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Fluid replacement following dehydration reduces oxidative stress during recovery

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ABSTRACT

To investigate the effects of hydration status on oxidative DNA damage and exercise performance, 10 subjects ran on a treadmill until exhaustion at 80% VO_{2max} during four different trials [control (C), 3% dehydration (D), 3% dehydration + water (W) or 3% dehydration + sports drink (S)]. Dehydration significantly decreased exercise time to exhaustion (D < C and S). Plasma MDA levels were significantly higher at pre-exercise in D than C. Plasma TAS was significantly lower at pre-exercise in C and S than in D, and was significantly lower in S than D at 60 min of recovery. Dehydration significantly increased oxidative DNA damage during exercise, but fluid replacement with water or sports drink alleviated it equally. These results suggest that (1) dehydration impairs exercise performance and increases DNA damage during exercise to exhaustion; and (2) fluid replacement prolongs exercise endurance and attenuates DNA damage.

Introduction

Oxidative stress is generally considered as one of the major factors leading to DNA damage. DNA damage induced by oxidative stress occurs primarily at three levels: the single/double strand level, the base/nucleotide level, and the DNA–protein crosslink level. Oxidative damages including lipid peroxidation and protein and DNA damage occur when oxidative stress caused by reactive oxygen species (ROS) exceed the antioxidation capacity of the organism [1,2].

Exercise, especially that of long duration or high intensity, and its consequent tissue injuries are known to increase ROS production in mitochondria [3,4]. Exercise can induce dehydration if lost fluid is not quickly replaced during exercise. Dehydration of 2% of body mass can impair physiological functions and exercise performance [5] by increasing heart rate and core temperature over time, decreasing cardiac output, and altering CNS function [6,7]. In order to stabilize physiological conditions and minimize the stresses on cardiovascular, thermoregulatory and neuromuscular systems, it is important to replace fluids during exercise, thus prolonging exercising ability [8,9].

Relationship between exercise performance, dehydration and rehydration has been demonstrated by many researches [10,11]. However, no study to date has investigated the effect of hydration status on oxidative stress and subsequent DNA damage during exercise.

The purpose of this study was to determine the effect of dehydration and different types of fluid replacement on exercise performance, oxidative stress, and oxidative DNA damage during rest, exercise, and recovery.

Materials and methods

Subjects. Ten healthy and moderately active men between the ages of 21 and 29 years were recruited from Yonsei University. Subjects were injury- and disease-free as determined by a health history questionnaire and physical examination. All subjects provided informed consent, and the study protocol was approved by an institutional ethics review board in the department of physical education at Yonsei University.

Preliminary tests. VO_{2max} during running was determined during a continuous, graded exercise test on a treadmill (Q65, Quinton, USA) beginning at 1.7 mph and 10% grade and increasing 0.8–1.0 mph and 2% grade every 3 min until voluntary cessation. Subjects were instructed to maintain diet and physical activity levels throughout the entire experimental period. Body composition was determined by bioelectrical impedance analysis (M310, Biodynamic, USA).

General experimental design. After the preliminary tests, 10 subjects ran on a treadmill until exhaustion at 80% VO_{2max} during four different trials [control (C), 3% dehydration (D), 3% dehydration

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followed by rehydration with water (W) or sports drink (S)] in randomized order. Each trial was separated by 5–7 days. Subjects were fed with the standardized breakfast of 450 calories (65% carbohydrates, 20% fat, and 15% protein) on the day of the trial. Dehydration was induced by sauna (10 min of heat exposure followed by 5 min of rest for a total of 3 h) to achieve approximately 3% loss of body weight. Subjects were subsequently rehydrated with either water or sports drink (Gatorade, PepsiCo. Inc., USA) prior to the exercise to compensate 3% of the subjects' weight loss. Experimental protocol is shown in Fig. 1.

Blood sampling and analyses. Blood samples were taken at rest (pre- and post-dehydration, and pre-exercise), during exercise (15 min and exhaustion), and after 60 min of recovery. At each of the blood sampling time points, malondialdehyde (MDA) levels, total antioxidant status (TAS), and lymphocyte DNA damage were determined.

(1) Plasma MDA and TAS analyses. Plasma MDA and TAS levels were determined using the BIOXVTECH LPO-586 kit (Oxis, USA) and Randox Antioxidant status kit (Antrim, UK), as described in Buckingham [12] and Miller et al. [13], respectively.

(2) Lymphocyte DNA damage analyses. As described previously by Singh et al. [14], lymphocyte DNA damage was measured using a comet assay, which shows single or double strand DNA breaks. DNA in tail (%), DNA tail length (μm) and DNA tail moment (DNA in tail × DNA tail length) were also determined.

Statistical analyses. Data are presented as means ± standard error of mean (SEM). The significance in differences of the mean values among the four trials were determined by one-way analysis of variance (ANOVA) followed by Bonferroni's post-hoc test, using SPSS 12.0 for windows. Statistical significance was set at $p < 0.05$.

Results

Exercise time to exhaustion

The exercise time to exhaustion was significantly increased for groups C and S as compared to group D ($p < 0.05$). No significant differences were found among groups C, S and W (Table 1).

Plasma MDA and TAS levels

Plasma levels of MDA [MDA] and TAS [TAS] significantly increased from pre-dehydration to post-dehydration ($p < 0.05$) (Fig. 2A and B, respectively). Plasma [MDA] and [TAS] were significantly higher at exercise-15 min ($p < 0.05$), and at exercise-15 min and exercise-exhaustion ($p < 0.05$), respectively, as compared to those of pre-exercise. Plasma [MDA] at pre-exercise was significantly higher in group D as compared to group C ($p < 0.05$). Plasma [TAS] at pre-exercise was significantly lower in groups C and S as compared to group D ($p < 0.05$) and was significantly lower at recovery-60 min in group S as compared to group D ($p < 0.05$).

Table 1
Physical characteristics of subjects. Values are means ± SEM. Group C, control; group D, 3% dehydration; group W, 3% dehydration + rehydration with water; group S, 3% dehydration + rehydration with sports drink; VO_{2max}, maximal oxygen consumption. $^{*}p < 0.05$ vs group C and S.

Variable	Groups			
	Group C	Group D	Group W	Group S
N		10		
Age (years)		25.6 ± 0.8		
Height (cm)		173.7 ± 2.8		
Weight (kg)	69.0 ± 2.4	69.9 ± 24	69.5 ± 2.5	69.6 ± 2.4
Body fat (%)	13.0 ± 1.3	14.2 ± 1.2	14.2 ± l.3	13.6 ± l.2
Fat mass (kg)	9.0 ± l.0	9.9 ± l.0	9.9 ± l.l	9.5 ± l.0
Lean body mass (kg)	60.0 ± 1.7	60.0 ± l.5	59.6 ± 1.7	60.l ± l.6
VO_{2max} (ml/kg/min)	53.6 ± 3.6	52.9 ± 3.5	53.2 ± 3.6	53.2 ± 3.5
(l/min)		3.7 ± 0.2		
Exercise time to exhaustion (min)	41.5 ± 2.5	28.0 ± l.9*	32.2 ± 2.8	40.3 ± 3.1

Lymphocyte DNA damage

Among three parameters representing lymphocyte DNA damage, tail DNA (Fig. 3A) significantly increased from pre-dehydration to post-dehydration, regardless of the conditions ($p < 0.05$), while no significant differences were seen in DNA tail length (Fig. 3B) or DNA tail moment (Fig. 3C). Exhaustive exercise significantly increased lymphocyte oxidative DNA damage (Fig. 3A–C, $p < 0.05$), regardless of the conditions. Furthermore, DNA tail moment appeared to be significantly lower in group S than in group D at recovery-60 min ($p < 0.05$).

Discussion

Exercise time to exhaustion

It is well known that excessive dehydration prior to or during exercise impairs exercising ability as it negatively affects cardiovascular and thermal control systems [8,10]. In our study, exercise time to exhaustion appeared to be significantly shorter in group D as compared to groups C and S. These results are in agreement with those of other recent studies [8,11,15], which demonstrated that a decrease in exercise performance were attributed to dehydration.

Carbohydrate supplementation is known to lead to improved exercise performance [16,17] as it is not only an energy substrate but also a mediator that activates reabsorption of electrolytes and fluid [18,19]. Therefore, it is important to maintain a certain level of both carbohydrates and electrolytes such as Na^+, Mg^{2+}, K^+

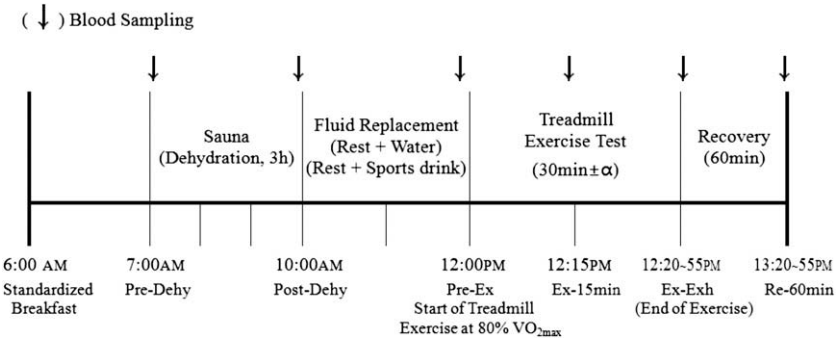

Fig. 1. Experimental protocol. Pre-Dehy, before dehydration; Post-Dehy, after dehydration; Pre-Ex, before exercise; Ex-15 min, exercise at 15 min; Ex-Exh, just prior to the termination of exercise; Re-60 min, recovery at 60 min.

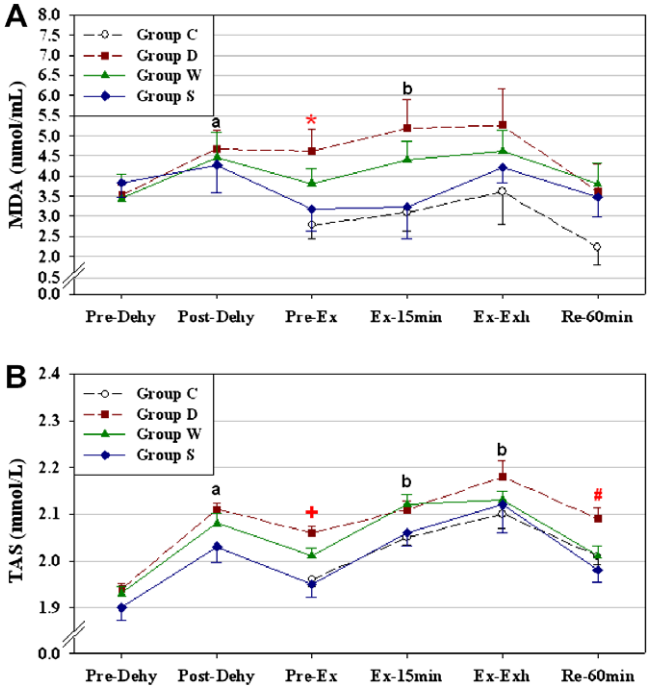

Fig. 2. Changes in plasma MDA (A), and TAS (B) levels. Values are means ± SEM. Group C, control; group D, 3% dehydration; group W, 3% dehydration + rehydration with water; group S, 3% dehydration + rehydration with sports drink. Pre-Dehy, before dehydration; Post-Dehy, after dehydration; Pre-Ex, before exercise; Ex-15 min, exercise at 15 min; Ex-Exh, just prior to the termination of exercise; Re-60 min, recovery at 60 min. $^{a}p < 0.05$ vs Pre-Dehy. $^{b}p < 0.05$ vs Pre-EX. $^{*}p < 0.05$ in group D vs group C at Pre-Ex. $^{\dagger}p < 0.05$ in group C and S vs group D at Pre-Ex. $^{\#}p < 0.05$ in group S vs group D at Re-60 min.

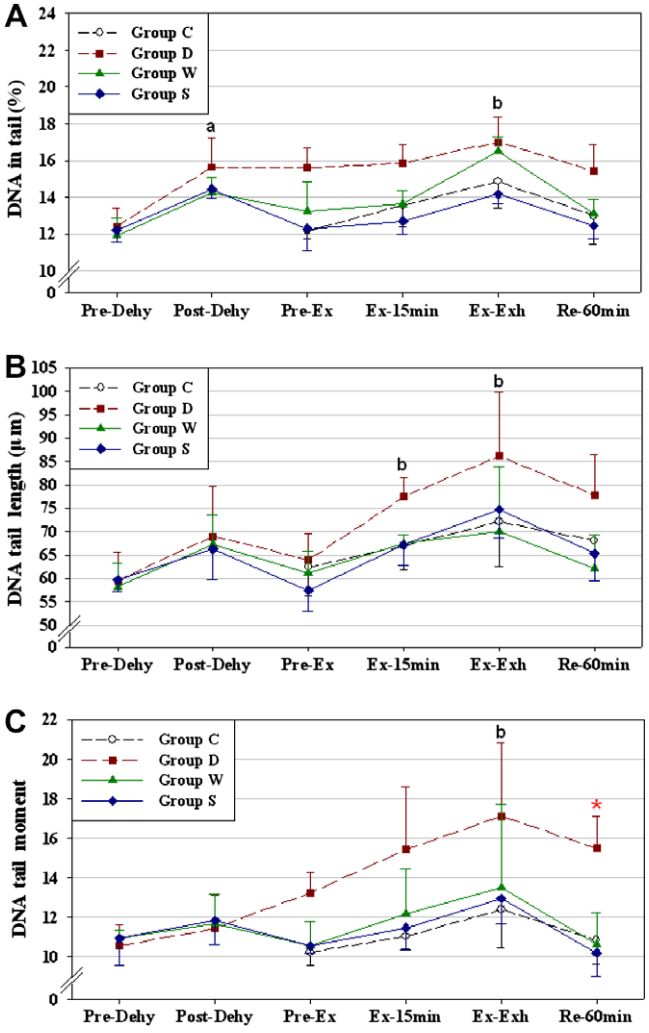

Fig. 3. Changes in lymphocyte DNA damage: DNA in tail (A), DNA tail length (B), DNA tail moment (C). Values are means ± SEM. Group C, control; group D, 3% dehydration; group W, 3% dehydration + rehydration with water; group S, 3% dehydration + rehydration with sports drink. Pre-Dehy, before dehydration; Post-Dehy, after dehydration; Pre-Ex, before exercise; Ex-15 min, exercise at 15 min; Ex-Exh, just prior to the termination of exercise; Re-60 min, recovery at 60 min. $^{a}p < 0.05$ vs Pre-Dehy. $^{b}p < 0.05$ vs Pre-Ex. $^{*}p < 0.05$ in group S vs group D at Re-60 min.

and Ca^{2+} that are essential to maintain physiological functions and body fluid levels following loss, as even a small loss can cause muscular dysfunction and exercise performance impairment [20,21]. In this study, exercise time to exhaustion in group S was significantly longer and was similar to that of group C. It is assumed that carbohydrate and electrolytes contents in the sports drink alleviated the detrimental effects of dehydration by inducing fast absorption and replacement of water and electrolytes. Relatively shorter exercise time to exhaustion in group W compared to that of group S may be due to delayed fluid reabsorption [22] and insufficient replacement of electrolyte loss from plain water ingestion during the rehydration period.

Plasma MDA and TAS levels

ROS produced during energy metabolism are usually stabilized through the oxidation–reduction reaction triggered by an antioxidant defense mechanism of the organism [23]. Overly produced ROS beyond the capacity of the defense mechanism, however, become very reactive with polyunsaturated fatty acids (PUFA), the major constituent of cell membranes, leading to the production of lipid peroxidation [4,24]. MDA, a reactive aldehyde produced when ROS degrade PUFA, is a common marker of oxidative stress [25] and is often used as a blood index of oxidative stress in response to exercise [26]. On the other hand, TAS is widely accepted as an integrated parameter of antioxidants, which reflects the balance between oxidants and antioxidants *in vivo* [27]. Previous studies have demonstrated an increased [TAS] due to oxidation stress imposed by exercise [27,28].

In this study, all individuals in the dehydration groups showed an increased [MDA] following dehydration. Group D showed a continuous increase in [MDA] until pre-exercise with a significantly higher [MDA], as compared to those in group C. On the other hand, [MDA] in groups W and S, whose subjects had a rehydration period, appeared to decrease at pre-exercise as compared to post-exercise. The results of our study using higher organisms strengthen the findings from previous studies that water deficiency in the yeast Saccharomyces cerevisiae causes an increase in the MDA level and generates lipid peroxidation [29,30].

Plasma [MDA] increased from pre-exercise to exercise-exhaustion and decreased at recovery—60 min, regardless of the conditions. This corresponds with the results from previous studies that demonstrated that ROS production increased during high intensity endurance exercise, while O_2 consumption for mitochondrial respiration increased by 10- to 20-fold [3,4].

Group D showed the highest [MDA] suggesting that a mismatch between higher O_2 demand in muscle cells and a decrease in fluid volume intake induces increased oxidation stress in muscle cells. On the other hand, oxidative stress induced by higher O_2 demand following dehydration seems to be alleviated by rehydration as seen in groups W and S. Groups W and S showed 15.5%, 17.5% and 12.4%; and 31.4%, 20.0% and 37.6% lower [MDA] than those

of Group D at pre-exercise, exercise-15 min and exercise–exhaustion, respectively. Notably, the [MDA] difference between D and S was significant at pre-exercise. Relatively lower [MDA] in group S than in group W is in agreement with the results of other studies reporting a faster recovery of plasma volume and lower degree of dehydration with sports drinks replacement as compared to water ingestion [9,31]. Accordingly, these results indicate that fluid replacement with sports drinks is more effective in relieving oxidative stress from high O_2 demanding exercise after dehydration.

Analysis of [TAS] in our study showed that all dehydrated groups had increased [TAS] post-dehydration. Noteworthy is that the [TAS] matches the [MDA] at pre-exercise, suggesting that the operation of the antioxidant system is to maintain homeostasis under oxidation stress from dehydration. It is also notable that, as was seen in group S, rehydration with sports drink resulted in a lower [TAS] at pre-exercise than was seen in group D suggesting alleviated oxidation stress. Remarkably, individuals in group S showed a significantly lower [TAS] compared to those in group D at pre-exercise and recovery-60 min, whereas the [TAS] difference between groups D and W was not significant. This result implies that sports drink ingestion more effectively contributes to the stable redox homeostasis from dehydration and exercise than ingestion of plain water.

Lymphocyte DNA damage

Lymphocyte DNA damage shown as DNA in tail appeared to be significantly higher at post-hydration compared to that at pre-dehydration, which is consistent with a previous study using a lower level organism demonstrating that oxidative stress induced by dehydration is 10 fold higher in dehydrated yeast cells than in non-dehydrated cells [32]. The results of this study on the parameters of DNA damage implies that dehydration induced by sauna-imposed oxidative stress damaged DNA by lowering body fluid volume.

Results of the current study demonstrating DNA damage parameters in all groups appeared to be higher at exercise-exhaustion compared to that of pre-exercise corresponds with results of previous studies. As reported by Niess & Simon [2], an increase in O_2 consumption in tissues during high intensity exercise resulted in excessive ROS production beyond antioxidative capacity, which subsequently damaged DNA [33]. Significant increases in DNA in tail and in DNA tail moment after exercise were also observed in a recent study that investigated the effect of prolonged high intensity exercise on DNA damage [34]. Additionally, it was found that the insufficient supply of O_2 for the increased demand by mitochondria may trigger ischemia-reperfusion mechanisms [35,36], which then may result in DNA damage [37]. It is assumed that the DNA damage seen in group D in this study increased as O_2 delivery was hindered due to abnormal blood circulation caused by dehydration, whereas the damage in group S seems to be alleviated due to the maintenance of blood volume through rapid fluid absorption. As described earlier, ingesting sports drinks containing both electrolytes and carbohydrates may curtail the time for restoring plasma volumes compared to ingestion of water following dehydration [18,38] and, therefore, decrease oxidative stress.

It is notable that DNA tail moment, the major indicator of DNA damage, decreased in groups W and S to a level similar to that in group C at pre-exercise and was relatively lower at exercise–exhaustion while continuously increasing in group D from pre-dehydration to exercise–exhaustion. At recovery—60 min group S, especially, showed a significantly lower DNA tail moment than group D, demonstrating that dehydration imposes greater oxidative stress, but fluid replacement, especially with sports drinks, alleviates DNA damage from exercise and dehydration.

In conclusion, we found that not only a single bout of exercise at 80% of VO_{2max} but also 3% dehydration by thermal effect impose oxidative stress, which subsequently causes lymphocyte DNA damage. Fluid replacement following dehydration appeared to have positive effects in maintaining physiological homeostasis and protection from oxidative stress. Furthermore, the results of this study suggest that fluid replacement with sports drinks, rather than simple water, is more effective in maintaining exercise endurance, relieving oxidative stress, and alleviating lymphocyte DNA damage.

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