Effect of Ginger Supplementation and EnduranceTraining on Serum Levels of IL-1α and TNF-α

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Received : 08 Aug 2015
Revised: 12 Aug 2015
Accepted: 07 Nov 2015

ABSTRACT

Background and Objective: Exercise training and supplementation have different effects on the immune system. The aim of the present study was to evaluate the effect of ginger supplementation and endurance training on serum levels of Interleukin 1 alpha (IL1α) and tumour necrosis factor α (TNFα) in untrained young women.

Methods: The study was performed on 32 untrained young women with mean age of 30±2 years from city of Abbas Abad, in 2014. The participants were randomly assigned into four groups of endurance training (E), endurance training and ginger supplementation (EG), ginger supplementation (G) and control (C). Endurance training was performed at 60-70% heart rate reserve for six weeks, three times a week, and for 60 minutes per session. Daily supplementation with 10 mg/Kg/day of ginger extract was carried out. T-test and ANOVA were used to evaluate the effect of independent variables, and make comparisons between the groups.

Results: The mean level of IL-1α decreased significantly after the training period in the G and EG groups. There were significant differences between E and EG groups and EG and C groups. The results of intergroup comparison showed that the mean levels of TNFα decreased significantly after the training in the E, G and EG groups. There were significant differences between E and EG groups, E and G groups, EG and C groups, and G and C groups.

Conclusion: Ginger consumption and adaptation to endurance training can counteract the negative effects on immune function and stability of mast cell membrane.

Keywords: Endurance Training, Ginger, IL-1alpha and TNF-alpha.

This paper should be cited as: Barari AR[Effect of Ginger Supplementation and EnduranceTraining on Serum Levels of IL-1a and TNF-a]. mljgoums. 2016; 10(4): 58-63

INTRODUCTION

Cytokine response may vary depending on exercise type, intensity, duration, recovery duration between bouts and training status. Cytokine production can also be affected by other physiological factors of exercise such as stress hormones, acidosis, oxidative stress, and heat. The present study focuses on the cytokine response to endurance training (1). Endurance training has been introduced as a model of stress response. Several studies have reported that exercise induces an acute phase response, which has some similarities to the acute phase response to sepsis and trauma (2). Cytokines facilitate an influx of lymphocytes, neutrophils, monocytes and other cells, which participate in antigen clearance and healing (3). The local inflammatory response is accompanied by a systemic response known as the acute phase response. Infusion of Interleukin1α (IL-1α) in humans will result in fever, but does not cause shock or capillary leakage-like syndrome as observed with the prototypical proinflammatory cytokines such as IL-1α and tumour necrosis factorα (TNF-α.). Unlike IL-1 and TNF-α, IL-6 does not upregulate major inflammatory mediators such as nitric oxide or matrix metalloproteinases (4). Ginger is a medicinal plant with anti-inflammatory properties that has been used in Asia and tropical countries for treatment of asthma, diabetes, nausea, and pain. It is classified as a food additive by the Food and Drug Administration (5, 6). The plant is important in traditional medicine, particularly for treatment of inflammation (7, 8). Several studies have shown that ginger extract balances immune response to intense inflammation (8). The plant has analgesic properties due to presence of acetic acid (6-8), and can inhibit prostaglandins, nitride oxide and even interleukins productions, which are involved in inflammation process (8, 9). The other reasons for the anti-inflammatory effects of ginger could be the inhibitory effects on lipoxygenase activity and arachidonic acid metabolism. Due to its antioxidant activity, this plant is also useful for protection against cancer (10, 11). Ginger has strong antimicrobial components, which are effective against influenza. This medicinal plant triggers the production of sweat that can excrete viruses and cut shorter the period of influenza. Furthermore, it can be used to reduce the accompanying pain associated with influenza (9-11). It also strengthens heart muscles and reduces blood pressure. Its anti-flatulence property is also effective in preventing stomach ulcer (12). Cytokines are proteins that are secreted by specific cells of immune system. They are produced in response to microbes and other antigens. Different cytokines stimulate various responses in cells involved in immunity and inflammation. Cytokines stimulate growth and differentiation of lymphocytes in activation of the immune response (11, 12). The results of studies on the effect of training on cytokine response have been inconsistent (13). In some studies, training and ginger consumption increased cytokine levels (12, 13), while another study reported no significant change in cytokine levels after training (14). A study showed that one-year of endurance training in women caused a steady increase in their cytokines' levels. Cytokine levels appear to be unaffected by training, which indicates that they may be a sensor of negative energy balance as suggested previously (13, 14). All studies performed so far have measured total cytokines in acute training (12-14), which is a limitation of these types of studies. Hypothesized role of cytokines in the adaptive response to inflammation would be better supported if cytokine levels were changed in endurance training. The present study aimed to evaluate the effect of ginger supplementation on pro-inflammatory cytokines (IL-1a, TNF-α).

MATERIAL AND METHODS

This semi-experimental study included 32 sedentary women (mean age: 32 ±2 years) from city of Abbas Abad who were randomly assigned into four groups of endurance training (E, n=8), training and ginger supplementation (EG, n=8), ginger supplementation (G, n=8) and controls (C, n=8), stratified by body mass index (BMI). After the intervention, participants in the E, EG and G groups experienced significant weight loss (n=8). The participants were sedentary at baseline, as defined by 40 min selective endurance training for six weeks. They were non-smokers and free from gastrointestinal, cardiovascular, or metabolic disorder. All participants in the E and EG groups performed 40 min of endurance training, three days per week at 60-70% maximum heart rate reserve (15, 16). The participants were required to attend all

sessions during the intervention. Daily consumption of 10 mg ginger per kg of body weight was monitored throughout the study (15, 16). The weight and height were measured using a balance beam scale and studio meter to the nearest 0.1 Kg and 0.1 cm, respectively. BMI was calculated as the weight in kilograms divided by the square of the height in meters (Kg/m^2). After 12h over-night fasting in pre- and post-test stages, blood sampling was done for cytokine analysis. Plasma levels of cytokines were measured by commercially available ELISA kits. All results were expressed as means ± standard deviation (SD). Independent t-test was used to compare baseline descriptive characteristics between the three test groups and the control group. T-test and ANOVA were used to evaluate the effect of independent variables, and make comparisons between the groups. Scheffe's test was used to determine significant changes in the variables between the groups. Statistical analysis was performed using SPSS Software and p-values less than 0.05 were considered as statistically significant.

RESULTS

Body weight and BMI decreased significantly in the E and EG groups ($\alpha \leq 0/05$). VO_2 max showed no increase in the E, EG and G groups ($\alpha \geq 0/05$). IL-1α level decreased significantly in the EG and G groups (P=0/002, P=0/021). The mean of variables in the E, EG and G groups had significant differences after the intervention (P=0.001, P=0.007, P=0.004) (Tables 1 and 2). Furthermore, there were significant differences in the level of IL-1α between the four groups (p= 0.000). The Scheffe's test showed a significant difference between E-EG and EG-C groups. There was a significant difference in the level of TNF-α between the four groups (p= 0.000). The Scheffe's test indicated a significant difference between E-EG, E-G, EG-C and G-C groups.

Table 1- Characteristics of subjects in the study groups

P-value	After training Mean ±SD	Before training Mean ±SD	Group	Characteristic
-	30.12 ± 7.1	30.12 ± 7.1	E	
-	30.28 ± 9.1	30.28 ± 9.1	EG	Age
-	29.6 ± 3.2	29.6 ± 3.2	G	
-	30 ± 8.2	30 ± 8.2	C	
-	1.60 ± 7.5	1.60 ± 7.5	E	
-	1.60 ± 3.4	1.60 ± 3.4	EG	Height (m)
-	1.61 ± 7.2	1.61 ± 7.2	G	
-	1.57 ± 5.1	1.57 ± 5.1	C	
0.026	74.8 ±4.9	75.8 ± 8.9	E	
0.004	73.5 ± 3.7	77.7 ±9.8	EG	Weight (kg)
0.064	77.1 ± 8.7	79.5 ±7.8	G	
0.545	69.9 ±3.8	69.5 ± 3.7	C	
0.686	39.7 ± 7.1	39.5 ± 4.1	E	
0.098	39.69 ± 6.1	38.7 ± 7.2	EG	VO_2max
0.20	37.7 ±7.3	37.4 ± 6.3	G	(ml/kg/min)
0.59	38.7 ± 5.2	38.9 ± 2.2	C	
0.025	28.9 ± 3	29.25 ± 3.3	E	BMI
0.003	29.11 ±2.9	30.74 ± 3.3	EG	($Kg.m^2$)
0.10	29.33 ± 4	29.46 ± 3.7	G	
0.43	28.45 ±5.3	28.27 ± 4.8	C	

Table 2- Dependent variables before and after the training intervention

P-value	After training M±SD	Before training M±SD	Group	Variable
0.12	8.15± 2.29	8.7 ± 1.6	E	
0.002	4.8± 1.47	8.1 ± 2.17	EG	IL-1a
0.021	6.1 ± 2.5	7.7 ± 2.5	G	(Pg/ml)
0.929	8.94 ± 1.29	8.9 ± 1.34	C	
0.001	92.27 ± 36	103.6 ± 36	E	
0.007	32.7 ± 12.4	90.4 ± 35.3	EG	TNF-a
0.004	78.9 ± 19	116.4 ± 30	G	(Pg/ml)
0.398	97.9 ± 41.6	103.03 ± 31	C	

DISCUSSION

The present study investigated the effects of endurance training and ginger supplementation on pro-inflammatory cytokines. Ginger consumption significantly affected bodyweight and BMI in the E and EG groups ($P < 0.05$). VO_2 max improvement after endurance training may be attributed to attenuated levels of oxidative stress, which in turn may reduce cytokine expression. Previous studies on healthy older adults showed that endurance training programs are more effective in improving VO_2 max than a continuous diet that produces greater cumulative oxidative stress (8, 16). In this study, VO_2 max was not significantly changed in the training groups that received a reasonable volume of exercise to elicit functional capacity changes. A limitation of the present study was the lack of evaluating frequency (sessions/week), duration (number of weeks), and intensity of trainings that have greater effects on VO_2 max levels. Ginger supplementation reduced IL-1 α and TNF-α level in untrained women. The level of IL-1α decreased significantly in the G and EG groups, while TNF-α decreased significantly in the E, EG and G groups. Studies have shown that exercise training can increase cytokine levels in athletes (16, 17). Adequate nutrition can help neutralize the adverse effects of endurance training on immune function (15-17). However, a study has suggested that IL-1α produced by exercising muscles, exerts an anti-inflammatory effect (5, 8). These findings suggest that production and removal of TNF-α and IL-1α may have relatively independent mechanisms and effects (inflammatory or anti-inflammatory) (18). Daily supplementation of ginger causes a reduction in acute-phase inflammatory response. Considerable evidence support the anti-inflammatory activity of ginger and its constituents (especially gingerols, shogaols, paradols, and zingerones) in reduction of *TNF-α and IL-1 α* gene expression (6,14) and inhibition of cyclooxygenase 1 and 2 (7,14,16). These well-established biological actions suggest that consumption of ginger could block the IL-1α increase (8, 18). Endurance training increases cytokine expression in the skeletal muscles. Several studies suggest that a sudden imposition of a training program which is associated with substantial increase in energy expenditure leads initially to an increase in pro-inflammatory cytokines (3, 8, and 13). Although the mechanisms underlying exercise-associated immune changes are multifactorial, it is worth mentioning that supplementation with nutrients such as glutamine, carbohydrate, antioxidants, or prostaglandin inhibitors may affect exercise-associated changes of the immune function (7, 16, and 18).

Strenuous exercise is thought to cause a 2- to 3-fold increase in concentrations of TNF-α (8, 19). Although the mentioned studies suggested that the level of cytokines may increase in response to exercise, other studies have shown a decrease, no increase and/or only a modest increase (2, 5, 16). Certain amount of free cytokines are released and rapidly excreted during physical activity. Increased level of IL-1α in damaged skeletal muscle after exercise indicates the role of this cytokine in the inflammation process and damaged skeletal muscle repair (9, 14, and 18).

The results of the present study showed that IL-1α decreased significantly in the EG and G groups, while TNFα decreased significantly in the E, EG and G groups. Endurance training significantly reduces the expression of TNF-α and IL-1-α in skeletal muscles of young women. It also improves both basal endothelial nitric oxide formation and agonist-mediated endothelium-dependent vasodilation of the skeletal muscle vasculature in untrained women. There is a correlation between endothelium dysfunction and significant increase in exercise capacity (5, 8, and 19). Studies showed that one hour of water polo training in young females (average age of 14-16 years old) increases IL1-α and IL-6 levels. However, the amount of TNFα decreases significantly after the training leading to an increase in lymphocyte and monocytes (6, 15, and 17). The present study showed that cytokine levels decrease after six weeks of endurance training and ginger consumption. Sirvan et al. recently reported that ginger could reduce inflammation either with or without endurance training (16). Several studies have shown that active components of ginger are capable of producing prostaglandin, nitride oxide and even interleukins, which are involved in the inflammation process. Thus, ginger inhibits the activity of enzymes

involved in inflammatory response. A study evaluated the effect of ginger supplementation on nonathletic girls after one session of training, and reported that ginger contains compounds with anti-inflammatory potential (14) that could inhibit the production of cytokines in active macrophages (11). It has been reported that ginger contains compounds that block prostaglandins' synthesis (7, 18). Consistent with previous studies, the present study reported that ginger consumption with or without endurance training decrease cytokines. Further studies are required to examine the effect of endurance training, trauma and infection on novel cytokines. It is also essential to elucidate the significance of cytokine regulation via physical activity and the effects of short- and long-term physical activity on the immune function and health (19, 20). Previous studies on the alteration of immune response by endurance training have shown that training increases cytokines in athlete's body, but supplementation may neutralize the adverse effect of high intensity activity on the immune function. Cytokines' reduction following endurance training in the participants of the present study had beneficial effects. Decreased level of IL-1α in damaged skeletal muscle after endurance training indicates the role of this cytokine in the inflammation process and reduction of muscle damage (5, 17, and 20).

CONCLUSION

In addition to the beneficial effects on exercise capacity, endurance training has anti-inflammatory effects on untrained women. Decreased level of IL-1α may indicate the important role of this cytokine in tissue repair following endurance training. Alteration of anabolic and catabolic hormones and inflammatory mediators' balance during the training exercise may help elite athletes and coaches in preparation for competitions.

ACKNOWLEDGEMENTS

The author would like to thank all the participants and colleagues who cooperated in this study.

CONFLICT OF INTEREST

We have no conflict of interest to declare.

REFERENCES

1. Ramadan G, Al-Kahtani MA, El-Sayed WM. *Anti-inflammatory and anti-oxidant properties of Curcuma longa (turmeric) versus Zingiberofficinale(ginger) rhizomes in rat adjuvant-induced arthritis.*Inflammation. 2011;34(4):291-301.doi: 10.1007/s10753-010-9278-0.

2. KochAJ. *Immune Response to Exercise.*Brazilian Journal of Biomotricity. 2010; 4(2): 92-103.

3. Abdullah Al-Nahain,1Rownak Jahan,2 and Mohammed Rahmatullah1. Zingiberofficinale: A Potential Plant against Rheumatoid Arthritis. Volume 2014. ID 159089, 8 pages.

4. ChangHY,Sheu MJ, Yang CH, Lu TC,Chang YS, PengWH,et al. *Analgesic Effects and the Mechanisms of Anti- Inflammation of Hispolon in Mice.*Evid Based Complement Alternat Med. 2011;2011:478246. doi: 10.1093/ecam/nep027.

5. Denguezli-BouzgarrouM,Jabrallah MB, Gaid S, TabkaZ.*Effects of brief maximal training on interleukin-6 and tumor necrosis factor-alpha.*Biology of sport. 2006; 23(1):3-15.

6. GrzannaR, PhanP,Polotsky A, LindmarkL,Frondoza CG. *Ginger Ttract inhibits beta- amyloid peptide induced cytokine and chemokine Tpression in cultured THP-1 monocytes*. J Altem complement Med. 2004;10(6):1009-1013.

7. Haghighi M, KHalvat AT, Toliat T, JallaeiS. *Comparing the Effects of Ginger (ZingiberOfficinale) Ttract and Ibuprofen on Patients with Osteoarthritis.*Archives of Iranian Medicine.2005;8(4):267-271.

8. Ostrowski K, Rohde T, Asp S, Schjerling P, Pedersen BK.*Pro-and anti-inflammatory cytokine balance in strenuous training in humans.*Journal of physiology.1999;515(1):287-291.

9. Mahluji S, Ostadrahimi A, MobasseriM,EbrahimzadeAttari V, Payahoo L. *Anti-Inflammatory Effects of ZingiberOfficinale in Type 2 Diabetic Patients.*Adv Pharm Bull. 2013; 3(2): 273-276. doi: 10.5681/apb.2013.044.

10. SeaidSM, Barari A, AlaviSH. *Effect Of Short-Term Resistance Training And Silymarin Consumption On Some Of Preinflammatory Cytokines, Growth Mediators And Immune System Performance*. Australian Journal of Basic and Applied Sciences. 2012; 6(9): 73-77.

11. Lantz RC, Chen CJ, Sarihan M, Solyom AM, Jolad SD, TimmermannBN. *The effect of Ttracts from ginger rhizome on inflammatory mediator production.*phytomedicine.2007; 14(2-3):123-128.

12. LevyASA,SimnoO,Shelly J, Gardener M.*6-Shogaol Reduced Chronic Inflammatory Response in the Knees of Rats Treated with Complete Freuns,sAdjuvant.*Biomed Central.Pharmacology.2006;6: 12-20.doi:10.1186/1471-2210-6-12.

13. Ojewole JA. *Analgesic, anti-inflammatory and hypoglycemiceffects of ethanol Ttract of Zingiberofficinale (Roscoe) rhizomes (Zingiberaceae) in mice and rats.*Phytother. 2006; 20(9):764-772.

14. PhanPV, SohrabiA, Polotsky A, Hungerford DS, Lindmark L, FrondozaCG.*GingerTtract components suppress induction of chemokine Tpression in human synoviocytes*. J Altern Complement Med.2005;11(1):149-154.

15. barari A. *Endurance training and ginger supplement on TSH, T3, T4 and testosterone and cortisol hormone in obese men*.Persian Journal of Medical Sciences,Vol:3,no:1.96-103.

16. AtashakS, PeeriM, Azarbayjani MA, Stannard SR, MosalmanHaghighiM.*Obesity-related cardiovascular risk factors after long- term endurance training and ginger supplementation*. Journal of Sports Science and Medicine.2011; 10(4): 685-691.

17. Thissenjp. *How proinflammatory cytokines may impair growth an cause muscle wasting*. Hormone research.2007; 67(1): 64-70.doi:10.1159/000097555.

18. Tripathi S, Majer KG, Bruch D, KitturDS.*Effect of 6-Gingerol on pro- inflammatory Cytokine production and Costimulatory molecule Tpression in Murine peritoneal Macrophages*.Journal of surgical Research.2007; 138(2): 209-213.

19. Chatzinikolaou A, Fatouros IG, Gourgoulis V, Avloniti A, Jamurtas AZ, Nikolaidis MG, et al. *Time course of changes in performance and inflammatory responses after acute plyometric exercise.* J Strength Cond Res. 2010;24(5):1389-98.doi: 10.1519/JSC.0b013e3181d1d318.

20. Liburt NR, Adams AA, Betancourt A, Horohov DW, McKeever KH. *Exercise-induced increases in inflammatory cytokines in muscle and blood of horses.* Equine Vet J Suppl.2010;38:280-8.doi: 10.1111/j.2042-3306.2010.00275.x.