

28 - THE CUSHING AND PHYSICAL EXERCISE

DANILO SILVA BARBOSA
 ESMAC - Belém-PA/Brazil
 JOSÉ FERNANDES FILHO
 UFRJ - Rio de Janeiro-RJ/Brazil
 xdanilo@msn.com

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INTRODUCTION

Because cushing is still a poorly understood endocrine pathology, a brief history of it will be made. In 1912, the American neurosurgeon, Harvey William Cushing, also known as the father of "modern neurosurgery," immortalized his name in the history of medicine, when he discovered an endocrinological syndrome caused by malfunctioning of the pituitary gland. Extensively described in his article "The Pituitary Body and Its Disorders", where in 1926 he won the Pulitzer Prize. This condition of cushing's syndrome was actually identified in 1932, and the first scientific records on it were born. However, even after decades of its discovery, an effective diagnosis for this condition is still a challenge for clinical endocrinology.

The clinical suspicion of SC is directly related to a laboratory evaluation, using as reference the dosages of cortisol and ACTH (Adrenocorticotrophic), however, even the basal dosages of these hormones are not sufficient to confirm the diagnosis, requiring dynamic tests that stimulate or inhibit the HHA (Hypothalamic-Hypothesis-Adrenal) axis. (CASTRO MOREIRA, 2002).

It is important to emphasize that there are two pathological incidences for cushing, one is cushing's disease, which for the Brazilian Society of Clinical Pathology (BSCP), occurs when there is excessive stimulation of the adrenal glands by ACTH, produced by a tumor in the pituitary gland. The other is cushing's syndrome, which, on the other hand is a set of signs and symptoms caused by excess cortisol or exogenous corticosteroids, such as medicines. (BSCP- access: <https://www.endocrino.org.br/doenca-de-cushing-neuroendocrinologia/>).

As cortisol is one of the triggers of cushing (Freire, 2009) and physical exercises also raise the rates of this hormone, this study, through a qualitative-quantitative, exploratory, explanatory approach and a field research composed by open and closed questions aims to identify when physical exercise is related to cushing, as well as its importance in the recovery of the quality of life of people who had this condition and more specifically to describe the etiology, physiopathology and its symptomatology, related to know more about this endocrinological disorder, clarifying if there are deleterious effects caused by the increase of cortisol through the physical exercises to then identify the most propitious moment to establish the relationship between cushing and physical exercise.

ETIOLOGY AND PHYSIOPATHOLOGY

Cushing's syndrome can be caused by endogenous (internal) factors, divided into ACTH-Dependent and ACTH-Independent, and / or exogenous (external) factors also known as iatrogenic, resulting from the use of glucocorticoid-containing drugs, the most common cause of CS, caused by the excess of synthetic hormones. On the other hand, the endogenous causes are caused by excess production of cortisol (immunosuppressive, anti-inflammatory) by the adrenal, independent of the level of ACTH (adrenal gland stimulation hormone), or by excess ACTH production known as Cushing's syndrome pituitary. It then becomes apparent that CS can occur from a pituitary or adrenal alteration. Endogenous causes of SC are the rarest, affecting more women than men at a ratio of 8: 1 for Cushing's disease (pituitary tumor producing ACTH), 4: 1 for adrenal adenomas, and 2: 1 for adrenal carcinomas. However, CS ACTH-dependent ectopic ACTH secretion affects more men than women (FREIRE, 2009). In the table below, a demonstrative summary of the causes of cushing:

Table 1: Causes of cushing's syndrome

Exogenous (iatrogenic)			
Endogenous	ACTH-independent (25%)	Adrenal Tumors	Adenomas
			Squamous
		Nodular hyperplasia	Macronodular
		Micronodular	
	ACTH-dependent (75%)	Cushing's disease	
		Ectopic ACTH secretion	
		Ectopic secretion of CRH	

Source: Freire, 2009

ACTH-independent Cushing's syndrome has its cause attributed to adrenal tumors and nodular (macronodular or micronodular) hyperplasia. Adrenal tumors are the most common causes of ACTH-independent cushing's syndrome. Tumors can be benign (adenomas) or malignant (adenocarcinomas). The differential diagnosis between adenomas and carcinomas is made by a set of 9 histological criteria, the Weiss criteria. Tumors with less than 3 criteria are adenomas and present no risk of metastatic dissemination; on the other hand, the presence of more than 3 Weiss criteria indicates the diagnosis of adrenal adenocarcinomas (FREIRE, 2009).

Nodular adrenal hyperplasia are rare causes of ACTH-independent CS, which may be macronodular or micronodular. Macronodular are characterized by massive and bilateral glandular increase, occasionally asynchronous. The micronodular adrenal hyperplasia, also known as adrenal pigmentosa hyperplasia, is caused by activating mutations of the 1-alpha regulatory subunit of protein kinase A, and may present alone or in combination with atria or cutaneous myxomas, pigmented skin lesions, acromegaly, thyroid or mammary nodules, ovarian cysts or testicular tumors, constituting the Carney complex. ACTH-dependent Cushing syndrome can be caused by cushing's disease (ACTH-secreting pituitary adenomas) and by extra-hypophyseal ACTH-secreting tumors, or more rarely CRH (Freire, 2009).

The CS is considered rare, according to the World Health Organization (WHO) there are approximately 50,000 people living with this pathology currently, the age group most affected is between 20 and 50 years. In Denmark this incidence is in the proportion of 2 cases per million inhabitants per year and in Spain 2.4 cases per million inhabitants per year (SMITH, 2016).

THE SYMPTOMATOLOGY

Freire (2009) shows that cushing has a series of symptoms very characteristic of its pathology, but a person with CS may not have the same symptoms as the other, or it may occur from a single person presenting all their symptoms, mainly when its cause is of endogenous origin. Cushing causes serious symptoms that should receive attention and care, such as rapid and sudden weight gain, even without small or large changes in eating habits, culminating in centripetal obesity, which is the accumulation of fat in the central regions of the body, especially in the abdomen, leaving it swollen and protruding, the face appears full moon shape and in the cervical region occurs the hump, resembling the hump of a camel. In the limbs, proteolysis occurs, which triggers weakness and loss of muscle mass in these regions. Large, violet streaks appear, usually in the abdomen and proximal limbs and ecchymosis (purple spots). The thinning of the skin occurs, causing the appearance of bruising very easily, low of the immune system causing in great slowness of any cicatrizing and infectious process. Increased thirst, micturition and the appearance of acnes, as well as alterations in the menstrual cycle are also part of its symptoms, such as the appearance of other diseases such as osteoporosis, diabetes, hypertension, headache, anxiety, irritability, cognitive dysfunction and depression. In children, obesity and slowed growth are the most recurrent symptoms.

PHYSICAL EXERCISE

Bueno and Gouvêa (2011), inform us that physical exercises are vital for the health of the human body in several aspects and proportions. There are countless studies that line the countless benefits of physical exercise, playing a key role in our lives. Because of this, its practice has been winning great numbers of fans, whether for aesthetic purposes, to improve a pathological clinical picture or just seeking a better quality of life. It is always valid to emphasize that regardless of its purpose, any and all physical activities should be prescribed, oriented and supervised by a physical education professional.

When performing physical exercise, we promoted the activation of the hypothalamic-pituitary-adrenal axis (HPA), which occurs in physiological energetic, metabolic and vascular response to exercise needs, resulting in this cortisol axis, whose prolonged increase or decrease causes health problems. However, the relationship between exercise and cortisol is something that has not yet been fully clarified by science (BUENO E GOUVÊA, 2011).

METHODOLOGY

It is a bibliographical review, through an analytical empirical approach, of the applied type regarding its nature, which in the approach of the problem is qualitative-quantitative, exploratory and explanatory, in the databases Medline Plus, NIH (National Institutes of Health), Scielo, Pub Med, CSRF (Cushing's Support and Research Foundation) and MedicinaNet, reviewed twenty articles, studies and publications related to Cushing, describing its etiology, symptomatology and physiopathology, as well as its relation with physical exercise.

The field research was conducted through interviews with 10 people who had this condition, where the information analyzed were: age group, genre, waiting time to receive diagnosis, cause of cushing (exogenous or endogenous), if they did physical exercises before and returned to do them after CS, what symptoms developed and the importance of physical exercises after this process. The interviews took place through the social networks with the participation of members of the groups "Cushing's Syndrome Brazil and Cushing's Syndrome", composed of closed and open questions.

Only those people affected by cushing and already cured, regardless of the causes and their recurrence, are part of the sample. People who were still in the process of being diagnosed or in the process of being treated were not part of the sample.

RESULTS AND DISCUSSION

In the course of this study, it was detected that the main boost trigger for the development of this pathology is the hormone cortisol, making it necessary to study the influence of physical exercise on cortisol control, to only then abstract and ponder the variables that involve this pathology with the practice of physical exercise (Castro Moreira, 2002).

Table 2- descriptive table on the interviews of cushing

Sample (n)	Sex		Age (years)		T.Diag. (months)	
	Mal	Fem	(x ±)	(min-max)	(x ±)	(min-max)
10	20%	80%	33±6	25-49	10±20	5-72
%C.EXOG		%C.ENDOG		%E.F.A		%E.F.D
50%		50%		100%		50%

Source: Authors, 2017

T.DIAG: time of diagnosis. - % C.ENDOG: endogenous causes - % C.EXOG: Exogenous cause - % E.F. : Exercise Before Cushing % E.F.D: exercise after the Cushing. (x ±) average and standard deviation; min-max: minimum and maximum value

In the analyzed sample, composed by 10 people (n=10), we obtained the following results: 80% of the sample is represented by females (%S.F.), while the males (%S.M.) was only 20%, age min-max = 25-49 with mean standard deviation of $x \pm = 33 \pm 6$, the mean time for the diagnosis of cushing (T.Diag (months) was min-max = 5-72, with an average standard deviation of $x \pm = 10 \pm 20$, regarding the causes of CS, 50% of them were (%C.EXOG exogenous and endogenous) 50% (%C.ENDOG), 100% of the sample reported performing physical exercises before the CS (%E.F.) and only 50% of those people were able to return to perform them (%E.F.D).

One case in particular, of endogenous origin, has been noted because it is the rarest type of cushing, cyclic CS. According to Albiger, Nora Maria Elvira; Cyclic Cushing's syndrome is a disease in which glucocorticoid levels are alternately normal and elevated the latter occurring in episodes that can last from a few days to several months. It is more common in children than in adults. Cyclic CS may manifest as one of two different forms of CS (ACTH-dependent or independent).

The studies of Freire (2009) and Castro and Moreira (2002), present great similarity with the results presented here. Regarding the symptomatology reported by the sample in general, all showed the standard symptoms very characteristic of cushing (see symptomatology), with slight variations in intensity, some have had hair loss others not, and all women reported disorder in the menstrual cycle.

All those who were able to resume their physical exercise routines after cushing emphasized the importance of exercise as an indispensable tool in controlling body mass, muscle mass recovery, muscle tone, physical vigor, in the improvement of the disposition, energy, concentration, sleep and the search for quality of life.

The table no 2 describes the results of research in all parameters analyzed:

Considering the results, it was observed that CS affects more women than men, the average waiting time for the

diagnosis is 5 to 72 months, which represents a significant problem for the patient with cushing, because the longer the exposure time to high levels of cortisol, larger and more severe became their symptoms, there was a case in the interviews that reported having waited 6 years to have their diagnosis. About 80% complained about the delay in receiving the correct diagnosis and 40% reported that in some consultations (after diagnosis) the doctors did not even know what cushing was.

In the general context, the exogenous causes are much more frequent than the endogenous ones, but in this sampling they have been equated. What is striking is the percentile of people who were unable to resume their physical exercise routine after CS, which indicates that 100% of people reported to do exercise before Cushing and that only 50% of them were able to return. This low percentile of return has an interesting explanation, of the 50% who did not return to the practice of physical exercises, 30% reported that after a period (between 1 and 2 years) there was a recurrence of tumor in the pituitary, being necessary the accomplishment of a procedure called adrenalectomy (removal of the adrenal glands), as a consequence, the organism significantly reduces the production of hormones, including cortisol, being necessary to replace it with medication, if there are reports of muscle weakness, body aches and discomfort after this procedure, with the remaining 30% failing to return. Of the remaining 20% who did not return to exercise, 10% said they still felt muscle weakness and indisposition, and the other 10% said that after reorganizing their normal life routine, they ended up having no time for exercise.

The bearers of Cushing, on the other hand, have high levels of cortisol in the body and since physical exercise also raises the levels of this hormone, how can physical exercise be beneficial to those who have cushing's?

Firstly, it is important to clarify that during CS the practice of exercises is almost impossible to perform due to the pain in the proximal joints from osteoporosis, followed by muscle weakness, indisposition, dizziness, among other aspects. Only after treatment and with most of the controlled symptomatology, especially cortisol levels, is it possible to practice the exercises.

Yes, physical exercises increase cortisol levels in the human body, just as stress also does, however when the physiological reactivity of the HPA axis increases to stressors, the physical exercise in turn acts at the same time reducing the axis response to other stressors leading to an adaptive response (LUGER et al., 1987).

Physical exercise induces the development of several defense mechanisms, potentiating our immune system, inhibiting the deleterious actions of the cortisol momentary increase through physical activity. This is because physical exercise stimulates the modulation of serum free cortisol levels (active form) by binding to cortisol binding globulin and activation of the cortisol-converting enzyme in cortisone (inactive form), thereby making the body less responsive to stress, which has beneficial effects on physical and mental health, protecting it against the consequences of chronic stress and stress-related diseases (BUENO & GOUVÊA, 2011).

CONCLUSIONS

Cushing's disease is in fact a rare pathological disorder and although it has clinical manifestations and symptoms that are highly suggestive, it is a condition of difficult investigation, almost always leading to numerous diagnostic misconceptions if not followed a well elaborated and monitored laboratory routine by a physician. Its causes, independent of being endogenous or exogenous, have in common the hormone cortisol. This disease affects more women than men, causing serious damages to the human body that can lead to death if not treated in time and "time" ends up being one of the most important variables when we speak of cushing, because as this study showed, time for the diagnosis is 5 to 72 months and this delay entails terrible consequences for its carrier, and may have his body completely disfigured along that waiting. The exercises were of fundamental importance for people who were cured of this pathology, where we concluded that although physical exercises also increase cortisol levels in the body, our body gets less responsive to stress and its deleterious effects, promoting beneficial results to physical and mental health. We thus perceive that the best time to relate cushing to physical exercises is after treatment and stabilization of his symptomatology, where exercise acts fundamentally helping them to control body mass, muscle mass recovery, physical tone, improvement of disposition, concentration, sleep and contributing to a better quality of life that had long been subtracted from them.

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ADDRESS FOR CORRESPONDENCE

DANILO SILVA BARBOSA

73 Passagem Andrade, Rd. Transcoqueiro, Cabanagem, CEP: 66625-015

Belém do Pará, Brazil

EMAIL: xdanilo@msn.com

THE CUSHING AND PHYSICAL EXERCISE

Cortisol is a glucocorticoid that plays an important role in the metabolism of proteins, lipids and carbohydrates, among other functions. The exposure of the human organism to high levels of cortisol over a prolonged period may lead to the appearance of hyperadrenocorticism or hypercortisolism, also called Cushing's syndrome (CS). This research aims to describe the etiology, symptomatology and physiopathology of CS as well as its relation with physical exercises. Using a qualitative-quantitative approach, with a sample of 10 people who had this pathology, an interview was made up of closed and open questions, in order to analyze some variables such as: average age, female and male percentile had Cushing, average time to diagnosis, percentile of exogenous and endogenous causes, and the percentile of people doing physical exercises before and after Cushing, as well as the symptomatology presented and the importance of physical exercise after this process. The following were obtained: RESULTS: The sample consisted of 10 people (n = 10), age = 33 ± 6, 80% of the sample was represented by females, while males were only 20%, average time to diagnosis of Cushing (T. Diagnosis (months)) was 10 ± 20 months, 50% of the causes were exogenous (% C.EXOG) and 50% were endogenous (% C.ENDOG), the percentile of those who performed physical exercises before Cushing (% EFA) it covered 100% of the sample and 50% was the percentile of the people who were able to resume exercise (% E.F.D). The symptomatology presented by the sample was the pattern of the studied pathology, with small variations that did not interfere in the results of the study and 100% of the sample that was able to return to exercises, reported their importance as fundamental for the control of body mass and the search for a better quality of life.

Keywords: Cushing, Cortisol, physical exercise.

LE CUSHING ET L'EXERCICE PHYSIQUE

Le cortisol c'est un glucocorticoïde qui joue un rôle important dans le métabolisme des protéines, des lipides et des glucides, entre autres fonctions. L'exposition de l'organisme humain à des niveaux élevés de cortisol pendant une période prolongée peut provoquer l'apparition de hyperadrenocorticism ou hypercorticisme, aussi appelé syndrome de Cushing (SC). Ce travail de recherche a pour but décrire l'étiologie, la symptomatologie et physiopathologie de SC et ainsi comme sa relation avec des exercices physiques. En utilisant une recherche d'approche qualitative et quantitative, avec un échantillon de 10 personnes qui ont eu cette maladie, une interview a été faite, composée des questions ouvertes et fermées, afin d'analyser certaines variables telles que : l'âge moyen, et le percentile du sexe masculin et féminin qui avait le Cushing, le temps moyen pour le diagnostic, le percentile des causes exogènes et endogènes et le percentile des personnes qui font des exercices physiques avant et après le Cushing ainsi que les symptômes présentés et l'importance de l'exercice physique après ce processus. On a eu obtenu ces résultats: un échantillon de 10 personnes (n = 10), l'âge = 33 ± 6, 80% de l'échantillon a été représentée par le sexe féminin tandis que le sexe masculin était 20% seulement, le temps moyen pour le diagnostic du Cushing (T. Diag (mois)) était de 10 ± 20 mois, 50% étaient des causes exogènes (C.EXOG%) et 50% étaient endogènes (C.ENDOG%), le percentile de ceux qui ont effectué l'exercice physique avant le Cushing (% EPT) a couvert 100% de l'échantillon et 50% était le percentile des personnes qui étaient capables de reprendre l'exercice physique (% E.F.D). Les symptômes présentés par l'échantillon était le modèle standard de la pathologie étudiée, souffrant des petites variations qui n'interfèrent pas avec les résultats de l'étude, et 100% de l'échantillon qui pourrait revenir à faire des exercices, a rapporté son importance comme fondamentale pour le contrôle de la masse corporelle et l'intention d'une meilleure qualité de vie.

Mots clés: Cushing, cortisol, exercice physique.

EL CUSHING Y EL EJERCICIO FÍSICO

El cortisol es un glucocorticoide que desempeña un papel importante en el metabolismo de las proteínas, de los lípidos y de los carbohidratos, entre otras funciones. La exposición del organismo humano a altos niveles de cortisol durante un largo período puede ocasionar el surgimiento del hiperadrenocorticismismo o hipercortisolismo, también llamado Síndrome de Cushing (SC). Este trabajo de investigación tiene como objetivo describir etiología, sintomatología y fisiopatología de la SC, así como su relación con los ejercicios físicos. En el presente trabajo se analizó la relación entre el peso de la mujer y el peso de la mujer en el momento de la lactancia. El Cushing, tiempo medio para diagnóstico, percentil de causas exógenas y endógenas y el percentil de personas que realizaban ejercicios físicos antes y después del Cushing, así como la sintomatología presentada y la importancia del ejercicio físico después de ese proceso: La muestra compuesta por 10 personas (n = 10), edad = 33 ± 6, 80% de la muestra fue representada por el sexo femenino, mientras que el sexo masculino fue de apenas el 20%, el tiempo promedio para el diagnóstico del Cushing (T.Diag (%)), fue de 10 ± 20 meses, el 50% de las causas fueron exógenas (% C.EXOG) y el 50% fueron endógenas (% C.ENDOG), el percentil de los que realizaban ejercicios físicos antes del Cushing (% EFA) abarcó 100% de la muestra y el 50% fue el percentil de las personas que lograron reanudar la práctica de los ejercicios (% E.F.D). La sintomatología presentada por la muestra fue la patología de la patología estudiada, sufriendo pequeñas variaciones que no interfieren en el resultado del estudio y el 100% de la muestra que logró volver a realizar ejercicios, relataron su importancia como fundamental para el control de la masa corporal y en la búsqueda de una mejor calidad de vida.

Palabras clave: Cushing, Cortisol, Ejercicio Físico.

O CUSHING E EXERCÍCIO FÍSICO

O cortisol é um glicocorticoide que desempenha importante papel no metabolismo das proteínas, lipídios e carboidratos, entre outras funções. A exposição do organismo humano a altos níveis de cortisol durante um período prolongado pode ocasionar no surgimento do hiperadrenocorticismismo ou hipercortisolismo, também chamado de Síndrome de Cushing (SC).

Este trabalho de pesquisa tem por objetivo descrever a etiologia, sintomatologia e fisiopatologia da SC, bem como, sua relação com os exercícios físicos. Utilizando uma pesquisa de abordagem quali-quantitativa, com uma amostragem de 10 pessoas que tiveram essa patologia, realizou-se uma entrevista composta por perguntas fechadas e abertas, afim de analisar algumas variáveis como: média de idade, percentil do sexo feminino e masculino que tiveram o cushing, tempo médio para diagnóstico, percentil de causas exógenas e endógenas e o percentil de pessoas que faziam exercícios físicos antes e após o cushing, bem como a sintomatologia apresentada e a importância do exercício físico após esse processo. Obteve-se os seguintes resultados: Amostra composta por 10 pessoas ($n = 10$), idade = 33 ± 6 , 80% da amostra foi representada pelo sexo feminino, enquanto o sexo masculino foi de apenas 20%, o tempo média para o diagnóstico do cushing (T.Diag (meses)) foi de 10 ± 20 meses, 50% das causas foram exógenas (%C.EXOG) e 50% foram endógenas (%C.ENDOG), o percentil dos que realizavam exercícios físicos antes do cushing (%E.F.A) abrangeu 100% da amostra e 50% foi o percentil das pessoas que conseguiram retomar a prática dos exercícios (%E.F.D). A sintomatologia apresentada pela amostra foi a padrão da patologia estudada, sofrendo pequenas variações que não interferem no resultado do estudo e 100% da amostra que conseguiu voltar a realizar exercícios, relataram sua importância como fundamental para o controle da massa corporal e na busca de uma melhor qualidade de vida.

Palavras-chave: Cushing, Cortisol, Exercício Físico.