



## Dead Sea Marathon-Induced Muscle Damage and Acute Oral Vitamin E Supplementation

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### ABSTRACT

**Bataineh M, Ali-Nawaiseh A, Taifour A, Judge L.** Dead Sea Marathon-Induced Muscle Damage and Acute Oral Vitamin E Supplementation. **JEPonline** 2017;20(3):1-13. Downhill running and eccentric muscle contractions provoke muscle damage. The Dead Sea Marathon has a unique race course with a 1368 m decline in elevation from start to finish. The aim of this study was to determine the magnitude of muscle damage and the effectiveness of short term  $\alpha$ -tocopherol (Vitamin E) supplementation in reducing muscle damage induced by the Dead Sea Marathon. Fourteen well-trained distance runners were randomly assigned to a control group ( $n = 7$ ) or a Vitamin E group ( $n = 7$ ). The vitamin E group was orally supplemented with vitamin E ( $400 \text{ IU}\cdot\text{d}^{-1}$ ) for 5 days (3 days pre-marathon, marathon day, and post-marathon day). Dietary and training logs were obtained and analyzed. Fluid consumption, running pace, and rate of perceived exertion (RPE) were collected for each participant before, during and immediately after the race without any significant differences between groups. During-race weight loss was significantly higher in the Vitamin E group (control:  $-5.8 \pm 0.9\%$  vs. Vitamin E:  $-6.31 \pm 0.3\%$ ;  $P=0.001$ ). Serum creatine kinase (CK) activity was analyzed 24 hrs post-race, and although values were high in both groups, no difference existed between groups (control:  $5351.6 \pm 1331.9 \text{ U}\cdot\text{L}^{-1}$  vs. Vitamin E:  $5337.3 \pm 1058.4 \text{ U}\cdot\text{L}^{-1}$ ;  $P>0.05$ ). In conclusion, the Dead Sea marathon induced high muscle damage with no protection from Vitamin E supplementation.

**Key Words:** Antioxidant Vitamins, Dead Sea Marathon, Downhill Running, Exercise Induced Muscle Damage

## INTRODUCTION

Recreational or competitive running is one of the most beneficial and most popular physical activities to improve one's well-being (25,44,45). In Jordan, the Dead Sea Marathon (42.2 km) and Ultra-Marathon (50 km) have been run annually since 1993. The racecourse itself is interesting physiologically, as it has approximately 21 km of downhill running.

Runners consider many marathons to be tough specifically because of the downhill or decline component of its racecourse. Examples of such marathon courses include St. George Marathon (Total decline: 768 m), Tucson Marathon (Total decline: 671 m), Bizz Johnson Trail Marathon (Total decline: 335 m), SteamTown Marathon (Total decline: 291 m), Whistle-stop Marathon (Total decline: 155 m), Boston Marathon (Total decline: 137 m), and California International Marathon (Total decline: 104 m). In comparison, the total decline of the Dead Sea marathon and Ultra-Marathon is 1318 and 1368 m, respectively. The downhill portion of the marathon starts after the 1st and 9th km, and the start line altitudes are approximately 900 and 950 m above sea level in the marathon and the Ultra-Marathon, respectively. Both events share the same finish line at an altitude of 418 m below sea level, namely why "Run to the Lowest Point on Earth" is the slogan for the event.

The inability to walk for days after such events is likely a result of exercise-induced muscle damage (EIMD), which is typically most evident after high intensity exercise. However, strong evidence supports the effect specifically of the eccentric component of muscle contraction as being the main cause of muscle damage (31). The EIMD contributes to fatigue and muscle soreness due to leakage of muscle content into the bloodstream that is permitted by physical disruption of the muscle membrane. This process triggers an inflammation cascade and induces irritation of the nerve endings (17,31). Furthermore, marathon running itself produces significant physiological challenges, such as depleted energy resources (31,36), dehydration, hyponatremia (12), hyperthermia, thermoregulations (11,40), oxidative stress (16,29), transient insulin resistance (20), and immune system depression (14). In the Dead Sea Marathon, the steep downhill path, the change in altitude, and the increase in temperature and humidity as the race progresses add additional stress to the challenges presented by marathon running.

Downhill running has a large eccentric contraction component resulting from the absorption of body weight in each stride when landing on one foot from a higher starting point. With longer strides, in steep downhill courses, runners clear more distance during the flight phase and this augments the impact of landing on each foot, which increases the eccentric component of running that enhances the magnitude of runners' EIMD (40). Also, since the running distance is extensive and the runners' oxidative system is the main source of energy during the run, it is expected that oxidation by-products may contribute to further muscle damage (16). Since the Dead Sea Marathon lasts around 3 hrs of racing that is mostly a downhill race course, we assumed that running this event would induce more muscle damage than other types of eccentric contractions commonly reported in literature.

Blood or urine markers are often used to evaluate EIMD. In particular, creatine kinase (CK) levels in blood are good indicators of skeletal muscle damage when measured in the CKm isoforms, and they usually peak in the bloodstream 24 to 48 hrs post-exercise (6,21,43,).

Long distance aerobic events are significantly related to increased oxidative stress that can also induce muscle damage (43).

Several researchers have suggested that Vitamin E supplementation as a preventative strategy to reduce the damage of oxidative stress that is associated with submaximal aerobic long distance events (5,16,18,39). However, since long-term supplementation with Vitamin E appears to reduce the adaptations to exercise training, such supplementation should be avoided in order to minimize the negative effects (30). Interestingly, in this regards, only a few studies have reported an effective role for Vitamin E in attenuating muscle injury associated with eccentric contractions and oxidative stress, due to its antioxidant ability to scavenge free radicals and stabilize the sarcolemma (4,23,37,38).

The Dead Sea Marathon has yet to be studied with respect to its extreme running conditions. Hence, we decided to carry out the current study with two main objectives in mind: (a) quantify the magnitude of exercise-induced muscle damage following the Dead Sea Marathon; and (b) examine possible preventative effects of the antioxidant Vitamin E on muscle damage markers induced by eccentric contractions and oxidative stress associated with Dead Sea Marathon running.

## METHODS

### Subjects

Fourteen competitive male runners (Table 1) who voluntarily participated in the Dead Sea Marathon were recruited by word of mouth to be subjects in this study. After informing the subjects about the risks and benefits of the study, they signed an IRB-approved informed consent. The recruitment process was divided into two stages.

**Table 1. Descriptive Data of the Subjects.**

Conditions	Control (n = 7)	Vitamin E (n = 7)	P-Value
<b>Age</b> (yrs)	29.8 ± 4.1	32.2 ± 2.2	0.622
<b>Height</b> (m)	1.67 ± 0.012	1.72 ± 0.19	0.04
<b>Weight</b> (kg)	61.32 ± 1.64	61.7 ± 1.3	0.861
<b>BMI</b> (kg·m <sup>-2</sup> )	22.12 ± 0.55	20.75 ± 0.25	0.064
<b>Training</b> (min·wk <sup>-1</sup> )	508.3 ± 148.3	648.4 ± 144.4	0.536

At Stage 1, only 27 of the 77 registered participants met our study's initial inclusion criteria (i.e., male, aged 20 to 39 yrs, more than 5 yrs experience in competitive distance running, previous participation in local and/or international marathons, and not ingesting any type of supplements). Twenty-two runners initially agreed to participate in the current study.

At Stage 2, we excluded 8 runners for failing to comply with the inclusion standard of this stage, which required that the runners had not practiced on the race course in the past 30 days and that pre-race CK levels were normal. The subjects were randomly and equally divided into two groups (i.e., Vitamin E Supplement and Control). All subjects reached the finish line and did not require medical care during or after the event. Blood samples were obtained 24 hrs after the conclusion of the race at a local private hospital laboratory and processed for subsequent analysis. The experimental procedure complied with The Declaration of Helsinki.

## **Procedures**

### ***Dietary Analysis***

The subjects maintained their regular dietary behavior and did not receive any nutritional advices from the research team. For dietary analysis purposes, the subjects received training from a nutritionist on how to fill and keep detailed food records for the duration of the 2-wk study. The food records were collected and analyzed using NUTRITIONEST PRO (Axxya Systems; Stafford, TX, USA), and information about essential nutrients intake was obtained for each subject. Additionally, nutritional strategies and special nutritional considerations were recorded for all subjects.

### ***Vitamin E Supplementation***

The subjects were randomly assigned to two groups. The Vitamin E group supplemented for 5 days with Vitamin E soft gels ( $400 \text{ IU} \cdot \text{d}^{-1}$   $\alpha$ -Tocopherol), which were obtained commercially. The Vitamin E group began intake of vitamin E 3 days before the event, continued on the morning of the race, and finished the following morning. The Control group did not receive any treatment (i.e., Vitamin E), and they were unaware that the second group was consuming Vitamin E.

### ***Creatine Kinase Assessment***

We determined (and research supports) that post-event CK levels peak 24 hrs post-exercise (21,31,43). Blood sampling was done in a local hospital while following a standardized procedure. A blood sample (5 mL) was drawn from the antecubital vein of the right arm into a vacutainer tube with separating gel. Samples were centrifuged for 15 min at  $2500 \text{ rev} \cdot \text{min}^{-1}$  followed by separation of serum into an Eppendorf tube. The CK values were measured enzymatically using ARCHITECT C8000 system (Abbott Diagnostics, Abbott Park, IL USA).

## **Statistical Analyses**

Normality of data was assessed by the Shapiro-Wilk test. The test of normality verified that the data were normally distributed ( $P > 0.05$ ). Results are expressed as mean  $\pm$  standard deviation (SD). Main effect was detected using a two-way ANOVA with repeated measure test (Treatment and Time). A cross-group comparison was performed using an independent *t*-test and paired *t*-tests for pre- and post-comparisons within the same group, both followed by Bonferroni adjustment for multiple comparisons when appropriate. Relationships between measured study variables were assessed using Pearson product-moment correlations (*r*). All statistical analyses were performed using the statistical package IBM SPSS statistics 20. We set the alpha level at 0.05 and accepted significance when  $P < 0.05$ .

## RESULTS

### Performance

All subjects crossed the finish line within their expected performance time. Running speed during the event ranged from 12.24 km·h<sup>-1</sup> to 19.13 km·h<sup>-1</sup>, and total time to finish the event ranged from 131.7 min to 245.0 min (Figure 1). There were no significant differences in average running speed (Control: 16.11 ± 3.8 km·h<sup>-1</sup> vs. Vitamin E: 16.16 ± 2.6 km·h<sup>-1</sup>) (Figure 1a) nor time to finish (Control: 168.1 ± 63.9 min vs. Vitamin E: 166.3 ± 43.9 min) (Figure 1b).

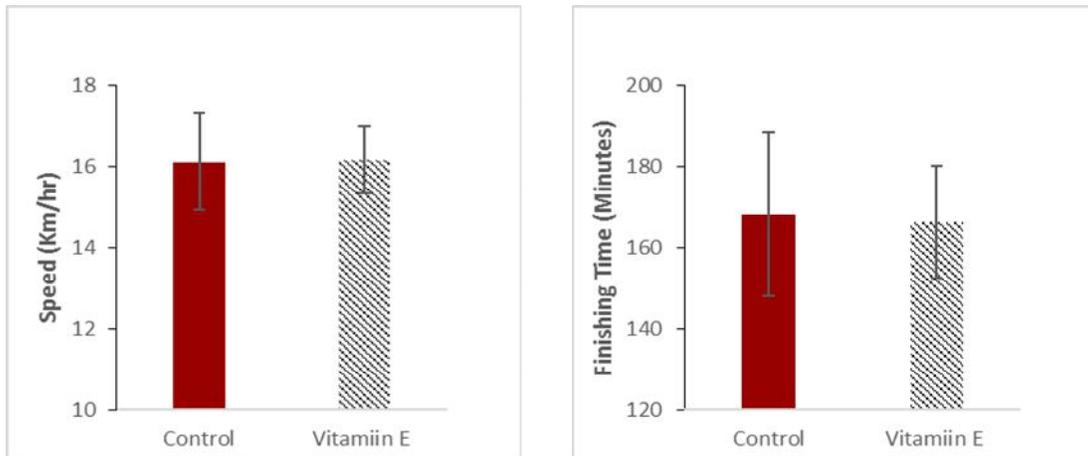


Figure 1. Running Pace and Finishing Time for Dead Sea Marathon According to Group.

The subjects' body weight was significantly reduced ( $P = 0.000$ ) from start to finish by  $3.5 \pm 0.54$  kg (5.81%) though all subjects followed their regular during-event fluid consumption protocol (1 to 1.5 L·h<sup>-1</sup>), and there were sufficient water stations evenly distributed every 2.5 km along the race course. Between-group differences in weight loss were significant (Control:  $5.8 \pm 0.9$  % vs. Vitamin E:  $6.34 \pm 0.3$ %;  $P = 0.001$ ), indicating higher sweat rate in the Vitamin E supplementation group (Figure 2).

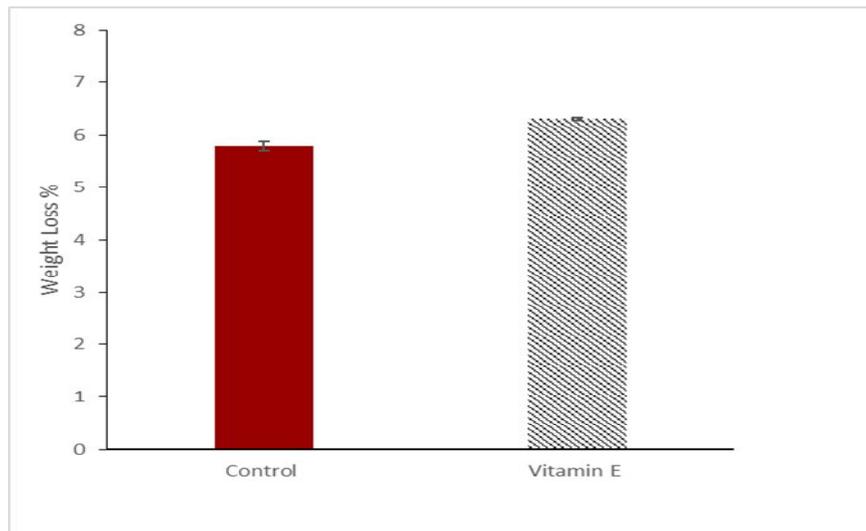


Figure 2. Percentage Weight Loss during Dead Sea Marathon.

## Energy Intake

The energy intake during the week before the event was similar among all subjects (Control:  $3154.5 \pm 174.5$  kcal·d<sup>-1</sup> vs. Vitamin E:  $3250.7 \pm 186.8$  kcal·d<sup>-1</sup>). Furthermore, percentage contributions of carbohydrates (nearly 60%), fat (nearly 25%), and protein (nearly 15%) were not significantly different between the two groups. Dietary Vitamin E consumption also was similar in both groups (nearly 30 IU·d<sup>-1</sup>). Pre-race-day energy intake was significantly reduced ( $P=0.000$ ) by ~39% when compared to previous days where there were no significant differences between groups (Table 2). Pre-race-day decreases in energy intake were distributed evenly between energy yielding nutrients.

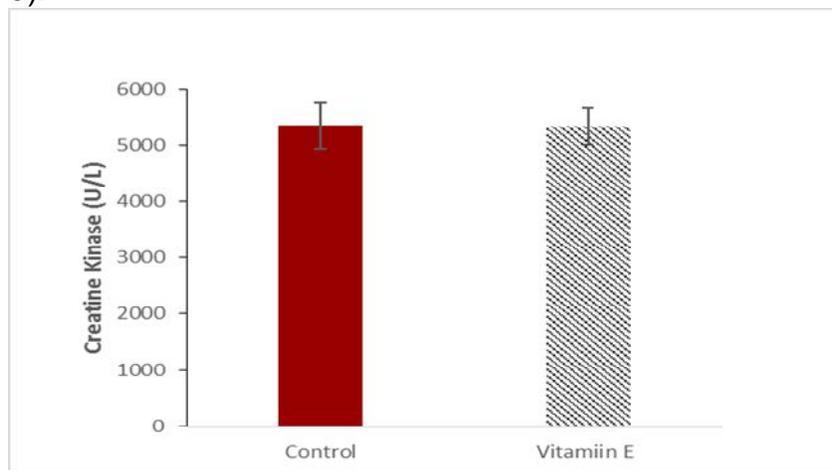
**Table 2. Measured Changes in Energy Intake during Study Period.**

Variable	Control (n = 7)	Vitamin E (n = 7)	P-Value*
<b>Regular Energy Intake</b> (kcal)	$3154.5 \pm 174.5$	$3250.7 \pm 186.8$	0.498
<b>24 hrs Pre-Race Energy Intake</b> (kcal)	$1493.4 \pm 911.5$	$2238.6 \pm 658.4$	0.543
<b>Pre-Race Energy Intake</b> (Percentage of regular intake)	$48.1 \pm 13.0$	$68.9 \pm 20.4$	0.588

\*P value for comparison between groups.

## Muscle Damage

All subjects in both the control and the supplement groups were within normal range of CK before the race. Only after the event did the subjects exceed the upper normal cutoff point for serum CK levels ( $170$  U·L<sup>-1</sup>), varying from  $927$  to  $8501$  U·L<sup>-1</sup> 24 hrs post-event. No significant correlation was detected between serum CK levels and running speed ( $r = 0.49$ ;  $P=0.15$ ), age ( $r = 0.36$ ;  $P=0.31$ ), regular energy intake ( $r = 0.69$ ;  $P=0.20$ ), pre-race day energy intake ( $r = 0.65$ ;  $P=0.24$ ) nor weekly training time ( $r = 0.006$ ;  $P=0.99$ ). Post-24-hr serum CK levels were significantly elevated in both groups (Vitamin E:  $5337.3 \pm 1058.4$  U·L<sup>-1</sup>; Control:  $5351.6 \pm 1331.9$  U·L<sup>-1</sup>) in comparison with the pre-24-hr levels ( $P=0.000$ ). However, supplementation with Vitamin E did not attenuate post-event serum CK values compared to the control group ( $P=0.98$ ) (Figure 3).



**Figure 3. Creatine Kinase (U·L<sup>-1</sup>) Post-24 hrs the Dead Sea Marathon.**

Perceived fatigue (RPE values) was similar in both groups whether assessed at the end of the race (median = 20) or after 24 hrs (median = 18) ( $P \geq 0.05$ ).

## DISCUSSION

To our knowledge this is the first reported investigation on the magnitude of Dead-Sea-Marathon-induced muscle damage. The purpose of this study was to determine the magnitude of muscle damage resulting from running a downhill marathon and the effectiveness of Vitamin E supplementation in preventing muscle damage. The main finding of the current study was an unveiling of a 20-fold to 30-fold increase in serum [CK], which is considered the highest values reported in the literature (Table 3).

**Table 3. Magnitude of EIMD Marker (CK) Post-Marathon and Eccentric Muscle Contractions.**

Author	Subjects, Gender, Age & Fitness Level	Exercise Mode	CK Assessment Timing	CK Level
Newham et al. 2004 (33)	16 M & F non-athletes	20 min stepping	NA	<400 U·L <sup>-1</sup>
Nosaka & Clarkson (34)	10 M 21.7 yrs old, activity level not reported	24 maximal eccentric actions of the elbow flexors	NA	236 IU
Goodman et al. 2014 (17)	6 (3 M and 3 F) 26.3 yrs of age, recreationally active subjects	Eccentric knee extensor exercise	24 hrs post-exercise	339 IU/L
Lippi et al. 2008 (26)	15 M, healthy trained	Half marathon (21K)	24 hrs post-	<600 IU
Del Coso et al. 2013 (13)	40 amateur runners, 34 M and 6 F	Marathon	10 min post-race	453 IU
Zbigniew et al. 2012 (47)	14 M, amateur athletes, 43 yrs of age	42 K run	Post marathon	786.9 IU
		12 hrs run	Post 12 hrs run	4,284 IU
		24 hrs run	Post 24 hrs run	17,502 IU
Kłapcińska et al. 2013 (21)	7 M, amateur runners 35-59 yrs	48 hrs run	24 hrs post-race	6277 IU

Our results cannot specify whether or not the leakage of muscle content was due specifically to the eccentric component of muscle contractions in downhill running or from the oxidative stress caused by the long aerobic exercise (19). However, we measured serum CK values in

subjects running the 21-km event, which was run on a flat race course at an altitude ranging between ~300 to 370 m below sea level and revealed though lower than marathoners' values yet higher than usual (results not shown in this study), suggesting a higher oxidative stress coinciding with hyperbaric below sea-level running conditions. In addition, no previous studies have reported a similar increase in CK levels with a marathon distance run (Table 3).

### **Downhill Component Effect**

The magnitude of the CK values in the current study has not been reported in any other marathon event or in any 24-hr or longer races (43). Thus, the current findings are likely to be attributed to the downhill component rather than the distance of the race. The steepness of the first half of the race course and the eccentric form of contraction while running in such conditions resulted in the transfer of mechanical energy to thermal energy (8,10,40). Muscle temperature also increased, causing a higher rate of reactions within the muscles with an increase in loss of water for thermoregulation. Furthermore, increased energy oxidation in the competitive setting imposes higher demands for oxygen, which when coupled with reduced plasma volume creates a situation similar to exercising under much higher intensities (8,13), thus inducing higher muscle damage than expected.

### **Hyperbaric Contribution**

In the second half of the marathon, the race course changed dramatically. This section of the race course is characterized by an almost flat running course under increased barometric pressure (800 mmHg) at an altitude of 350 to 400 m below sea level. This decrease in altitude along the race course was accompanied by an increase in barometric pressure from 763 mmHg to 800 mmHg near the finish line. The increase in barometric pressure attenuates blood flow, increases  $PO_2$ , hinders  $O_2$  kinetics, and challenges the runners' thermoregulation due to increased heat and humidity in the Jordan Valley area as compared to mountain weather (7,22,26,27,32). Additionally, oxygen toxicity caused by the increased  $PO_2$  (reaching 168 mmHg in our case) is assumed to further increase oxidative stress that leads to more muscle damage.

### **Dehydration**

The eccentric component of downhill running and shock absorption of the muscles are well-known to generate abnormal amounts of heat leading to runners' elevated sweating rate and dehydration in an attempt to maintain homeostasis and avoid hyperthermia (10). Dehydration is known to deteriorate the ability to stabilize core temperature resulting in hyperthermia, which results in Delayed Onset Muscle Soreness (DOMS) and a higher perceived pain lasting up to 48 hrs post-exercise (10). Indeed, our results revealed augmented dehydration (>5% weight loss), which might explain the magnitude of muscle damage evident through the observed high CK values and the high RPE, both immediate and 24 hrs post-race.

### **Energy Intake**

For fear of gastrointestinal problems and fatigue, the majority of distance runners fail to meet energy requirements or proper nutrition in the day preceding competition (29,35). Hence, the subjects in this study also reduced their energy and nutrient intake during the 24 hrs leading up to the race. Taking into consideration that the subjects did not receive any scientific advice about the amount and type of food to ingest from the research team might partially explain the reduced intake the day before the race. Additionally, the small sample size, which was a

major limitation in the present study, also explains the lack of significance when comparing energy intake and other energy yielding nutrient differences.

### **Supplementation**

Contrary to anticipated preventative effects of Vitamin E ( $\alpha$ -Tocopherol) supplementation in reducing EIMD, results of our study raise doubts about the effectiveness of Vitamin E as a useful agent against muscle damage induced by long distance downhill running. While we did not measure plasma  $\alpha$ -Tocopherol levels in this study, it has been well-established that supplementation with vitamin E ( $\alpha$ -Tocopherol) for five days was enough to double its levels in the plasma (46). Therefore, we are suggesting that low plasma Vitamin E levels did not affect our results. Furthermore, several studies have failed to report any beneficial effects of higher plasma Vitamin E on altering redox status of blood and muscle, as well as muscle damage resulting from long distance running or eccentric muscular contraction exercises (30,41,42). Many studies suggest that subjects should have hypovitaminosis E to detect an effect of supplementation (3,42); however, none of our subjects had hypovitaminosis at study entry, as determined by dietary analysis of their food records.

### **CONCLUSIONS**

The magnitude of Dead-Sea-Marathon-induced muscle damage is far superior to any other muscle damage reported post-marathon. It is driven by the extreme running conditions (race course and environmental factors), thus exposing the event participants to a great health burden. Though literature suggests Vitamin E supplementation as a potential ergogenic and preventative agent against eccentric EIMD, our results do not support these claims in the case of Dead Sea Marathon. Future studies are required to test effectiveness of strategies to attenuate Dead Sea Marathon EIMD.

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