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HETEROZYGOUS GENOTYPE OF MONOCARBOXYL TRANSFERASE 1 (rs1049434) POLYMORPHISM COMMONS IN A TURKISH ATHLETE COHORT

TÜRK ATLET TOPLULUĞUNDA MONOKARBOKSİL TRANSFERAZ 1 (rs1049434) POLİMORFİZMİ'NİN HETEROZİGOT GENOTİPİ YAYGINDIR

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Abstract

There are many parameters that have effects the success of athletes, like exercise, motivation, determination, nutrition, all of which have genetic backgrounds. To have the optimal approach, all of these conditions should complement each other. In this study, we aimed to analyze and compare the monocarboxyl transferase 1 (MCT1) rs1049434 polymorphism, which is important to determine the lactate levels, in long and short distance running athletes. A total of 30 athletes, 15 of which were power athletes and 15 were endurance, were enrolled for the study. DNA isolations were carried out by using commercially available DNA isolation Kit, and genotyping process was by real-time PCR. Of the 15 power athletes, 14 (93%) and 1 (7%) athletes had AT and TT genotypes, respectively. We detected no AA genotype in power athletes. In endurance cohort, 4 (27%), 8 (53%) and 3 (20%) athletes had AA, AT and TT genotypes, respectively. When we count the alleles, A allele was counted as 14 (47%) and 16 (53%) in power and endurance athletes. For T allele, 16 (53%) and 14 (47%) were counted in power and endurance cohorts. No statistically significant difference was found between groups in the terms of genotype and allele. In our cohort, AT genotype was higher in both groups, whereas both alleles were equal in our cohort. Our basic goal is to be able to channel the athlete correctly and carry it to maximum success in a shorter period of time considering the genetic predisposition.

Keywords: MCT1, sport, genetic, DNA, athletic performance

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Öz

Egzersiz, motivasyon, azim, beslenme, sahip olunan tüm genetik geçmiş gibi atletlerin başarılarına etki eden çok sayıda parametre bulunmaktadır. Optimal bir yaklaşıma sahip olmak için, bu koşulların tamamı birbiri ile tamamlayıcı olmalıdır. Bu çalışmada uzun ve kısa mesafe koşucu atletlerde laktat düzeylerini saptamada önemli olan monokarboksil transferaz 1 (MCT1) rs 1049434 polimorfizmini karşılaştırmak ve analiz etmeyi amaçladık. Çalışmamızda 15 güçlü, 15 dayanıklı toplam 30 atlet kaydedildi. DNA izolasyonları ticari olarak mevcut DNA izolasyon kiti ve genotip süreçleri real time PCR kullanılarak gerçekleştirildi. 15 güçlü atlette sırasıyla 14 (% 93) AT, 7 (%1)'inde TT genotipi olduğu tespit edildi. Güçlü atletlerde AA genotipi tespit edilmedi. Dayanıklı toplulukta AA, AT ve TT genotipleri sırasıyla 4 (% 27), 8 (% 53) ve 3 (% 20)'idi. Alleller sayıldığında, güçlü ve dayanıklı atletlerde sırasıyla A alleli 14 (% 47), ve 16 (% 53) olarak sayıldı. T alleli için güç ve dayanıklı topluluklarda sırası ile 16 (% 53) ve 14 (% 47) olarak sayıldı. Geneotip ve allel bakımından gruplar arasında istatistiksel bir anlamlılık bulunmamıştır. Çalışmamızda AT genotipi her iki grupta da daha yüksektir, oysa diğer allelller eşittir. Temel hedefimiz genetik yatkınlık dikkate alınarak kısa bir zaman periyodunda atletin maksimum başarıya ulaşmak için doğrudan mı ya da taşıyıcı mı bağlantısını kurabilmektir.

Anahtar Kelimeler: *MCT1, spor, genetik, DNA, atletik performans*

1. Introduction

Athletic performance is a component of the athlete's ability to produce athletic work, production quality and production capacity both positive and negative factors. Twin studies showed that, on average, 66 % of the variance in the athlete status is explained by the contribution of genetic factors (depending on sports discipline). Factors that effect athletic performance like endurance, strength, stiffness, flexibility, neuromuscular coordination and psychological properties are all considered to be enhanced by genetic factors (Ulucan et al., 2014). Based on these findings, it is possible to say that the athletic condition is largely influenced by heredity. The remaining variances can be explained as unshared environmental factors, like nutrition, mental guidance, sleep etc. The association of the genetics with the sportive performance can be understood by examining the distribution of alleles in the athlete. If the related allele is more common among the elite athletes than the general population, it is understood that the allele influences the athlete's athletic performance (Weyerstraß et al., 2018; Sawczuk et al., 2015; Guth and Roth, 2013; Eynon et al., 2010).

Many spawning performances require long duration low level activities and repeated short duration high intensity exercise sessions. In this type of repeated metabolic activity, aerobic and anaerobic respiration occurs. In continuous exercise sessions, the level of the corresponding lactate could reach to very high levels. The accumulation of lactate in the cell leads to inhibition of glycolysis. In order to maintain continuous high density contractile activity and prevent acidosis, it is necessary to transmit lactates accumulated in white skeletal muscles using glycolysis as an ATP source to neighboring red muscle fibers. Here, the neighboring red muscle fibers can transform lactate transduction, which is transferred, and oxidize it as fuel (Lund et al., 2018). A study by Pilegaard et al. reported that individuals have different lactate transport capacities and very high capacity has been observed in well-educated people. This observed difference in capacity may also indicate hereditary athletic abilities (Pilegaard et al., 1999).

Monocarboxyl transferase 1 (MCT1) and Monocarboxyl transferase 4 (MCT4) play a role in the transport of lactate between white muscle fibers and red muscle fibers. MCT4 is involved in the transport of lactate out of the cell to prevent accumulation of lactate in the hyper-glycosylated white muscle fiber, while MCT1 is involved in the transport of white muscle fibers through the MCT4 to the red skeletal muscle to transform lactate into pyruvate. There is a great correlation between the amount of MCT1 exerting in muscle fibers and oxidative capacities (Fedotovskya et al., 2014; Merezhinskaya et al., 2009). A common functional polymorphism (A/T transversion, rs1049434) within MCT1 leads to a glutamic acid and aspartic acid replacement at position 490, and effects lactate transport rates. Minor "T" allele was found to have 60-65 % reduced transport rates during heavy intensity weight training when compared to "A" allele (Cupeiro et al., 2010).

In this study, we hypothesized that MCT1 rs1049434 polymorphism will effect athletic performance and differ in long and short distance runners. Therefore, we aimed to compare the genotypic and allelic differences of rs1049434 polymorphism between long and short distance runners.

2. Materials and Methods

2.1. Subjects

The study involved 30 athletes, 15 of them were sprinters (short-distance athletes) and 15 were endurance (long-distance athlete), were enrolled in the study, all of whom are over 18 years. Athletes were grouped according to their distance that they perform. All are a member of a different amateur athletic team. They have 2 sessions of training, at least 5 hours/ week. Üsküdar University Ethics Committee approved the study protocol, and the study protocol was in agreement with the principles of Helsinki Declaration II. All the athletes signed the informed consents, indicating they have understood and confirmed the study.

2.2. DNA Sample Collection and Genotyping

DNA collector swaps were used to collect buccal cells, and DNA samples were isolated by using DNA purification kit (Thermofisher Scientific Invitrogen, USA. Catolog no: K1820-02). MCT1 rs1049434 genotyping was carried out by Real-Time Polymerase Chain Reaction (RT-PCR) by using Taqman Genotyping Assay (Catolog no: 4362691, Thermofisher, USA). Manufacturers recommended instruction were followed in both isolation and genotyping protocoles.

2.3. Statistical Analysis

Genotype frequencies of MCT1 rs1049434 polymorphism

and the allele frequencies were compared among the groups using the x2 test (SPSS version 21 software). $p < 0.05$ values were considered as statistically significant.

3. Results

30 athletes were successfully genotyped in the study. 15 of those were power athletes and the rest were endurance athletes. 4 (27%) of the endurance athletes had AA genotype, 8 (53%) had AT and 3 had TT genotype. For sprinters, 8 (93%) had AT and one (7%) athlete had TT genotypes. AA genotype was not detected in power athletes. As a total; AA, AT and TT genotypes and frequencies were 4 (13%), 22 (74%) and 4 (13%), respectively. Table 1 lists the genotypes of the alleles. The genotypic percentages of our cohort is found to be statistically significant (p=0.036) between short and long distance athlete groups.

When we consider the allelic distribution, A allele was counted as 16 (53%) and T allele as 14 (47%) in endurance athletes. In power athletes, A and T alleles were counted as 14 (47%) and 16 (53%), respectively.

In total, A and T alleles were counted as the same; 30 (50%) (Table 1). Alleles numbers showed no statistically significant difference (p=0.605).

Table 1. MCT1 Rs1049434 Genotype Numbers And Frequencies Of The Athlete Cohort

	Endurance Athletes			Power Athletes		
Genotype	**AA**	**AT**	**TT**	**AA**	**AT**	**TT**
Number	4	8	3	0	14	1
Percentage (%)	27	53	20	0	93	7

Table 2. MCT1 Rs1049434 Allele Numbers and Frequencies.

	Endurance Athletes		Power Athletes		Total	
Alleles	A	T	A	T	A	T
Number	16	14	14	16	30	30
Percentage (%)	53	47	47	53	50	50

4. Discussion

Gene variants influence on athletic status and analyzing these variants is a matter of investigation worldwide nowadays. MCT1 gene is one of the important gene effecting athletic performance in different sport disciplines. In the present study, we aimed to determine the genotypic frequency distribution of MCT1 rs1049434 polymorphism and alleles in long and short professional distance athletes. To date, according to best of our knowledge, population this is the first study conducting MCT1 rs1049434 polymorphism on long and short distance athletes (Fedotovskya et al., 2014; Merezhinskaya et al., 2009).

Lactate transporters (MCT proteins) play crucial roles in muscle metabolism, especially in skeleton muscles. The functional rs1049434 polymorphism effects gene activity, therefore considered to affect muscle capacity. Before, lactate transporter deficiencies were associated with muscle cramping and fatigue after prolonged exercise due to the delayed removal of protons. As T allele of MCT1 rs1049434 is associated with decreased transport of lactate from arterial blood into the muscles, it is considered to be linked with improved athletic performance. The main finding of our study is that AT genotype dominated in both groups, and also in total, which showed statistically significant difference. A and T alleles were counted as equal, whereas A allele was higher in endurance athletes, and T allele was higher in power athletes. Allelic distribution showed no statistically difference (Merezhinskaya et al., 2000).

Studies including MCT1 rs1049434 polymorphism and athletes are not enough to debate on them. Sawczuk et al. reported in a recessive genetical model that MCT1 T allele was related with sprint/power performance and TT genotype frequency was higher in sprint/power athletes compared to both control and endurance athletes.

These results are in agreement with ours in the terms of the high frequency of T allele in short distance runners (Sawczuk et al., 2015).

In the meantime, there is a number of biochemical evidence which is related to MCT1 rs1049434 polymorphism with performance in human beings. Cuperio et al. analyzed the accumulation of lactate in those who are with MCT1 A1470T polymorphism and performed high and longtime nonstop training in a pilot study (Cuperio et al., 2010). They concluded that MCT1 AT or TT genotypes had a limited and less lactate transporting capacity for oxidation in their muscles. In another study, Cuperio et al. studied the effect of the same polymorphism on blood lactate levels both in males and females after varied exercise protocols. Venous blood lactate levels were found to be higher in AA genotyped males than that of both TT and TA. The results for females remained unchanged (Cuperio et al., 2012). Fedotovskya et al. studied the relation between MCT1 rs1049434 polymorphism and maximum oxygen consumption, and maximum lactate concentrations in Russian rowers. They found that lactate levels were high in the male rowers with T allele when compared to endurance athletes (Fedotovskya et al., 2014).

Ben-Zaken et al. reported that the frequency of T allele was high in Israeli long-distance swimmers when compared to long and mid-distance runners. Additionally, its frequency was also higher in the swimmers than that of runners. In our cohort, T allele was higher in power based short distance runners, which is controversial to the findings of the latter study. Athletes' ethnicity and sample size may help us to explain the controversial results. As T allele decrease lactate transport, high lactate levels may enhance athletes' anaerobic metabolism (Ben-Zaken et al., 2015). Also there is evidence that high lactate levels are associated with muscle hypertrophy, which in turn is associated with anaerobic metabolism (Bonen et al., 1998). Environmental factors, like training, nutrition have crucial effects on athletic performance (Corak et al., 2017).

In our study, to eliminate the training effect on athletic performance, we recruited the athletes who had the same training sections, that's why our sample size remained in 30 athletes. This is the main limitation of our study. Another limitation is the lack of information about

blood lactate levels. We could not optimize the athletes' nutrition, and this can affect blood lactate levels. That's why we did not calculate blood lactate levels.

Patient informed consent: Informed consent was obtained.

Ethics committee approval: Ethics committee approval was obtained.

Conflict of interest: There is no conflicts of interest to declare.

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