Changes in serum creatinine, uric acid, creatine kinase and glomerular filtration in street runners

Alturações dos níveis séricos de creatinina, ácido úrico, creatina cinase e da taxa de filtração glomerular em corredores de “rua”

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Abstract – The strategies adopted by corridors “street” during the evidence from interference of the race distance and levels of technical and physical competition. The objective of this study was to examine the biochemical effects of Creatinine (C), Uric Acid (AU), Creatine Kinase (CK) and Glomerular Filtration Rate (GFR) caused by a test run of “street” of 6 (six) Km participated n=(15) male athletes (40.53 ± 8.65 years) divided into three groups: Group 1 Best Times (G1MT) n = 5, Group 2 Intermediate Times (G2TI) n = 5; Group 3 Times Worst (G3PT) n = 5. Blood samples were collected 30 min before and immediately after the race. Data were analyzed by Two-Way ANOVA, Wilcoxon and Mann Whitney test. It was considered significant levels (p<0.05). The results showed that there were significant increases in serum activities of intra-group (C) in G1MT before: 1,18±0,04 mg.dL-¹ after: 1.60±0.15 mg.dL-¹; G2TI before: 1,04±0,15 mg.dL-¹ after: 1,56±0,21 mg.dL-¹; G3PT before: 1,08±0,13 mg.dL-¹ after: 1,52±0,32 mg.dL-¹ and (AU) G1MT before: 3,80±0,75 mg.dL-¹ after: 4,56±0,94 mg.dL-¹; G2TI before: 4,36±1,62 mg.dL-¹ after: 5,0±1,69 mg.dL-¹; G3PT before: 4,62±1,08 mg.dL-¹ after: 5,42±0,86 mg.dL-¹, while (CK) and (GFR) showed no significant difference.

Key words: Athletic performance; Biochemistry; Running.

Resumo – As estratégias adotadas pelos corredores de “rua”, durante as provas, sofrem interferência da distância da corrida e dos níveis técnico e físico dos competidores. Assim, o objetivo deste estudo foi de examinar os efeitos bioquímicos da Creatinina (C), Ácido Úrico (AU), Creatina Cinase (CK) e da Taxa de Filtração Glomerular (TFG) provocados por uma prova de corrida de “rua” de 6 (seis) Km. Participaram n=(15) atletas masculinos (40,53±8,65 anos) separados em 3 grupos: Grupo 1 Melhores Tempos (G1MT) n=5; Grupo 2 Tempos Intermediários (G2TI) n =5; Grupo 3 Piores Tempos (G3PT) n=5. Foram coletadas amostras de sangue 30 min antes e imediatamente após a corrida. Os dados foram analisados através da ANOVA Two-Way, Wilcoxon e Mann Whitney test. Consideraram-se os níveis significativos (p<0,05). Os resultados permitem concluir que ocorreram aumentos significativos intragrupos nas atividades séricas de (C) no G1MT pré: 1,18±0,04 mg.dL-¹ pós: 1,60±0,15 mg.dL-¹; G2TI pré: 1,04±0,15 mg.dL-¹ pós: 1,56±0,21 mg.dL-¹; G3PT pré: 1,08±0,13 mg.dL-¹ pós 1,52±0,32 mg.dL-¹ e no (AU) G1MT pré: 3,80±0,75 mg.dL-¹ pós 4,56±0,94 mg.dL-¹; G2TI pré 4,36±1,62 mg.dL-¹ pós 5,0±1,69 mg.dL-¹; G3PT pré 4,62±1,08 mg.dL-¹ pós 5,42±0,86 mg.dL-¹, enquanto a (CK) e a (TFG) não apresentaram diferença significativa.

Palavras-chave: Corrida; Bioquímica; Desempenho atlético.
INTRODUCTION

The number of people today seeking physical activity is growing exponentially. Among these activities, Street Races or Marathons are one of the most sought after. This can be proven by the increasing number of competitions and those that practice this sport. Its easy access to the entire population, low cost, ease of training, and few materials needed (socks, shoes, shorts, shirt) are factors that contribute to making this sport more popular and thus increases the level of competition among the athletes.

By setting up parameters that make it possible to visualize physiological adaptations due to training allows any changes to be monitored to which metabolism is submitted during physical activity, so that it is possible to extract the maximum performance of the runners and avoid harmful situations such as overtraining and additionally muscle injuries. To prevent these situations there are physiological indicators considered to be important parameters for monitoring the volume and intensity of training such as plasma concentrations of Creatine Kinase (CK).

The strategies adopted by the runners during races vary depending on the distance and technical level of the race and their objective. Due to the time that it takes to complete a race, the supply of energy is carried out primarily by the oxidative system. However, in most cases, athletes use sprints, which can be defined as the act of increasing the pace at certain times of the race. Characterized by intense but short muscle contractions, this running strategy increases the demand for ATP, exceeding the capacity of the muscle cell in resynthesis.

According to Maughan et al., the lowering of the energy load at the beginning of the contraction (momentary decrease of the ATP and increase of the ADP and AMP) accelerates both the anaerobic and oxidative resynthesis of the ATP, as well as the degradation of the nucleotides. The fall in the ATP/ADP ratio in intense contractile activity leads to inhibition of the contractile resulting in muscle fatigue. These mechanisms are attenuated by biochemical pathways (phosphocreatine, purine synthesis, purine salvage pathway, and adenine nucleotide degradation pathway), mediated by enzymes with kinase, deaminase, and transferase activity (creatine kinase, ribose-phosphate pyrophosphokinase, hypoxanthine phosphoribosyl transferase, adenylyl kinase, and AMP deaminase).

The hydrolysis of the phosphocreatine in the beginning of submaximal exercise and during high-intensity exercise (sprints) occurs at the higher transfer potential of the phosphate group for ATP resynthesis. Thus, the muscle cell with a low energy load cannot rephosphorize it, producing Creatinine (C) as a result of the nonenzymatic dehydration and going from the muscle tissue into the plasma from where it is removed almost entirely at a relatively constant velocity by glomerular filtration. The Glomerular Filtration Rate (GFR) has its importance once we notice that the smaller the filtration, the greater will be the athlete’s dehydration. This data is in line with the results found by authors such as Hellsten et
al.13 that, through the study of muscle biopsies and blood samples showed that phosphocreatine is reduced by doing knee extension exercises (50-70W) until exhaustion, and that the AMP is deaminated to IMP (inosine monophosphate) until the formation of Uric Acid (UA), representing the loss of nucleotides.

It is believed that athletes who intensify their training through sprints have a higher tolerance to muscle fatigue during maximum racing effort quantified by the lower C and UA serum levels. This data is also supported by the inhibition of the AMP-deaminase enzyme by the elevations of the resynthesis in the ATP molecules, reducing the flow of the adenine nucleotide loss pathway and the increase of the purine salvage pathway14.

These results should be viewed with caution since the levels of UA, for example, tend to be elevated immediately after the activity is finished, causing it to be considered as an acute effect of the effort. The post-activity CK peak, however, is dependent on the intensity and type of effort and a considerable increase in its concentration can be detected after the race, although other studies show increased levels of this enzyme between 24 and 72 hours after the activity15.16. Another concern is with GFR because the levels are commonly reduced in distance runners17 characterizing a decrease in the renal function.

Given this scenario, the main objective of this study was to examine the acute biochemical effects from the effort caused by a 6-kilometer street race, more specifically, the levels of C, UA, CK, and GFR.

**METHODS**

**Sample**

The participants in this study were 15 male street runners with a mean age of 40.5±8.6 years. The sample was selected by the ranking resulting from the first stage of the Campos dos Goytacazes/RJ 2011 Circuit of Street Races where the 15 best times of the athletes were tested within the procedures described below.

**Data gathering**

An anamnesis was done consisting of a standard interview regarding the use of medications, training time, musculoskeletal injuries, and distances run in a week. The criterion was applied that all those selected for the sample had to have more than two years of training prior to starting the study.

The athletes were instructed during the technical workshop (one day before the race) to not change their eating habits prior to blood collection. There were two moments when blood was collected. The first took place 30 minutes prior to the race and the second immediately after the race was finished by the athlete. The race was 6 kilometers long and part of the Campos dos Goytacazes/RJ 2011 Circuit of Street Races.

The athletes signed a Consent Form in accordance with Resolution 196/1996 of the National Health Council. This study was approved by
the Ethics Committee on Human Research from the Institutes of Higher Education of Censa (ISECENSA-RJ) under protocol number 0017.0.413.000-11/2011.

Because it is an official competition with the measurements being taken immediately before and after it, some variables could not be controlled. But we understand and admit that the intensity of the race, as well as the pace of the runners, were at their maximum for the distance. Furthermore, water loss could not be controlled because there were hydration stations during the race and it was not possible to control what each athlete drank during the race.

**Blood collection and analysis**

The blood was collected in a specific room for the purposes of this study, which was set up at the site of the start and finish of the race. One athlete at a time had the following material collected from him: The blood was collected (±5 mL) from the antecubital vein of the individuals who were sitting at the time of collection. Disposables needles and syringes were used. After collection, the blood was deposited in sealed glass containers that were immediately taken to the Chemistry of Biomolecule Lab of the Institutes of Higher Education of Censa (ISECENSA-RJ) where it was centrifuged (Centrifuga Basic® / Sislab Tecnologia Laboratorial Ltda. - Brazil) to separate the serum. Colorimetry alkaline picrate methods were adopted to determine the levels of creatinine, uric acid, and creatine kinase - Jaffé, enzymatic-Trinder, and enzymatic, respectively, in all analyses of the blood samples. Creatinine K, Liquiform Uric Acid, and CK-NAC (Labtest Diagnóstica SA - Brazil) kits were used and an automatic analyzer Labmax Plenno® (Labtest Diagnóstica SA - Brazil).

**Determination of the Glomerular Filtration Rate (GFR)**

The GFR was determined using the formula Modification of Diet in Renal Disease (MDRD) using serum creatinine and age. A multiplier is used to adjust the estimate depending on race and gender. The equation was validated by the inulin clearance method and urine collections for 12 or 24 hours of creatinine.

\[
GFR = 186^* \text{(serum creatinine)}^{-1.154} \times \text{(age in years)}^{-0.203} \times \text{multiplier}
\]

The multiplier: 1.21 for blacks, 0.742 for non-black women

**Statistical Analysis**

The athletes were divided into 3 groups based on their times of the street race by the statistical tool Tertile Score: Group 1 - Best Times (G1MT) n=5, Group 2 - Intermediate Times (G2TI) n=5, Group 3 - Worst Times (G3PT) n=5. For the homogeneity of the data, the Levene’s test was used (C p=0.31, UA p=0.19, CK p=0.04, and GFR p=0.07). The comparison of the serum levels of C, UA, and GFR were analyzed by the two-way ANOVA for repeated
measurements, using the test of Post hoc of Bonferroni. As for CK, the tests used were the nonparametric Wilcoxon signed rank test (intragroups) and Mann Whitney test (intergroups). Differences were considered significant at p<0.05. Data from the procedures described above were analyzed by the GraphPad Prism® software version 5.0 (GraphPad, USA).

**RESULTS**

Table 1 shows the general characteristics as mean values with their standard deviations of the groups of athletes.

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Age (years)</th>
<th>Race time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1MT</td>
<td>5</td>
<td>38.02±9.20</td>
<td>24.62±3.17</td>
</tr>
<tr>
<td>G2TI</td>
<td>5</td>
<td>41±8.80</td>
<td>28.15±0.59</td>
</tr>
<tr>
<td>G3PT</td>
<td>5</td>
<td>42.4±9.39</td>
<td>33.08±3.53</td>
</tr>
</tbody>
</table>

G1MT-Group 1 Best Times; G2TI-Group 2 Intermediate Times; G3PT-Group 3 Worst Times

Figure 1 shows the levels of creatinine with G1MT at Pre-Race at 1.18±0.04 mg.dL⁻¹ and Post-Race at 1.60±0.15 mg.dL⁻¹ in serum levels; G2TI at Pre-Race at 1.04±0.15 mg.dL⁻¹ and Post-Race at 1.56±0.21 mg.dL⁻¹; and G3PT at Pre-Race at 1.08±0.13 mg.dL⁻¹ and Post-Race at 1.52±0.32 mg.dL⁻¹ with significant differences in intragroups G1MT, G2TI, and G3PT (p=0.00, p=0.02, and p=0.01), respectively.

Figure 2 shows the levels of uric acid with G1MT at Pre-Race at 3.80±0.75 mg.dL⁻¹ and Post-Race at 4.56±0.94 mg.dL⁻¹ in serum levels; G2TI at Pre-Race at 4.36±1.62 mg.dL⁻¹ and Post-Race at 5.0±1.69 mg.dL⁻¹; and G3PT at Pre-Race at 4.62±1.08 mg.dL⁻¹ and Post-Race at 5.42±0.86 mg.dL⁻¹ with significant differences in intragroups G1MT, G2TI, and G3PT (p=0.00, p=0.00, and p=0.01), respectively.
Biochemical changes in street runners  Morales et al.

Figure 2. Levels of Uric Acid (UA) in the pre and post-race moments of the groups: G1MT-Group 1 Best Times; G2TI-Group 2 Intermediate Times; G3PT-Group 3 Worst Times. * Different compared to pre-race moment (p<0.05).

Table 2 presents the pre-and post-race of the CK without significant differences within and between the groups (p=0.06, p=0.06, and p=0.06 / p=0.69, p=1.00, and p=1.00), respectively.

Table 2. Serum activity of the CK enzyme before and after the race of the athletes.

<table>
<thead>
<tr>
<th></th>
<th>Pre-Race CK (U.L⁻¹)</th>
<th>Post-Race CK (U.L⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Min)</td>
<td>(Q1) 25%</td>
</tr>
<tr>
<td>G1MT</td>
<td>97</td>
<td>128</td>
</tr>
<tr>
<td>G2TI</td>
<td>101</td>
<td>124</td>
</tr>
<tr>
<td>G3PT</td>
<td>125</td>
<td>125</td>
</tr>
</tbody>
</table>

(G1MT) Group 1 Best Times; (G2TI) Group 2 Intermediate Times; (G3PT) Group 3 Worst Times; (Min) Minimum, (Q1) First Quartile; (Md) Median, (Q2) Second Quartile; (Max) Maximum.

Figure 3 shows the rates of functional changes of the renal system through the estimation formula (MDRD) with G1MT at Pre-Race at 73.97±5.44 mL.min.1.73m² and Post-Race at 70.20±6.22 mL.min.1.73m², G2TI at Pre-Race at 86.08±16.67 mL.min.1.73m² and Post-Race at 62.60±8.62 mL.min.1.73m², and G3PT at Pre-Race at 81.25±12.69 mL.min.1.73m² and Post-Race at 69.00±24.15 mL.min.1.73m² without significant differences within and between the groups G1MT, G2TI, and G3PT (p=1.00, p=0.67, and p=0.89 / p=0.07, p=0.10, and p=0.08), respectively.

Figure 3. Glomerular Filtration Rate (GFR) in the pre and post-race moments of the groups: G1MT-Group 1 Best Times; G2TI-Group 2 Intermediate Times; G3PT-Group 3 Worst Times. * Different compared to pre-race moment (p<0.05).
DISCUSSION

At the end of the Street Race of 6 kilometers, the three groups studied showed a significant increase in the levels of C in relation to the pre-race condition (p<0.05). It is believed that one of the factors that influenced the levels of C to increase in the post-race of the groups was the lowering of the capacity of these athletes to re-synthesize the Creatine phosphate (PCr) molecules. This fact may be related to the high intensity of the route (6 Km), thereby altering the production of free creatine in the muscle and consequently leading to high levels of serum C after the race. These sharp changes in the levels of serum C in athletes have been reported by Banfi, Del Fabbro & Lippi who studied the concentrations of C in elite male athletes of rugby, alpine skiing, and cycling characterized based on different Body Mass Indexes (BMI), finding significant differences in rugby (p=0.00) and in skiing (p=0.02), but not observing differences for cycling (p=0.25), concluding that the changes in concentrations of C in athletes should not only take into account only the sport practiced and BMI, but also the possible variations in intensity and volume in training and in the competitions.

Forbes et al. reported that the resynthesis of PCr can be divided into two phases: the initial phase (glycolytic production of ATPs) and the final stage (oxidative production of ATPs), indicating an important predictor in evaluating the pathways of generating energy (ATPs) after the activity. Furthermore, Duteil et al. using nuclear magnetic resonance simultaneously with quantification of myoglobin saturation found in endurance athletes a high correlation (r=0.75) between the resaturation of myoglobin molecules and rephosphorylation of PCr, indicating a greater oxidative capacity than sprint athletes. Yoshida found in five long distance runners a significant reduction in PCr molecules and lower levels of acidification in high intensity knee flexion exercises compared with six sedentary individuals.

It is understood, therefore, that the changes of serum C in athletes presented in our study after the race are associated with a lower efficiency of the pathways that generate ATP molecules because these ATPs generated by these pathways (glycolytic and oxidative) favor the resynthesis of PCr molecules where they will be used as a means of synthesizing ATPs and buffering of free H⁺.

The results presented in high levels of UA by the groups of runners (G1MT, G2TI, and G3PT) compared to the pre-race condition (p<0.05) are related to trying to keep the energy needs of the cell under high intensity exercises. The reaction catalyzed by the AMP deaminase (AMP → IMP + NH₃) indirectly minimizes the accumulation of ADP by removing the AMP to UA, allosterically activating the enzyme Adenylate Kinase (AK), shifting the reaction to the right (2ADP → ATP + AMP), thereby increasing the energy load (ATP)¹. For these reasons it is suggested that the loss of adenine nucleotide is important for muscle function in conditions of metabolic crisis during
maximal exercises (sprints) and during prolonged submaximal exercises, increasing UA serum levels. On the other hand, lower serum levels of UA were found, reduced activities of the AMP-deaminase (AMPD) enzymes and increased activity of the Hypoxanthine Phosphoribosyl Transferase (HPRT) enzymes in athletes who underwent training on a cycle ergometer three times per week for six weeks. The salvage pathway of the nucleotides utilizes the 5-phosphoribosyl-1-pyrophosphate (PRPP) by the enzyme HPRT along with a reduction of the activity of the AMPD enzyme, reducing thereby the UA levels and increasing the levels of Inosine Monophosphate (IMP) in which the molecules of AMP and ADP undergo rephosphorylation until ATP.

Strenuous physical exercising can cause an overload on the muscles. Therefore, the increased plasma activity of the muscle enzymes such as CK may be a typical physiological response during strenuous physical exercises and is generally used as markers of muscle damage. When the exercise is strenuous, this results in excessive muscle damage, a condition known as exertional rhabdomyolysis in which CK levels after exercising can be up to 5 or 10 times higher than the normal limit for men and women. In this study, one athlete from the group G3PT showed high levels of (CK) (11.688 U.L⁻¹) after the race, which is considered a clinical condition of exertional rhabdomyolysis.

The results presented by the groups did not show significant elevated levels compared to the pre-race condition (p>0.05), leading us to believe that these changes in absolute levels of concentrations of CK are specific to this individual since these levels are usually high in athletes. However, these values can be more conclusive when the Delta differences (Δ = value of CK after test - value of CK before the test) are correlated with the performance levels of the athletes. confirmed this information when they studied the Delta difference in the CK values, reporting a significant correlation coefficient (r=−0.64, p=0.02) between the high levels of peak power with the lowest Delta CK differences in twelve (12) college football athletes, having found in these athletes absolute values of CK (11.634 U.L⁻¹, 18.823 U.L⁻¹) close to the levels found in our study.

The levels of estimated GFR by the equation Modification of Diet in Renal Disease (MDRD) in the groups G1MT, G2TI, and G3PT did not undergo significant reductions (p>0.05) compared to before the race. Authors such as Tian et al. found different results when they investigated the changes in the biomarkers of the renal function and estimated GFR in 10 male runners (16.2±0.6 years) during the recovery periods of 2 h, 4 h, 24 h after a 21-kilometer race, concluding that the decline in the renal function does not return to the pre-race levels during the recovery period of 24 hours. It is believed that the duration of the race (6 Km) in our study was an important factor in not influencing these changes in GFR because the time these athletes were exposed to dehydration factors (high temperature and high humidity) was less. The effects of dehydration in the smaller GFR are explained by the greater reduction in
renal blood flow produced by the production of catecholamines such as
adrenaline, causing intense constriction of afferent arterioles with a great
reduction in pressure in the glomerular capillaries that can drastically
reduce the plasma filtration and consequently increase the glomerular
colloid osmotic pressure (increase of the plasma proteins). Studies such
as those done by authors Machado et al. have demonstrated a reduction
in GFR, increases in serum $C$, and a high correlation between high levels
of $C$ in women performing a strength training on a circuit with 3 sets
of 12 repetitions with intervals of less than 15 seconds with a lower GFR
calculated by the equations of estimates Modification of Diet in Renal
Disease MDRD ($r = -0.924, p=0.01$), Cockcroft-Gault CG ($r = -0.884,
p=0.01$) and Mayo Clinic Quadratic Equation MCQE ($r = -0.644, p=0.05$).
Another factor caused by the dehydration during and after the physical
exercise is an increased secretion of Aldosterone or Vasopressin because
this steroid hormone regulates diuresis through water reabsorption in
the collecting ducts.

The equations of estimates of the levels of GFR are strong predictors
of risk of complications of the renal function. After the race, only two
athletes in our study had a GFR of 51 mL.min.$^{-1}.73$ m$^2$ classified in stage
3 with a moderate decrease in GFR. Within this context Lippi et al. studied the variations of the equations for estimating GFR using equations
of CG, MDRD, and MCQE at rest in 60 professional cyclists compared to
60 healthy sedentary subjects. The results pointed to the following results:
MDRD (119 versus 104 mL.min.$^{-1}.73$m$^2$, $p<0.001$), MCQE (137 versus 135
mL.min.$^{-1}.73$m$^2$, $p=0.128$), and CG (127 versus 127 mL.min.$^{-1}.73$m$^2$, $p=0.490$),
respectively, concluding that the CG and MCQE equations are more ade-
quate that the MDRD equation because it seems to present more robustness
against variations in the regime of training of endurance athletes. Thus,
the GFR values of the two athletes may have been underestimated by the
MDRD equation used in our study because to estimate GFR through the
CG and MCQE equations, the 24h urine volume and body mass (kg) are
needed and these variables were not included in the methodology of this
study because as it was an official sporting event.

**CONCLUSION**

According to the data found in this study, it can be inferred that there was a
significant increase in post-race values in the levels of Creatinine (C) in all
groups (G1MT, G2TI, and G3PT), a fact that can be attributed to the high
intensity of the activity considering that it was a relatively short distance (6
km). The Uric Acid (UA) was also high in all groups compared to pre-race
values, while the Glomerular Filtration Rate (GFR) levels estimated by the
equation Modification of Diet in Renal Disease (MDRD), although they
underwent reduction compared to pre-race levels, did not show statistically
significant differences probably because the time the athletes were exposed
to climatic factors was less. CK did not show significant changes, though
its concentration was increased, probably due to the fact that the damage caused in the muscle fibers were relatively mild for the population tested.

It is important to point out that, despite the results make it possible to monitor silent injuries and are of good reliability, further studies should be made in relation to the variables investigated, mainly measuring the changes that occur with an increased recovery time (24, 48, 72 hours) after the race, as well as to try to control variables that were not addressed in this study such as the pace of the athletes, hydration levels, among others.

REFERENCES


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