J. Basic. Appl. Sci. Res., 1(12)3483-3488, 2011

ISSN 2090-4304
Journal of Basic and Applied Scientific Research
www.textroad.com

Intravenous Heparin Injection Does not Affect Aerobic Capacity and some Carbohydrate Metabolism Markers during Cycling Exercise

Short Running title
Heparin injection and glucose concentration during cycling

Afsharmand Zohreh[1], Eizadi Mojtaba[2], Behbudi Laleh[3], Daraei Shokrabad Firooz[4]

Department of physical education and sport science, Islamshahr Branch, Islamic Azad University, Islamshahr, Iran

ABSTRACT

Background and Objective: Scientific researches suggest that a high fat availability during prolonged exercise is accompanied with low carbohydrate usage in the whole body and skeletal muscle and delay in onset of fatigue. The aim of this study was to investigate the effect of heparin injection on some factors involved in carbohydrate metabolism and aerobic capacity during cycling.
METHODS: For this purpose, twenty eight none-trained male students aged 18 – 24 years were divided to experimental (intravenous heparin) and placebo (Lactose injection) groups randomly. All participants of two groups completed a submaximal cycling test for 20 min at 70% maximal O_2 uptake (VO_2max) without intravenous injection. After 7 days, the subjects repeated this cycling test 30 min after intravenous heparin and Lactose injection in experimental and placebo groups orderly. In order to measure the lactate and glucose concentration and lactate dehydrogenase activity (LDH), venous blood samples were immediately taken after exercise. Maximum oxygen consumption (VO2max) was measured using a cycling test. Statistical analysis was performed using an independent-paired t-test.
RESULTS: Heparin injection did not affect glucose and lactate concentration and lactate dehydrogenase activity in experimental group ($P<0.05$). In addition, VO2max did not change after Heparin injection in these subjects ($P<0.05$). All variables remained without change in placebo group ($P<0.05$).
CONCLUSION: Based on these findings, we conclude heparin injection can not affect aerobic capacity and carbohydrate metabolism substrate during submaximal exercise. Further studies are needed to clarify possible mechanisms by which heparin or other supplementation on fat-carbohydrate metabolism during exercise.
KEYWORD: Carbohydrate metabolism, Lactate, Aerobic capacity.

INTRODUCTION

The importance of carbohydrates as an energy source during exercise has been in the spotlight since the first years of this century and its vital role in prolonged endurance performance has always been underlined [1]. Muscle and liver glycogen depletion or hypoglycemia has been identified as one of the primary factors of fatigue during prolonged exercise [2]. The main reason for this phenomenon is the depletion of the body's limited carbohydrate supplies. On the other hand, fats are known to be the inexhaustible fuel reserves even during extremely prolonged endurance activities [3].

The required energy for exercise in particular endurance activities is related to fat-carbohydrate metabolism. In the beginning of this type of activities, the highest amount of energy is generated by carbohydrates and when the length of activity increases, the contribution of fat to produce energy gradually increases while that of carbohydrate declines [3]. To maintain activity in the final stages of endurance exercise, which is marked by the gradual depletion of the limited carbohydrates reserves of liver or muscle, it is essential to preserve these reserves in order to keep beta-oxidation metabolism and to retard fatigue [3, 4]. Therefore, several studies have been carried out on creating favorable conditions for increasing energy generation of fat metabolism for energy production especially during prolonged exercise in order to reduce carbohydrate burning and to maintain it for the final stages and for delay in fatigue onset. In this regard, different ways to increase free fatty acid (FFA) availability during exercise, have been studied; fasting, caffeine intake, L-carnitine supplementation, or use of triglyceride containing solutions or intravenous injection of certain compounds decomposing major sources of fat are among the most significant solutions studied [5-7].

Increase in FFA mobilization by heparin injection is effective in improving exercise performance [3]. Heparin has anticoagulant property and increases and accelerates lipoprotein lipase activity which breaks down triglycerides into FFA. Intravenous heparin injection is associated with increased FFA availability [3]. But the question here is whether heparin

***Corresponding author:** Eizadi Mojtaba, Department of physical education and sport science, Islamshahr Branch, Islamic Azad University, Islamshahr, Iran. Email address: izadimojtaba2006@yahoo.com

injection is associated with the reduction of glucose intake or maintaining muscular glucose or liver glycogen, changes in blood lactate concentration, increased aerobic capacity or maximum oxygen consumption (VO2max) that is characterized by endurance capacity during activity [3].

Most studies have dealt with the effects of heparin injection on oxidative metabolism variables or factors such as physical fitness in hemodialysis patients [8], chronic effort angina patients [9, 10], ischemic disease [11] and atherosclerosis patients [12]. However, the some study findings which have assessed these variables in healthy people are arbitrary and contradictory and there is no consensus on this subject. In this regard, the study of Dyck et al showed that heparin injection decreased muscle glycogen intake without change in blood lactate during a 15-minute ergometry exercise [13]. But the findings of Van Beck study indicate no effect of heparin injection on plasma lactate and glucose concentration during exercise [14]. Another study showed that while concentration of FFA and glycerol significantly increased by heparin injection, it did not result in any significant change in lactate and glucose concentration and endurance performance [14]. Another study showed that increased fatty acid availability due to diet results in increased fat oxidation, VO2max as well as running time [15]. The study by Graham et al showed that caffeine intake which has similar effects to those of heparin leads to increase in endurance and speed, but does not lead to any change in VO2max [16]. Therefore, this study aims to determine the effect of intravenous heparin injection on blood glucose and lactate, lactate dehydrogenase activity rate, VO2max and heart rate in a group of students.

MATERIALS AND METHODS

The purpose of this double-blind clinical trial performed was to investigate the effects of intravenous heparin injection on glucose and lactate concentration, lactate dehydrogenase activity and maximal oxygen consumption during a cycling test on stationary leg ergometer. For this purpose, twenty eight none-trained male students of Saveh University with an age range of 21±3 years and weight range of 75±15 kg participated in study by randomly. Then, these participants were divided into experimental (heparin injection) and placebo (Lactose injection) groups. Each participant received written and verbal explanations about the nature of the study before signing an informed consent form. After the nature of the study was explained in detail, informed consent was obtained from all participants. Their medical history showed no specific disease history or orthopedic or metabolic disorders such as diabetes and dyslipidaemia. All subjects were non-smokers. All participants had not participated in regular exercise/diet programs for the preceding 6 months. The subjects were advised to avoid any physical activity or exercise 48 hours before the blood sampling. Body weight and height were measured with a standard physician's scale and a stadiometer, respectively when subjects were in a fasting state when the participant had thin clothes on and was wearing no shoes.

All participants completed a graded bicycle-ergometry test (F90 Tuntury, Finland) according to Astrand protocol guideline (work load = 98 Watt) for 20 minutes [17]. Exercise tests were performed in two stages, with a one-week interval. Resting heart rate (HR) was measured after a 15-min rest in a sitting position and in a quiet environment. The ergometery test performed after an overnight fast. At the first test, the exercise test was performed without heparin injection in the experimental group or lactose (placebo) in the control group. But in the second test, all participants were completed exercise test 30 min after intravenous heparin or Lactose injection (10000 U) in experimental and control groups respectively. In exercise test, at first each subject pedaled for 2 minutes on a cycle ergometer without any load. Then the main phase of the test was carried out at the pedaling speed of 50 rpm and the work intensity of 98 watts. Work intensity rate and pedaling speed remained constant during the test. The duration of implementation of this test was considered 6 minutes for the purpose of calculating the maximum oxygen consumption. In order to activate the oxidative mechanism, the test was continued up to 20 minutes.

Immediately after the test, venous blood samples were taken from subjects in order to measures the concentrations of lactate and glucose factors and lactate dehydrogenase activity. Measurement of serum glucose, by glucose oxidase enzymatic method was done using Pars Azmoon Test Kit made in Iran. Lactate and lactate dehydrogenase values were measured by by Kobas Auto-analyzer with kits manufactured by Randox Company of England. Maximum oxygen consumption was calculated by Astrand nomogram [17].

STATISTICAL ANALYSIS

Statistical analysis was performed with the SPSS software version 15.0. Comparisons of parameters between the two groups in first exercise test were made by independent sample T-test. Paired Student T-test was used to determine significance levels of changes in any of the variables in response to heparin or Lactose injection compared to first blood sampling in two groups. P-value less than 0.05 were considered statistically significant.

RESULTS

The study subjects of both groups completed Astrand cycling test successfully. Baseline and posttraining of anthropometric and metabolic characteristics of the study participants are shown in Table 1. There are no significant differences in all variables between placebo and experimental groups in baseline (P>0.05). The statistical results showed that heparin injection had not significant effect on glucose concentration during cycling test (P>0.05, Fig 1). The statistical results of this study suggested that plasma lactate concentrations did not change due to heparin injection in experimental groups (P>0.05, Fig 2). Maximum oxygen consumption as determinative index of cardiovascular fitness was not affected by intravenous heparin infusion in experimental groups (placebo group: 33±5 versus 33±6 ml/kg/L, experimental group: 32±7 versus 36±5 ml/kg/L) (P>0.05). The activity range of lactate dehydrogenase enzyme was not affected by heparin injection during exercise test in experimental groups (placebo group: 333±43 versus 345±51 IU/L, experimental group: 342±38 versus 358±41 IU/L) (P>0.05). All variables remained without change in placebo group (P>0.05).

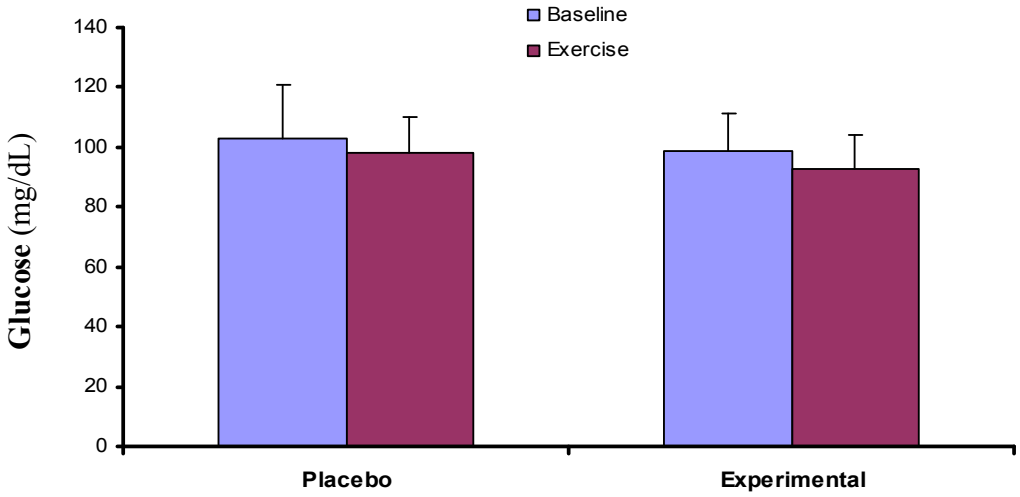

Fig 1. Mean and standard deviation of glucose concentration in response to Lactose and heparin injection after cycling test in placebo and experimental groups orderly

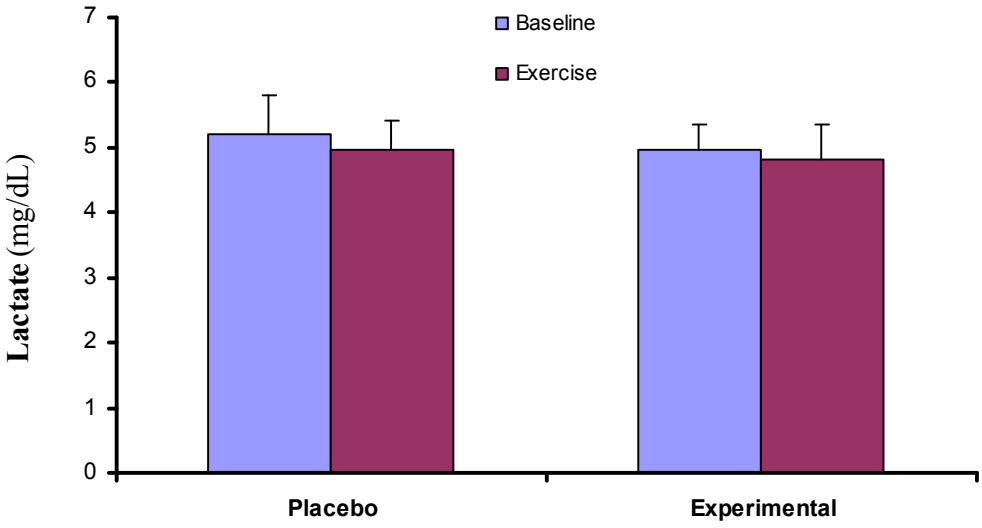

Fig 2. Mean and standard deviation of Lactate concentration in response to Lactose and heparin injection after cycling test in placebo and experimental groups orderly

DISCUSSION

Athletes are often vulnerable to temptations to use of various kinds of supplements to improve athletic performance and use different dietary methods, such as carbohydrate loading and using energizing substances to improve athletic performance. Addition to being anticoagulant heparin leads to increased activity of a kind of lipase called lipoprotein lipase that results in boosted conversion of triglycerides to FFA [3]. These findings are confirmed by Mora's study on sub-maximal exercise conducted in 2001 [18]. In a study by Hawley et al, intravenous injection of heparin to seven male athletes, also led to increased fat oxidation [19].

The increase of blood glucose concentration during exercise after heparin injection is indicative of reduced consumption of this substrate or reduced carbohydrate oxidation the outcome of which is increased fat oxidation. However, scientific resources represent that excessive accumulation of lactate during anaerobic or progressive aerobic exercise is considered a fatigue factor [3]. If lactate accumulation during any type of exercise could be reduced by continue training or a specific type of diet or taking certain supplements, it would represent greater reliance of produced energy on aerobic metabolism especially lipids and would lead to decreased carbohydrate oxidation or decreased glucose consumption and delayed onset of fatigue. Decreased activity of lactate dehydrogenase, which converts pyruvate back to lactate, also leads to reduced lactate production during maximal or exhaustive exercise [20].

Heparin injection altering the said variables has always been controversial and research findings in this field are more or less contradictory. One study in this area has shown that intravenous heparin injection leads to reduced consumption of glycogen in the experimental group than in the control group during cycling exercise [13]. In another study, heparin injection led to reduced consumption of muscular glycogen during exercise on stationary bicycle [21]. In Saloranta's study, increased FFA caused by heparin injection was associated with a 20-percent decrease of glucose consumption and reduced carbohydrate oxidation [22]. The results of some other studies also show that the combination of heparin injection and exercise training leads to increased exercise capacity and reduced recovery time after exercise in some diseases such as chronic effort angina and in coronary artery patients [23, 24]. In another study, extended exhaustion time and delayed onset of fatigue during exercise due to heparin injection has also been observed in six male athletes [25]. But in Layden's study, despite a significant increase in FFA concentration during exercise due to heparin injection compared with saline, no change was observed in plasma glucose, triglycerides, heart rate, oxygen consumption, and fat or carbohydrate oxidation [26]. Heart rate, oxygen consumption and respiratory exchange ratio remaining unchanged during exercise has also been reported in some other studies [25]. Another study also reports the concentrations of glucose, lactate and glucose 6-phosphate during exercise remaining unchanged after heparin injection [27]. Recent findings of Rantzau et al also show that injection of heparin does not result to a significant change in the blood glucose concentrations during exercise [28]. Findings of Everett et al also support these results [29]. The results of this study also showed heparin injection would not lead to any significant changes in lactate, glucose, and lactate dehydrogenase activity and maximum oxygen consumption. The limitations of this study include failure to measure simultaneously such variables affecting lipid metabolism as FFA and triglycerides the simultaneous measurement of which would have undoubtedly brought about more important results regarding the effects of heparin administration on carbohydrate - fat metabolism. It is necessary to mention that most studies suggest the increase in FFA and decrease in triglycerides by injection of heparin in both patients and healthy groups [30, 31]. Some studies also suggest that increased FFA due to heparin injection is not associated with changes in the amount of plasma glucose or lactate or VO2max [15]. However, although plasma FFA concentration seems to increase due to the injection of heparin or other supplements and is considerably important in athletic performance; regardless of its high concentration in plasma, its transport into mitochondria is of higher importance. In fact, it seems that it is the increase in FFA transfer into mitochondria by the some other supplements such as carnitine [32, 33,34], which leads to increased fat oxidation and energization which is in turn associated with decreased glucose consumption and increased plasma concentration of it.

CONCLUSION

Increased availability of FFA by heparin injection has been demonstrated repeatedly. In some studies, this increase has been reported together with decreased blood glucose consumption or maintaining muscle and liver glycogen reserves. Some studies, however, have reported no change in the consumption of glucose or carbohydrate reserves. Our study findings also show that heparin injection does not result in significant changes in the concentrations of glucose or lactate and aerobic capacity during exercise and does not alter the process of oxidative metabolism against the control group. It is likely that the rate of fat oxidation during exercise depends more on the mechanisms of free fatty acid entry into mitochondria than on its availability in plasma. Some studies also suggest extended exhaustion time and delayed onset of fatigue during exercise without a change in the metabolic pattern the need which signifies further studies in this field.

Acknowledgment

The authors would like to thank the Health Department of Saveh County, Research Deputy of Islamic Azad University, Danesh hematology laboratory and all students who have collaborated in the research.

REFERENCES

1. Krogh A, Lindhard J. The Relative Value of Fat and Carbohydrate as Sources of Muscular Energy: With Appendices on the Correlation between Standard Metabolism and the Respiratory Quotient during Rest and Work. Biochem J 1920; **14**: 290-363.
2. Coyle EF. Fuels for sport performance. In: Lamb DR, Murray, R, eds. Perspectives in exercise science and sport performance. vol. 10. Optimizing Sport Performance. Carmel: Cooper Publ Group. 1997; 96-137.
3. Maughan RJ, Gleeson M, Maughan R. Biochemistry of exercise & Training. (Oxford Medical Publications), Oxf University Press, USA 1997; 130-7.
4. Coyle EF, Coggan AR, Hemmert MK, et al. Muscle glycogen utilization during prolonged strenuous exercise when fed carbohydrate. J Appl Physiol, 1986; 61: 165-72
5. Cha YS, Choi SK, Suh H, et al. Effects of carnitine coingested caffeine on carnitine metabolism and endurance capacity in athletes. J Nutr Sci Vitaminol (Tokyo). 2001; 47(6):378-84.
6. Hathcock JN, Shao A. Risk assessment for carnitine. Regul Toxicol Pharmacol 2006; 46(1):23-8.
7. Hawley JA. Effect of increased fatty availability on metabolism and exercise capacity. Med Sci Sports Exercise. 2002; 34(9): 1485-91.
8. Nasstrom B, Olivercrona G, Olivercrona T, et al. Lipoprotein lipase during heparin infusion: lower activity in hemodyalisis patients. Scand J Clin Lab Invest 2003; 63(1): 45-53.
9. Fujita M, Sasayama S, Asanoi H, et al. Improvement of treadmill capacity and collateral circulation as a result of exercise with heparin pretreatment in patients with effort angina. Circulation 1988; 77(5):1022-9.
10. Fujita M, Yamanishi K, Hirai T, et al. Comparative effect of heparin treatment with and without strenuous exercise on treadmill capacity in patients with stable effort angina. Am Heart J 1991; 122(2):453-7.
11. Fragasso G, Leonardo F, Piatti P, et al. Detrimental effects of acute heparin administration on ischemic threshold in patients with coronary artery disease. Ital Heart J 2000; 1(6): 407-11.
12. Shioji K, Fujita M, Yamada T, et al. heparin and exercise treatment in the patients with arteriosclerosis obliteransS. Circ J 1997; 61(8): 715-8.
13. Dyck DJ, Putman CT, Heigenhauser GJ, et al. Regulation of fat-carbohydrate interaction in skeletal muscle during intense aerobic cycling. Am J physiol Endocrinol Metab 1993; 265(6): 852-859.
14. Van Baak MA, Mooij JM, Wijnen JA. Effect of increased plasma non-esterified fatty acid concentrations on endurance performance during beta-adrenoceptor blockade. Int J Sports Med 1993; 14(1): 2-8.
15. Muoio DM, Leddy JJ, Horvath PJ, et al. Effect of dietary fat on metabolic adjustments to maximal VO2 and endurance in runners. Med Sci Sports Exerc 1994; 26(1):81-8.
16. Graham TE. Caffeine, coffee and ephedrine: impact on exercise performance and metabolism. Can J Appl Physiol 2001; 26 Suppl: S103-19.
17. Assessing VO2max in edipemiological studies: Modification of the Astrand- Ryhming test. Medicine and science in sports and exercise 1982; 14(5): 335-8.
18. Mora-Rodrigues R, Hodgkinson BJ, Laury O, et al. Effects of bete-adrenergic receptor stimulation and blockade on substrate metabolism during submaximal exercise. Am J Physiol Endocrinol Metab.2001; 280(5): 752-60.
19. Hawley JA, Burke LM, Angus DJ, et al. Effect of altering substrate availability on metabolism and performance during intense exercise. Br J Nutr 2000; 84(6):829-38.
20. Huertas R, Campos Y, Diaz E, et al. Respiratory chain enzymes in muscle of endurance athletes: effect of L-carnitine. Biomechanical and biophysical research communications 1992; 188(1): 102-7.

21. Vukovich MD, Costill DL, Hickey MS, et al. Effect of emulsion and fat feeding on muscle glycogen utilization during cycle exercise. Appl Physiol 1993; 75(4): 1513-8.

22. Saloranta C. contribution of muscle and liver to glucose-fatty acid cycle in human. Am J physiol. 1993. 264(4); 599-605.

23. Fragasso G, Leonardo F, Piatti P, et al. Detrimental effects of acute heparin administration on ischemic threshold in patients with coronary artery disease Ital Heart J 2000; 1(6): 407-11.

24. Fujita M, Yamanishi K, Hirai T, et al. Comparative effect of heparin treatment with and without strenuous exercise on treadmill capacity in patients with stable effort angina. Am Heart J 1991; 122(2): 453-7.

25. Pitsiladis YP, Smith I, Maughan RJ. Increased fat availability enhances the capacity of trained individuals to perform prolonged exercise. Med Sci Sports Exerc 1999; 31(11): 1570-9.

26. Layden JD, Malkova D, Nimmo MA. During exercise in the cold increased availability of plasma nonesterified fatty acids doas not affect the pattern of substrate oxidation. Metabolism. 2004; 53(2): 203-8.

27. Hargreaves M, Kiens B, Richter EA. Effect of increased plasma free fatty acid concentrations on muscle metabolism in exercising men. J Appl Physiol 1991; 70(1):194-201.

28. Rantzau C, Christopher M, Alford FP. Contrasting effects of exercise, AICAR, and increased fatty acid supply on in vivo and skeletal muscle glucose metabolism. J Appl Physiol 2008; 104(2):363-70.

29. Everett-Grueter C, Edgerton DS, Donahue EP, et al. The effect of an acute elevation of NEFA concentrations on glucagon-stimulated hepatic glucose output. Am J Physiol Endocrinol Metab 2006 Sep; 291:449-59.

30. Garcia-Roves P, Huss JM, Han DH, et al. Raising plasma fatty acid concentration induces increased biogenesis of mitochondria in skeletal muscle. Proc Natl Acad Sci USA 2007; 104(25):10709-13.

31. Odland LM, Heigenhauser GJ, Spriet LL. Effects of high fat provision on muscle PDH activation and malonyl-CoA content in moderate exercise. J Appl Physiol. 2000; 89(6):2352-8.

32. Murosaki S, Lee TR, Muroyama K, et al. A combination of caffeine, arginine, soy isoflavones, and L-carnitine enhances both lipolysis and fatty acid oxidation in 3T3-L1 and HepG2 cells in vitro and in KK mice in vivo. J Nutr 2007; 137(10):2252-7.

33. Muller DM, Seim H, Kiess W, et al. Effect of oral L-carnitine supplementation on in vivo long-chain fatty acid oxidation in healthy adult. Metabolism 2002; 51(11): 1389-91.

34. Kim E, Park H, Cha YS. Exercise training and supplementation with carnitine and antioxidants increases carnitine stores, triglyceride utilization, and endurance in exercising rats. J Nutr Sci Vitaminol (Tokyo). 2004; 50(5):335-43.