Effects of exercise on plasma adiponectin levels in athletes

Efekat treninga na vrednosti adiponektina u plazmi vrhunskih sportista

Mirjana Popović[1], *Dejan Nešić*[1,2]

[1] Faculty of Medicine, University of Belgrade
[2] Institute of Medical Physiology „Richard Burian"

Abstract

Adipose tissue is an endocrine organ which releases biologically active adipokines. Adiponectin, an adipocyte-derived protein structurally similar to complement 1q, plays a significant role in metabolic disorders, due to its insulin sensitizing, anti-inflammatory and anti-atherogenic properties. AdipoR$_1$ and AdipoR$_2$, mediate the metabolic actions of adiponectin by activating adenosine monophosphate-activated protein kinase (AMPK) and peroxisome proliferator-activated receptors-alpha (PPAR-α) which leads to an increase in fatty acid combustion and energy consumption, fatty acid oxidation and glucose uptake in myocytes and reduces gluconeogenesis and thus leads to increased insulin sensitivity. Plasma adiponectin level is affected by multiple factors: gender (females have higher plasma adiponectin levels), obesity-linked diseases (metabolic syndrom, diabetes mellitus type 2 and atherosclerosis are associated with lower adiponectin levels), lifestyle - including exercise. Yet, to date, little is known about the response of adiponectin concentrations to exercise and, in particular, the response of this hormone to training in population of athletes. The aim of this review is to overview the published evidence for the effects of exercise on adiponectin levels in athletes.

Adiponectin concentration presents a delayed increase (30 min) after short-term intense performance, by athletes, both male and female. It seems that adiponectin concentrations do not change in response to long-term exercise. No significant difference was found in total adiponectin and/or high-molecular weight (HMW) oligomers in long-term effects of high physical training in athletes. Adiponectin can serve to monitor training loads and the establishment of individual limit values of training loads. Further studies are needed to clarify possible mechanisms by which adiponectin might influence energy homeostasis during heavy training in elite athletes.

Key words: adiponectin, adipose tissue, athlets, exercise.

Sažetak

Masno tkivo je endokrini organ, koji oslobađa biološki aktivne adipokine. Jedan od adipokina je adiponektin, protein strukturno sličan komplementu 1q, koji ima značajnu ulogu u metaboličkim poremećajima zbog antiinflamatornog dejstva, anti-aterogenih svojstava i dejstva na insulin. Receptori AdipoR$_1$ i AdipoR$_2$ posreduju metaboličko dejstvo adiponektina aktiviranjem adenozin-monofosfat aktivirane proteinkinaze (AMPK) i peroksizom proliferator aktiviranog receptora alfa (PPAR- α), što dovodi do povećanog katabolizma i oksidacije masnih kiselina, preuzimanja glukoze u miocitima, smanjenja glukoneogeneze i povećanja osetljivosti na insulin. Na nivoe adiponektina utiče više činilaca: pol (žene imaju više vrednosti adiponektina u plazmi), bolesti povezane sa gojaznošću (metabolički sindrom, tip 2 dijabetesa melitusa i ateroskleroza su povezane sa nižim vrednostima adiponektina) i način života (uključujući vežbanje). Do danas se ipak malo zna o uticaju rekretivnog vežbanja na nivoe adiponektina, a posebno o uticaju treninga na nivo adiponektina u populaciji sportista. U ovom radu smo prikazali pregled literature o efektima treninga na nivoe adiponektina u plazmi vrhunskih sportista.

Koncentracija adiponektina pokazuje odloženo povećanje (30 min) nakon kratkotrajnog intenzivnog treninga u sportista oba pola. Prema podacima iz literature, koncentracije adiponektina se ne menjaju kao odgovor na dugotrajno vežbanje. Kod sportista posle treninga nema značajne razlike u nivou ukupnog adiponektina vs. oligomera visoke molekularne težine (HMW). Adiponektin može da služi za praćenje opterećenja tokom treninga i postavljanje individualnih normi za intenzitet treninga. Potrebna su dalja istraživanja radi pojašnjenja mogućih mehanizama kojima adiponektin utiče na energetsku homeostazu kod vrhunskih sportista tokom treninga.

Ključne reči: adiponektin, masno tkivo, sportisti, trening.

Adipose tissue functions as an endocrine organ (1). In addition to its role in fuel storage, thermal insulation and mechanical protection, it releases biologically active and diverse cytokines, called adipokines (2). Adiponectin, an

adipocyte-derived protein (3), plays a significant role in metabolic disorders, such as obesity, type 2 diabetes, coronary heart disease and metabolic syndrome (4, 5) due to its insulin sensitizing, anti-inflammatory and anti-atherogenic properties (6). Structurally, adiponectin contains three distinguishable domains: an N-terminal sequence, a collagenous region and a globular domain structurally similar to complement 1q (7). It belongs to a family of proteins that form characteristic multimers. Adiponectin exists in a wide range of multimer complexes in plasma and combines via its collagen domain to create 3 major oligomeric forms: a low-molecular weight (LMW) trimer, a middle-molecular weight (MMW) hexamer and high-molecular weight (HMW) 12- to 18-mer adiponectin (8, 9). Several investigations support the hypothesis that HMW adiponectin is a more active form of the protein and has a more relevant role in insulin sensitivity and in protecting against diabetes (10). $AdipoR_1$ and $AdipoR_2$, mediate the metabolic actions of adiponectin through phosphorylation and activation of adenosine monophosphate-activated protein kinase (AMPK) (11). The AMPK activation stimulates phosphorylation of acetyl-CoA carboxylase, fatty acid oxidation and glucose uptake in myocytes and reduces enzymes involved in gluconeogenesis in liver, leading to reduction of glucose levels. Adiponectin also increased the expression levels of peroxisome proliferator-activated receptors-alpha (PPAR-α) *in vivo*, increasing fatty acid combustion and energy consumption, which led to decreased triglyceride content in the liver and skeletal muscle and thus increased insulin sensitivity (12).

There is a sexual dimorphism in the circulating levels of adiponectin. Females have higher plasma adiponectin levels (16.6 ± 5 mg/ml) than males (7.9 ± 0.5 mg/ml), suggesting that sexual hormones regulate the production of adiponectin (13). Plasma adiponectin level is affected by multiple factors: gender, aging, obesity-linked diseases (insulin resistance, diabetes mellitus type 2 and atherosclerosis), lifestyle, including exercise. It is well documented that exercise or regular physical activity has beneficial effects on metabolic and cardiovascular diseases (14). Considering previous literature, it is unclear whether exercise increases adiponectin in circulation and its receptors in insulin-sensitive tissues (15). Complicating interpretation of the existing data is dependent on multiple factors, including the pathological condition, types (endurance *vs* resistance exercise), intensity (low, moderate and intense) and duration of exercise (acute *vs* chronic, short-term *vs* long-term) and sex. For example, in healthy, young subjects, it seemed that both acute and chronic aerobic exercise did not alter plasma level of adiponectin (16). However, exercise in combination with diet-induced weight loss (17), significantly increases plasma adiponectin levels in both obese and insulin-resistant subjects. Furthermore, recent data suggest that exercise training might modulate the expression of $AdipoR_1$ and $AdipoR_2$ in PBMCs (peripheral blood mononuclear cells) in young men (18). On the other hand, there is a fact that a relationship between exercise and increased adiponectin levels was not observed in the majority of randomized controlled trials (16). Only moderate-high intensity resistance training, not low intensity, increased plasma adiponectin in inactive subjects, suggesting that the intensity of exercise may be an important factor in the expression of adiponectin.

From the point of view of the intensity of exercise, what are the possible mechanisms by which adiponectin might influence energy homeostasis during heavy training in elite athletes? Vigorous training program represents a physical stress condition in which heavy changes in energy expenditure might increase adiponectin concentration in athletes, but a number of different hormones are known to be immediately altered during intense exercise (19), such as insulin, catecholamines, and cortisol (20), and they may affect adiponectin levels via suppressed adiponectin gene expression (20).

Adiponectin influences metabolic adaptations that would prove beneficial to the endurance of athletes, but there aren't many studies that have investigated the response of this hormone to training in a population of athletes and how adiponectin is regulated during cumulative exercise.

In professional cyclists, adiponectin significantly increased during the cycling race and recovery periods (21), when compared to the baseline. Lombardi G. et al (21) found adipokines trends were clearly related to the power output and the energy expenditures. In another study about adiponectin, significant increases were observed in cumulative exercise (22) within 5 days of commencing the race of cyclists, with these elevated values failing to return to baseline levels after 3 days of recovery, suggesting that adiponectin can serve to monitor training loads and the establishment of individual limit values.

In a study with graded treadmill walk/run protocol in trained runners (23), significant increases in post-exercise levels of adiponectin were elicited. On the other hand, no significant changes were noted in serum adiponectin levels during an ultra-marathon endurance race (24).

Jurimae et al. (25) found a significant reduction in adiponectin levels immediately after-high intensity rowing exercise and correction in plasma volume expansion, but adiponectin was significantly increased above the resting value after the first 30 min of recovery (uncorrected for plasma volume + 19.3%; corrected for plasma volume + 20.0%). Adiponectin does not change throughout the prolonged training period in elite male rowers (26). Jurimae J et al. observed differences in the study (27) of ad-

iponectin responses before and after the training period in SEL (selected) and N-SEL (not selected) rowers for the national team. Decreased postexercise adiponectin values in N-SEL rowers, with lower performance capacity, may be indicative of the inadequate recovery of these athletes. In the same study (27), the acute effects of volume-extended rowing training produced significantly greater adiponectin levels in the athletes selected for a national team immediately and 30 min post-exercise. Significant increases in plasma adiponectin concentration occurred, in response to maximal exercise after completion of the high-intensity interval rowing training but not after traditional ergometer (28).

No significant difference was found in total adiponectin and/or HMW oligomers in long-term effects of high physical training in professional male water polo players (29). In this study, (29) a direct relationship was found between total adiponectin and monocytes, that could represent a mechanism by which adiponectin participates in exercise-induced anti-inflammatory functions and/or cardiovascular health.

Serum adiponectin levels were significantly higher in X/X genotype than R/R or R/X genotype of α-actinin-3 (ACTN3) in rugby players (30). This may be useful information when determining the individual responses of anti-atherogenic markers to exercise.

Elite rhythmic gymnasts (RGs) constitute a unique metabolic model and they are prone to developing Anorexia Athletica. The possible role of salivary adiponectin levels as a predictive factor of reproductive dysfunction and bone mass acquisition in elite RGs was evaluated.

In a study by Roupas ND et al. (31) no association of salivary adiponectin levels was documented with either reproductive function or bone mass acquisition. Parm A.-L et al. (32) found that adiponectin and ghrelin levels did not predict increases in measured bone mineral density (BMD) value in rhythmic gymnasts. In elite rhythmic gymnasts salivary adiponectin is upregulated after chronic intensive exercise and negative energy balance, while salivary adiponectin is suppressed after short term intensive anaerobic exercise (33).

Adiponectin significantly increased, when compared to the baseline, in young female handball and basketball players (16.7 ± 7.8 vs 21.0 ± 9.8 μg/ml, $p < 0.001$) after intensive fitness and speed exercise (34). Plasma adiponectin remained unchanged during long-term moderate aerobic exercise in young female handball and basketball players (34) and in elite female water polo athletes throughout a season (35).

Conclusion

Adiponectin is secreted by adipocytes and has been implicated in the regulation of energy homeostasis. Vigorous training program represents a physical stress condition in which heavy changes in energy expenditure might increase adiponectin concentration in athletes. Adiponectin concentration presents a delayed increase (30 min) after short-term intense performance by trained athletes, male and female. It seems that adiponectin concentrations do not change in response to long-term exercise. Adiponectin can serve to monitor training loads and the establishment of individual limit values. Further studies are needed to clarify possible mechanisms by which adiponectin might influence energy homeostasis during heavy training in elite athletes.

Literature

1. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. J Clin Endocrinol Metab 2004; 89: 2548-56.
2. Aldhahi W, Hamdy O. Adipokines, inflammation, and the endothelium in diabetes. Curr Diab Rep 2003; 3: 293-8.
3. Pajvani UB, Du X, Combs TP, Berg AH, Rajala MW, Schulthess T et al. Structure-function studies of the adipocyte-secreted hormone Acrp30/adiponectin. Implications for metabolic regulation and bioactivity. J Biol Chem 2003; 278: 9073-85.
4. Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y. et al. Novel modulatorfor endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. Circulation 1999; 100: 2473-76.
5. Salmenniemi U, Ruotsalainen E, Pihlajamäki J, Vauhkonen I, Kainulainen S, Punnonen K et al. Multiple abnormalities in glucose andenergy metabolism and coordinated changes inlevels of adiponectin, cytokines, and adhesionmolecules in subjects with metabolic syndrome. Circulation 2004; 110: 3842-48.
6. Berg AH, Scherer PE. Adipose tissue, inflammation, and cardiovascular disease. Circ Res 2005; 96: 939-949.
7. Scherer PE, Williams S, Fogliano M, Baldini G, Lodish HF. A novel serum protein similar to C1q, produced exclusively in adipocytes. J. Biol. Chem. 1995; 270: 26746-49.
8. Lara-Castro C, Luo N, Wallace P, Klein RL, Garvey WTC. Adiponectin multimeric complexes and the metabolic syndrome trait cluster. Diabetes 2006; 55: 249-9.
9. Ebinuma H, Miyazaki O, Yago H, Hara K, Yamauchi T, Kadowaki T. A novel ELISA system for selective measurement of human adiponectin multimers by using proteases. Clin. Chim. Acta. 2006;372(1-2):47-53.
10. Fisher FFM, Fisher ME, Trujillo W, Hanif AH, Barnet PG, McTernan P, Kumar S et al. Serum high molecular weight complex of adiponectin correlates better with glucose tolerance than total serum adiponectin in Indo-Asian males. Diabetologia. 2005; 48: 1084-7.
11. Yamauchi T, KamonJ, Minokoshi Y, ItoY, Waki H, Uchida S, et al. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. Nat. Med. 2002; 8: 1288-95.
12. Evans RM, Barish GD, Wang YX. PPARs and the complex journey to obesity. Nat. Med. 2004; 10: 355-61.
13. Xu A, Chan KW, Hoo RL, Wang Y, Tan KC, Zhang J et al. Testosterone selectively reduces the high molecular weight form of adiponectin by inhibiting its secretion from adipocytes. J. Biol. Chem. 2005; 280: 18073-80.
14. Ivy JL. Role of exercise training in the prevention and treatment of insulin resistance and non-insulin-dependent diabetes mellitus. Sports Med. 1997; 24 (5): 321-36.

15. Röhling M, Herder C, Stemper T, Müssig K. Influence of Acute and Chronic Exercise on Glucose Uptake. J Diabetes Res. 2016; 2016: 2868652.
16. Simpson AK, Fiatarone Singh MA. Effects of Exercise on Adiponectin: A Systematic Review Obesity 2008; 16: 241–56.
17. Ryan AS. Insulin resistance with aging: effects of diet and exercise. Sports Med. 2000; 30 (5): 327-46.
18. Lee SH, Hong HR, Han TK, Kang HS. Aerobic training increases the expression of adiponectin receptor genes in the peripheral blood mononuclear cells of young men. Biol. Sport 2015; 32:181-186
19. Kraemer RR, Aboudehen K, Carruth A, Durand R, Acevedo E, Hebert E. Adiponectin responses to continuous and progres-sively intense intermittent exercise. Med Sci Sports Exerc 2003; 35: 1320-5.
20. Fasshauer M, Klein J, Neumann S, Eszlinger M, Paschk R. Adiponectin gene expression is inhibited by beta-adrenergic stimulation via protein kinase A in 3T3-L1 adipocytes. FEBS Lett2001; 507: 142-6.
21. Lombardi G, Lanteri P, Graziani R, Colombini A, Banfi G, Corsetti R. Bone and Energy Metabolism Parameters in Professional Cyclists during the Giro d'Italia 3-Weeks Stage RacePLoS One. 2012; 7(7): e42077.
22. Voss SC, Nikolovski Z, Bourdon PC, Alsayrafi M, Schumacher YO. The effect of cumulative endurance exercise on leptin and adiponectin and their role as markers to monitor training load. Biol Sport. 2016; 33 (1): 23-8.
23. Kraemer RR, Aboudehen KS, Carruth AK .Adiponectin responses to continuous and progressively intense intermittent exercise. MedSci Sports Exerc 2003; 35: 1320-5.
24. Roupas ND, Mamali I, Maragkos S, Leonidou L, Armeni AK, Markantes GK, et al. The effect of prolonged aerobic exercise on serum adipokine levels during an ultra-marathon endurance race. Hormones 2013, 12(2): 275-82.
25. Jurimae J, Purge P, Jurimae T. Adiponectin is altered after maximal exercise in highly

trained male rowers. Eur J Appl Physiol 2005; 93: 502-5.

26. Jürimäe J, Purge P, Jürimäe T. Effect of prolonged training period on plasma adiponectin in elitemale rowers. Horm Metab Res. 2007; 39 (7): 519-23.
27. Jurimae J, Purge P, Jurimae T. Adiponectin and stress hormone responses to maximal sculling after volume-extended training season in elite rowers. Metabolism 2006; 55: 13-9.
28. Shing CM, Webb JJ, Driller MW, Williams AD, Fell JW. Circulating adiponectin concentration and body composition are altered in response to high-intensity interval training. J Strength Cond Res. 2013; 27 (8): 2213-8.
29. Nigroa E, Sangiorgiob D, Scudieroa O, Monacoa ML, Politoa R, Villonee G at al. Gene molecular analysis and Adiponectin expression in professional Water Polo players. Cytokine 2016; 81: 883.
30. Shinsuke N, Mami F, Kokoro T, Sachiko F, Akihiko U, Yasuharu K. at al: ACTN3 gene R577X polymorphism associated with high–density lipoptotein, cholesterol and adiponectin in rugny players. Endocrine Practice. Rapid Electronic Article in Press AACE 2016; DOI:10.4158/EP15963. OR
31. Roupas ND, Maïmoun L, Mamali I, Coste O, Tsouka A, Mahadea KK et al. Salivary adiponectin levels are associated with training intensity but not with bone mass or reproductive function in elite Rhythmic Gymnasts. Peptides. 2014; 51: 80-5.
32. Parm A.-L, Jürimäe J, Saar M, Pärna K, Tillmann V, Maasalu K. et al. Bone mineralization in rhythmic gymnasts before puberty: no longitudinal associations with adipocytokine and ghrelin levels. Horm Res Paediatr. 2012; 77 (6): 369-75.
33. Roupas ND, Maïmounb L, Mamalia I, Costeb O, Tsoukaa A, Kunal Mahadeaf K. et al. The influence of intensive physical training on salivary adipokine levels in Elite Rhythmic Gymnasts. Horm Metab Res. 2012; 44 (13): 980-6.
34. Plinta R, Olszanecka-Glinianowicz M, Drosdzol-Cop A, Chudek J, Skrzypulec-Plinta V. The effect of three-month pre-season preparatory period and short-term exercise on plasma leptin, adiponectin, visfatin, and ghrelin levels in young female handball and basketball players. J Endocrinol Invest. 2012; 35 (6): 595-601.
35. Varamenti EI, Kyparos A, Veskoukis AS, Bakou M, Kalaboka S, Jamurtas AZ. et al. Oxidative stress, inflammation and angiogenesis markers in elite female water polo athletes throughout a season. Food Chem Toxicol. 2013; 61: 3-8.