Effects of histamine-receptor blockade and exercise on blood-glucose concentration

Sabrina Raqueno-Angel, Matt Ely, Dylan Sieck, John Halliwill
Department of Human Physiology, University of Oregon, Eugene OR

ABSTRACT

Histamine has been found to be an important component during the exercise recovery period, particularly in mediating vasodilation, hyperemia, and hypotension. Blocking H_1/H_2 histamine receptors produced altered outcomes during recovery, including a decrease in interstitial glucose concentrations and reductions in blood flow and whole-body insulin sensitivity. It is unknown if blood glucose concentrations change with histamine receptor blockades, specifically during the exercise period. PURPOSE: To determine if H_1/H_2 histamine receptor blockades decrease blood glucose concentrations during exercise. HYPOTHESIS: It was hypothesized that histamine receptor blockade would decrease blood glucose concentrations during exercise. METHODS: Nine competitive cyclists performed 120 minutes of cycling exercise at 50% VO_2 peak. 60 minutes prior to exercise, subjects were given either a placebo or histamine receptor blockades (540 mg Fexofenadine and 300 mg Ranitidine). Blood glucose concentrations were measured using a handheld Precision Xtra Blood Glucose Monitoring System (Abbot Diabetes Care INC, Alameda CA). Measurements were taken from the earlobe pre-exercise and three times during exercise at 15, 60, and 120 minutes. A repeated-measures two-way ANOVA (RM ANOVA, Group X Time) was used for statistical analysis. RESULTS: No differences were found between placebo and histamine receptor blockades groups (p = 0.801), and no Group X Time Interaction was determined (p = 0.881). Blood glucose levels at 15, 60, and 105 minutes were lower than the pre-exercise levels (p<0.001). CONCLUSION: No significant differences in blood glucose concentrations were found between placebo and histamine receptor blockade groups.

INTRODUCTION

- Blood glucose concentration decreased with cycling exercise at 50% VO_2 peak (Zinker 1990).
- Histamine receptor blockade (H_1/H_2) reduced interstitial glucose concentrations within skeletal muscle during recovery from exercise (Pellinger 2010).
- Histamine receptor blockade (H_1/H_2) reduced blood flow and therefore glucose delivery to skeletal muscle following exercise, and the effect may be more relevant in highly fit individuals (Emhoff 2011).
- Additionally histamine receptor blockade (H_1/H_2) reduced whole-body insulin sensitivity by 25% following exercise (Pellinger 2013).
- The effect of histamine receptor blockades (H_1/H_2) on blood glucose during exercise is unknown.
- The purpose of this experiment was to determine if H_1/H_2 histamine receptor blockades would decrease blood glucose concentrations during exercise. It was hypothesized that blood glucose concentration would decrease during exercise with the histamine receptor blockade (H_1/H_2).

METHODS

This was a double-blind placebo-controlled study. 6 men and 3 women completed two familiarization 10K time trials prior to the study visits. Study visits were performed in a semi-random order and all time trials were performed at the same time of day in a 18°C, 45% RH controlled environment. 1 hour before performing 120 minutes of cycling exercise at 50% VO_2 peak, subjects received either placebo or an oral H_1/H_2 histamine receptor blockade (540 mg Fexofenadine, and 300 mg Ranitidine). Blood samples were acquired from an ear lobe puncture and measured using a handheld Precision Xtra Blood Glucose Monitoring System (Abbot Diabetes Care INC, Alameda CA) pre-exercise and 3 times during exercise at 15, 60, and 105 minutes).

Statistics. The results were analyzed with a repeated-measures two-way ANOVA (RM ANOVA, Group X Time) to estimate differences between groups (Placebo vs. Antagonist) over time (Pre-Exercise, 15, 60, 105 minutes).

Table 1. Subject Characteristics

n	9 (3F, 9M)
Age (yrs)	27 ± 6
Height (cm)	175.7 ± 9.8
Weight (kg)	70.52 ± 13.75
Body Fat (%)	16.7 ± 10.7
Peak Power (Watts)	897 ± 262
$VO_{2\ peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	58.1 ± 6.8
Knee-extension isometric force (N)	581.7 ± 235.1
50% $VO_{2\ peak}$ Workload (Watts)	155 ± 35

Values are means ± SD.

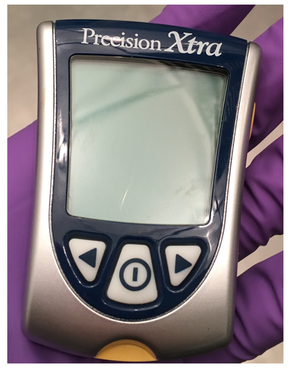

Table 2. Study Design:

120-min Seated Rest / 50% VO2peak			
Time (min)	0	60	120
Blood Glucose	| |	|	|

RESULTS

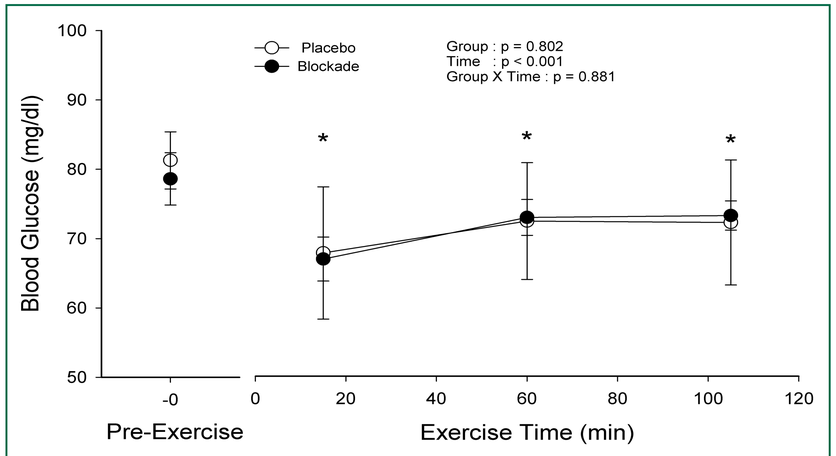

Fig. 1. Blood glucose concentrations of 120 minutes of steady state exercise at 50% of VO_2 peak.

No differences were found between placebo and histamine receptor blockade groups (p = 0.801), and no Group X Time Interaction was determined (p = 0.881). Blood glucose levels at 15, 60, and 105 minutes are lower than the pre-exercise levels (p<0.001).

CONCLUSIONS

The primary findings from this study are:

1. Both placebo and histamine receptor blockade groups rose in blood glucose levels between 20-60 minutes, then stayed consistent between 60-105 minutes. No significant differences were found between the groups.
2. A significant difference in blood glucose concentrations over time was found. Pre-exercise blood glucose levels are higher than at minutes 15, 60, and 105 of exercise.

FUTURE STUDIES

The future study goals are:

- To learn the effects of histamine receptor blockade during exercise on skeletal muscle glucose concentration in a very fit population.

REFERENCES

1. Emhoff, C.W., Barrett-O'Keefe, Z., Padgett, R. C., Hawn, J. A., Halliwill, J. R. (2011). Histamine-receptor blockade reduces blood flow but not muscle glucose uptake during postexercise recovery in humans. *Experimental Physiology, 96*(7), 664-673.
2. Pellinger, T. K., Dumke, B. R., Hallwill, J. R. (2013). Effect of H_1/H_2 histamine receptor blockade on postexercise insulin sensitivy. *Physiological Reports, 1*(2), 1-11.
3. Pellinger, T. K., Simmons, G. H., MacLean, D. A., Halliwill, J. R. (2010). Local histamine H_1/H_2 histamine-receptor blockade reduces postexercise skeletal muscle interstitial glucose concentrations in humans. *Applied Physiology, Nutrition, and Metabolism, 35*(5), 617-626.
4. Zinker, B. A., Britz, K., Brooks, G. A. (1990). Effects of a 36-hour fast on human endurance and substrate utilization. *The American Physiological Society, 69*(5), 1849-55.