59 - THE COLLATERAL EFFECTS RELATED WITH THE ANDROGENIC PROPERTIES OF THE ANABOLIC STEROIDS IN WISTAR MALE ADULT MOUSE

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1. INTRODUCTION

Searching for better results, the athletes often improve their scores in high level competitions. Trying to reach better performance, the athletes have been using on the recent years substances or phenomenon that improve the performance, then called (ergogenic assistants) acrogenic auxiliary (McARDLE, et al., 1998; WILMORE e COSTIL, 2001). Among them there is the anabolic androgenic steroid (EAA). With the past of the time, the EAA started to be used as a way to increase strength, hypertrophy and the athletic performance by world classes athletes competitors or those people whom want to turn better their physical looking (LABREE, 1991, 2002; MILES et al., 1992). Besides the collateral effect diseases caused by the EAA use (in over recommended doses), the users are more suitable to be involved with illicit drugs as alcohol and tobacco (BAHRKE et al., 2000).

1.2 OBJECTIVE

To analyze the possible alteration of the weight on testicle, prostate, epididymis and seminal vesicle and also alteration on immunological system (monocytes, leukocytes, neutrophil e lymphocytes) of the mouse, due to the over recommended use of EAA.

1.3 JUSTIFICATION

Based on studies from (BUCKLEY et al., 1988; WINDSOR and DUMITRU,1989; KOMOROSKI and RICKERT,1992 ; BAHRKE et al.,1998;JOHNSTON et al., 2002) that shown that the number of male teenagers non-athletes that are using EAA is increasing recently with the application of over recommended doses that exceed the standard from 10 to 100 times (LISE et al., 1999). The studies presented by literature, until now, are not in complete agreement with the related collateral effects diseases caused by the wrong use of EAA

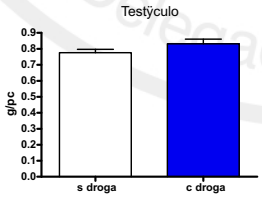
2. LITERATURE REVISION

The testosterone is synthesized since 1935. During the second war it was used by the German army to increase aggressiveness and hostility among the soldiers. In this period, its therapeutic use was restricted to the cure of patients recently passes by surgery, or burned or deeply depressed (LISE et al., 1999; FONSECA and THIESEN, 2000). In 1939 it was mentioned that its application could increase the performance of athletes (LIZE et al.1999). The researchers (LISE et al.,1999) tells that the standard of abuse of EAA use by athletes exceed from 10 to 100 times the physiological levels and therapeutic doses, what configure over recommended doses, justifying this way the additional toxic effects once the specific pharmacology receptors are saturated with lower doses.

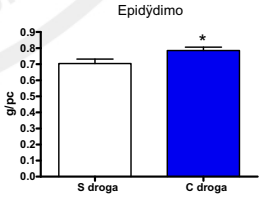
3.METHODOLOGY

The group of male mouses of Wistar gender was composed by 16 mouses with medium weight of 360gm. The animals receive the administration of following drug: Durateston® (testosterone deaconates, testosterone phenylproprionate, testosterone isocanoate organon, 50mg/ml). The doses applied corresponds to 5mg/kg from the mouse corporal mass (over recommended doses) (BRONSON e MATHERNE, 1997). The administration of EAA was made everyday during 10 days. The same procedure was applied to the group treated with peanut oil (psycho stimulation). In the end of the experimental period, the animals received a dose of anesthetic Tiopental® (100ml/kg), then they were sacrificed by cervical displacement. To compare the groups (with and without EAA) it was used the T test student been considerate statistic significantly to $< 0,05$.

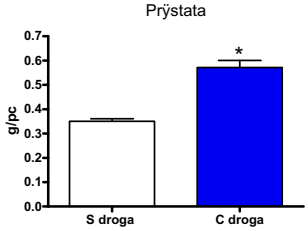
4. RESULTS



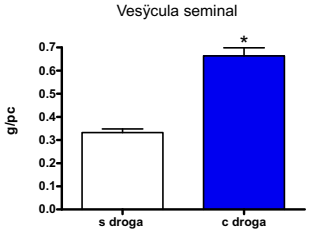
Picture 1
Without drug 0,7762±0.02
With drug 0,8313±0.02
N=8 P<0,05



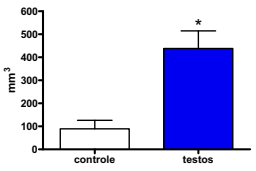
Picture 2
Without drug 0,7038±0.02
With drug 0,7850±0.02
N=8 P<0,05



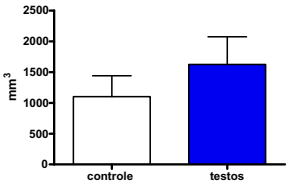
Picture 3
Without drug 0,3500±0.01
With drug 0,5713 ±0,02



Picture 4
Without drug 0,3325±0.02
With drug 0,6638 ±0,03

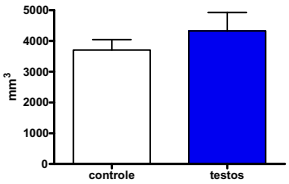


Picture 5
Without drug 89,00±37,46 mm
With drug 438,47±6,22 mm^3



Picture 6
Without drug a1100 ± 339,6 mm^3
With drug 1625 ± 448,6 m

Picture 7
Without drug 4950 ± 460,6 mm^3
With drug 6413 ± 977,3 mm^3



Picture 8
Without drug 3703 ± 334,9mm^3
With drug 4324± 598,3mm^3

5. DISCUSSION

The main discover of this study was that the 10 days infusion of EAA caused weight increase on prostate, epididymis and seminal vesicle, what did not happened on the testicle. Concerning the prostatic hypertrophy,our results are in accordance with the literature data that shows among the colaterall effects diseases in male adults and adolescent men, a reduction on the production of spermatozoon, atrophy of testicles, impotence, difficult or pain when piss and prostatic hypertrophy (LABREE, 1991; LISE et al., 1999). However in this research, we could not verify atrophy on the testicle maybe due to the short period that the mouses were submitted to the EAA. About epididymis and seminal vesicle, it was noticed weight increase as shown by (LABREE, 1991; LISE et al., 1999), where the testosterone influence in the action of those structures, so a higher concentration of this hormone would lead to the increase of the mentioned organs showing this way that those organs are influenced by the testosterone level increase. We could realize that the immunological system was changed related to the monocytes but those changes were not relevant when compared to the leukocytes, neutrophil and lymphocytes. Related to pictures 2 and 4: Epididymis and seminal vesicle was noticed: weight increase of these structures as mentioned(LABREE, 1991; LISE et al., 1999), where the testosterone influence in the action of those structures ,so a higher concentration of this hormone would lead to the increase of the mentioned organs. On pictures 6, 7, 8 respectively: neutrophil, lymphocytes, leukocytes, did not present a relevant statistic difference, this is due to the period of expose with EAA. Picture 5 shows a relevant statistic difference to the number of monocytes with an increase of (YU et al, 2003) it was noticed 32 weeks of application of 20 mg/kg per Day followed by a recuperation of 24 weeks presented a reduction on the spermatogenesis, but with no reduction on the leukocytes and lymphocytes as per those authors these results shown that an over recommended dose of EAA does not affect the immunological parameters. Our data is different due to the period of recuperation used by the authors. Many literature studies show the effects of testosterone deaconates drug, one of the drugs that is part of the composition of Durateston® drug, on spermatogenesis of animals and human being, but it were not noticed effects over the immunological system (YI QUN GU et al, 2003; YU et al, 2003).

6. CONCLUSION

According the found data, we can conclude that the application per 10 days of Durateston® on the measure of 5mg/kg were enough to increase the weight on seminal vesicle,epididymis, prostate and on the number of monocytes in male sedentary adult mouses of Wistar gender what agree with the hypothesis of this research. On the other hand, this fact did not happened to the testicle weight and the number of neutrophil, lymphocytes and leukocytes in accordance with the null hypothesis. This is probably due to the low period of exposion to the EAA (Durateston®). For future researched we suggest the accomplishment of new studies related to this issue, using other EAA (with base of synthetic testosterone), to a compare the relation between the data and an analysis with more criteria about the collateral effects and the proposal of investigation of such and other parameters.

7. REFERENCE

ANDREW DAVIS;CECIL KIDD;ASA G.H. BLAKELEY,JG. MC GEOWN.*"Fisiologia Humana"* Artemed s/a. São Paulo,2001

BACURAU, Reury Frank Pereira; NAVARRO, Francisco; ROSA, Luiz Fernando B.P.. *"Nutrição e suplementação esportiva"* 2. ed. rev. e ampl. Guarulhos: Phorte, 2001.

BAHRKE, M.S.; YESALIS, C.E.; BROWER, K.J. *"Anabolic-androgenic steroid abuse and performance-enhancing drugs among Adolescents"*. Child and Adolescent Psychiatric Clinics of North America; 7(4): 821-38, 1998

BRONSON E MATHERNE. "*Medicine science in Sports Exercise"* 29.5 (1997): 615-619

BUCKLEY, W.E.; YESALIS, C.E.; FRIEDL, K.E. ET AL. "*Estimated prevalence of anabolic steroid use among male high school seniors"*. Journal of the American Medical Association, 260:3441-3445, 1988

DAWSON, R.T. *Hormones and sport: drugs in sport* "*the role of the physician. J. Endocrinol."*, v. 170, p. 55-61, 2001.

EVANS, N.A; BOWREY, D.J.; NEWMAN, G. "*Ultra structural analysis of ruptured".*

FONSECA, E.P.; THIESEN, F. V. "*Esteroides anabólicos e suas alterações em análises clinicas"*. RBAC, (PUCRS) Pontifícia Universidade Católica do Rio Grande do Sul v.32, n.4, p.255-260, 2000

GAUTHIER, J.*"Effects cardiovasculaires du dopage. Ann. Cardiol. Angéiol*"., v. 50, p.293 - 298, 2001

GEORGE, S.J.; DWIVEDI, *"MMPS, cadherins, and cell proliferation"* TCM, v.14, p. 100-105, 2004.

GUYTON, Arthur C. *"Fundamentos de Guyton Tratado de fisiologia médica"* Rio de Janeiro: Guanabara Koogan, 2000.

HEDGE, GA.; COLBY, HD,; GOODMAN, R.L. *"Fisiologia Endocrina Clinica* ". São Paulo: Interlivros Edições LTDA, 1988 pp. 151-175

JOHNSON, M.D.; JAY, S.; SHOUP, B. RICHERT, V.I. *"Anabolic steroid use by male adolescents"*. Pediatrics, 83(6): 921 - 924, 1989.

JOHNSTON, L. D.; O'MALLEY, P. M. , BACHMAN, J. G. e cols. *"Monitoring the future national results on adolescent drug use: Overvew of Key finding"*, 2001.(NIH PUBLICATION N 02 - 2105) BETHESDA, MD: National Institute on Drug Abuse, 236., 2002.

KOMOROSKI, E.M. & RICHERT, V.I. *"Adolescent body image and attitude to anabolic streroid use"*. America Journal of diseases of children, 145:823 - 828, 1992.

LABRE, M. "*A review of anabolic steroids:uses and effects"*. J. Sport Med. Phys. Fit., v.31, n. 4, p.618 - 626, 1991.

LABRE, M.P. *"Adolescent boys and the muscular male body idea"*I. J. Adolescent Health, v.30, p.233-242, 2002.

LISE, M.L.Z. et al. *"O abuso de esteróides anabólicos androgênicos em atletismo".* Ver. Ass. Med. Brasil, Rio Grande do Sul, v.45,n.4, p. 364 - 370, 1999.

LISE, M.L.Z.; GAMA-E-SILVA, T.S.; FERIGOLO, M. & BARROS, H.M.T. *"O abuso de esteróides anabólico-androgênicos em atletismo".* Revista da Associação Médica Brasileira, 45:1-11, 1999

McARDLE, W. D.; KATCH, F. I.; KATCH, V. L. *"Fisiologia do exercicio: energia, desempenho e nutrição humana*". 4.ed. Rio de Janeiro: Guanabara Koogan, 1998.

MILES, J. W. et al. *"The effect of anabolic steroids on teh biomechanical and histological proprerties of rat tendon".* J.Bone Joint Surg., v. 74, p.411 - 422, 1992.

NATIONAL RESERCH COUNCIL.*"Guide for the care and use of laboratoty animals".*Washington, D.C: National Academy Press,1996

PARSSINEN, M. et al. *"The effect of supraphysiological doses of anabolic androgenic steroids on collagen metabolism"*. Int. Sports Med., v.21, p. 406-411, 2000.

PAVLATOS, A, M. et al. *"Review of oxymetholone: a 17 alfa alkylated anabolic-androgenic steroids"*. Clin. Ther., v.23, n.6, p.789 - 801, 2001.

SILVA, M. P.; MARCONDES, M.C.C.G.; MELLO, M.A,R. *"Exercício aeróbio e anaeróbio: efeitos sobre a gordura sérica e tecidual de ratos alimentados com dieta hiperlipidica"*. Ver. Bras. Ativ. Fís. Saúde, Londrina, v.4, n.3, p. 3 - 56, 1999.

SILVA, P. R. P.; DANIELSKI, R.; CZEPIELEWSKI, M. A, *"Esteróides anabolizantes no esporte".* Ver. Bras. Méd. Esporte., v. 8, n.6, p. 238-243, nov./dez. 2002.

STEDMAN.*"Dicionario Medico. Rio de Janeiro*": Guanabara Koogan, 1979.

TAKAHASHI, M.; TATSUGI, Y.; KOHNO, T. *"Endocrinological and pathological effects of anabolic-androgenic steroid in male rats"*. 51, n. 4, p.425 - 434, 2004.

YI-QUN GU, XING-HAI WANG, DWO XU, LIN PENG, LI-FA CHENG, MING-KONG HUANG,ZHEN-JIA HUANG, AND GUI-YUAN ZHANG. "*A Multicenter Contraceptive Efficacy Study of InjectableTestosterone Undecanoate in Healthy Chinese Men J Clin Endocrinol Metab."* 2003 Feb;88(2):562-8

Yu M,Cao X, Xu J, Wang X,Yang J, Wang X, Ben *"Effects of testosterone undecanoate as a male contraceptive candidate on rat immunological featuresImmunopharmacol Immunotoxicol".* 2003 Nov;25(4):627-43.

WILMORE, J. H.; COSTILL, D. L. *"Fisiologia do esporte e do exercicio".* 2 ed. Manole: São Paulo, 2001.

WILSON, J.D. : Goodman e Gilman, *"As Bases Farmacológicas da Terapêutica".* 8ed. Rio de Janeiro: Guanabara Koogan, 1991

WINDSON, R.E. & DUMITRU, D. *"Prevalence of anabolic steroid use by male and female adolescents".* Medicine and Science in Sports and Exercises. 21: 494: 497, 1989.

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THE COLLATERAL EFFECTS RELATED WITH THE ANDROGENIC PROPERTIES OF THE ANABOLIC STEROIDS IN WISTAR MALE ADULT MOUSE

ABSTRACT

The use of anabolic androgenic steroid (EAA) has been described in many situation as liable of diverse collateral effect diseases. The purpose of this research was analyze the weight alteration that could have occurred on the main organs of the male reproduction system (prostate, epididymis, testicle, seminal vesicle), and on the immunological system in sedentary group of adults male mouse of race Wistar. The animals were divided in two groups : Group 1 with peanut oil injection , Group 2 EAA injection. The EAA (DURATESTON® 5mg/kg) was injected via subcutaneous intersect through the sural triceps on the back paw being alternated between right and left during 10 consecutive days. After that period the animals were sacrificed and the weight of the testicle, prostate, epididymis, seminal vesicle was analyzed and also the blood for immunologic system verification (monocytes, lymphocytes, neutrophil, leukocytes total). Analyzing the results, It was found relevant statistic difference on the weight of the organs prostate, epididymis and, seminal vesicle. In the immunological system it was noticed relevant modifications on the monocytes ($p < 0,05$) figures. Thought this research it was possible to realize that the 10 days application of Durateston® lead to the weight increase on the seminal vesicle, epididymis, prostate and also on the monocytes figures.

KEY-WORDS: Anabolic androgenic steroid (EAA); Immunological system; Male reproductor system

LES EFFETS COLLATÉRAUX RAPPORTÉS AUX PROPRIÉTÉS ANDROGÊNICAS DE ESTERÓIDES ANABOLIZANTES À DES RATS WISTAR DU TYPE MASCULIN

RESUMÉ

L'utilisation d'esteroides anabólicos - androgénicos (EAA) il a été présenté dans diverses vezes comme responsable par différents effets latéraux. Le deste objectif étude a été d'analisar le possible changement de poids dans les principaux organes du système reproducteur masculin (prostate, epidídimo, testicule, vesícula séminal), et dans le système immunologique dans des souris de la race Wistar de de celui adulte sédentaire masculin gênero. Les animaux ont été divisés deux groupes : Groupe 1 avec injection d'huile d'amendoin, Groupe 2 avec injection de EAA. L'EAA (DURATESTON® 5mg/kg) a été appliqué par voie sous-cutanée en transférant le tríceps sural dans la jambe postérieure en étant alterné entre droite et gauche par dix jours rapprochés. Passé cette période, les animaux ont été sacrifié et a été analysé le poids des testicules, prostate, epidídimo, vesícula séminal et analizis du sang pour vérification du système immunologique (monócitos, linfócitos, neutrófilos, leucocytes en total). A été observées des différences estatísticas significatives pour le poids de la prostate, epidídimo et vesícula séminale. Dans le système immunologique il y a eu des changements significatifs dans le nombre de monócitos ($p < 0,05$). Cette étude a informé que l'application pour la période de 10 jours de Durateston® a été sufuciente pour augmenter le poids dans la vesícula

séminale, epidídimo, prostate et dans le nombre de monócitos.

MOT- CLÉ: D'esteroides anabólicos - androgénicos (EAA); Système immunologique ; Système reproducteur masculin.

EL EFECTO COLATERAL RELACIONADOS A LAS PROPIEDAD ANDROGÉNICA DE LOS ESTEROIDES ANABÓLICOS EN RATON WISTAR DE LOS GENERO MASCULINO

RESUMEN

La utilización de esteroides anabólicos - androgénicos (EAA) ha sido presentada en diversas vezes como responsable por distintos efectos laterales molestadores. El objectivo deste estudio fué analisar el posible cambio de peso en los principales organos del sistema reproductor masculino (próstata, epidídimo, testículo, vesícula seminal), y en el sistema inmunológico en ratónes de la raza Wistar del gênero masculino adulto sedentário. Los animales fuerón divididos en dos grupos: Grupo 1 con inyección de aceite de amendoin, Grupo 2 con inyección de EAA. El EAA (DURATESTON® 5mg/kg) fué aplicado por via subcutánea traspasando el tríceps sural en la pata posterior siendo alternada entre derecha y izquierda por diez dias seguidos. Pasado este periodo, los animales fuerón sacrificados y fué analizado el peso de los testículos, próstata, epidídimo, vesícula seminal y analizis de la sangre para verificación del sistema inmunologico (monócitos, linfócitos, neutrófilos, leucócitos en total). Fué observado significativas diferencias estatísticas para el peso de la próstata, epidídimo y vesícula seminal. En el sistema inmunológico hubo significativos cambios en el numero de monócitos ($p < 0,05$). Este estudio informó que la aplicación por el período de 10 días de Durateston® fué sufuciente para aumentar el peso en la vesícula seminal, epidídimo, próstata y en el numero de monócitos.

PALABRA-LLAVE: Esteroides anabólicos - androgênicos (EAA) ; Sistema inmunológico; Sistema reproductor masculino

OS EFEITOS COLATERAIS RELACIONADOS ÀS PROPRIEDADES ANDROGÊNICAS DOS ESTERÓIDES ANABOLIZANTES EM RATOS WISTAR DO GÊNERO MASCULINO

RESUMO

O uso de esteróides anabólicos - androgênicos (EAA) tem sido descrito em diversas situações como causadores de diversos efeitos colaterais indesejáveis. O objetivo deste trabalho foi analisar possíveis alterações do peso dos principais órgãos do sistema reprodutor masculino (próstata, epidídimo, testículo, vesícula seminal), e no sistema imunológico em ratos da raça Wistar do gênero masculino adultos sedentários.Os animais foram divididos em dois grupos: Grupo 1 com injeção de óleo de amendoim, Grupo 2 com injeção de EAA. O EAA (DURATESTON® 5mg/kg) foi administrado via subcutânea atravessando o tríceps sural na pata posterior alternando entre direita e esquerda dos animais durante dez dias consecutivos. Após esse período os animais foram sacrificados e foi analisado o peso de testículo, próstata, epidídimo, vesícula seminal e análise do sangue para verificação do sistema imunológico (monócitos, linfócitos, neutrófilos, leucócitos totais). Notaram-se diferenças estatisticamente significativas para o peso dos órgãos próstata, epidídimo, vesícula seminal. No sistema imunológico houve alterações significativas no número de monócitos ($p < 0,05$).O estudo demonstrou que a aplicação pelo período de 10 dias de Durateston® foram suficientes para aumentar de peso na vesícula seminal, epidídimo, próstata e no número de monócitos.

PALAVRAS -CHAVES: esteróides anabólicos - androgênicos (EAA) ; Sistema imunológico; Sistema reprodutor masculino.