Intense Walking Exercise Affects Serum IGF-1 and IGFBP3

TaeHo Kim[1,†], Jae Seung Chang[1,†], Hanul Kim[1], Kwang Ho Lee[2], In Deok Kong[1,*]

[1]Department of Physiology and Center for Exercise Medicine, [2]Department of Anesthesiology and Pain Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea

Background: Insulin-like growth factor (IGF-1) is associated with chronic diseases such as diabetes, cardiovascular disease, and hypertension, as well as muscle dysfunction. Previous studies of exercise interventions yield controversial results regarding plasma IGF-1, IGFBP3, and IGF-1/IGFBP3 ratio. In this study, we examined whether 100 km walking exercise affects serum levels of IGF-1 and IGFBP3 and IGF-1/IGFBP3 ratio. We also investigated several metabolic-related blood parameters before and after walking.

Methods: Participants were 14 healthy middle aged men (41.0 ± 6.78 years of age). We assessed body composition and measured metabolic-related blood indicators, such as such as lipid profiles, glucose, renal and hepatic metabolic bio-markers before and after a 100 km walking race. Blood samples from all participants were taken before and immediately after the walkathon. We also analyzed serum levels of IGF-1 and IGFBP3, and calculated the IGF-1/IGFBP3 ratio.

Results: After participants completed a 100 km walking race, some of their metabolic profiles were markedly changed. Serum levels of IGF-1 and IGFBP3 were significantly decreased, and therefore the IGF-1/IGFBP3 ratio also decreased before and after 100 km of walking.

Conclusion: Our results indicate that intense walking exercise affects serum levels of IGF-1 and IGFBP3 as well as metabolic bio-markers including high density cholesterol, glucose and triglycerides.

Key Words: IGF-1, IGFBP3, Walkathon

INTRODUCTION

Sedentary lifestyles and lack of physical activity have led to increases in mortality and chronic diseases such as hypertension, type 2 diabetes, and obesity. Lack of activity is also closely associated with elevated incidences of cancers. Regular physical activity improves diverse health conditions such as diabetes and cardiovascular disease [1-4]. Walking is a relatively simple and safe type of exercise with many health benefits. It is known to reduce the risk of heart disease and can help prevent dementia, depression, and Alzheimer's disease. Some findings suggest that walking exercises improve both mental health and quality of lifestyle [5]. However, the physiological and pathophysiological effects of extreme exercise are not fully understood. Some previous studies have reported that prolonged moderate intensity walking caused muscular injury and injury to the ankle and knee [6]. Several studies have demonstrated that prolonged strenuous physical exercise can induce hydration, severe electrolyte abnormalities, dysfunction of heart and kidney, and myocardial infarction causing sudden death [7].

Insulin-like growth factor (IGF-1), also called somatomedin C, is synthesized in the liver and is regulated by pituitary growth hormones which plays a major role in cell growth, cell development, and energy metabolism. IGF-1 se-

cretion causes hypoglycemia by glucose uptake and is synthesized by the liver and pituitary hormone. A number of studies have shown that impaired liver function causes decreases in IGF-1 secretion [8,9]. IGF-1 affects growth hormones (GHs) whose deficiencies are related to kidney dysfunction. Various studies showed that IGF-1 levels are correlated with metabolic diseases such as type 2 diabetes, hypertension, and insulin resistance. Insulin-like growth factor binding protein 3 (IGFBP3) is a family of IGFBP encoded by the IGFBP3 gene. IGFBP3 binds to IGF-1in the blood. Recently, IGF-1 and IGFBP3 have been found to affect energy balance, body weight, and body fat mass. Decreased serum levels of IGF1 are associated with energy balance and body composition in rhythmic gymnastics athletes [10]. Cumulative studies argue the effects of exercise intervention associated with plasma levels of IGF-1 and IGFBP3. It has been known that exercise increase IGF-1 secretion [11,12] with inconsistent results with relevant studies [13,14].

Long-distance (100 km) walking is an extreme sport that is becoming more popular. It is one of the most usable and accessible forms of physical activity. Nevertheless the effects of long-distance walking are not known. There are few previous studies regarding the effects of prolonged exercise, such as swimming and marathon running, and the associated physiological changes remain unclear. In the present study, we investigate the effect of intense exercise on metabolic hepatorenal indicators including serum IGF-1 and IGFBP3.

MATERIALS AND METHODS

1. Subjects and study protocol

The subjects were recruited among the participants of a 100 km walk festival in W city. All subjects were healthy middle aged men (Table 1). All participants completed an essential medical questionnaire, medical history check-up,

and body composition analysis 1 hour prior to the start of the race. Only 14 of 20 subjects completed the race, while the remaining 6 failed to complete all 100 km. The race began at 2:00 p.m., and the average finishing time was 21 hours. The participants were allowed to ingest water and food freely on their own time during the event.

2. Blood sampling and analysis

Blood samples from all participants were obtained through the antecubital vein immediately before and after walking. Blood samples were centrifuged at 3,000 rpm for 10 min and metabolic profiles were measured with an automatic chemical blood analyzer (Samsung® IVD-A10A, Korea). The serum IGF-1 and IGFBP3 levels were also measured with IGF-1 and IGFBP3 ELISA kits.

3. Data analysis

All data were analyzed using the SPSS 19.0 software. Descriptive statistics were calculated to identify the means and standard deviations. Before and after prolonged moderate intensity walking, data analyses were performed using a Wilcoxon signed rank test. Statistical significance was set at $p < 0.05$. IGF-1 and IGFBP3 serum levels and IGF1/IGFBP3 ratios were calculated as dependent outcomes. The molar ratio was obtained as follows: IGF-1/IGFBP3 = [IGF-1 (ng/mL) $\times$ 0.13] / [IGFBP3 (ng/mL) $\times$ 0.036] [15].

RESULTS

Data values were represented as the mean $\pm$ SD, before and after the 100 km walk. The subjects' weights (66. 6 $\pm$ 5.1 vs 65.6 $\pm$ 5.0 kg; $p < 0.001$) and %body fat (23.9 $\pm$ 8.5 vs 18.8 $\pm$ 5.53%; $p < 0.05$) were significantly decreased after the 100 km walking. Serum biomarkers indicating liver function including ALT, AST, BUN and total bilirubin were increased after the 100 km walk (Fig. 1). Next, hemodynamic factors such as systolic blood pressure,

Table 1. Physical characteristics of participants

	n	Age (yr)	Height (cm)	Weight (kg)	BMI (kg/m^2)	%BF (%)
Participants	14	41.8 $\pm$ 6.8	165.5 $\pm$ 5.5	58.2 $\pm$ 11.2	23.7 $\pm$ 2.0	23.8 $\pm$ 8.5

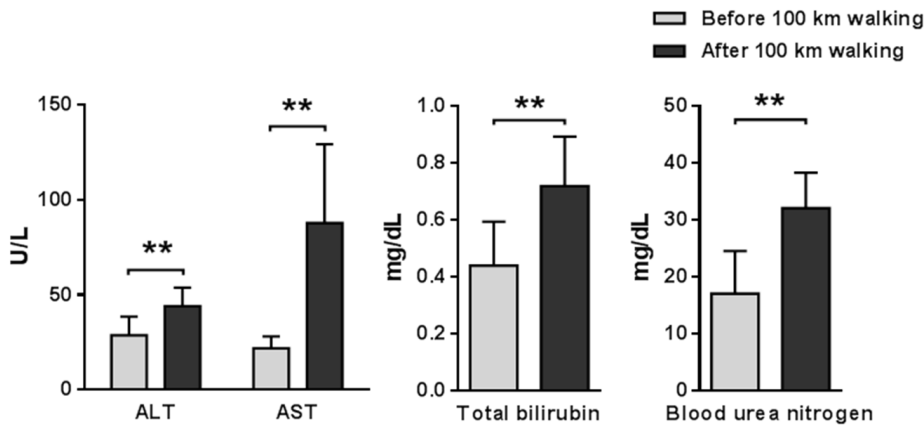Values are mean $\pm$ S.D., BMI: body mass index, %BF: percent body fat.

Fig. 1. Changes in metabolic indicators of the liver and kidney before and after 100 km walking.

diastolic blood pressure, and heart rate were examined before and after 100 km walking. Whereas systolic blood pressure (133.0 ± 13.7 vs 122.3 ± 9.8 mmHg; $p < 0.05$) and diastolic blood pressure (85.0 ± 8.9 vs 76.8 ± 4.2 mmHg; $p < 0.05$) were decreased, heart rate (75.1 ± 16.6 vs. 91.6 ± 13.4 beats/min; $p < 0.001$) was increased after the 100 km walking. In addition, we analyzed several metabolic-related blood factors. Blood glucose, insulin, and triglyceride were significantly decreased, while high-density lipoprotein was significantly increased after walking 100 km (Fig. 2 and 3). However, serum level of total protein, total and low-density cholesterol, γ-GTP, creatinine, and albumin were not altered after walking. IGF-1 and IGFBP3 and IGF-1/IGFBP3 ratio levels were significantly decreased after 100 km walking (Fig. 3).

DISCUSSION

In this study, we examined the effects of 100 km walking exercise on the serum concentration of IGF-1 and IGFBP3 and the IGF-1/IGFBP3 ratio. The IGF-1/IGFBP3 ratio is also an important factor for the assessment of IGF-1 and IGFBP3 [15]. Previous studies demonstrated that exercise influences circulating IGF-1 and IGFBP3 which are depend on exercise intensity and types. In most studies, exercise interventions led to increases in IGF-1 and IGFBP3 secretion [12,16], however, some reports argue that IGF-1, IGFBP3, and the IGF-1/IGFBP3 ratio were decreased or not affected by exercise interventions [14,17]. Circulating serum levels of IGF-1 and IGFBP3 are associated with both aging and exercise [18,19]. Moderate intensity treadmill exercise led
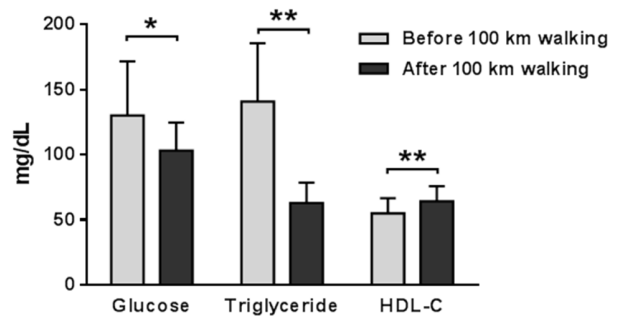

Fig. 2. Changes in bio-markers of glucolipid-metabolism before and after 100 km walking.

to increases in IGF-1 in both young and old animals [19,20].

Interestingly, the serum IGF-1, IGFBP3, and IGF-1/IGFBP3 ratio were significantly decreased in our study. Many studies have reported that long-duration moderate exercise results in the decrease of insulin, glucose, triglyceride, total cholesterol, and low-density lipoprotein, and the increase of high-density lipoprotein [21]. We also found that 100 km walking exercise caused decrease of insulin, glucose, and triglyceride, while high-density lipoprotein level was increased. We also observed decreased blood glucose and insulin and increased serum level of indicators for hepatorenal function such as ALT, AST, BUN and total bilirubin. IGF-1 is produced in the liver and function as an endocrine hormone that is regulated by glucose and insulin independently of caloric restriction such as fasting and protein supplementation [22]. Our results suggest that intense walking may decrease serum level of insulin and glucose induced by decrease of serum IGF-1 and IGFBP3. We allowed subjects ingestion of food and water freely during walking which
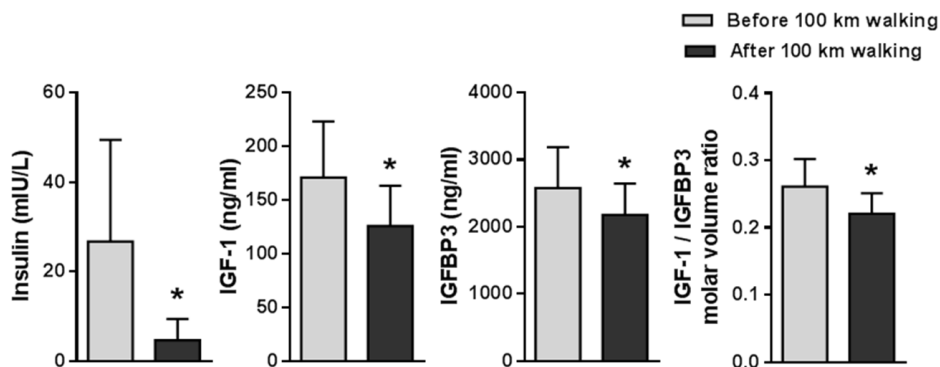
Fig. 3. Changes in insulin, IGF-1, IGFBP3 and IGF-1/IGFBP3 before and after 100 km walking.

may affect the IGF-1 and IGFBP3 levels. Energy intake was not analyzed in the present study that should be considered for prolonged walking exercise in future studies.

Exercise intensity and time are important factors governing the beneficial effects of exercise on body function. Most studies have detected negative effects of long-duration exercise such as marathons and ultra-marathons [23]. Generally, excessive exercise impairs body functions such as kidney and liver [24,25]. In our study, hepatic markers such as ALT and AST markedly increased in blood samples after completing a 100 km walking. Impaired liver function might lead to decrease of IGF1 and IGFBP3 levels through functional impairments of gluconeogenesis.

Generally, increased level of HDL-c is known to prevent obesity and enhance vascular function through improved transportation of LDL-c to the liver. In addition to exercise-induced decrease of triglyceride, other benefits have been observed in terms of ischemic vascular events [26]. Recent studies have demonstrated that decreased level of IGF-1 is associated with reduced body weight and fat mass. It should be noted that decreased IGF-1 level affects obesity after exercise regardless of intensity, type, or time of exercise. We found that 100 km walking exercise led to decreased and increased level of triglyceride and high- density lipoprotein, respectively, suggesting that IGF-1 and IGFBP3 associated with metabolic biomarkers with additional benefits. The effect of exercise on IGF-1 secretion in the context of energy supplementation and exercise intensity, type, and time awaits future investigation.

ACKNOWLEDGEMENTS

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