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Basal and postprandial intermediary metabolism in normal male high altitude dwellers

Abstract

Objectives: To investigate the differences in basal and post prandial intermediary metabolism between male high altitude dwellers adapted to an environment of low barometric and oxygen pressures with chronic hypoxia and sea level dwellers in response to a mixed meal

Methods: A group of 15 normal male high altitude dwellers (Cusco, Peru, 3395 meters above sea level) and 17 normal male sea level dwellers (Lima, Peru, 150 meters above sea level) were given a mixed meal containing 730 Kcal and their responses assessed by directly measuring blood glucose, total cholesterol, high density lipoproteins, triglycerides, insulin and non-sterified fatty acids basally and at intervals for 6 hours afterwards. Low density lipoproteins, very low density lipoproteins and non-high density lipoprotein cholesterol were calculated.

Results: High altitude dwellers showed significantly lower fasting blood glucose and higher triglycerides and very low density lipoproteins than sea level dwellers, whereas no significant differences were found in insulin, total cholesterol, high density liproproteins, non-sterified fatty acids and non-high density lipoproteins cholesterol. Postprandially, high altitude dwellers showed significantly higher levels of insulin, triglycerides and non-sterified fatty acids but similar blood glucose values.

Conclusions: Normal male high altitude dwellers possess different intermediary metabolism than sea level dwellers both at fasting as well as postprandially.

Keywords: high altitude, men intermediary metabolism

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Introduction

Lower blood glucose (BG) levels in high altitude dwellers (HAD) compared to sea level dwellers (SLD) was first reported by Forbes[1] & San Martin.[2] Later on, further studies confirmed the lower glycemic values in this population.[3–11] This lower BG levels in the HAD was found not to be dependent on a higher hematocrit nor on an increased insulin secretion [8-10]. It has been shown that HAD have a higher triglycerides (TG) and non-sterified fatty acids (NEFA) levels than SLD.[12,13] Altogether these findings led to believe that HAD are more sensitive to endogenous insulin, and, due to lower glucose availability, there is a metabolic shift to lipids as energy source, and there is a corresponding elevation of counter regulatory hormones such as cortisol, growth hormone and glucagon in order to maintain euglycemia.[14–18] So far, most studies were conducted in the fasting state, in young males and in response to stimuli different from daily life. By investigating a more representative older age group of normal males in terms of their response to a normal mixed meal both fasting as well as post-prandially we provide in this study further insight into their intermediary metabolism.

Material and methods

Informed consent was obtained from all participants. The HAD group consisted of 15 normal males residing in Cusco, Peru (3,395 meters above sea level, barometric pressure 510 mm Hg., oxygen partial pressure 106.7 mm Hg.), ages 40-65 years (mean 51,3 ± 1,57). The SLD group was comprised of 17 normal males living in Lima, Peru (150 meters above sea level, barometric pressure 750 mm Hg, oxygen partial pressure 150 mm Hg.), ages 52 to 69 years (mean 56.4 ± 1.83). Further characteristics are shown in Table 1. Fasting BG, total cholesterol (TC), high density lipoproteins (HDL), and TG were determined by conventional enzymatic methods, insulin (I) by RIA and NEFA by Duncombe`s method.[19] Very low density lipoproteins (VLDL), low density lipoproteins (LDL) and non-HDL cholesterol were calculated using Friedewald`s formula.[20] A standard mixed breakfast, consistent of 45 Gms fat, 68 Gms carbohydrates and 13.4 Gm protein for a total of 730 Kcal, was given orally.[21] Blood samples were obtained at 30, 60, 120, 240 and 360 minutes thereafter for the measurement of BG, TG, insulin and NEFA. Statistical analysis was done using the Student`s "t" test.

Results

As shown in Table 1, the HAD group was significantly higher in body weight, height, diastolic blood pressure and pulse rate. No difference in body mass index (BMI) was observed. When looking at basal values (table 2), the HAD group had significantly lower BG than SLD group. Significantly higher TG and VLDL were also observed in the HAD. A tendency to higher NEFA, I, TC, LDL and non-HDL cholesterol was found in HAD but did not reach statistical significance (Table 1) (Table 2). After the mixed meal ingestion, the BG levels were not significantly different between the two groups. In contrast, I, TG and NEFA were significantly higher in the HAD group as illustrated in Figure 1. Towards the last part of the study period it was clear that both TG and NEFA did not return to basal values, more so in the HAD group than in SLD. During this stage both I and BG were identical in both groups (Figure 1).

Table 1 Sample general characteristics

	Sea level	High altitude	p
n	17	15	
Age, years	58,5± 1,30 (*)	56,4 ± 1,21	0,36
Weight, kg	64,8 ± 1.56	70,3 ± 2,26	<0,05
Height, m	1,61 ± 0,01	1,67 ± 0,01	<0,009
BMI	24,8 ± 0,46	25,0 ± 0,50	0,77
SBP, mmHg	123,0 ± 3,48	126,0 ± 2,89	0,51
DBP, mmHg	73,1 ± 1,76	80,3 ± 2,26	<0,01
Pulse rate, beats/min	74,1 ± 2,14	64,7 ± 3,27	<0,02

(*)Mean ± standard error of de mean. SBP systolic blood pressure; DBP diastolic blood pressure

Table 2 Basal biochemical values

	Sea level	High altitude	P
Glucose, mg/dl	85,3 ± 1,95 (*)	79,0 ± 2,0	<0,03
Insulin, uIU/ml	9,34 ± 1,38	13,1 ± 1,61	0,08
Total cholesterol, mg/dl	179,3 ± 6,01	194,4 ±8,16	0,14
HDL cholesterol mg/dl	35,1 ± 1,75	35,3 ±1,42	0,93
Triglycerides, mg/dl	125,8 ± 12,7	171,8 ± 13,7	<0,02
VLDL, mg/dl	24,7 ± 2,55	34,2 ± 2,76	<0,01
LDL, mg/dl	119,2 ± 5,87	125,0 ±8,29	0,56
Non-HDL cholesterol mg/dl	144,1 ± 5,34	159,0 ± 8,08	0,12
NEFA, uEq/L	509,7 ± 44,9	555,7 ± 43,4	0,47

(*)Mean ± standard error of de mean.

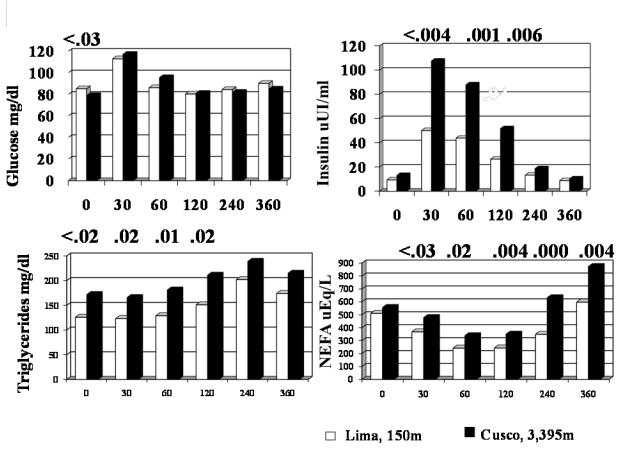

Figure 1 Comparison of the biochemical mean values both at fasting as well as during the postprandial period.

Discussion

In the present study we report that the HAD behave quite differently than the SLD in terms of their intermediary metabolism both under basal conditions as well as postprandially. The group of normal male HAD showed significantly lower basal BG and higher TG and NEFA but similar I levels than SLD, an observation previously reported by others.[1–14] We also found a trend towards higher fasting NEFA, I, TC, LDL and non-HDL cholesterol in HAD as opposed to SLD, but not statistically significant probably due to a small subject sample. After given a mixed meal (730 Kcal) a significantly different behavior was also found between HAD and SLD, namely higher I, TG, NEFA, and a slower return to basal values in the former group as compared to the latter. Their glycemic response, however, was identical. Regarding HAD metabolic physiology, it has been reported that their BG levels gradually increase when they migrate to sea level conditions. Conversely SLD lower their BG levels when living at high altitude.[22,23] These changes are not racially nor nutritionally related but due to purely environmental factors.[22] HAD showed a much faster BG return to basal values after an oral glucose tolerance test as compared to SLD[4,9] An intravenous glucose tolerance test demonstrated a higher glucose utilization in the HAD as compared to SLD [5,6,13]. In vitro studies showed that hypoxia increases the transport and utilization of glucose in endothelial cells.[24] and increases the expression of GLUT-1 glucose transporter in muscle cell cultures.[25] In the basal state, the HAD have higher growth hormone.[14–17] glucagon.[10–17] and cortisol.[10–18] levels than SLD. These higher levels are also shown during induced hypoglycemia.[26–28] On the other hand we know from previous reports that the glycemic as well as lipemic responses are influenced by the oral intake of fat.[29] carbohydrates.[30] and protein.[31–33] Our study lends further support to the known differences between HAD and SLD. Under chronic hypoxia the HAD shows a much more efficient handling of BG levels as evidenced by a significantly lower basal values, most likely representing higher sensitivity to insulin. Because hypoxia increases glucose utilization and disposal, in order to maintain BG close to normal, it is necessary to elevate counter regulatory hormones such as growth hormone, glucagon, cortisol and catecholamines. In turn, all the above changes trigger a shift of metabolic pathways towards lipids such as TG and NEFA as fuel sources for daily activities. This is quite evident by the much higher TG and NEFA response to a mixed meal by the HAD. We also observed a significantly briskier and sustained insulin response to a mixed meal in the HAD compared to SLD. The significance of this is not clear but may imply a different incretin effect present in HAD as compared to SLD. The increased sensitivity to insulin in the HAD previously reported by others, appears to apply only for basal condition, since our study shows a completely different hormonal response in the postprandial state. These results allow us to conclude that the HAD has a different intermediary metabolism that sets them apart from SLD in order to adapt to the environmental high altitude chronic hypoxia.

Acknowledgment

None.

Conflict of interest

Authors have declared no conflict of interests.

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