and reversing the processes that trigger excess deposition central possible to be modified. Among the main goals are to reduce weight and waist circumference, the normalization of dyslipidemia and control of blood pressure (BP) and glucose. Associated with pharmacological strategies for the treatment of Metabolic Syndrome, the practice of regular physical activity and changes in eating habits play a central role in these actions (Petersen et al., 2005).

METHODOLOGY

Controlled cross-sectional study, based on a historical sample obtained by drawing lots among the records of the database of patients with metabolic syndrome, in the absence and presence of established cardiovascular disease, classified according to the NCEP/ATP III, in the Outpatient of Cardiometabolic Risk hospital PUC-RS, from 03/2008-12/201. From a sample of 200 individuals were randomly selected 80 patients with metabolic syndrome, 40 with no disease and 40 with Cardiovascular Disease Cardiovascular established to develop the study. Metabolic syndrome was defined by the criteria of the NCEP/ATPIII the presence of three or more criteria such as:

1.Abdominal obesity: waist > or = 102 cm in men and> 88 cm in women;

2.Hypertriglyceridemia: > or = 150 mg/dl;

3. Low HDL cholesterol: < 40 mg/dl in men and < 50 mg/dl in women;

4. High blood pressure: SBP (systolic) > or = 130 mmHg and DBP (diastolic) > or = 85 mmHg .

Cardiovascular disease has been established defined as:

1.A history of acute myocardial infarction confirmed by electrocardiogram, Myocardial scintigraphy, or angiography, performed at this hospital.

2.Myocardial revascularization prior.

3.Coronary artery catheter (angioplasty with or without stent placement).

4.The waist circumference was performed in the standing position, after expiration, with the tape measure, between the costal margin and the iliac crest.

The values considered for men and women, according to the criteria of NCEP-ATP III. Weight and height were assessed by precision balance and the value of Body Mass Index (BMI) was calculated by dividing weight (kg)/height 2(m).The

determination of blood pressure was performed in the sitting position on arrival at the clinic and after standing for 5 minutes. Will be made and the average value obtained shall be considered for registration.

The variable, regular physical activity was obtained by patient information through a structured questionnaire that serves as the basis for the database of the clinic. The answers provided were: sedentary lifestyle and regular physical activity.

A blood sample was collected after fasting for 12 hours for the following dosages: Glucose, Total Cholesterol, HDL - cholesterol, LDL - cholesterol and triglycerides. Interleukin - 6 was measured by Elisa and other variables such as fasting glucose and lipid levels were measured using the dry chemistry method, the Vitros 5.1 Chemistry, Johnson - Johnson ®, a sample from the serum of these patients, which is stored C at the Institute of Research. -70 blood was collected under consent of the patients with the term of free and informed consent, according to the research project number 06/03546, endorsed by the Committee of Ethics and Research. Data collection and blood to the exams were collected on the first day of consultation when patients are assessed for metabolic syndrome, laboratory tests and tests performed to assess cardiovascular disease part of routine outpatient.

RESULTS AND DISCUSSION

For the analysis of this study, quantitative data were presented as mean and standard deviation and categorical variables were expressed as frequency and percentage. The amounts of interleukin-6, due to its strong asymmetry received logarithmic transformation prior to analysis. The data were expressed as geometric mean and value minimum and maximum.

Below, Table 1 shows the baseline characteristics of patients with metabolic syndrome classified as sedentary and regular physical activity. There were no significant correlations between IL-6 and the variables described below, and all coefficients were observed < rs 0.30.

Table 1 - Baseline characteristics of the groups of sedentary and physically active regular

Characteristics	Sedentary n=74	Active regular n=6	P
Age, years	60±10	58±9	0,71
Male, nº (%)	44 (60)	4 (67)	?0,99
BMI, Kg/m^2	32,4±4,9	28,2±3,9	0,044
Waist, cm	107±11	102±13	0,42
C/Q	1,00±0,09	1,00±0,07	0,81
SBP, mmHg	152±27	138±22	0,19
DBP, mmHg	89±13	83±12	0,23
Fasting glucose, mg/dL	144±75	135±52	0,70
Total Cholesterol, mg/dL	199±53	187±38	0,51
LDL Cholesterol, mg/dL	119±45	114±36	0,76
HDL Cholesterol, mg/dL	45±11	41±7	0,22
Triglycerides, mg/dL	211±123	166±55	0,12

Data are presented as mean ± standard deviation or counts (percentage)

Comparisons of quantitative data between groups were performed by ANOVA and Student t test procedure with robust standard errors (Welch). Categorical data were compared by chi-square or Fisher's exact test, when necessary.

In Figure 1, it can be seen that the group with regular physical activity, even with a reduced number of patients showed statistical significance as compared with the group of sedentary as serum levels of the inflammatory cytokine interleukin-6 in patients with Metabolic Syndrome.

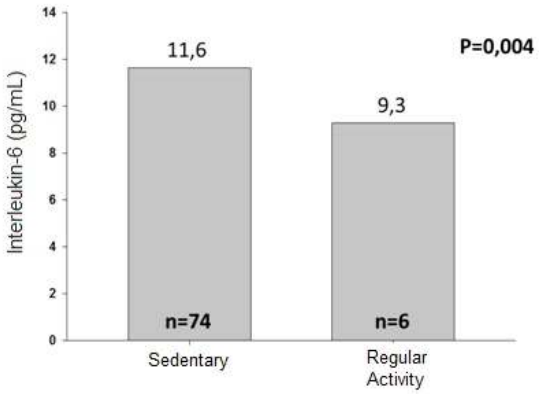

Figure 1- Bar graph representing the geometric means for interleukin-6 in patients with metabolic syndrome according to two groups, regular physical activity and sedentary.

Covariates to adjust the values of IL-6 were used in the analysis of covariance procedure with robust standard errors. The significance level was 5%. Data were processed and analyzed using SPSS version 21.0.

Below, Table 2, shows a summary comparison of unadjusted and adjusted between sedentary patients with regular physical activity for interleukin-6, and the data presented as geometric means.

Table 2 -Unadjusted comparison between patients with sedentary versus regular physical activity for interleukin-6 (IL-6)

			unadjusted analysis		analysis adjusted for age		analysis with additional adjustment [a]	
denouement	Sedentary *	regular physical activity*	mean ratio (IC95%)	P	mean ratio (IC95%)	P	mean ratio (IC95%)	P
IL-6,pg/mL	N=74	N=6	1,25	0,004	1,27	0,008	1,26	0,037
	11,63	9,28	(1,07 to 1,46)		(1,06 to 1,52)		(1,01 to 1,57)	

* The data are presented as the geometric mean. IC, confidence interval; P, statistical significance; [a] additional adjustment for age, sex and presence of cardiovascular disease

CONCLUSION

Therefore, IL-6 is involved in the pathogenesis of metabolic syndrome and the association of clinical outcomes in high cardiovascular morbidity and mortality, such as cerebrovascular accident (CVA) and acute myocardial infarction (AMI).

For the two groups of sedentary and physically active regularly, statistical significance was obtained, however, it is known that the sample used for this analysis has little statistical power.

However, we note that among the various risk indicators that are associated with the etiology of cardiovascular diseases, there is the sedentary lifestyle, characterized by the absence or lack of physical activity in these individuals with metabolic syndrome and changes in habits and lifestyle, especially related to balanced diet and exercise.

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EVALUATION OF SERUM INTERLEUKIN-6 IN PATIENTS WITH METABOLIC SYNDROME ASSOCIATED WITH CARDIOVASCULAR DISEASE AND ITS RELATION TO PHYSICAL ACTIVITY.

ABSTRACT

Introduction: Patients with Coronary Artery Disease, both in its acute forms as chronic, have high levels of inflammatory adipokine interleukin-6 (IL-6) compared with the general population, presumably healthy. Interleukin-6 is a multifunctional cytokine that regulates body's immune response, hematopoiesis, acute phase response and inflammation. In skeletal muscle, the expression of IL-6 increases after physical exercise and is expressed by the muscle fibers during contraction being released in large quantities into the circulation of the muscle during the practice. Methods: Cross-sectional study controlled based on a historical sample obtained by drawing lots among the records of the database of patients with metabolic syndrome, according to the absence or presence of established cardiovascular disease, classified according to the NCEP/ATP III, the Outpatient Risk Cardiometabolic Hospital PUCRS, from 03/2008-12/201. Conclusion: IL-6 is involved in the pathogenesis of

metabolic syndrome and the association of clinical cardiovascular outcomes. For the two groups of sedentary and physically active regularly, statistical significance was obtained, however, it is known that the sample used for this analysis has little statistical power.

KEYWORDS: Interleukin-6, Metabolic Syndrome, Physical Activity.

EVALUATION DE SÉRUM L'INTERLEUKINE-6 EN PATIENTS PRÉSENTANT SYNDROME METABOLIQUE ASSOCIÉ AUX MALADIES CARDIOVASCULAIRES ET SA RELATION AVEC L'ACTIVITE PHYSIQUE.

RÉSUMÉ

Introduction: Les patients atteints de maladie coronarienne, tant dans ses formes aiguës que chroniques, des niveaux élevés de adipokine inflammatoire interleukine-6 (IL-6) par rapport la population générale, probablement en bonne santé. L'interleukine-6 est une cytokine multifonctionnelle qui régule la réponse immunitaire, de l'hématopoïèse, la phase aiguë réponse et l'inflammation de l'organisme. Dans le muscle squelettique, l' expression de l'IL-6 augmente après l'exercice physique et est exprimé par les fibres du muscle pendant la contraction d'être libéré en grande quantité dans la circulation du muscle au cours de la pratique. Méthodes: Etude transversale contrôlée sur un échantillon historique obtenu par tirage au sort parmi les dossiers de la base de données des patients atteints de syndrome métabolique, selon l'absence ou la présence d' une maladie cardiovasculaire établie, classé selon le NCEP/ATP III, le risque ambulatoire cardiométabolique Hôpital PUCRS, à partir de 03/2008 à 12/2011. Conclusion: IL-6 est impliquée dans la pathogenèse du syndrome métabolique et l'association des résultats cliniques cardio-vasculaires. Pour les deux groupes de sédentarité et de l'activité physique régulièrement, la signification statistique a été obtenue, toutefois, il est connu que l'échantillon utilisé pour cette analyse a peu de puissance statistique.

MOTS-CLÉS: interleukine-6, syndrome métabolique, l'activité physique.

EVALUACIÓN DE SUERO INTERLEUCINA-6 EN PACIENTES CON SÍNDROME METABÓLICO ASOCIADO CON LA ENFERMEDAD CARDIOVASCULAR Y SU RELACIÓN CON LA ACTIVIDAD FÍSICA.

RESUMEN

Introducción: Los pacientes con enfermedad coronaria, tanto en sus formas agudas como crónicas, tienen altos niveles de adipoquinas inflamatoria interleucina-6 (IL-6) en comparación con la población general, presumiblemente sanas. La interleucina-6 es una citocina multifuncional que regula la respuesta inmune del cuerpo, la hematopoyesis, la respuesta de fase aguda y la inflamación. En el músculo esquelético, la expresión de IL-6 aumenta después de ejercicio físico y se expresa por las fibras musculares durante la contracción de ser liberado en grandes cantidades en la circulación del músculo durante la práctica. Métodos: Estudio transversal controlada sobre la base de una muestra histórica obtenida por sorteo entre los registros de la base de datos de los pacientes con síndrome metabólico, según la ausencia o presencia de enfermedad cardiovascular establecida, clasificados según el NCEP/ATP III, el riesgo para pacientes ambulatorios hospital de cardiometabólico PUCRS, de 03/2008 a 12/ 2011. Conclusión: La IL-6 está implicada en la patogénesis del síndrome metabólico y la asociación de los resultados clínicos cardiovasculares. Para los dos grupos de sedentaria y actividad física regular, se obtuvo significancia estadística, sin embargo, se sabe que la muestra utilizada para este análisis tiene poco poder estadístico.

PALABRAS CLAVE: La interleucina-6, el síndrome metabólico, la actividad física.

AVALIAÇÃO DOS NÍVEIS SÉRICOS DE INTERLEUCINA-6 EM PACIENTES COM SÍNDROME METABÓLICA ASSOCIADA À DOENÇA CARDIOVASCULAR E SUA RELAÇÃO COM ATIVIDADE FÍSICA.

RESUMO

Introdução: Pacientes com Doença Arterial Coronariana, tanto em suas formas agudas quanto crônicas, apresentam níveis elevados da adipocina inflamatória Interleucina-6 (IL-6) quando comparados à população geral, presumidamente saudável. A Interleucina-6 é uma citocina multifuncional que regula a resposta imune do organismo, a hematopoiese, a resposta da fase aguda, e a inflamação. No músculo esquelético, a expressão de IL-6 aumenta após o exercício físico e é expressa por fibras musculares durante a contração, sendo liberada em grandes quantidades do músculo para a circulação durante essa prática. Metodologia: Estudo transversal controlado, baseado em uma amostra histórica obtida por sorteio entre os registros do banco de dados de pacientes com Síndrome Metabólica, segundo ausência e presença estabelecida de Doença Cardiovascular, classificados conforme os critérios NCEP/ATP III, atendidos no Ambulatório de Risco Cardiometabólico do Hospital da PUCRS, no período de 03/2008 a 12/2011. Conclusão: A IL-6 está envolvida na patogênese da Síndrome Metabólica e na associação de desfechos clínicos cardiovasculares. Em relação aos dois grupos estudados de indivíduos sedentários e praticantes de atividade física regular, obteve-se significância estatística, porém, sabe-se que a amostra utilizada para essa análise possui pouco poder estatístico.

PALAVRAS-CHAVE: Interleucina-6, Síndrome Metabólica, Atividade Física.