ORIGINAL ARTICLE

Physical Exhaustion Unmasking Underlying Diseases

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Abstract

Physical exhaustion is the temporary physical inability of the muscles to perform optimally. The onset of muscle fatigue during physical activity is gradual and can be reversed by rest and replenishment of electrolyte and hydration. For maximal physical fitness, one should require optimal function of all the body parts and system. It is our humble attempt to find out the underlying disease in patients who presented to us with signs and symptoms of physical exhaustion.

Materials and methods: The study was conducted at medical center located at southern part of India from March 2017 to February 2019, and 213 healthy individuals from a physical training institute aged between 18 and 21 was selected, and pre- and post-run blood parameters were measured.

Discussion: In our study, more than 20% persons have more than 2-fold rise in blood creatine phosphokinase level which ultimately comes to normal within 48 hours. Eighty-one people among the study population have increase in serum AST/ALT level, and most of them come to normal within 48 hours.

Conclusion: For optimal performance and to avoid major catastrophe, it is suggested that before undergoing exhaustive physical exhaustion, one should be properly evaluated.

Keywords: Gilbert's syndrome, G6PD, Physical exhaustion, Thalassemia minor.

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Introduction

Appropriate exercise is helpful in health promotion and prevention of disease, such as hypertension, hyperlipidemia, and diabetes. Endurance exercise induces cellular changes within the body, increasing cytokine levels and changes in the muscle, cartilage, heart, liver, and kidneys.[1–6] Muscles are damaged as a result of metabolic and mechanical factions caused by intense, long-time exercise. Muscle injury induces rhabdomyolysis via structural damage to the myocytes and protein leakage. Studies have found that atraumatic rhabdomyolysis occurs in healthy persons after extreme exercise.[7–9]

Increases in serum enzymes that are isolated within the blood, such as creatinine kinase (CK) and lactate dehydrogenase (LDH), serve as markers of acute or chronic muscular damage and cell necrosis. Activation of CK and LDH may increase symptoms such as pain, fatigue, and a decline in muscular strength during high-intensity, long-distance exercise because of damaged skeletal muscles. Alanine transaminase (ALT) and aspartate aminotransferase (AST) serve as markers of liver disease, and increases in AST, ALT, and LDH after long-distance exercise induces chronic liver injury.

However, such reports estimate changes in biochemical markers after a single type of long-distance running, and there are few studies examining differences in biochemical markers based on distance.

It is our humble attempt to find out the correlation of enzymes with physical exercise.

Aims and Objectives

To find out the correlation of enzymes with physical exercise and duration of exercise so that necessary action can be taken to prevent untoward effects of exhaustion and exacerbation of the underlying diseases.

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Materials and Methods

The study was conducted at medical center located at southern part of India from March 2017 to February 2019. A total of 213 healthy individuals from a physical training institute aged between 18 and 21 were selected. After taking informed consent, height and weight were measured. Blood samples were taken for biochemistry analysis before commencement of the study. After proper hydration, they were allowed to run 14 km within 1 hour. After completion of run, those who felt sick were evaluated clinically, blood parameters were measured, and pre–post difference in parameters were analyzed. They are divided into five groups (groups I–V) depending on performances (time taken to complete the run),

- Group I being first 40 individuals who finished the run
- Group II 41st to 80th individuals who finished the run

- Group III 81st to 120th individuals who finished the run
- Group IV 121st to 160th individuals who finished the run
- Group V 161st to rest 53 individuals who finished the run last

Results

A total of 213 healthy individuals are included in the study. Different blood parameters are checked before and after the run and analyzed.

After data analysis it is observed that median age was 20 with BMI of 22.3 and SD of 0.5 (Table 1).

It is observed that there is rise in serum creatine phosphokinase (CPK) level more than 2-fold for 28.64% of people. In all, 42.25% of people has mild rise in serum levels, and the remaining has no change. After 48 hours, most of the patients showed almost normal value of CPK (Table 2).

It is observed that there is rise in serum AST/ALT ratio level for 38.03% of the people. In all, 29.58% of people have AST/ALT ratio of <1, and the remaining people have normal value. After 48 hours, most of the patients show almost normal value of CPK.

From the Table 3, it is obvious that there is no significant variation between the groups.

Discussion

The study was conducted at hospital located at southern part of India. Total 213 healthy male individuals were included in this study. After initial height and weight measurements, blood parameters were checked.

In our study, mean age was 20 with none of the candidates having obesity or underweight.

On measuring pre-run blood parameters, all candidates had normal picture. After completion of the run, there was significant alteration in blood parameters, and most of the people come to normal value within 48 hours of the run.

Table 1: Level of blood creatine phosphokinase (CPK) level on just after completion of run and after 48-hour

	>2-fold rise of CPK	*Mild rise of CPK*	*No significant rise*
After completion of run	61	90	62
After 48-hour of completion	5	23	185

Table 2: Level of bl AST/ALT ratio on just after completion of run and after 48-hour

	Rise in level of ALT, AST with AST/ALT ratio >1	*Rise in level of ALT, AST with AST/ALT ratio <1*	*No significant change*
After completion of run	81	63	69
After 48-hour of completion	14	29	170

All candidates finished their run within 55 minutes, with minimum time being 48 minutes and maximum time 55 minutes, although there is no significant difference in change of blood parameters between the groups. According to Jastrzębski et al., higher running speed has a positive correlation with elevated liver enzymes, but he did not find any correlation between the speed of run and enzyme level. In our study, we also have not found such correlation.[1]

In our study, more than 20% persons have more than 2-fold rise in blood CPK level which ultimately comes to normal within 48 hours.

Eighty-one people among the study population have rised serum AST/ALT level, and most of them come to normal within 48 hours. Sixty-three people had increase in serum ALT level initially but became normal within 48 hours.

Waśkiewicz et al.[10] reported a 14-fold increase in AST activity and a 4-fold increase in ALT activity. However, Smith et al.[11] and Wu et al.[12] observed only a slight increase in liver markers in marathon runners. In our study, we also found rise in AST level much more compared to ALT level. According to Jastrzębski et al., it was revealed that the highest level of liver enzymes activity occurred 24 hours after termination of the run.[1] But in our study, we found maximum rise in the level of liver enzymes within 4 hours of the run in most of the runners.

In our study, three people during follow-up failed to show normalization of values even after 72 hours, so we did further study.

Case Descriptions

Case 1

A 19-year-old trainee was admitted in hospital with features of disorientation following run of 14 km. On evaluation, his AST/ALT was 756/875, and CPK was elevated. So, initially he was diagnosed as a case of physical exhaustion and was managed with intravenous (IV) fluid and supportive treatment. He responded well with treatment but subsequently complained of abdomen pain, vomiting, and loose motion. On examination, he was found to have icterus and nontender hepatomegaly. Initial investigation revealed bilirubin (total/direct 7.8/4.4) with AST/ALT 839/978 IU/mL, and he was diagnosed provisionally as a case of viral hepatitis, so through evaluation was done. On further workup, viral markers were found negative. He was managed as a case of viral hepatitis, and general condition improved. Liver enzymes became normal within 15 days, but indirect bilirubin was still raised; so, further investigations were advised. PBS and USG abdomen were normal. On consultation with medical specialist, caloric deprivation test was done which revealed rise in serum bilirubin by 3.1 from 7.3 to 10.4 and also elevation of indirect bilirubin by 3.4 from 6.0 to 9.4, suggestive of underlying Gilbert's syndrome.

The cause of fluctuation in level of unconjugated bilirubin without signs of hemolysis is still not clear. In all, 25% of the patient shows normal values of bilirubin during routine follow-up, and level of bilirubin rises following stress, fatigue, reduced caloric intake, and intercurrent infections, while reduced levels of

Table 3: Number of people in each group with dearranged blood enzymes level just after completion of run

Enzymes elevated	*Group I*	*Group II*	*Group III*	*Group IV*	*Group V*	*p value*
CPK	33	23	29	29	29	>0.05
AST	14	21	23	15	17	>0.05
ALT	13	15	17	18	11	>0.05

bilirubin in patients is found with increased caloric intake. Gilbert syndrome generally diagnosed by variety of biochemical tests such as reduced UGTA activity and increased activity of bilirubin monoglucuronidase. In our case, although initially it seems to be a case of physical exhaustion, but actually physical stress or less caloric intake of the patient uncovered the underlying Gilbert's syndrome.[2,3]

Case 2

A 19-year-old trainee presented with unconsciousness following long route run of 13.5 km and was provisionally diagnosed as a case of physical exhaustion, as his CPK and liver enzymes were elevated. He was initially treated with IV fluids and supportive treatment and responded well to treatment. On investigation, CPK and liver enzymes were elevated and was normalized during the course of treatment but found deranged blood indices, his Hb was 12.4 g, MCV 63.6 fl, and MCH 20.4 pg. As his blood indices were deranged, he was advised further workup in the form of iron studies which revealed normal study. On further studies, hemoglobin electrophoresis was done which revealed raised HbA2 level. In view of the abovementioned findings, a diagnosis of thalassemia minor was made.

Thalassemia minor, a genetic disorder asymptomatic, presents with microcytosis and hypochromia with minimal anemia. Mean corpuscular volume is rarely >75 fL, hematocrit is rarely <30 33%. Hemoglobin analysis shows elevated HbA2 (3.5–7.5%) and or elevated HbF. In our case, the underlying thalassemia trait manifested following prolonged stress or fatigue may be due to increased requirement of oxygen.[2]

Case 3

A 19-year-old trainee presented with signs of physical exhaustion following long route run of 13.5 km, and his CPK and liver enzymes were elevated. He was initially treated with IV fluids and supportive treatment and responded well to treatment. On subsequent investigation, bilirubin was still elevated with normalization of liver enzymes, and peripheral blood smear shows signs of hemolysis. So on the background of physical exhaustion with signs of hemolysis clinch the diagnosis and glucose-6-phosphate dehydrogenase (G6PD) level was assessed which reveals significantly reduced level of G6PD (0.86).

Generally, G6PD-deficient individuals are asymptomatic. However, those suffering a certain type of G6PD deficiency are at risk of severe acute hemolytic anemia under the effect of oxidative stress, such as physical exhaustion. G6PD catalyzes the first reaction of the pentose phosphate pathway involving the conversion of glucose into pentose sugars while providing reducing power in the form of NADPH. The NADPH produced is crucial for the protection of cells, particularly erythrocytes, from oxidative stress. Heavy exercise can accelerate the generation of reactive oxygen species (ROS) frequently exceeding the capacity of antioxidant defenses and resulting in oxidative stress, which can induce adverse effects on health. Erythrocytes are susceptible to oxidative damage because of the high polyunsaturated fatty acid content in their membranes and the high concentrations of oxygen and hemoglobin. During exercise, where the production of ROS increases, erythrocytes are at an increased risk of oxidative damage. Several reports in the literature have shown that G6PD-deficient individuals exhibit increased oxidative stress in several tissues[4,5] that may ultimately leads to hemolysis and rise in bilirubin level in susceptible individuals.

Case 4

Nineteen year old trainee admitted in hospital with h/o altered sensorium along with 2 episodes of GTCS following 14 km run. His CPK was found elevated, 3400 IU/L and AST/ALT was 818/217. As his CPK level was elevated following run, he was diagnosed as a case of physical exhaustion and treated conservatively with IV fluids and other supportive management. After 2 days of conservative treatment his CPK became normal 186 IU/L and AST/ALT was 141/145 IU/L and he was discharged from the hospital. But within 4–5 days he developed fever, pain abdomen and diarrhea followed by progressive severe pain in muscles without any history of headache, rash, weight loss, anorexia, joint pain or Reynaud's effects. His provisional diagnosis was acute gastroenteritis and treated conservatively. But on investigation, his CPK was highly elevated 32700 IU/l and AST/ALT was 2386/ 551 IU/L and blood count was normal. For further workup muscle biopsy was done which showed intramyceal edema, margination of nuclei with scattered inflammatory cells comprises of lymphocytes and polymorphs without any myonecrosis, inclusion bodies suggestive of viral myositis. He was treated conservatively and within two weeks, his CPK became normal. Muscle soreness reduced to some extent with time and he was rehabilitated. Within one month he became symptom free and he was advised for restricted physical activity for the time being. Influenza is the most common viral etiology followed by HIV infection and enteroviral infection. The presenting symptoms in the patients whose case was reported included myalgia, weakness, muscle tenderness. Exact pathophysiology of viral myositis is not known but thought to be due direct muscle invasion causing muscle necrosis or toxin mediated. Muscle biopsies of patients with rhabdomyolysis that have shown a lymphocytic infiltrate, viral inclusions, and, recently, DNA from varicella-zoster virus was identified by PCR analysis of muscle specimens from patients with rhabdomyolysis.[7]

Conclusion

Physical exhaustion is very common among active young age population. One should be very cautious in diagnosing a case of physical exhaustion following vigorous physical activity, as there may be hidden underlying disease that may become unmasked following stress which ultimately leads to prolonged hospitalization and difficult rehabilitation. For optimal performance, and to avoid major catastrophe, it is suggested that before undergoing exhaustive physical exhaustion one should be properly evaluated.

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