FREQUENCY OF GENE ACE I POLYMORPHISM I-D IN ATHLETES OF DIFFERENT SPORTS

FREQUÊNCIA DO POLIMORFISMO I-D DO GENE ECA I EM ATLETAS DE DIFERENTES ESPORTES

FRECUENCIA DEL POLIMORFISMO I-D DEL GEN ECA I EN ATLETAS DE DIFERENTES DEPORTES

ABSTRACT

Introduction: The angiotensin-converting enzyme I-D (ACE) polymorphism gene is one of the most widely investigated genetic variations in sports science. Apparently, allele I is related to endurance sports, while allele D is related to power-strength activities. Nevertheless, studies have presented controversial results when it comes to its occurrence in a variety of sports. Objective: This study aims to evaluate the frequency of gene ACE polymorphism I-D in professional athletes of collective or individual sports. Methods: Five mL blood were collected from 189 subjects divided into two groups: athletes (AG, n=127, wrestling, taekwondo, soccer, futsal and handball) and non-athletes (NAG, n=62). The athlete group was subdivided by group modalities, into collective and individual. Both groups were further subdivided into male and female. Thus, we have the groups FAC= collective female, FAI= individual female; MAC= collective male, and MAI= individual male. The statistical analysis was carried out by frequency test, and the Hardy-Weinberg equilibrium by the x² test. Results: The results for the AG group indicated the following frequencies: DD=7%, ID=44% and II=49%. Allele frequency: D=29% and I=71%. For the NAG, the results were: DD=6.5%, ID=45.2% and II=48%. Allele frequency: D=29% and I=71%. The AG genotypic and allele frequencies did not differ statistically from those of the NAG (p= 0.982 and p= 0.984, respectively). However, we noticed that the genotypes II and ID frequencies were significantly higher than those of the DD. Conclusion: It can be concluded that the genotypic and allelic I-D frequencies of the ACE gene do not seem to influence performance in either group or individual sports. ACTN3 genotype frequencies did not vary significantly between male and female control subjects, and overall, there was no significant deviation from Hardy-Weinberg (H-W) equilibrium. Level of evidence I; Diagnostic studies-Investigating diagnostic test.

Keywords: Genetics; Sports; Angiotensin converting enzyme.

RESUMO

Introdução: O polimorfismo I-D do gene da enzima convertidora da angiotensina (ECA) é uma das variações genéticas mais amplamente investigadas na ciência do esporte. Apparentemente, o alelo I está relacionado aos esportes de resistência e o alelo D às atividades de força. Entretanto, os estudos têm apresentado resultados controversos quanto a sua ocorrência em diversos esportes. Objetivo: O presente estudo pretende avaliar a frequência do polimorfismo I-D do gene da ECA em atletas profissionais de esportes coletivos ou individuais. Métodos: Cinco mL de sangue foram coletados de 189 indivíduos divididos em dois grupos: atletas (GA, n=127, praticantes de luta livre, taekwondo, futebol, futsal e handebol) e não atletas (NAG, n=62). O grupo de atletas foi subdividido de acordo com a modalidade: coletiva e individual. Ambos os grupos foram também subdivididos em masculino e feminino. Portanto, temos os grupos FAC = feminino coletivo, FAI = feminino individual, MAC = masculino coletivo, MAI = masculino individual. A análise estatística foi realizada através do teste de frequência e o equilíbrio de Hardy-Weinberg pelo teste x². Resultados: Os resultados para o GA indicaram as seguintes frequências: DD=7%, ID=44% e II=49%. Frequência alélica: D=29% e I=71%. Para o NAG, os resultados foram: DD=6,5%, ID=45,2% e II=48%. Frequência alélica: D=29% e I=71%. As frequências genotípicas e alélicas do GNA não se diferem estatisticamente daquelas do GNA (p=0,982 e p=0,984, respectivamente). Entretanto, notamos que as frequências dos genotipos II e ID se apresentaram significativamente maiores do que aquelas do DD. Conclusão: Pode-se concluir que as frequências I-D genotípicas e alélicas do gene da ECA não pareceram influenciar o desempenho tanto nos esportes individuais como coletivos. As frequências do genótipo ACTN3 não variaram significativamente entre os indivíduos de controle de ambos os sexos, e, no geral, não houve um desvio significativo do equilíbrio de Hardy-Weinberg (H-W). Nível de evidência I; Estudos diagnósticos-Investigação de um exame para diagnóstico.

Descritores: Genética; Esportes; Enzima converidora de angiotensina.

RESUMEN

Introducción: El polimorfismo I-D del gen de la enzima convertidora de la angiotensina (ECA) es una de las variaciones genéticas más ampliamente investigadas en la ciencia del deporte. Aparentemente, el alelo I está relacionado a los deportes de resistencia y el alelo D a las actividades de fuerza. Entretanto, los estudios han presentado resultados controvertidos cuanto a su ocurrencia en diversos deportes. Objetivo: El presente estudio pretende evaluar la frecuencia del polimorfismo I-D del gen de la ECA en atletas profesionales de deportes colectivos o individuales. Métodos: Cinco...
INTRODUCCIÓN

Los polimorfismos genéticos son frecuentemente asociados con el rendimiento atlético en diferentes deportes. Es probable que los genes influyan en fenotipos como fuerza muscular y resistencia. El estudio de estos polimorfismos en deportes se ha ampliado en los últimos años. Un polimorfismo del gen ACE, la enzima que convierte la angiotensina I en angiotensina II, es una de las más estudiadas en el rendimiento atlético. El estudio del polimorfismo ID de ACE ha producido resultados contradictorios.

MATERIALS AND METHODS

El presente estudio se realizó en 189 individuos de ambos géneros (hombre, n = 127 y mujer, n = 62). Los individuos fueron subdivididos en grupos de atletas y no atletas. Los atletas participaron en diferentes deportes, siendo el taekwondo el más representativo. Se recolectaron muestras de sangre para realizar el análisis genético. Los resultados mostraron que no hubo desviación significativa del equilibrio de Hardy-Weinberg (H-W) para los genotipos ACE ID y IID. Las frecuencias del genotipo IID fueron significativamente mayores que las del DD. Se puede concluir que los genotipos I-D y IID no influyen en el rendimiento en los deportes individuales y colectivos.

Table 1. Characterization of the experimental group by sports.

| Sports (n) | SEX | MALE (n) | FEMALE (n) | Age (Mean ± dp) |
|-----------|-----|----------|------------|-----------------|
| Wrestling (8) | 6 | 2 | 25.60 ± 7.09 |
| Taekwondo (20) | 17 | 3 | 21.55 ± 5.80 |
| Soccer (31) | 18 | 13 | 21.22 ± 4.13 |
| Futsal (41) | 14 | 27 | 21.82 ± 3.24 |
| Handball (27) | 17 | 10 | 25.44 ± 4.89 |
| Total (127) | 72 | 55 | 22.84 ± 5.03 |

El estudio concluye que los polimorfismos genéticos del ACE ID y IID no influyen significativamente en el rendimiento atlético en diferentes deportes.
The ACE gene amplification may generate fragments with 491 or 191 pairs of bases (pb) in alleles I or D, respectively. Therefore, three different genotypes may appear: insertion homozygote I, heterozygote ID and deletion homozygote DD. It is relevant to highlight that during PCR preferential amplification of allele D over allele I may occur. In order to confirm the DD genotype a new PCR was carried out, making use of primers Forward: 5’ – TGGGACCACAGCGCCCGCCACTAC – 3’ and Reverse 5’ – TCGCCAGCCCTCCCATGCCCATAA – 3’, with similar conditions to the first PCR, except for the anelament temperature, which was 61º in the confirmation and 5% DMSO addition. The samples were applied in agarose gel 2%, however, none of the samples presented alteration in the result.

Figure 1. ACE gene polymorphisms. 1M is the marker with 100pb and 1C - is the negative control. DD = homozygous deletion polymorphism (191pb); II = homozygous insertion polymorphism (490pb); ID = heterozygous polymorphism (191 and 490pb) if the count was performed at inferior and superior regions, respectively.

Statistical analysis

The statistical treatment was done according to the descriptive analysis. The genotypic and allelic frequencies were calculated using the statistics SPSS program (version 21.0). The Hardy-Weinberg equilibrium was measured by the tx2 test. The genotypes percentages were determined through the cross reference tables, while the allelic frequencies proportions were done based on the 2x2 contingency tables.

RESULTS

The ACE genotypes frequency data of the total sample, as well as its stratificated form for the athlete group (AG) and the non-athlete group (NAG) is shown in Table 2. The results indicate that there was no significant difference (p = 0.982) in the genotypic frequency between the groups AG and NAG. However, when the analysis was intragroup, a difference was observed (p = 0.0001) due to the low frequency of the DD genotype. The frequency of insertion or deletion alleles followed the same pattern, being insignificant between groups (p = 0.984), although different both inside the GE (p = 0.0001) and in GNA (p = 0.0001).

Figure 2 shows ACE genotypic frequency in the respective types of AG. There was difference (p < 0.05) in the genotypes proportions when the sports were grouped. Nevertheless, when each sport was accessed, the three genotypes did not differ in Taekwondo (p = 0.259).

The samples were also separated by individual and collective characteristics. The genotypic and allelic frequencies are shown in Figures 3a and 3b. The grouping of the two did not present differences among genotypes II, ID and DD (p = 0.129). Similar result was verified in the genotypic frequency of individual sports (p = 0.208), however for team sports genotypes II, ID and DD were significantly different (p = 0.0001). The allelic frequencies were different among individuals (p > 0.05), and significantly different among male spices (p = 0.0001). In total, the frequency of allele I was higher than the allele D (p = 0.0001).

Figure 4a and 4b show data of ACE genotypic and allelic frequencies from groups separated by gender and aerobic or anaerobic sports. There was no difference in the genotypes of sports when grouped (p = 0.323), however, there was important difference (p = 0.0001) in collective and individual female groups, as well as in collective male groups. The only frequency that showed no difference was the individual male sports (p = 0.108).

The allelic frequency of the grouped sample was not significantly different (p = 0.140). However, when divided by gender and sport (individual and collective) the allele I frequency in the sample was significantly higher than D (p = 0.0001). Nevertheless, the alleles did not show difference (p = 0.527) for the female individual group.

DISCUSSION

The present study had the objective of analyzing the genotypic and allelic frequencies of professional athletes in various sports. The results of the study showed there was no significant difference among genotypes frequencies, as well as the allelic frequencies when AG and NAG were compared. However, genotype DD and the allele D were less frequent among the groups.

Some studies with similar lineation have shown no difference of genotypic and allelic frequencies among athletes and non-athletes,
while other investigations have identified important differences in the athletes and non-athletes groups. Costa et al.19 and most of the published data refers to an I/D polymorphism leading to the presence (I allele) did not find differences among ACE genotypes when swimmers were compared to non-athletes. Likewise Gunel et al.21 and functional ACE I/D and ACTN3 R577X polymorphisms have been associated with sprinter performance. The aim of this study was to determine the effect of these polymorphisms on sport performance among 37 elite athletes and 37 healthy controls. The ACE II genotype was identified in 32.43% of the control group and 51.35% of the elite athletes, and the ID genotype in 29.73% of the control group and 40.54% of the elite athletes. With regard to the ACTN3 gene, the XX genotype, which confers an advantage for endurance activities, was identified in 10.81% of the control group and 19.14% of the elite athletes. The XX genotype was observed more frequently in non-athletes (above 8000 meters) were homozygotes II (n = 6) or heterozygotes II (19,14%), then, the genotypes did not present difference (P = 0,85). Bordoni et al.23 have tested the association between ACE I-D polymorphism, corporal composition and hydration state in 306 Italian young and verified frequencies DD (41%), ID (44%) and II (15%). The data shows an inversely proportional relationship between frequencies of genotypes DD and II when compared to the frequencies of this study. It is important to highlight that any of the investigations aforementioned were carried out in the Northern region of Brazil, site of the present study. Coelho et al.22 verified the following frequencies in soccer players of different categories from Southeast region in Brazil: DD (29,42%), ID (51,42%) and II (19,14%), then, the genotypes did not present difference (P = 0,85). Moreover, the purpose of the present study was to determine the interaction between both ACE ID and ACTN3 R577X polymorphisms and sprint and endurance performance in swimmers. Genomic DNA was extracted from oral epithelial cells using GenElute Mammalian Genomic DNA Miniprep Kit (Sigma, Germany) that identified, both in the swimmers and its stratification in short or long distance competitors, difference when compared to the non-athlete.

Researches involving athletes13,22 elderly23 or children and adolescents24 showed different frequencies when compared to this study. It is important to highlight that any of the investigations aforementioned were carried out in the Northern region of Brazil, site of the present study. Coelho et al.22 verified the following frequencies in soccer players of different categories from Southeast region in Brazil: DD (29,42%), ID (51,42%) and II (19,14%), then, the genotypes did not present difference (P = 0,85). Bordoni et al.23 have tested the association between ACE I-D polymorphism, corporal composition and hydration state in 306 Italian young and verified frequencies DD (41%), ID (44%) and II (15%). The data shows an inversely proportional relationship between frequencies of genotypes DD and II when compared to the frequencies of the present study.

It has been suggested that allele I presents distinctive relationship with sports which the endurance capacity is preponderant.24,25 Montgomery et al.24 related the genotypic and allelic frequency of ACE I-D polymorphism into two groups. The first one was made of 25 mountaineers who competed climbing to heights above 7000 meters, while the second one was made of 123 military from the UK DD. Both were subjected to exercises to assess the upper limbs muscular stamina. Results showed that the mountaineers who achieved longer distances (above 8000 meters) were homozygotes II (n = 6) or heterozygotes II (n = 9). As for the military, genotypes homozygotes II did the exercise...
for 79.4 ± 25.2 seconds, heterozygotes ID for 24.7 ± 8.8 seconds and homozygotes DD for 14.9 (p = 0.001).

Grenda et al.14 the purpose of the present study was to determine the interaction between both ACE ID and ACTN3 R577X polymorphisms and sprint and endurance performance in swimmers. Genomic DNA was extracted from oral epithelial cells using GenElute Mammalian Genomic DNA MiniPrep Kit (Sigma, Germany) verified that in 49 Polish long-distance elite swimmers the frequency of genotype DD was under 10%, whereas, in 147 sprinters that frequency rose to 26.7%. Even though these results have confirmed the hypothesis that the allele I may be related to better performance at endurance events, other findings present results that disagree with such hypothesis.12,26 Amir et al.12 the allele promotes more power-oriented events. We tested this hypothesis by determining the frequency of ACE ID alleles amongst 121 Israeli top-level athletes classified by their sporting discipline (marathon runners or sprinters verified higher proportion of genotype DD (62%) in comparison to genotypes ID (29%) and II (9%) in Israeli elite marathonists. Another study with endurance elite athletes carried out by Grealy et al.26 diagnosed, in 196 Ironman contestants, 42.3% of genotypes DD, 46.9% ID and 10.7% II, corroborating Amir et al.12 the allele promotes more power-oriented events. We tested this hypothesis by determining the frequency of ACE ID alleles amongst 121 Israeli top-level athletes classified by their sporting discipline (marathon runners or sprinters results).

On the other hand, other investigations indicate that allele D frequency is higher in sports that demand higher muscle strength-power.27,28 Nevertheless, when Heffernan et al.,27 evaluated in the frequency in 505 Rugby players did not find significant genotypic differences (DD = 21.4%, ID = 49.7%, e II = 28.9%). Opposing these results, Costa et al.29 and most of the published data refers to an I/D polymorphism leading to the presence (I allele evaluated the frequency of 39 Portuguese elite swimmers (25 of up to 200m racers and other 14 of races ranging from 400 to 1500m). The genotypic frequencies of the short-distance swimmers were DD 56% and ID 44%, while for mid-distance athletes the frequencies were DD (43%), ID (21%) and II (36%). These results indicate an increased presence of allele D in short-distance races athletes, however, the more distant the race, the more evident is the frequency of allele I. The same authors evaluated 58 high-performance athletes (35 swimmers and 23 triathletes), grouping them into long or mid-distance types. Genotype II was not find in the short-distance group, while there was no important difference found in the mid-distance group, Costa et al.30 This data corroborates Papadimitriou et al.31 who verified better results in Olympic-level sprinters carriers of allele D. Likewise, Massidda et al.31 even if this association has been often conflicting. The aim of the present study was to investigate the association between the ACE and the ACTN3 genotypes and elite performance in Italian male athletes. The ACTN-3 R577X and the ACE I/D genotype distributions of 59 elite male Italian athletes practicing gymnastics (G, n = 17) did not find a genotype II carrier in a group of 12 sprinters. Moreover, the frequency of genotype DD was above 50% in gymnasts and soccer players.

Once this investigation assessed predominantly anaerobic sports, it was reasonable to expect that allele D would present frequency of at least 50%. Instead, it was shown that in collective sports, 73% of allele I and 23% of allele D (P = 0.001), while in individual sports, the proportion was 39% of allele I and 61% of allele (P = 0.102). Although the results found in individual sports are similar to other studies,12,25,28 when the groups were united, the total frequency was 71% I and 29% D. Therefore, the sample allele frequency of this study differed significantly from those found in studies aforementioned.

Wang et al.23 compared the genotypic frequencies of American and European short and mid-distance swimmers (≤ 400 meters, n = 130) and long-distance (> 400 meters, n=70) against Asian sprint swimmers (≤ 100 meters, n = 166) and mid-distance ones (200-400 meters, n = 160). Caucasian sprint and mid-distance swimmers showed higher frequencies of genotypes DD (40.7%) and ID (39.8%) in comparison to II (19.5%). However, long-distance contestants showed similar genotypic frequencies between II 24.2% e DD 28.8%. Among Asians, frequencies corroborate the results of the present study. Short-distance athletes presented the following percentage, DD 9.6%, ID 34.9% and II 55.4%, while for mid-distance, genotypes DD, ID and II presented frequencies 7.5%, 49.4% and 43.1%, respectively. Ginevičienė et al.32 the angiotensin-converting enzyme (ACE) also identified correlation between allele I and anaerobic sports. Apparently, the frequencies found in the present study are similar to the ones found in studies with Asian populations.10,33-34 Park et al.19 and to determine the association between ACE genotype and cardiovascular risk.

Forty hypertensive adolescents (16-17 years old, systolic blood pressure (BP) found higher frequencies of genotypes ID and II than genotype DD in young Koreans. Meanwhile, Chiu et al.33 verified frequencies of DD (7%), ID (44%) and II (49%) in young female Asian athletes. Malhotra et al.34 a sub-mountainous population of the Himalayan region, are known for strength and bravery. In the present study when “Gorkha”u201du201d is used without brackets, we are mentioning Gorkhas of Tibeto-Burman origin. Physical capability, strength and endurance are important components of fitness associated with genetic traits. The aim of this study was to examine the endurance potential of male Gorkha soldiers, based on endurance-related genetic markers ACE I/D, ACTN3 Arg (R identified frequencies DD (10%), ID (47%) and II (43%) in 374 Asian military from sub-mountainous regions. In this way, two points could be made: 1) The I-D polymorphism frequency of the ACE is presented in different ways in different populations and, 2) allele D is not always related to strength-power events nor is allele I linked to endurance events.

CONCLUSION

The present study evinces that genotypic and allelic frequencies of gene ECAI did not differ between athletes and non-athletes. In addition, in the athletes group of collective sports it was observed higher frequency of the homozygous insertion genotype.

All authors declare no potential conflict of interest related to this article

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