

A Prospective Evaluation of Anterior Pituitary Functions In Football Players (Chronic Head Trauma)

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Abstract

This first clinical study that evaluated the hypothalamo-pituitary dysfunction in professional football player. The GH and ACTH levels were found to be in the normal range in football players playing professional football for 5–18 years. Other neuroendocrine values were found higher than the normal values. The probability of pituitary dysfunction in professional football players who play less than 18 years is not high. Broader studies are needed to investigate pituitary dysfunction and treatment options, as well as the pathophysiology of brain injury in sports. This study must be supported by new studies that include neuropsychological and radiological subjects. This is a “circumstance ascertain” study, so it has no impact on clinical practice.

Purpose: This study aims to investigate the changes in anterior pituitary hormones in professional football players.

Material and Method: This study was carried out at the Department of Emergency Medicine, Faculty of Medicine and Gaziantep University between 01.01.2012 and 31.10.2012. The study included 51 professional football players [group 1] who suffered chronic head traumas (heading) and 21 healthy male volunteers [group 2] for comparison. Blood samples were collected from both groups and centrifuged to measure the Thyroid-Stimulating Hormone (TSH), Growth Hormone (GH), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin (PRL) and Adrenocorticotrophic Hormone (ACTH) values. The samples were kept at -80°C. The results were analyzed using SPSS version 18 and $p \leq 0,05$ was considered to be statistically significant.

Findings: GH values were 40%, and ACTH values were 12% below the normal range in football players. However, a comparison with the control group showed that this low level was statistically insignificant ($p = 0,284$). TSH was 10%, PRL was 6%, LH was 4% and ACTH was 6% over the normal range in football players. TSH, FSH, PRL and ACT values were found to be higher in football players compared with the control group. The high TSH and PRL hormone levels was statistically significant ($p = 0,001$). Gonadotropins and ACTH levels increased with longer playing times, but this increase was not statistically significant.

Conclusions: Playing professional football and heading the ball cause no significant changes in anterior pituitary hormones, except for the GH. No correlations exist between ball possession and hormonal changes.

Keywords: Football player; Chronic head trauma; Growth hormone; Pituitary dysfunction

Introduction

Hypopituitarism (pituitary insufficiency) develops as a result of insufficient production and release of the pituitary hormone one or more times. Lack of one or more pituitary hormones is known as partial hypopituitarism, and the lack of all pituitary hormones is known as panhypopituitarism. Its prevalence is 45/100.000, and its incidence is 4/100.000/year. Mortality increases 2 times compared with normal individuals [1]. Pituitary hormones act to respond properly to stress and maintain vital bodily functions in addition to many other functions. Clinical findings, basal hormone measurements and various dynamic tests are used to evaluate the functions [2,3]. Major

causes of pituitary insufficiency include pituitary adenoma, treatment complications, craniopharyngioma, hypothalamic region tumors, idiopathic and congenital causes, lymphocytic pituitaritis, apoplexia and postpartum pituitary necrosis, infiltrative diseases and traumatic brain injury [4,5].

Contact sports including box, football, American football, ice hockey, and martial arts (karate, taekwondo, judo, kick box etc.) cause acute and chronic traumatic brain injuries [6]. Another contact sport, football has also been described among the causes of chronic traumatic brain injury. Chronic head traumas in football players occur due to the direct impact of head contacts with other players and the ground, or due to the cumulative power generated by the act of heading the ball [7–9]. Increased exposure to the ball, possession time and increased competition are the risk factors for chronic head traumas in football players [7]. Although traumatic brain injury analyses have been performed in football players, hypothalamo-pituitary function analyses are unavailable [10].

The prevalence of neuroendocrine anomalies is high in traumatic brain injury patients who have been rehabilitated for a long time after the injury [11]. Gonadotropin and GH deficiencies appear to be the most common disorders [12,13]. Although its pathophysiology remains unclear, direct mechanical trauma and vascular injury are the most common underlying causes. As a result, hypopituitarism develops at the anterior lobe of the pituitary gland due to necrosis, ruptured pituitary stalk, or decreased blood flow [14].

This study aims to evaluate the pituitary functions in football players [post chronic head trauma] considering that heading the football is a chronic head trauma. Our study, different from other similar studies, is important as it investigates neuroendocrine changes in football players.

Material and Methods

Patients and Ethics

This study was carried out at the Department of Emergency Medicine, Faculty of Medicine, and Gaziantep University between 01.01.2012 and 31.10.2012. The study included 51 professional football players (group 1) who played professional football for at least 5 years and suffered chronic head traumas (heading) and 21 healthy male volunteers (group 2) for comparison to evaluate the effects of chronic head trauma due to heading the football.

Ethical Committee approval was obtained before the study from the Medical Ethical Committee of the Faculty of Medicine, Gaziantep University (Ethical committee resolution no: 06-2009/237, date: 18.06.2009) and the ethical standards of Helsinki Declaration were adopted. The study was funded by the Commission for Scientific Research Projects of Gaziantep University [Project no: TF.12.31].

All included groups were informed about the tests to be performed. Written and signed approvals were obtained from all participants in order to carry out the tests and perform the required physical examinations.

Inclusion criteria for football players [chronic head trauma]

1. Older than 18 years of age,
2. Understanding and accepting the study procedures,
3. Signing the informed consent,
4. Playing football professionally for at least 5 years,
5. Playing in the advanced, defense or midfield positions (due to high incidence of contact traumas),
6. No diagnosed meningitis, major depressions, SVO disease, and suffering no head traumas in the last 6 months,
7. Undergoing no hormone replacement (thyroid hormone, growth hormone, FSH, LH, ACTH) therapies for any reasons whatsoever.

Exclusion criteria for football players [chronic head trauma]

1. Failing to sign the informed consent,
2. Younger than 18 years of age,
3. Having no endocrinologic disorders that can cause Hypoprolactinemia, Hyperthyroidism, Hypothyroidism or other anterior pituitary hormone disorders,

4. Having no known history of acute, light, mild or severe head traumas,
5. Having no known history of intracranial pathologies (brain tumor, brain abscess etc.) and/or surgical operations,
6. Playing in the goalkeeper position (due to low incidence of contact traumas)

Collection of samples

The heights, weights, body mass indexes and waist circumferences of all football players were measured. Routinely measured serum sodium (Na), potassium (K), blood urea nitrogen (BUN), calcium (Ca), phosphorus (P), fasting blood glucose (FBG), total protein, albumin, high density lipoprotein (HDL), low density lipoprotein (LDL), triglyceride and total cholesterol levels were recorded. They were questioned for polyuria symptom to assess the occurrence of Diabetes Insipidus (DI).

In order to assess the basal hormone profile, venous blood samples were collected once from either the right or left arm antecubital vein from the football players and the control group to measure the parameters of the Thyroid-Stimulating Hormone (TSH), Growth Hormone (GH), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), Prolactin (PRL), and Adrenocorticotrophic Hormone (ACTH), which are anterior pituitary hormones. For the TSH, GH, FSH, LH and PRL hormones, bloods drawn into test tubes, 5 cc each, and into blood tubes, each 2,5 cc, for ACTH were centrifuged for 10 minutes at 4000 rev/min, and serums were separated. Serum samples taken into a test tube with a pipette were then put into separate Eppendorf tubes for the TSH, GH, FSH, LH, PRL hormones and ACTH, recorded, and kept until use at -80°C in a freezer at the laboratories of the department of Biochemistry, Faculty of Medicine Hospital, Gaziantep University.

Evaluation of samples

The GH level was measured using the Immunoradiometric (IRMA) method in an Immulite-2000 (DPC Cirrus Inc. Flanders NJ 07836 a subsidiary of Diagnostic Products Corporation, CA, USA) device [Intra-assay; CV: 5,9%, theoretical sensitivity: 0.01 ng/mL] Normal value: 0.05–8,6 ng/mL.

Since both the football players and the control group were composed of males, normal values were based on males. PRL, FSH, LH, and TSH were measured using the RIA method (Architech C2000, Germany) Normal values; PRL; 5,18–26,53 ng/ml, FSH; 0,7–11,1 mIU/ml. LH; 0,8–7,6 mIU/ml, TSH: 0,350–4,94 µg/dL.

ACTH levels were measured using the Immunoradiometric (IRMA) method in an Immulite 2000 (DPC Cirrus Inc. Flanders NJ 07836 a subsidiary of Diagnostic Products Corporation, CA, and USA) device. Normal value: 10–46 pg/ml.

Playing times

The Playing times of football players were grouped as follows: A (90–5 years), B (6–12 years) and C (13–18 years).

Statistics

The Kolmogorov-Smirnov test was used to evaluate whether the distribution of continuous variables was normal. The Wilcoxon Test was used to compare the two dependent groups of non-normally distributed variables; and the Paired-T Test was used for normally-distributed groups. Frequency, percentage and mean ± std.deviation values were used as descriptive statistics. SPSS for Windows version 18 was used for statistical analyses and $P \leq 0.05$ was considered to be statistically significant.

Results

The mean age of 51 football players was 25, 27 (age range: 18–36), and the mean age of the control group was 24, 18 (age range: 18–33). There was no statistically meaningful age difference between the groups. The FSH value was in the normal range for all football players.

In two (4%) football players, the LH value was above the normal values. LH was not found below the normal value for any football player.

Hormones	The reference values of measured hormones
GROWTH HORMON [15]	0.05–8,6 ng/mL
PROLAKTIN [16]	5,18–26,53 ng/ml
ACTH [17]	10–46 pg/ml
TSH [16]	0,350–4,94 µg/dL
FSH [16]	0,7–11,1 mIU/ml ^a
	26,72–133,41 mIU/ml ^b
	3,03–16,69 mIU/ml ^c
LH [16]	0,8–7,6 mIU/ml ^a
	10,39–64,57 mIU/ml ^b
	0–74,24 mIU/ml ^c

a: male, b: postmenopozal female, c: premenposal female.

Table 1: The reference values of measured hormones.

While in five (10%) football players, the TSH value was found to be higher than normal. No values were found to be below the normal value.

The PRL value was found to be above the normal value in 3 (6%) football players. No values were found to be below the normal value.

The ACTH value was below the normal value in 6 (12%) football players, above the normal value in 3 (6%) football players.

The GH value was found to be below the normal value in 20 (40%) football players. No values were found to be above the normal value.

A comparison of the hormone levels of football players and the control group showed statistically significant differences between TSH (p = 0,001) and PRL (p = 0,001) values, and no statistically significant differences between GH (p = 0,284), FSH (p = 0,069), LH (p = 0,350), and ACTH (p = 0,442) values (Table 2).

Hormones	Football Players Group (n : 51)	Control Group (n : 21)	p*
TSH	2,64 ± 1,32	1,17 ± 0,49	0,001
GH	1,41 ± 2,05	0,83 ± 0,52	0,284
FSH	3,64 ± 1,61	3,12 ± 1,97	0,069
LH	3,37 ± 1,62	3,53 ± 1,34	0,350
PRL	15,71 ± 6,89	9,59 ± 4,53	0,001
ACTH	22,98 ± 14,17	19,04 ± 7,56	0,442

*p: Mann-Whitney U test.

Table 2: A Comparison of the hormone levels of football players and the control group.

An analysis of the playing times of football players and the changes in the anterior pituitary hormones showed the following: A comparison of Group A, Group B, Group C found no significant differences between the TSH, FSH, LH, GH, PRL, and ACTH values (Table 3). A comparison of Group A and Group B found a significant FSH value (p = 0,022). The differences between the TSH, LH, GH, PRL, and ACTH values were insignificant (Table 3). A comparison of Group A and Group C found no significant differences between the FSH, TSH, LH, GH, PRL, and ACTH values (Table 3).

A comparison of Group B and Group C found significant differences between the TSH values ($p = 0,026$). The differences between the FSH, LH, GH, PRL, and ACTH values were insignificant (Table 3).

HORMONES	Group A (0-5 years)	Group B (6-12 years)	Group C (13-18 years)	p
TSH	3,2 ± 1,83	2,74 ± 1,09	2,15 ± 1,24	*p = 0,057 A-B = 0,064 A-C = 0,079 B-C = 0,026
FSH	2,7 ± 0,83	3,89 ± 1,67	3,76 ± 1,73	*p = 0,101 A-B = 0,022 A-C = 0,157 B-C = 0,826
LH	2,60 ± 0,53	3,43 ± 1,61	3,73 ± 1,94	*p = 0,103 A-B = 0,054 A-C = 0,054 B-C = 0,679
GH	2,35 ± 2,67	1,24 ± 1,53	1,17 ± 2,39	*p = 0,514 A-B = 0,320 A-C = 0,297 B-C = 0,727
PRL	18,12 ± 5,1	15,14 ± 5,33	15,27 ± 9,64	*p = 0,187 A-B = 0,180 A-C = 0,079 B-C = 0,407
ACTH	20,9 ± 13,18	23,82 ± 16,05	22,76 ± 11,99	*p = 0,211 A-B = 0,678 A-C = 0,671 B-C = 0,948

*p: Kruskal Wallis test ^{A-B}p, ^{A-C}p, ^{B-C}p: Mann-Whitney U test p: Comparison of all groups, A-B: Comparison of Group A and Group B, A-C: Comparison of Group A and Group C, B-C: Comparison of Group B and Group C.

Table 3: The correlation between the playing times of football players and their hormone levels.

Discussion

Chronic head traumas in football players occur due to the direct impact of head contacts with other players and the ground, or due to the cumulative power generated by the act of heading the ball [7-9]. Increased exposure to the ball, possession time and increased competition are the risk factors for chronic head traumas in football players [7]. Although traumatic brain injury analyses have been performed in football players, hypothalamo-pituitary function analyses are unavailable [10].

Jantsen, *et al.* have investigated neurophysiological correlation in sports-related traumatic brain injury using the MRI method in eight American football players. A comparison of the baseline pre- and post-concussion values has revealed that 50% of players with a concussion had specific neural trauma symptoms compared with the uninjured control group [18]. It has been reported that football, another contact sports, could be correlated with chronic traumatic brain injury, and that these injuries could occur due to the direct impact of head contacts with other players and the ground, or due to the cumulative power generated by the act of heading the ball [7-9]. No significant neuropsychological dysfunction findings could be found in Butler’s study [19] on 289 boxers where the pituitary gland functions were not investigated.

Kelestimur, *et al.* [4] have stated that 45% of amateur boxers suffered from GH deficiency. The study investigated the GH levels with the GHRH and GHRP-6 stimulation test and found the mean IGF-1 levels to be higher in healthy individuals compared with boxers. On the other hand, a significant negative correlation was found between the peak GH level and boxing time and peak GH level and number

of matches. However, the study concluded that further studies were needed with more both professional and amateur boxers and other martial artists or subjects who have suffered head traumas during sports in order to identify hypothalamo-pituitary dysfunction. Another study [20] reported that the GH was the first low hormone level identified in hypopituitarism due to different causes.

In this study, we investigated the anterior pituitary functions of 51 professional football players, considering that heading the football is a chronic head trauma. GH values were 40%, and ACTH values were 12% below the normal range in football players. However, a comparison with the control group showed that this low level was statistically insignificant ($p = 0,284$).

TSH was 10%, PRL was 6%, LH was 4% and ACTH was 6% above the normal range in football players although no other insufficiencies, except for GH and ACTH, were found in football players. Only the FSH was found in normal ranges. The TSH, FSH, PRL and ACTH values were generally found to be higher in football players compared with the control group. The high TSH and PRL hormone levels was statistically significant ($p = 0,001$). Gonadotropins and ACTH levels increased with longer playing times, but this increase was not statistically significant. Again, despite a relative insufficiency in the GH and PRL levels with the increase in such playing times, the increase was not statistically significant. Only the TSH levels meaningfully increased after playing football for 12 years. Chronic traumatic encephalopathy has been reported in 20% of retired professional boxers [21]. Zhang, *et al.* [22] have emphasized that normal MRI findings did not exclude microstructural damage in relation to chronic head trauma in the brain. Rabadi and Jordan have reviewed the literature for the clinical aspect of chronic head traumas caused by contact sports and reported the following risk factors for chronic head trauma: boxing for over 10 years, participation in ≥ 150 bouts; increased sparring exposure, previous history of a knockout and poor performance. On the other hand, apolipoprotein [Apo E] E4 genotype has also been proposed as a risk factor, with reports that the risk of chronic traumatic encephalopathy was not only due to recurrent head traumas, and could also have a genetic component [23].

A study by Jordan, *et al.* has reported that 93% of the CT images of 338 active professional boxers were normal and 6 had borderline atrophy [24]. It has also been reported that particularly new snowboarders had an increased risk of head traumas [25].

The inability to follow football players for prolonged periods for pituitary dysfunctions, inability to radiologically support the study, and the inability to include the thalamopituitary axis were the major limitations our study.

In conclusion, the GH and ACTH levels were found to be in the normal range in football players playing professional football for 5–18 years. Other neuroendocrine values were found to be above the normal values. No correlations were found between playing for long periods and pituitary dysfunction. However, we concluded that further studies were needed with more both professional and amateur boxers and other martial artists or subjects who have suffered head traumas during sports in order to identify hypothalamo-pituitary dysfunction. Also, the football players should be followed after they quit football to identify long-term pituitary dysfunction. A literature review showed that the studies investigating TBI in sports generally included radiological or neuropsychological subjects. Neuroendocrine changes received little attention. So, broader studies are needed to investigate pituitary dysfunction and treatment options, as well as the pathophysiology of brain injury in sports.

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