

# CREATINE KINASE LEVEL IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE TREATED WITH HYDROTHERAPY

## *Nível de creatina quinase em portadores de doença pulmonar obstrutiva crônica submetidos à hidroterapia*

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**RESUMO:** A pesquisa teve o objetivo de analisar o nível de Creatina Quinase (CK) frente à hidroterapia em portadores de Doença Pulmonar Obstrutiva Crônica (DPOC), assim como verificar o estado nutricional e a tolerância ao exercício desses pacientes. O estudo foi realizado com 16 voluntários, divididos em Grupo Experimental (n=8) formado por pacientes com diagnóstico de DPOC e Grupo Controle (n=8) formado por indivíduos saudáveis. O GE foi submetido ao protocolo de hidroterapia, enquanto o GC apenas passou pelo processo de avaliação. O método de avaliação ocorreu no tempo pré-intervenção T0 e pós-intervenção T20. As informações coletadas foram submetidas à análise estatística por meio do programa SSPS 19.0, onde se adotou a estatística descritiva (média e desvio padrão) com nível de significância para as inferências estatísticas de  $p \leq 0,05$ . O estudo utilizou uma análise comparativa dos dados obtidos a partir do teste t de Student. Os resultados mostraram prevalência de obesidade no GC ( $p=0,04$ ) e sobrepeso no GE ( $p=0,67$ ), assim como, aumento não significativo na distância percorrida no TC6 ( $p=0,09$ ). Os níveis séricos de CK no GE apresentaram discreta diferença de valores ( $p=0,89$ ), indicando ausência de dano na musculatura. O protocolo de exercícios no meio aquático proposto foi benéfico aos pacientes estudados GE, tendo em vista, a manutenção do estado nutricional e o controle do nível de CK.

**Palavras-chave:** Doença pulmonar obstrutiva crônica. Creatina Quinase. Hidroterapia.

**ABSTRACT:** The research aimed to analyze the Creatine Kinase (CK) level in connection with the usage of hydrotherapy in patients with Chronic Obstructive Pulmonary Disease (COPD) and to verify the nutritional condition and the tolerance of these patients to physical exercise. The study was carried out with 16 volunteers, divided into Experimental Group (n=8) formed by patients diagnosed with COPD and Control Group (n=8) formed by healthy individuals. The EG was submitted to the protocol of hydrotherapy, whilst the CG has undergone only an evaluation process. The evaluation method occurred at the pre-intervention time T0 and post-intervention time T20. The information collected was submitted to statistical analysis through the program SSPS 19.0, with the adoption of the descriptive statistic (mean and standard

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deviation) with a significance level for the statistical inferences of  $p \leq 0,05$ . The study used a comparative analysis of the data obtained from the Student test t. The results showed prevalence of obesity in the CG ( $p=0,04$ ) and overweight in the EG ( $p=0,67$ ) and there was no significant increase in the 6MWD ( $p=0,09$ ). The serum levels of CK of the EG presented a slight difference of values ( $p=0,89$ ), indicating absence of damage to the muscular system. The protocol of exercises in the proposed aquatic environment was beneficial to the EG patients studied, considering the maintenance of their nutritional condition and the control of their CK level.

**Keywords:** Chronic Obstructive Pulmonary Disease. Creatine Kinase. Hydrotherapy.

## INTRODUCTION

The Chronic Obstructive Pulmonary Disease (COPD) presents a high rate of morbidity and mortality in the world, affecting 5% of the adult population (SILVA *et al.*, 2012), and it is characterized by the decrease of the airway flux, which generates a significant disablement, detriment to the quality of life and metabolic losses that become more severe with the progression of the disease (PRESTO, 2009).

Studies have shown that the emergence of the COPD may be related to tobacco smoking, environmental factors, genetic factors, respiratory infections and the Alpha-1 antitrypsin deficiency (PRESTO, 2009; DWEIK; STOLLER, 2007). A clinical diagnosis must be taken into consideration for patients who present dyspnoea, chronic cough or the production of sputum and/or history of exposure to risk factors related to the disease (GRUFFYDD-JONES, 2012).

The COPD is considered by scholars as a multisystemic disease, and along its progression it normally tends to affect several organs and systems, including the skeletal muscles (MACHADO; ORLANDI, 2008). This may be explained under the light of new evidences which point at the skeletal muscles dysfunction syndrome, characterized by atrophy (sarcopenia) and loss of muscular strength in patients with COPD, which contributes to the reduction in the day to day activities of such individuals (VILLAÇA *et al.*, 2005).

Among the proteins most studied and analysed in the literature, the Creatine Kinase (CK) is the mostly utilized biomarker in what concerns the muscular damage (FOSCHINI; PRESTES; CHARRO, 2007; BRANCACCIO *et al.*, 2008), in view that the skeletal muscular tissue has the function of aiding the metabolism in the resynthesis of adenosine triphosphate (ATP), being involved in the first energy pathway and in the phosphorylation of the ATP (ALVES, 2014). The discharge of the protein CK is considered as evidence of muscle damage, since normally this enzyme is not able to cross the cell membrane. It is considered that the discharge of this enzyme through the lymphatic vessels would reflect important alterations occurred in the structure of the membranes, that is, alteration of the muscular fiber (NUNES; CURTY, 2012).

It is worth to emphasize also that, in addition to affecting the pulmonary and muscular condition, the COPD may also cause harm to the nutritional condition of the patient, leading to a progressive loss of weight, which contributes to a bad prognosis.

There are various factors that can influence the musculoskeletal disorder in patients with COPD. However the physical conditioning decrease is the main mechanism involved in this process (DOURADO; GODOY, 2006).

The purpose of this research was to analyse the level of CK, the nutritional condition and the tolerance to exercises in relation to the physical activity in an aquatical environment, in COPD patients.

## **METHOD**

This research is characterized as a observational, longitudinal, prospective and quantitative clinical trial, approved by the Ethics and Research Committee of the University of Amazônia, under register number 854.978.

The sampling was composed by 16 (sixteen) subjects, being subdivided into Experimental Group (EG, n=8, 4 men and 4 women) with clinical and spirometrical diagnosis of COPD, light to heavy degrees, aged 40 years plus, selected from the clinic of Respiratory Physiotherapy of the Unit of Study and Assistance to Physiotherapy and Occupational Therapy. The Control Group (CG, n=8, 3 men and 5 women) aged 40 years plus were volunteers, considered eutrophic, i.e. with no clinical diagnosis of COPD.

In order to evaluate the tolerance of the subjects from both of the groups to exercises, a 6 minutes walking test was applied (TC6). For the collection of data of the body composition, we used a Digital Scale and Body Fat AnalyserW939 (WisoCare®).

For the evaluation of the CK, the blood sampling was carried out in the laboratory of Biochemistry of the State University of Pará, with samples of 5ml of blood at the moment T(0) pre- intervention and T(20) after the 20<sup>th</sup> session. The blood was collected (in heparinized tubes) and immediately centrifugated at 2500 rpm, for 10 minutes and stored in a freezer at -80°C. The samples were stocked in duplicate and the determination of the CK was done through the enzymatic method in a spectrophotometer Celm® Model E225-D. The CK was determined with a specific kit of the laboratory Labtest Diagnóstica S.A.

The hydrotherapy program was conducted at the Clinic of Physiotherapy of the University of Amazônia, from March to June, 2014. Twenty sessions of hydrotherapy were carried out during the morning period, twice a week. It should be noted that only the EG was submitted to this treatment.

The program was composed by two adapted protocols (MOREIRA; CARMO; TANNUS, 2001), with 10 sessions each, being the second protocol more challenging for the patients. Each session encompassed warm-up, stretching, aerobic training and muscles relaxation exercises, with the duration of fifty minutes, including the resting intervals among the exercises.

The statistical data of the research were carried out through the Statistics Package SPSS 19.0, in which a level of significance for the statistical inferences of  $p \leq 0,05$  was

adopted.

The statistical data of the research were presented in tables and figure. The statistical treatment of the data was performed using the SPSS Statistical Package 19.0, which was adopted descriptive statistics (mean and standard deviation) for characterization of the sample for quantitative data and indexes absolute and relative to the qualitative data, and inferential statistics through the Student test t to compare the means of quantitative variables between the different times of testing (before and after treatment), the Chi-Squared test to compare prevalence in the classification of the variables studied in the two research groups (Control and Experimental), and the Pearson correlation coefficients to assess the association between variables investigated. A level of significance for the statistical inferences of  $p \leq 0,05$  was adopted.

## RESULTS

Table I shows the descriptive characteristics of the qualitative variables of the samples of the Control Group (CG), in addition to the comparative analysis of the prevalences observed for each variable studied. It was observed that the CG presented a slight prevalence of subjects of the feminine gender with overweight in the body mass index and with normal CK index; in addition, through the percentage of fat test, a significantly higher prevalence of obese subjects with muscle mass deficiency was also observed.

**Table I** – Qualitative characteristics (absolute and relative values) of the Control Group and the comparison of the prevalences. Belém, PA, 2014.

Variables	Prevalence			Comparison	
				$\chi^2$	p
Gender	Female		Male	0,50	0,48
	5 (62,5%)		3 (37,5%)		
Body Mass Index	Normal	Overweight	Ob. degree I	3,25	0,20
	2(25,0%)	5(62,5%)	1(12,5%)		
Fat Percentage	Healthy	Overweight	Obese	6,25	0,04*
	1(12,50%)	1(12,50%)	6(75,0%)		
Muscular mass percentage	Below		Normal	4,50	0,03*
	7 (87,5%)		1 (12,5%)		
Creatine Kinase	Below	Normal	Above	2,00	0,16
	---	6 (75,0%)	2 (25,0%)		

Source: from the author, 2014.

Table II shows the results of the analysis of the Experimental Group (GG), which showed a complete balance among the subjects of both genders, with four (4) subjects of each gender. There was a higher prevalence of subjects with a moderate degree of the dysfunction investigated, which occurred in 62% of the subjects of the sampling. With regards to the nutritional condition of this group, a degree of overweight was detected in the body mass index.

**Table II** – Qualitative characteristics (absolute and relative values) of the Experimental Group and comparison of the prevalences. Belém, PA, 2014.

Variable	Prevalence			Comparison	
				x <sup>2</sup>	p
<b>Gender</b>	<b>Female</b>	<b>Male</b>		0,00	1,00
	4 (50,0%)	4 (50,0%)			
<b>Dysfunction degree</b>	<b>Moderate</b>	<b>Heavy</b>		0,50	0,48
	5 (62,5%)	3 (37,5%)			
<b>BMI before</b>	<b>Normal</b>	<b>Overweight</b>	<b>Ob.Degree I</b>	1,00	0,61
	2(25,0%)	4(50,0%)	2(25,0%)		
<b>BMI after</b>	<b>Normal</b>	<b>Overweight</b>	<b>Ob.Degree I</b>	1,00	0,61
	2(25,0%)	4(50,0%)	2(25,0%)		
<b>% of Fat before</b>	<b>Normal</b>	<b>Above</b>		0,50	0,48
	3 (37,5%)	5 (62,5%)			
<b>% of Fat after</b>	<b>Normal</b>	<b>Above</b>		0,50	0,48
	3 (37,5%)	5 (62,5%)			
<b>% de Muscular Mass before</b>	<b>Below</b>	<b>Normal</b>		0,50	0,48
	5 (62,5%)	3 (37,5%)			
<b>% de Muscular Mass after</b>	<b>Below</b>	<b>Normal</b>		0,50	0,48
	5 (62,5%)	3 (37,5%)			
<b>Creatinokinase before</b>	<b>Below</b>	<b>Normal</b>	<b>Above</b>	3,25	0,20
	5(62,5%)	2(25,0%)	1(12,5%)		
<b>Creatinokinase after</b>	<b>Below</b>	<b>Normal</b>	<b>Above</b>	3,25	0,20
	5(62,5%)	2(25,0%)	1(12,5%)		
<b>Exercise Tolerance before</b>	<b>Below</b>			---	---
	8 (100,0)				
<b>Exercise Tolerance after</b>	<b>Below</b>			---	---
	7 (100,0)				

Source: from the author 2014.

Table III describes the quantitative results of the EG, which presented the average of age of 68,63±6,70 years, average weight of 53,85±8,36 kg, and average height 1,55±00,3 meters. It was also verified an altered nutritional condition, with little variation after the treatment, where it is possible to verify a Body Mass Index (BMI) of 22,24 ±3,41 and average fat percentage of 33,11±11,54%.

After the aquatic pulmonary rehabilitation program, it could be observed that the treatment did not promote any significant adaptation of any of the variables discussed herein. However it promoted slight increases on the body mass index, on the fat percentage, in the levels of CK and in the tolerance to exercises.

**Tabela III** – Quantitative characteristics of the Experimental Group. Belém, PA, 2014.

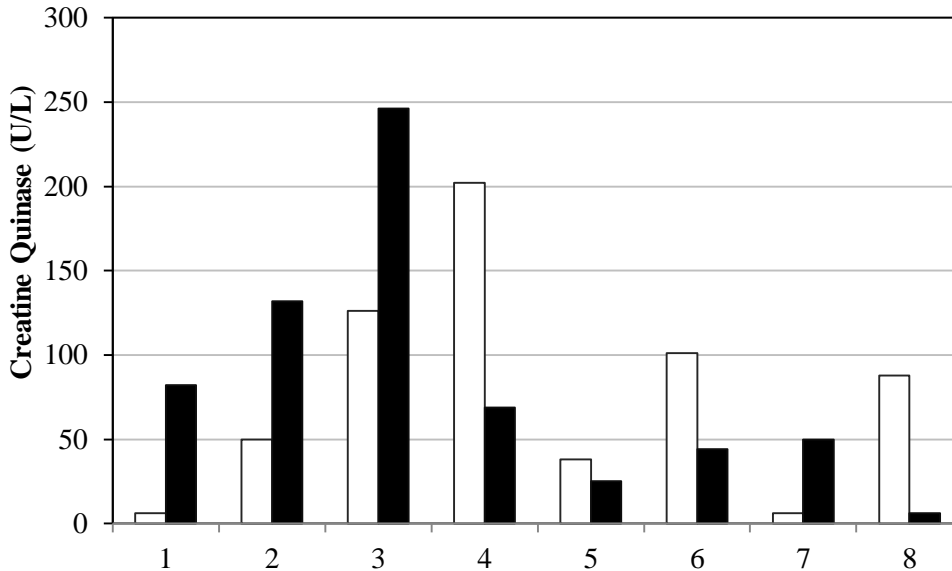
Variable	T0	T20	T	P
<b>Age</b>	68,63 ± 6,70	---	---	---
<b>Weight</b>	53,85 ± 8,36	53,85 ± 8,74	0,00	1,00
<b>Height</b>	1,55 ± 0,03	---	---	---
<b>Body Mass Index</b>	22,24 ± 3,41	22,30 ± 3,51	-0,45	0,67
<b>Fat percentage</b>	33,11 ± 11,54	33,75 ± 11,73	-0,56	0,59
<b>Muscular Mass Percentage</b>	36,49 ± 6,96	36,01 ± 6,58	0,84	0,43
<b>Creatine Kinase</b>	77,20 ± 66,51	81,79 ± 76,54	-0,15	0,89
<b>Tolerance to Exercises</b>	331,00±99,34	368,73±78,59	-1,99	0,09

Source: from the author, 2014.

Figure 1 show the levels of CK represented individually, in the moments T0 and T20.

It is possible to notice that each patient, after the proposed protocol, presented distinct alterations, although these alterations when considered within group data, cannot be considered significant in relation to the homogeneity of the group studied.

**Figure 1** – Individualized Level of Creatine Kinase of the sampling.



**Source:** from the author, 2014.

## DISCUSSION

There have been various researches carried out aiming at investigating the effects of aquatic exercises on the cardiopulmonary system and other systems, as well as its utilization on the construction of innovative protocols in the area of the aquatic pulmonary rehabilitation (ARRUDA, 2011).

In this research it was possible to observe that the CG presented a degree of obesity, revealing the nutritional condition of these subjects. In a research work carried out in the state of Rio Grande do Sul with 2.177 healthy individuals from 20 to 69 years of age, the prevalence of obesity was verified among the women (23,2 %) whereas among the men (14,4 %). It should be emphasized that the CG was composed in its majority by women (62,5%), which probably influenced the average of the results, thus confirming the findings of the research carried out in Rio Grande do Sul. In the same research, it was verified a direct relation between obesity and age, in which the individuals (men and women), after the age of 40 years have shown percentages over 20% in the increase of body fat with the rise of the age (GIGANTE *et al.*, 2006). The referred research corroborates the results of this research, which showed 75% of the individuals between 50 and 70 years with a degree of obesity (Table I).

When analysing the EG (Table III), it is possible to observe that the treatment in the pool promoted slight increases on the body mass index, which leads to the understanding that the exercises in the aquatic environment did not promote a change in the nutritional

condition of the analysed group. This result is similar to the research of Moreira (2011) which analysed the BMI of 23 COPD patients during the stage of pre-treatment with the treadmill and obtained results similar to those of this research, in which the BMI was of 23,2kg.

Nevertheless, an issue which requires further clarification is the fact that the literature indicates that the patients with COPD tend to present a significant weight reduction along the progress of the illness; some authors affirm that these patients present the loss of weight as a comorbidity component of the illness, (DOURADO; GODOY, 2006; WEHMEISTER *et al.*, 2011), which, however, did not occur with our experimental group, which presented a BMI average of  $22,24 \pm 3,41$  (before) and  $22,30 \pm 3,51$  (after), suggesting that the proposed treatment may be capable of promoting a maintenance of the nutritional condition of the COPD patients, taking into consideration the fact that the fat percentage  $33,11 \pm 11,54$  (before) and  $33,75 \pm 11,73$  (after) followed the slight increase of the BMI, classifying the sample as being a sample presenting overweight index.

The WHO recommends that the measurement of the BMI be accompanied with other indexes which may identify with higher precision, the issue of the nutritional condition (OMS, 2000); this research utilized another index (% of fat) for the body analysis of the subjects.

It was observed that after the physical activity in aquatic environment, the EG showed a considerable increase of the average distance covered during the TC6, however, not with significant values. Another research applied the TC6 to 90 male individuals, among healthy individuals and COPD patients with different degrees of obstruction and it was concluded that the higher the airway flux limitation is, the lower is the tolerance to physical strain (MARINO *et al.*, 2007). It can be stated that the results obtained in the TC6 of this research may have suffered influence from the findings of 62,5% of the individuals with moderate degree of obstruction (Table II).

There are factors which can influence the performance in the TC6; a research demonstrated that 70% of the COPD patients presented a decrease of muscular strength in the quadriceps (HAMILTON *et al.*, 1995). A fact that, in accordance with these authors, tends to adversely impact the distance covered, due to muscular weakness.

The CK has been receiving emphasis in the scientific circle as one of the main biochemical biomarkers which indicate the damage to the muscular tissue, being the analysis of this enzyme of utmost importance for the verification of muscular lesion, especially in patients that already show a deficiency in the muscular skeletal system (CESAR *et al.*, 2011).

In the evaluation of the values of lactate and of the serum activity of the enzyme creatine kinase in horses of the breed thoroughbred, submitted to effort tests in a treadmill, an increase in the level of CK was observed and this led to the conclusion that the increase of the serum activity of CK was related to the physical conditioning of the animal, where the animals in bad physical condition presented higher rates of the enzyme, compared to those regularly trained (KOWAL, 2006).

In a research with two synchronized swimming athletes during the training period, it was found that the levels of CK did not suffer alteration after the training, being possible that they may have gone through an adaptation effect which minimizes the rise of the serum levels of CK, due to their status of highly trained athletes (PAZIKAS, 2005). The results of that research are similar to the results of this research, in which it was not possible to detect alterations in the level of CK.

It should be noted that the COPD patients did not present a physical conditioning matching that of the athletes, however they are individuals that have undergone pulmonary rehabilitation for approximately 2 years, and this may also have led to a physical adaptation. The tendency is that the incidence of the serum findings of some determined enzymes such as the CK decrease (KOWAL, 2006).

It should be further noted that, in spite of the fact that this biomarker is widely utilized in the indirect analysis of the muscular lesion, the concentration of this enzyme (CK) does not always reflect the degree of muscular damage (KUIPERS, 1994). Therefore, the absence of alterations in the level of CK does not guarantee that the muscle did not suffer some type of strain during the proposed activity.

Some individuals may present high serum activity of CK, without showing signs of muscle damage and this may have been the case in this research (HARRIS; MARLIN; GRAY, 1998).

## CONCLUSION

Notwithstanding the reduced number of the sampling, the rehabilitation protocol proposed was beneficial to the participants of the research due to the fact that it promoted a maintenance of the nutritional condition and it helped in the gain of tolerance to exercise, even if not with significant values in the results of the TC6. Additionally it was possible to verify through the levels of CK that the aquatic activity performed did not cause damage to the muscle system of these patients. It is worth to emphasize that it is necessary to carry out additional researches with a higher number of samplings and with a longer period of treatment, which will enable the achievement of significant statistical results.

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ARRUDA, A.E. **Análise da função pulmonar de portadores de doença pulmonar**

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