PLASMA INSULIN, GROWTH HORMONE AND BLOOD SUGAR DURING EXERCISE IN MAN

R. C. SAWHNEY, A. S. MALHOTRA AND R. B. GUPTA

Defence Institute of Physiology and Allied Sciences, Delhi Cantt. - 110 010

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Summary : Alterations in plasma immunoreactive insulin (IRI), human growth hormone (hGH) and blood glucose were studied in five male volunteers undergoing exercise for 20 min on a bicycle ergometer at 750 kpm/min. Plasma IRI and hGH levels before exercise were 4.42 ± 1.35 *μU/ml* (Mean$\pm$SE) and 1.94 ± 0.88 *ng/ml* respectively. A significant decrease ($p < 0.01$) in plasma IRI was observed at 20 min postexercise and remained at lower levels upto 80 min of observations. hGH levels showed a signifcant increase ($p < 0.05$) to a mean value of 7.46 ± 0.71 *ng/ml* at 20 min of exercise with a peak value of 16.0 ± 5.04 *ng/ml* at 20 min postexercise. Sixty min after termination of exercise, hGH levels returned to pre-exercise values. Blood glucose rose progressively with the increase in the duration of exercise and peak levels were recorded at 20 min of exercise. Sixty min after termination of exercise, blood glucose levels returned to pre-exercise values. These observations suggest that exercise stress can lead to a physiological situation in which circulating insulin and glucose are not exclusively dependent on each other.

Key words : exercise growth hormone insulin

INTRODUCTION

Observations on stress induced alterations in glucose metabolism have suggested that all type of stresses including burns, hypothermia, exploratory laparotomy, cardiovascular shock and pheochromocytomas are associated with elevation of basal glucose levels, glucose intolerance and inhibition of the acute insulin response to intravenous glucose or tolbutamide (20). It is generally accepted that blood glucose is the physiological (endogenous) mechanism which regulates insulin secretion from the beta cells of pancreatic islets and the exercise stress leads to dissociation of this relationship between glucose and insulin (8). Pruett (13) observed a marked decrease in blood glucose and insulin levels during exercise to exhaustion at work loads of 50 and 70% of the subject's maximal oxygen consumption. The decrease in insulin levels was earlier than that of glucose levels. Hartley *et al.* (8) observed an increase in blood glucose and a decrease

in insulin levels during exercise. The exact mechanisms responsible for these alterations in glucose and insulin levels during exercise remains speculative. Since, growth hormone is intimately related to glucose homeostasis, its role during exercise remains to be elucidated. In the present study, alterations in circulatory levels of growth hormone, insulin and glucose were monitored in five healthy male volunteers undergoing exercise on a bicycle ergometer.

MATERIALS AND METHODS

Five healthy male volunteers with no family history of diabetes or any other endocrine dysfunction were used as subjects in this study. Their mean age, height and weight were 19.5±0.35 yr. 173.2±2.9 *cms* and 57.2±1.39 *kg* respectively. The subjects reported to the laboratory between 8 to 9 a.m. following an overnight fast and having performed no physical exertion prior to the test. An intravenous polythene catheter was inserted into an antecubtal vein and kept patent by a slow infusion of normal saline. The subjects rested for 30 min in a seated position on the bicycle ergometer before a pre-exercise control sample was withdrawn. Each subject exercised for 20 min on the bicycle ergometer at 750 *kpm/min.* Serial blood samples were withdrawn at 0,10,20, 40,60 and 80 min interval. Blood samples for glucose were taken into flouride oxalate tubes and for insulin and growth hormone into plain glass tubes.

The heart rate was noted by auscultation. The samples were analyzed for blood glucose (11) on the day of collection, whereas plasma immunoreactive insulin (IRI) and human growth hormone (hGH) were measured using the double antibody radio-immunoassay (RIA) techniques (9,19) at a later date. The anti hGH serum and hGH for labelling were supplied by the National Pituitary Agency/NIAMDD, Bethesda/Md, USA and hGH standard was provided by the National Institute of Medical Research, Mill Hill, London, England.

All samples for hGH and IRI measurements were processed in one assay to avoid larger intrassay variations. The sensitivity of hGH and insulin RIAs were 0.2 *ng/ml* and *uU/ml* respectively. The inter and intrassay variations at three different concentrations were less than 10%. Statistical analyses were done by analysis of variance (treatment by subject design).

RESULTS

The mean ± SE, heart rate of these subjects at 0,10,20, 40,60 and 80 min were

81.2±4.7, 177.6±4.6, 179±4.6, 106.2±2.1, 92.4±3.5 and 87.2±4.6 beats/min respectively. Blood glucose concentration before exercise varied between 82.2 to 97 *mg/dl* with a mean value of 89.64±2.39 *mg/dl*. Blood glucose increased significantly ($P<0.01$) to 96.34±3.56 *mg/dl* at 10 min of exercise with a peak at 20 min (99.12±3.20 *mg/dl)* (Fig. 1). Sixty minute after the termination of exercise, blood glucose decreased to 90.46±2.93 *mg/dl* which was not significantly different ($P>0.05$) than the mean of pre-exercise values.

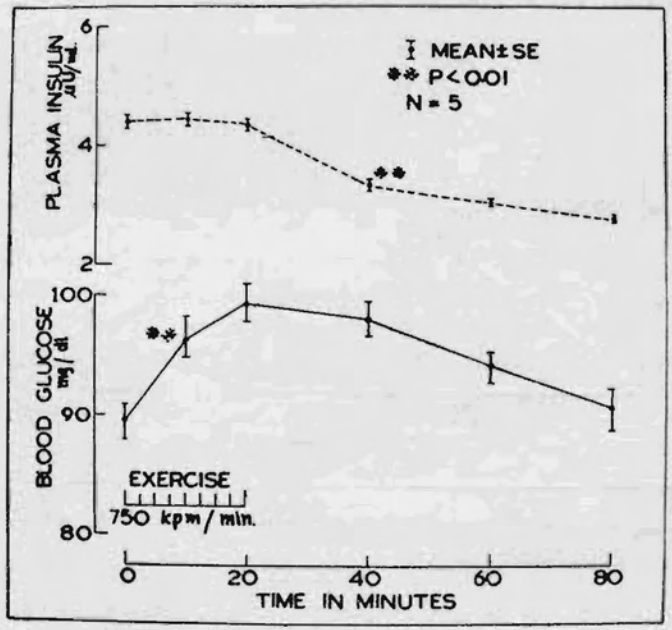

Fig. 1 : Showing plasma insulin and blood sugar before, during and after the exercise.

The mean plasma IRI before exercise was 4.42±1.35 *uU/ml* (range 1.4 to 7.8 *μU/ml)*. The mean values of 4.44±1.31 *uU/ml* and 4.02±0.97 *uU/ml* at 10 and 20 min of exercise respectively were not significantly different ($P>0.05$) than that of pre-exercise values (Fig. 1). Plasma IRI was significantly decreased ($P<0.01$) to 3.38±0.9 *μU/ml* at 20 min postexercise period. Further significant decrease ($P<0.05$) over the preceding levels was recorded 60 min after the termination of exercise.

Prior to exercise, hGH levels varied between 0.55 to 5 *ng/ml* with a mean value of 1.94±0.88 *ng/ml*. The mean value of 4.62±0.39 *ng/ml* at 10 min of exercise was

not significantly different ($P>0.05$) than the mean of pre-exercise values (Fig. 2). A significant increase ($P<0.05$) in hGH levels to 7.46 ± 0.71 *ng/ml* was recorded at 20 min of exercise and reached a peak at 20 min postexercise period (16.0 ± 5.04 *ng/ml*). Plasma hGH levels returned to pre-exercise values 60 min after the termination of exercise.

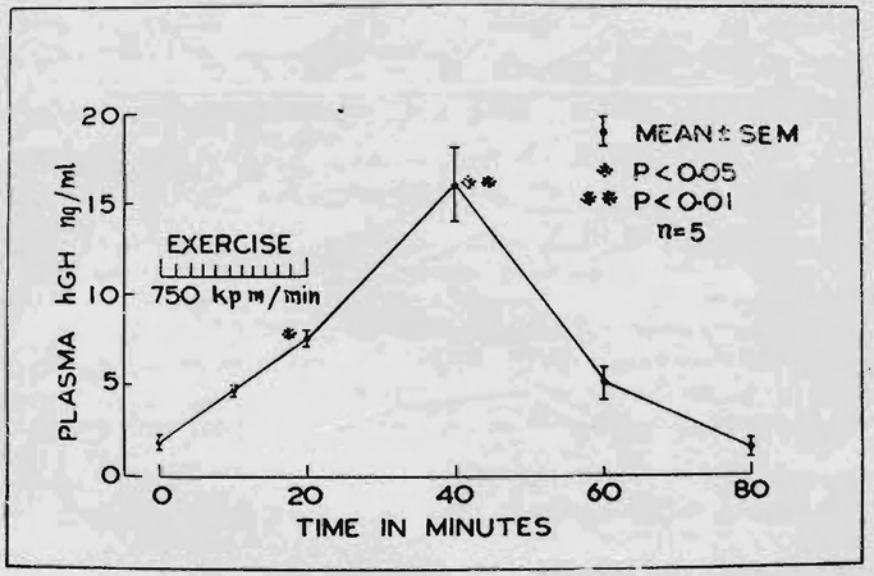

Fig. 2 : Plasma growth hormone before, during and after the exercise

DISCUSSION

The present study clearly demonstrates that exercise is associated with a rise in blood glucose and hGH levels and a decrease in plasma IRI. The commonly observed interrelation between blood glucose, insulin and hGH appears to be disturbed by the exercise stress. The increased levels of glucose during exercise appear to be hormonally mediated by glucagon and epinephrine which are markedly elevated during exercise (1.6) and facilitated by decreased levels of insulin. The exact mechanisms responsible for decreased levels of insulin remains speculative. The decreased levels could be either due to inhibition of the beta cells or to increased insulin utilization or degradation. Porte (12) has suggested an alpha receptor mechanism for suppression of insulin by adrenaline which could be blocked by phentolamine treatment (2). It is possible that exercise induced rise in catecholamines might have simultaneously increased hepatic glycogenolysis as well as decreased insulin secretion from the pancreatic beta cells.

The possibility that hormones or agents other than catecholamines could also result in hyperglycemia during exercise must be taken into consideration. Growth hormone is known to increase blood sugar concentration and inhibit the action of insulin but does not necessarily decrease plasma IRI levels. Although glucagon levels are also elevated during exercise but its administration has been shown to increase both glucose as well insulin levels in the circulation (5). In addition, an increase in blood ammonia during exercise may also contribute towards decreased insulin levels. The inhibitory effect of ammonia has been thought to be a direct effect on the beta cells and ammonia induced release of endogenous catecholamines from the pancreatic nerve endings (4).

The exact factors responsible for increased levels of hGH during exercise are unknown. Although, increased circulatory levels of hGH could be due to increased production, a decreased clearance rate or some combination of both, the magnitude of hGH elevation indicates that an increased pituitary secretion is the principal factor. An increase in lactate concentration has also been suggested to result in increased hGH levels during exercise (17,18). However, recent studies with artificial acidosis and alkalosis and sodium lactate infusion have disproven the lactate theory (16). Moreover, Lassare *et al.* (10) could observe no correlation between hGH and lactate, but instead observed a significant relationship between hGH levels and 0_2 deficit. While it seems difficult to accept how the 0_2 deficit could be stimulus for GH secretion, it is conceivable that it could be related to the accumulation of one or several metabolites or muscle hypoxia. Similarly, though alanine, pyruvate and other metabolites of rapid glycolysis are elevated during exercise they did not show any correlation with hGH levels (15). A rise in core temperature has also been postulated as mechanism for triggering hGH release from the pituitary gland (3). Since a correlation between hGH and core temperature was not observed in all the exercising subjects, and obsee subjects exhibited a diminished hGH response to exercise (7) this hypothesis also remains disputed.

In view of its role in regulation of glucose homeostasis, hGH levels could contribute to the stabilization of blood glucose through the decrease of muscle glucose uptake and utilization as well as stimulation of hepatic gluconeogenesis. It appears that exercise stress can lead to a physiological situation in which circulatory levels of insulin and glucose are not dependent on each other. Further investigations are required to explain control of hGH and insulin response to exercise in man.

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REFERENCES

1. Bottger, I., E.M. Schlein, G.R. Faloona, J.P. Knochel and R.H. Unger. The effect of exercise on glucagon secretion. *J. Clin. Endocr. Metab.*, **35** : 117-125, 1972.
2. Brisson, G.R. F., Malaisse-Lagae and W.J. Malaisse. Effect of phentolamine upon insulin secretion during exercise. *Diabetologia*, **7** : 223-229, 1971.
3. Buckler, J.M.H. Exercise as a screening test for GH release. *Acta Endocr.*, **69** : 219-229, 1972.
4. Feldman, J.M. and H.E. Lebovitz. Ammonia ion, a modulator of insulin secretion. *Am. J. Physiol.*, **221** : 1027-1032, 1971.
5. Gupta, P.R., M.K. Sinha, R.J. Dash, P.L. Wahi and G.K Rastogi. Insulin, free fatty acids and glucose response to intravenous glucagon following myocardial infarction. *Circulation*, **49** : 357-360, 19974.
6. Haggendal, J., L.H. Hartley and B. Saltin. Arterial noradrenaline concentrations during exercise in relation to the relative work levels. *Scand. J. Lab. Invest.*, **26** : 337-342, 1970.
7. Hansen, A.P. Serum growth hormone response to exercise in nonobese and obese normal subjects. *Scand. J. Clin. Lab. Invest.*, **31** : 175-178, 1973.
8. Hartley, L.H., J.W. Mason, R.P. Hogan, L.G. Jones, T.A. Kotchen, E.H. Mougey, F.E. Wherry, L.L. Pennington and P.T. Ricketts. Multiple hormonal response to graded exercise in relation to physical training. *J. Appl. Physiol.*, **33** : 602-606, 1972.
9. Hartog, M., A. Geafar, B. Meisser and R. Fraser. Immunoassay of serum growth hormone in acromegalic patients. *Brit. Med. J.*, **2** : 1229-1234, 1964.
10. Lassare, C., F. Girard, J. Durand and J. Raynaud. Kinetics of human growth hormone during sub-maximal exercise. *J. Appl. Physiol.*, **37** : 826-830, 1974.
11. Nelson, N. A photometric adaptation of Somogyi method for the determination of Glucose. *J. Biol. Chem.*, **153** : 575-578, 1944.
12. Porte, D. Jr. A receptor mechanism for the inhibition of insulin release by epinephrine in man. *J. Clin. Invest.*, **46** : 86-94, 1967.
13. Pruett, E. D.R. Plasma insulin concentrations during prolonged work at near maximal oxygen uptake. *J. App. Physiol.*, **29** : 155-158, 1970.
14. Schwartz, A.E., W. Lawrence, Jr. and K.E. Roberts. Elsvation of peripheral blood Ammonia following muscular exercise. *Proc. Soc. Exp. Biol. Med.*, **98** : 548-550, 1958.
15. Schwarz, F., D.J. Haar, Van Riet and J.H.H. Thijssen. Response growth hormone (GH), FFA, blood sugar and insulin to exercise in obese patients and normal subjects. *Metabolism.* **18** : 1013-1020, 1969.
16. Sutton, J.R., N.L. Jones and C.J. Toews. Growth hormone secretion in acid base alterations at rest and during exercise. *Clin. Sci. Mol. Med.*, **50** : 241-247, 1976.
17. Sutton, J. R., J.D. Young, L. Laz, J. B. Hickie and J. Maksvytis. The hormonal response to physical exercise. *Aust. An. Med.*, **18** : 84-90, 1969.
18. Vigas, M.S., S. Nemeth, J. Jurcoricora, L. Mikulaj and L. Komadel. The importance of lactate in exercise induced growth hormone release in man. In : Radio-immunoassay : methodology and applications in physiology and clniical studies. *Horm. Metab. Res.*, Suppl. **5,** pp. 166-169, 1974.
19. Welborn, T.A. and R. Fraser. Double Antibody immunoassay of insulin. A standardized second antibody reaction that eliminates spurious results with human serum. *Diabetologia*, **1** : 211-218, 1965.
20. Williams, R.H. and D. Porte, Jr. The Pancrease. In : The text book of Endocrinology by Williams, R.H., Philadelphia, W.B Saunders Company, p. 521, 1974.