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SABAH VE ÖĞLEDEN SONRA YAPILAN EGZERSİZİN GHRELİN VE VASPİN DÜZEYLERİNE ETKİSİ

THE EFFECT OF MORNING AND AFTERNOON EXERCISE ON GHRELIN AND VASPIN LEVELS

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ÖZ

Giriş: *Ghrelin ve Vaspin enerji metabolizmasında, vücut kompozisyonunda ve kardiyovasküler sağlıkta önemli rol oynamaktadır ve egzersizle yakından ilişkilidir. Çalışmanın amacı, sabah ve öğleden sonra yapılan egzersizde Ghrelin ve Vaspin seviyelerindeki değişimleri idrar ve tükürükte belirlemektir.*

Gereç ve Yöntem:*Genç sağlıklı futbolcuların antropometrik ölçümleri (n: 11) hesaplandı. Sporcular % 60 maksimum kalp atım hızında (HRmax) 60 dakikalık hafif egzersiz yaptılar. Egzersiz öncesi ve sonrası tükürük ve idrar örnekleri alındı (egzersiz öncesi saat 10.00 ve 16.00, egzersiz sonrası saat 11.00-17.00). Ghrelin ve Vaspin düzeyleri, ELISA yöntemi kullanılarak ölçüldü. İstatistiksel analiz, tekrarlanan ölçümlerde ANOVA testi ve Pearson Korelasyon analizi kullanılarak yapıldı.*

Bulgular: *Tükürük Ghrelin ve Vaspin düzeyleri, egzersiz öncesi (saat 10:00 ve 16:00'da) pozitif bir korelasyon gösterdi (sırasıyla $r = 0.664$, $p = 0.026$; $r = 0.657$, $p = 0.028$) ve saat 17:00'da alınan örnekler 10.00 ile karşılaştırıldığında anlamlı olarak artış gösterdi ($p = 0.017$, $p = 0.007$). Ghrelin düzeyleri ile vücut kütle indeksi (BMI) arasında negatif bir korelasyon gözlendi ($r = - 0.667$, $p = 0.025$). Egzersizden hemen önce ve hemen sonra alınan örnekler arasında (10.00 ile 11.00 arasında ve 16.00 ile 17.00 arasında) protein ölçümleri açısından bir fark belirlenmedi.*

Sonuç: *Sonuç olarak, bu proteinlerin ekspresyonu düşük yoğunluklu egzersiz etkisi ile değişmedi. Her iki proteinin öğleden sonra alınan tükürük numunelerinde öğleden önceye göre artmış olduğunu tespit ettik. Bu proteinler günün ilerleyen saatlerinde daha yüksek düzeyde olduklarından öğleden sonra yapılan egzersiz performansına olumlu katkıda bulunabilirler.*

SUMMARY

Introduction: *Ghrelin and Vaspin have important roles in energy metabolism, body composition and cardiovascular health, and are closely associated to exercise. The aim of the study was to determine the levels of Ghrelin and Vaspin in saliva and urine samples related to morning and afternoon exercise.*

Material and Method: *The anthropometric measurements ofyoung healthy football players (n:11) were calculated. The athletes performed 60 minutes of mild exercise at 60% maximum heart rate(HRmax). Saliva and urine samples were taken before and after exercise (at 10.00 and 16.00 for pre-exercise, at 11.00-17.00 for post-*

exercise). The Ghrelinand Vaspinlevels were measured using the ELISA method. Statistical analysis was performed with repeated measurements ANOVA test and Pearson Correlation analysis.

Results: *SalivaGhrelin and Vaspinlevels indicated a positive correlation (at 10:00 and 16:00) before exercise (r = 0.664, p = 0.026; r = 0.657, p = 0.028 respectively) and samples from 17:00 demonstrated a significant increasecompared to 10.00(p=0.017, p=0.007). A negative correlation was observed between Ghrelinlevels and body mass index (BMI) (r = – 0.667, p = 0.025). A difference in protein measurements at immediately before and immediately after exercise (between 10.00 and 11.00 and between 16.00 and 17.00) was not determined.*

Conclusion: *Consequently, the expression of these proteins did not change with low intensity exercise. Compared with in the morning, we detected increased levels of both these proteins in the saliva samples in the afternoon. Since these proteins are at a higher level later in the day, they can contribute positively to exercise performance in the afternoon.*

INTRODUCTION

Ghrelin, known as growth-hormone (GH) secretagogues, stimulates appetite and the release of growth hormones from the pituitary gland (1,2). Ghrelin regulates the feedback loop between central and peripheral, and plays a role in the hypothalamic regulation of energy homeostasis (2,3). This hormone is released mainly from stomach tissue and in addition also from the heart, kidney, thyroid, placenta, pancreas, spleen, pituitary gland and brain (4). Ghrelin is secreted into circulation as acyl-Ghrelin which is the biologically active form and unacyl-Ghrelin. Levels of both are elevated during fasting, and decrease after eating (1,5).

Ghrelin is effective in energy metabolism and insulin secretion and increases the metabolism of carbohydrates (3,6). Low Ghrelin levels result in insulin resistance, type 2 diabetes and increased body mass index and adiposity (7,8). Ghrelin has positive effects on cardiovascular function such as the preservation of endothelial functions, reduction of peripheral vascular resistance, improvement of cardiac contractility and cardiac output (9-11). Research on the relationship of Ghrelin and exercise are controversial. There are some studies reporting that acute exercise only temporarily affects the production of acylated Ghrelin in circulation and does not impact total Ghrelin circulation. Likewise, there is a suppression of acyl-Ghrelin levels in exercises above 75% maximal oxygen consumption (VO_2max) (12-14). On the other hand, a transient increase in Ghrelin levels after 2 hours of exercise at 80% HRmax and following 20 minutes of exercise at 80% VO_2max has been reported (15,16). The varying results may be due to different exercise types, fasting states, and short half-life (35 minutes) and rapid clearance of Ghrelin (17,18).

Vaspin is a recently discovered adipokine which increases insulin sensitivity, appears to compensate obesity and insulin resistance, and is secreted from visceral and subcutaneous adipose tissue (19). Similar to Ghrelin, it is effective in regulating energy-glucose metabolism and improving cardiovascular and inflammatory pathologies (11,20,21). It was demonstrated that serum Vaspin levels are directly associated with physical activity independent of body composition (22). In one study reported that serum Vaspin levels decreased in healthy men due to exercise-induced oxidative stress following both acute and long term (4 weeks) physical exercise (23). Another study indicated increased Vaspin levels in circulation after 4 weeks of exercise (24). Since there are different results reported in the literature, the effect of exercise on Vaspin levels is not clear.

The biological clock is affected by daylight, physical activity and exercise, and regulates the circadian rhythm (25). Serum Ghrelin levels which is higher in the evening, are influenced by the circadian rhythm (26,27). Similar to Ghrelin, serum Vaspin levels displayed diurnal variation with higher values in the evening (28). Both levels of protein decreased 1-2 hours after eating, and then increased (27,28). Some studies have indicated that serum levels of these two proteins exhibit parallel changes (29,30).

The exercise-related expressions of these proteins in the blood are controversial. Since proteolytic degradations and interactions with other homeostatic proteins may occur in the blood, measurements of other body fluids can provide supportive information concerning their expression. The changes in serum levels of these proteins in some physiological and pathological conditions (such as postpartum alterations, epilepsy, ischemic stroke, and anorexia nervosa etc.) are consistent with changes in urine and saliva samples (29,31-33). The aim of this study was to evaluate the changes in Ghrelin and Vaspin levels, which have positive effects on the cardiovascular system and glucose metabolism, in body fluids associated with exercise at different time of the day.

MATERIALS AND METHODS

The volunteer male young football players (n: 11) with a mean age of 18.5 ± 0.53, mean height of 173.37 ± 3.5 cm, and mean weight of 66.12 ± 8.74 kg were included in the study. The waist-to-height ratios and BMI were calculated for all subjects, and means and standard deviations were recorded (Table 1). The study was conducted in accordance with the Declaration of Helsinki and ethical approval of the study was obtained from the institutional ethics committee (approval number: 2019/14-34). All participants provided informed consent in the format requested by the ethics committee of the institution. The participants had breakfast and lunch with the same content in the morning and at noon. Two hours after breakfast and lunch (10.00 a.m. and 04.00 p.m.) they exercised (slow speed running)at 60% HRmax for 60 minutes. Saliva and urine samples were collected immediately before and after the exercise periods and the samples were stored at -85 °C until measurement. Samples were centrifuged immediately before protein measurement and the supernatants were separated.Protein levels in supernatants were measured using the ELISA method.

Ghrelin (Catalog no. E-EL-H1919, Elabscience®, USA; with assay sensitivity: 0.10 ng / mL and detection range 0.16-10 ng / mL) and Vaspin (Catalog no. E-EL-H1762, Elabscience®, U.S.A.; with assay sensitivity: 37.5 pg / mL and detection range 62.5-4000 pg / mL) levels were determined according to the kit protocol.

Statistics evaluation was performed by the SPSS Version 24 (IBM, Turkey) software program. The sample size for the ANOVA repeated measurement was calculated using the G Power method (effect size 0.5; α error 0.05; the power of 95% was accepted). Arithmetic means and standard deviations were determined for all parameters. Repeated measures ANOVA analysis with Bonferroni post hoc test was used to evaluate the difference between the measurements at different times and Pearson Correlations were used to evaluate the relationships between the variables. $p<0.05$ was considered significant.

RESULTS

Ghrelin levels present in saliva samples (four different hours, at 10.00, 11.00, 16.00 and 17.00) showed a significant difference between the hours of 10.00 and 17.00 ($p = 0.017$, Figure 1, Table 2). There was no significant difference in Ghrelin levels related with exercise in terms of urine Ghrelin levels and urine Ghrelin/creatinine ratios (Table 2). Similar to the Ghrelin levels, the Vaspin levels in saliva samples displayed a significant difference between the hours of 10.00 and 17.00 ($p = 0.007$, Figure 2, Table 2). There was no significant difference in urinary Vaspin levels and Vaspin/creatinine ratios between different time points (Table 2). A moderate positive correlation was observed between Ghrelin and Vaspin levels in saliva samples obtained at 10.00 and 16.00 ($r = 0.664$, $p = 0.026$; $r = 0.657$, $p = 0.028$ respectively, Figure 3). At 10.00, there was a strong negative correlation between Ghrelin levels and body mass index in saliva samples ($r = -0.667$, $p = 0.025$). No correlation was found between Vaspin levels and BMI, weight, height or waist-to-height ratios.

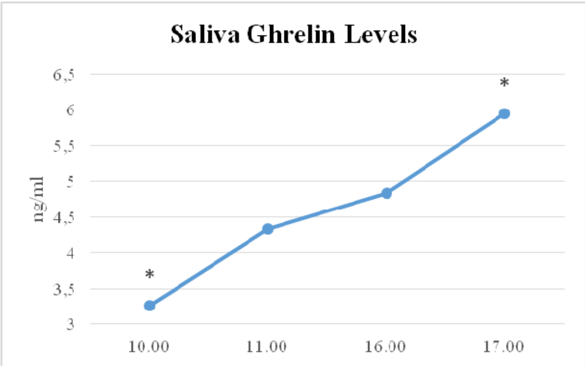

Figure 1. Ghrelin levels in saliva samples taken at different time points: Saliva samples were collected before exercise at 10.00 a.m., after exercise at 11.00 a.m. and before exercise at 04.00 p.m. and after exercise at 05.00 p.m. (*p:0.017).

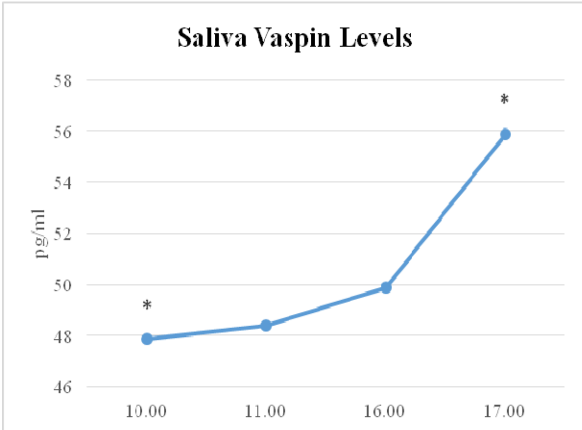

Figure 2. Vaspin levels in saliva samples taken at different time points: Saliva samples were collected before exercise at 10.00 a.m. after exercise at 11.00 a.m. and before exercise at 04.00 p.m. and after exercise at 05.00 p.m. (*p:0.007).

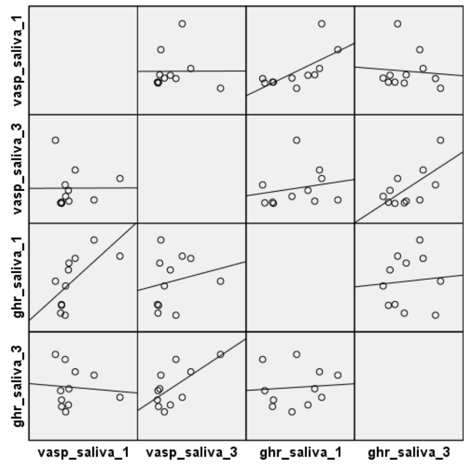

Figure 3. Correlation analysis of Ghrelin and Vaspin levels at morning and afternoon: There was a positive correlation between Ghrelin and Vaspin levels in saliva at 10.00 a.m. and at 04.00 p.m. (r=0.664, p=0.026 for at 10.00 a.m. and r=0.657, p=0.028 for at 04.00 p.m.). Ghr: Ghrelin, Vasp: Vaspin. Saliva 1: sample of 10.00 a.m., saliva 3: sample of 04.00 p.m.

Table 1. Descriptive data for the subjects.The ages andanthropometric measurements of the athletes participating in the study are given in the table. Data were presented with mean and standard deviation (mean±SD). BMI: body mass index.

	Age	Height (cm)	Weight (kg)	BMI (kg/m^2)	Waist-to-height ratio (cm/cm)
Participants Measurements	18.5± 0.53	174.18 ±4.2	67.90 ± 9.40	23.17 ± 3.44	0.45 ± 0.29

Table 2. The levels of Ghrelin and Vaspin in saliva and urine. Data were presented with mean and standard deviation (mean±SD), *, $^{\lambda}$: statistically significant. Cre:Creatinine.

Times	N	Saliva Ghrelin (ng/ml)	Urine Ghrelin (ng Ghrelin/mg Cre)	Saliva Vaspin (pg/ml)	Urine Vaspin (pg Vaspin/mg Cre)
10.00	11	3.26 ± 1.69*	0.22 ± 0.16	47.85 ± 12.34$^{\lambda}$	45.15 ± 15.24
11.00	11	4.32 ± 1.82	0.55 ± 0.17	48.41 ± 5.10	53.12 ± 40.72
16.00	11	4.83 ± 2.56	0.19 ± 0.27	49.90 ± 10.19	49.12 ± 23.35
17.00	11	5.93 ± 2.33*	0.23 ± 0.07	55.89 ± 15.18$^{\lambda}$	41.18 ± 16.99
P value		* p:0.017 (between 10.00-17.00)		$^{\lambda}$p: 0,007 (between 10.00-17.00)	

DISCUSSION

We investigated changes in Ghrelin and Vaspin levels associated with exercise and diurnal variations in different body fluids (urine and saliva) following a standard diet. Our results indicate that Ghrelin and Vaspin levels exhibit a positive correlation in saliva samples and increase gradually during the day, but the changes in the urine are not significant. Studies state the difficulty to accurately determine plasma levels of Ghrelin (6). Circulating Ghrelin is affected by secretion, proteolysis and clearance, and is bound to the transport proteins in plasma and delivered to the urine (17,18). It has been reported that Ghrelin passes through to the urine by glomerular filtration and tubular secretion. In addition, its passing is more efficient than unacyl-Ghrelin, and it is more stable in urine than in plasma (34). In our study we could not detect any changes related to Ghrelin in urine.Some previous studies reported that exercise-related Ghrelin and Vaspin levels did not change (13,35,36). We also did not detect any changes their levels between before and after each exercise trial. The exercise intensity of studies which demonstrated an increase in Ghrelin and Vaspin levels was higher than in our study (15,16,37). Studies have reported that high intensity exercise decreased splanchnic blood flow and increased sympathetic output which may affect the production of Ghrelin (12,38). A study reporting an increase in Ghrelin levels demonstrated that increased energy consumption and exercise triggered the Ghrelin signal to generate metabolic reactions required to cover the energy cost (15). Rising levels of Ghrelin have been associated with the shift of positive energy balance to negative balance. Our findings revealed that the expression of Ghrelin and Vaspin levels associated with low intensity exercise did not alter.It is possible our exercise intensity did not impact splanchnic blood flow or did not increase energy consumption for the induction of Vaspin and Ghrelin. In addition, we observed positive correlation between two protein before training but after training, we did not find a relationship between the two proteins.This may indicate that both proteins are affected by same pathway and exercise abolished these effects.

Studies showed that when compared to the morning hours, Vaspin and Ghrelin serum levels increase in the evening (26,28). In our study, similar to serum both to increase gradually from morning to afternoon. Research examining 24-hour Ghrelin and Vaspin changes showed a decrease in Ghrelin between 10.00-11.00 a.m. and 04.00-05.00 p.m. following breakfast and lunch (27,28). The pitting of the curve associated with food intake could be masked regarding sampling time in our study. Previous studies have shown that Vaspin, that is a member of the adipokine class associated with BMI in obesity and diabetes groups, but studies in healthy and lean young people are very rare (19). Lower Vaspin levels in sportsmen have been observed because they are leaner than normal healthy people (24). Vaspin increases have been reported to be compensatory for insulin resistance and obesity (39). We did not observe a relationship between exercise and anthropometric measurements corresponding to Vaspin levels in young healthy sportsmen. As expected, we observed a moderate negative correlation between Ghrelin levels with BMI at 10.00 a.m.. Until the 20s, GH secretion is higher to affect growth and body composition. Since the average age of our test group was 18, the force effect of Ghrelin may stimulate appetite and growth in the lower weight range. There was no effect of acute exercise on Ghrelin levels, but the relationship between Ghrelin and BMI disappeared after exercise. This may be related to an increase in Ghrelin levels in the afternoon.

CONCLUSION

Ghrelin and Vaspin are homeostatic mediators which play an important role in regulating energy metabolism and they are stimulated in parallel when energy needs increase. With low intensity exercise, there was no increase in the levels of these mediators which can alleviate cardiovascular disease, inflammation and insulin resistance. Steady levels of these mediators may be due to the lack of sufficient exercise which to discharge energy stores. Perhaps more severe exercise is required to induce these mediators.

Gradually increasing levels during the day are associated with the circadian rhythm and may be related to the cumulative discharge of energy stores. There was a moderate positive correlation between Ghrelin and Vaspin levels. Expressions of these proteins may be related to some common pathways. Late exercise in the afternoon can improve exercise performance due to the cardiovascular supportive effects (such as cardiac contractility, cardiac output and endothelial functions) of Ghrelin and Vaspin. These proteins can be isolated not only from serum, but also from urine and saliva as an alternative non-invasive method.

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