

INVESTIGATION OF PITUITARY DYSFUNCTION IN RETIRED PROFESSIONAL SOCCER PLAYERS

INVESTIGAÇÃO DE DISFUNÇÃO HIPOFISÁRIA EM JOGADORES DE FUTEBOL PROFISSIONAIS APOSENTADOS

INVESTIGACIÓN DE DISFUNCIÓN HIPOFISARIA EN JUGADORES DE FÚTBOL PROFESIONALES RETIRADOS



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ABSTRACT

Introduction: It is well-known that pituitary dysfunction can develop as a result of traumatic brain injuries. One reason for such injuries is collision during contact sports. **Objectives:** The aim of this study was to investigate the effects of heading the ball and concussion on pituitary function in retired soccer players. **Methods:** Thirty-two retired soccer players, with an average age of 43.38 ± 5.49 (35-59) and 26 sedentary individuals with an average age of 43.31 ± 6.38 (35-59) were included in this study. The subjects were questioned about their soccer-playing background, history of head trauma and concussion, and cardiometabolic diseases. One day one, blood samples were taken to investigate the baseline hematologic and biochemical parameters. On day two, the ACTH stimulation test was conducted, and on day three, glucagon stimulation tests were carried out. Resting EKG, transthoracic ECHO and exercise stress tests (for MET values) were also conducted. For the statistical analysis, The Student's t-test was used to compare the results of the two groups. The level of significance adopted was $p < 0.05$. **Results:** It was identified that 5 out of 32 soccer players (16%) had experienced concussion during their soccer careers. The growth hormone (GH) levels of 3 retired soccer players (9.2%) and 3 sedentary individuals (10%) was below 1 ng/dl, which was accepted as the threshold value. There were no significant differences between hematological, biochemical and cardiometabolic parameters of the soccer players with low GH levels and those with normal GH levels. There was no significant relationship between the number of headers performed and GH deficiency. **Conclusion:** Although low GH levels were detected in almost 10% of the retired soccer players, the frequency of hypopituitarism was not higher than in the sedentary control group.

Level of evidence I; Prognostic Studies.

Keywords: Soccer; Brain concussion; Hypopituitarism.

RESUMO

Introdução: É fato conhecido que a disfunção hipofisária sobrevém em decorrência de lesões cerebrais traumáticas. Uma das razões para essas lesões é a colisão durante esportes de contato. **Objetivo:** O objetivo deste estudo foi investigar os efeitos do cabeceamento de bola sobre a hipófise e suas funções em jogadores de futebol aposentados. **Métodos:** Participaram deste estudo 32 jogadores de futebol aposentados com média de idade de $43,38 \pm 5,49$ (35-59) e 26 indivíduos sedentários com média de idade de $43,31 \pm 6,38$ (35-59) que foram questionados quanto à experiência como jogador de futebol, história de traumatismo craniano, concussões e doenças cardiometabólicas. No primeiro dia, foram obtidas amostras de sangue para investigar os parâmetros hematológicos e bioquímicos basais. No segundo dia, foi realizado o teste de estimulação com ACTH; no terceiro dia, foram feitos os testes de estimulação com glucagon. Além disso, foram realizados ECG de repouso, ecocardiograma transtorácico e testes de esforço para obter o equivalente metabólico (MET). Na análise estatística, o teste t de Student foi usado na comparação dos resultados dos dois grupos. O nível de significância foi estabelecido em $p < 0,05$. **Resultados:** Identificou-se que cinco dos 32 jogadores de futebol (16%) sofreram uma concussão durante a carreira futebolística. Os níveis de hormônio de crescimento (GH) de três jogadores de futebol (9,2%) e de três indivíduos sedentários (10%) foram inferiores a 1 ng/dl, valor que foi aceito como limiar. Não houve diferença significativa entre os parâmetros hematológicos, bioquímicos e cardiometabólicos dos jogadores de futebol com deficiência de GH e os jogadores de futebol com nível normal de GH. Não houve relação significativa entre o número de cabeceamentos e a deficiência de GH. **Conclusão:** Embora a deficiência de GH tenha sido detectada em quase 10% dos jogadores aposentados, a frequência de hipopituitarismo não foi maior do que a dos controles sedentários. **Nível de evidência I; Estudos Prognósticos.**

Descritores: Futebol; Concussão encefálica; Hipopituitarismo.

RESUMEN

Introducción: Es un hecho conocido que la disfunción hipofisaria sobreviene a consecuencia de lesiones cerebrales traumáticas. Una de las razones para esas lesiones es la colisión durante deportes de contacto. **Objetivo:** El objetivo de este estudio fue investigar los efectos de la cabezada en la pelota sobre la hipófisis y sus funciones en jugadores de fútbol retirados. **Métodos:** Participaron en este estudio 32 jugadores de fútbol retirados con promedio de edad de $43,38 \pm 5,49$ (35-59) y 26 individuos sedentarios con promedio de edad de $43,31 \pm 6,38$ (35-59) que fueron cuestionados



cuanto a la experiencia como jugador de fútbol, historia de traumatismo craneano, concusiones y enfermedades cardiometabólicas. En el primer día, fueron obtenidas muestras de sangre para investigar los parámetros hematológicos y bioquímicos basales. En el segundo día, fue realizado el test de estimulación con ACTH. En el tercer día, fueron hechos los tests de estimulación con glucagón. Además, fueron realizados ECG de reposo, ecocardiograma transtorácico y tests de esfuerzo para obtener el equivalente metabólico (MET). En el análisis estadístico se usó el test t de Student en la comparación de los resultados de los dos grupos. El nivel de significancia fue establecido en $p < 0,05$. Resultados: Se identificó que cinco de los 32 jugadores (16%) sufrieron una concusión durante la carrera futbolística. Los niveles de hormona de crecimiento (HC) de tres jugadores de fútbol (9,2%) y de tres individuos sedentarios (10%) fueron inferiores a 1 ng/dl, valor que fue aceptado como umbral. No hubo diferencia significativa entre los parámetros hematológicos, bioquímicos y cardiometabólicos de los jugadores de fútbol con deficiencia de HC y los jugadores de fútbol con niveles normal de HC. No hubo relación significativa entre el número de cabezadas y la deficiencia de HC. Conclusión: Aunque la deficiencia de HC haya sido detectada en casi 10% de los jugadores retirados, la frecuencia de hipopituitarismo no fue superior a la de los controles sedentarios. **Nivel de evidencia I; Estudios pronósticos.**

Descriptor: Fútbol; Conmoción encefálica; Hipopituitarismo.

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INTRODUCTION

It is a known fact that pituitary dysfunction develops due to traumatic brain injuries. One of the reasons for these injuries is collision and contact sports.¹ It has been revealed in various studies that pituitary dysfunction develops in boxers, kickboxers,^{2,3} and retired American football players.⁴ Hypopituitarism⁵ and transient hypogonadism cases have also been reported in athletes having a concussion due to multiple head traumas.⁶

The world's most popular sport, soccer, is a contact and collision sport.⁷ For this reason, sports injuries are frequent. Although not much, there are also head and face traumas among these injuries.⁸⁻¹¹ Concussions constitute the most important part of the head and face traumas.¹²

Soccer is a sports branch that is open to chronic microtraumas, in addition to acute head traumas. One of the most important causes of chronic microtrauma is heading. It is claimed that cognitive functions of particularly the soccer players performing headings very frequently are worse when compared to other athletes due to the heading. This condition is parallel with the number of concussions and the number of headings.¹³ There are also studies indicating that there is a correlation between the heading and abnormal EEG activity.¹⁴ It is indicated that the heading is more dangerous in children and adolescents and thus the heading should not be trained until 14 years of age.¹⁵

The objective of this study was to investigate if frequent headings and concussions had any delayed pathological effects on the pituitary functions of retired soccer players.

MATERIALS AND METHODS

Participants

32 retired soccer players with the average age of 43.38 ± 5.49 (35-59) years having professionally played soccer at least for 5 years in the Turkish Football (Soccer) Leagues were included in the study, and 29 healthy male sedentary volunteers were included in the study as the control group. Looking at previous studies, glucagon cutt off was taken 1 ng/dl.¹⁶ The GH values of 3 volunteers from the control group were found to be below 1 ng/dl. Single GH stimulation test (glucagon stimulation test as we have applied) is not enough for the diagnosis of hypopituitarism in subjects without any organic lesion such as healthy volunteers.¹⁷ Therefore the data of these individuals were excluded from the study and the results of 26 volunteers with the average age of 43.31 ± 6.38 (35-59) years were accepted as the control group.

Those who experienced head trauma due to a reason other than soccer, experienced a pituitary disease, underwent a brain surgery, using

corticosteroid, diagnosed with cancer and suffering from neurologic and psychiatric diseases were excluded from the study.

Before the study, approval was obtained from Locale Ethic Committee (2014/189), and the conditions of the Declaration of Helsinki were complied with in the study. All of the participants signed the free and informed consent term.

Test protocols

All volunteers were examined in terms of their soccer history, head trauma, concussion and growth hormone (GH) deficiency.

Hematological and biochemical tests: Hemoglobin, glucose, TG, total cholesterol, HDL, LDL, fT3, fT4, TSH, prolactin, FSH, LH, total testosterone, insulin, ACTH and IGF-1 values were measured.

ACTH stimulation test: Cortisol values were measured with the RIA method in the nuclear medical laboratory of our hospital.

Glucagon stimulation test: GH levels were measured by the RIA method (IRMA GH, REF IM1397, Beckman Coulter Inc. 2015).

Cardiometabolic Measurements: The height the body weight, BMI, BF%, FFM (Tanita, Japan, 2013) were measured with the electrical bioimpedance method. The resting heart rate, SBP, DBP were measured, and resting EKG, transthoracic echo and the effort tests with Bruce protocol were conducted.

Statistical Analysis

The mean and standard deviation values were obtained for the data exhibiting normal distribution and the median, 25th and 75th percentile values were acquired for the data not showing normal distribution. Student's t-test was conducted in the comparison of the groups. The Mann-Whitney U test was conducted in the comparisons of the independent groups not showing normal distribution. The significance level was accepted as $p < 0.05$.

RESULTS

It was identified that 5 (16%) of the 32 soccer players experienced a concussion during their soccer career. While the GH values of 29 soccer player (90.8%) were within normal limits, the GH level of 3 soccer players (9.2%) was found to be below 1 ng/dl which was accepted as the threshold value. Although the GH values of the soccer players were higher than the sedanteries group, there was no statistically significant difference. In addition, mean GH values were above the normal limits in both groups.

There was no significant difference between the soccer players with the normal GH level and the soccer players with GH deficiency in terms of the concussion rate, the number of heading and soccer years. (Table 1)

When the average values of the soccer players and sedentaries were compared, while the MET values were statistically significantly high in favor of soccer players, Hb, ACTH, fT4, prolactin, and heart rate values were found to be lower when compared to the sedentaries ($p < 0.05$). (Table 2) However, all values were within the reference ranges. There was no significant difference between hematological, biochemical and cardiometabolic parameters of the soccer players with GH deficiency and the soccer players with the normal GH level. (Table 3)

No significant relationship was determined between the number of concussions and GH deficiency, and between the number of heading and GH deficiency ($p > 0.05$, $r = 0.210$, $r = -320$).

Table 1. Characteristics of soccer players.

	Soccer players with GH deficiency (n:3) 9.2%	Soccer players with GH normal (n:29) 90.8%	p
Soccer duration (yr)	20.67 (18.50-22.50)	21.10 (15.00-26.00)	0.919
Professional soccer duration (yr)	12.67 (9.00-16.50)	8.41 (5.00-11.00)	0.095
Mean heading per match	11.00 (6.50-15.00)	8.58 (4.00-10.00)	0.531
Mean heading per year (40 matches were taken annually)	440.00 (275.00-500.00)	343.50 (150.00-520.00)	0.531
Concussion rate	0.33 (0.00-0.50)	0.17 (0.00-0.00)	0.582

Parameters were given median p(25)-p(75).

Table 2. Biochemical, hormonal and cardiometabolic parameters.

	Soccer players (n:32)	Sedanteries (n:26)	p
Age (yr)	43.38 ± 5.49	43.15 ± 6.67	0.890
Height (cm)	175.94 ± 5.38	175.77 ± 5.45	0.907
Weight (kg)	85.35 ± 11.65	84.13 ± 10.64	0.681
BMI (kg/m ²)	27.58 ± 2.73	27.19 ± 2.84	0.617
Fat%	21.67 ± 5.65	22.86 ± 4.73	0.341
FFM (kg)	64.99 ± 10.88	64.56 ± 7.26	0.830
Hb (g/dL)	15.02 ± 0.83	15.69 ± 0.94	0.006*
Glucose (mg/dL)	76.91 ± 9.62	85.08 ± 20.98	0.700
TG (mg/dL)	139.86 ± 73.30	155.86 ± 67.20	0.346
Chol (mg/dL)	196.93 ± 35.20	196.85 ± 36.18	0.706
HDL (mg/dL)	45.66 ± 12.97	53.99 ± 9.58	0.093
LDL (mg/dL)	120.25 ± 39.32	120.26 ± 35.99	0.809
fT3 (pg/mL)	3.41 ± 0.43	3.60 ± 0.38	0.078
fT4 (ng/mL)	1.27 ± 0.13	1.36 ± 0.16	0.020*
TSH (μIU/mL)	2.23 ± 1.39	2.06 ± 1.12	0.621
Prolactin (ng/mL)	8.09 ± 3.21	10.57 ± 4.02	0.011*
FSH (mIU/mL)	4.48 ± 2.97	4.26 ± 2.82	0.771
LH (mIU/mL)	4.68 ± 1.57	5.31 ± 2.28	0.224
tTestosterone (ng/dL)	486.54 ± 160.32	477.37 ± 186.09	0.841
Insulin (μIU/mL)	7.49 ± 4.23	9.25 ± 4.61	0.988
ACTH (pg/mL)	42.21 ± 18.63	60.24 ± 24.34	0.002*
Cortisol (peak) (μg/dL)	22.40 ± 3.89	25.34 ± 7.41	0.057
IGF-1 (ng/mL)	130.73 ± 43.33	153.99 ± 48.15	0.058
GH (stimulated peak growth hormone) (ng/dl)	8.23 ± 6.72	5.97 ± 5.42	0.171
Heart rate	66.56 ± 4.96	71.23 ± 8.32	0.010*
SBP (mmHg)	117.13 ± 10.79	110.19 ± 18.03	0.075
DBP (mmHg)	72.97 ± 10.61	74.42 ± 9.42	0.588
EF (%)	64.00 ± 2.93	63.69 ± 3.07	0.698
MET	15.62 ± 1.88	13.74.62	0.002*

Parameters were given mean ± standart deviation.

Table 3. Biochemical, hormonal and cardiometabolic parameters.

	Soccer Players with GH normal (n:29)	Soccer Players with GH deficiency (n:3)	p
Age (yr)	42,00 (40,00-47,00)	38,00 (38,00-39,00)	0.096
Height (cm)	175,00 (172,50-178,00)	183,00 (171,00-183,00)	0.286
Weight (kg)	83,00 (78,20-89,05)	95,30 (77,10-95,30)	0.286
BMI (kg/m ²)	27,60 (25,55-28,75)	28,50 (26,40-28,50)	0.538
Fat%	22,00 (18,25-24,50)	20,70 (18,40-20,70)	0.903
FFM (kg)	64,90 (62,85-69,70)	62,90 (20,00-62,90)	0.624
Hb (g/dL)	14,80 (14,40-15,55)	15,90 (14,80-15,90)	0.144
Glucose (mg/dL)	78,00 (71,50-81,00)	72,00 (70,00-72,00)	0.258
TG (mg/dL)	120,00 (70,50-178,00)	202,00 (135,00-202,00)	0.096
Chol (mg/dL)	194,00 (175,50-208,70)	209,00 (166,50-209,00)	0.760
HDL (mg/dL)	44,70 (36,35-55,50)	32,20 (27,00-32,20)	0.317
LDL (mg/dL)	118,60 (99,20-138,64)	117,60 (93,62-117,60)	0.952
fT3 (pg/mL)	3,38 (3,17-3,66)	3,32 (3,31-3,32)	1.000
fT4 (ng/mL)	1,28 (1,18-1,36)	1,22 (1,06-1,22)	0.164
TSH (μIU/mL)	1,72 (1,29-2,58)	4,30 (1,72-4,30)	0.082
Prolactin (ng/mL)	7,91 (5,95-9,84)	6,17 (5,09-6,17)	0.760
FSH (mIU/mL)	4,33 (2,53-5,35)	3,05 (2,35-3,05)	1.000
LH (mIU/mL)	4,30 (3,71-5,65)	3,21 (3,06-3,21)	0.394
tTestosterone (ng/dL)	506,60 (385,80-603,80)	318,60 (237,90-318,60)	0.497
Insulin (μIU/mL)	6,77 (3,82-10,15)	7,30 (3,80-7,30)	0.714
ACTH (pg/mL)	38,87 (30,14-49,15)	39,02 (25,00-39,02)	0.903
Cortisol (peak) (μg/dL)	22,57 (20,02-24,27)	24,28 (19,58-24,28)	0.580
IGF-1 (ng/mL)	134,04 (89,32-154,31)	129,40 (102,21-129,40)	0.624
GH(peak) (ng/dl)	8,48 (3,45-12,00)	0,26 (0,20-0,26)	0.001*
Heart rate	65,00 (64,00-68,50)	71,00 (68,00-71,00)	0.144
SBP (mmHg)	120,00 (110,00-130,00)	120,00 (110,00-120,00)	0.855
DBP (mmHg)	75,00 (70,00-80,00)	80,00 (70,00-80,00)	0.286
EF (%)	64,00 (61,00-66,00)	65,00 (64,00-65,00)	0.580
MET	15,90 (13,95-17,10)	17,00 (10,80-17,00)	0.903

Parameters were given median p(25)-p(75).

DISCUSSION

It is indicated in various studies that head and face traumas in soccer players are 2.2-8.3%^{8,12,18} and the concussion rate is 0.06-0.6/1000 participation hours.^{9,19,20} It was determined that 5 (16%) of the 32 retired soccer players we included in the study experienced head trauma resulting in concussion (4 of them for one time, one of them for 2 times). Since the concussion rate we have found covers the entire soccer life of soccer players, it is higher when compared to the results of other studies because Asken et al. indicated that male soccer players with ten years of soccer life experienced concussion at the rate of 50% and female soccer players experienced it at the rate of 22%.²¹

In 3 (9.2%) of the 32 soccer players included in the study, the GH level was determined to be below 1 ng/dL which is the threshold value. It is considered that this rate can also be in the normal population because the GH values were found to be below 1 ng/dL in 4 of the 29 volunteers in the sedanteries group. In our study, the GH amount was found to be below normal values only in two (40%) of the 5 football players with head trauma resulting in concussion and no deficiency was determined in the other pituitary hormones. No significant relationship was found considering the relationship between the number of concussions and the GH level. However, while Kelly et al. determined 23.5% pituitary dysfunction in retired American football players, they also identified that 19% growth hormone deficiency and 50% metabolic syndrome developed.⁴ While Keleştemur et al. indicated growth hormone (GH) deficiency and

its relationship with the boxing age in boxers,² Tanrıverdi et al. determined that pituitary dysfunction with GH deficiency developed at the rate of 21.9% in boxers and kickboxers, and the body mass index (BMI) values of the athletes with GH deficiency were higher when compared to the normal athletes.³ However, multiple head traumas occur more frequently and intensely in boxing, kickboxing, and American Football when compared to soccer. While soccer is a contact and collision sport, the number of head traumas resulting in concussion is small. This condition does not cause the development of pituitary dysfunction at a significant rate, and thus metabolic syndrome does not develop.

Although there was a difference in testosterone between the GH deficiency group and GH normal group, the values were within the reference limits (275-800 ng/dl). For this reason, hypogonadism was not considered. GH values were higher in soccer players than in sedanteries groups, whereas IGF-1 values were higher in sedanter groups. Furthermore normal IGF-1 values were in the GH deficiency group. However, there may be normal GH peak with high IGF -1 or low GH peak with normal IGF-1 (20)

While head trauma is not frequently observed in soccer players, the heading is a frequently performed. In our study, the average number of heading for a soccer player per match was found to be 8.81. It is stated that, in the long term, microtraumas occurring in the head cause brain damage. It is indicated that the cognitive functions of soccer players frequently performing headings are worse due to the heading when compared to other athletes.²² This condition is parallel with the number of concussions and the number of headings.^{13,23} Moreover, it is suggested that there is microstructural disorder in the white matter of the brain mantle depending on the increase in the number of headings.⁹ Matser et al. determined in the study they conducted in the Danish Soccer League that there was a negative correlation between the heading and concussion, and cognitive functions.²⁴ It was observed that neurochemical parameters of the Swedish retired soccer players were higher when compared to the controls.²⁵ According to our results, no significant relationship was determined between the number of headings and GH deficiency. The effect of the heading on the brain is minimized with the fact that the muscle mass of professional athletes is high and they use the right technique. It was reported that less harmful effect is observed when the soccer player protects himself by locking his neck muscles while performing the heading.²⁶ Furthermore, some researchers stated that not the heading in soccer but concussions caused chronic brain injury symptoms,²⁷ and not the heading but head-on collisions increased the

risk of concussion. Moreover, Jones could not determine a relationship between dementia and heading in the study conducted with retired soccer players.²⁸ It is also indicated that currently used synthetic balls do not cause both masked and unmasked concussions.²⁹ On the other hand, since the muscle mass is lower in children, it is indicated that the risk is higher and it is asserted that pituitary dysfunction due to traumatic brain injury in children and adolescent athletes is an important problem.³⁰

Pituitary dysfunction is especially observed with growth hormone deficiency. Growth hormone deficiency causes an increase in cardiovascular disease risk factors such as performance decrease, an increase in the BMI, hypercholesterolemia, and an increase in the waist circumference. In our study, no significant difference was found in any parameters in the comparison between the group with the normal GH level and the group with GH deficiency. However, the number of subjects in the GHD group is insufficient. We made this comparison considering that possibility of deterioration of metabolic factors in the GHD group. If we had used enough subjects, we could have found significant results probably.

Study Limitations

Not conducting the insulin tolerance test (ITT) which is a gold standard in the diagnosis of GH deficiency is the most important limitation of our study. However, this test was abandoned since the side effects that might occur during this test would decrease the participation of volunteers. It was decided to conduct the GHRH+arginine test instead. However, this test was also canceled since it was difficult to obtain arginine. In addition, the low number of soccer players with pituitary deficiency reduces the power of statistical comparisons.

CONCLUSION

According to these results, it is possible to say that the heading in soccer does not cause pituitary dysfunction as in boxing and other martial arts. However, it is required to be aware of the fact that head traumas resulting in concussion may cause GH deficiency in retired soccer players.

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