Insulin Suppresses Fatty Acid Binding Protein and Omentin Levels

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ABSTRACT

Circulating omentin and Fatty Acid Binding Protein (FABP) have been reported to be altered in insulin resistance (IR). However, the role of insulin in the regulation of these adipokines remains unclear. We tested the hypothesis that insulin alters circulating omentin and FABP, measuring omentin and FABP responses to elevated insulin in a group of healthy participan

Following an overnight fast, participants (N=9, age: 28±2 yrs, BMI: 21.8±7.3 kg/m2, glucose: 85.6±28.5 mg/dL, insulin: 6.1±2.0 U/mL, C-peptide 1.1±0.1 ng/mL) underwent a hyperinsulinemic euglycemic clamp (target glucose 90mg/dL), at insulin of 10mU/m2/min (low dose: LD: 0-180 min), followed by 40mU/m2/min (high dose: HD: 180-360 min). Participants underwent serial sampling for glucose, insulin, C-peptide, omentin and FABP at baseline (Bl and during steady state (SS) of the LD and HD periods. Participants underwent a second identical procedure after 14 days to assess reproducibility.

Data are presented as mean ± SEM. At SS, glucose levels were 89.7±0.7 (LD) and 92.6±1.3 mg/dL (HD), insulin were 5.6±1.0 (LD) and 13.0±1.6 U/mL (HD), and glucose disposal rates were 3.5±0.4 (LD) and 11.5±0.8 mg/kg/min (HD), and were reproducible between first and second clamp procedures (r² from 0.72 to 0.52). At BL, C-peptide levels correlated with FABP (r²=0.72, p<0.01) and with omentin (r²=0.43, p=0.054). Significant (p<0.05) decreases from BL were observed in plasma FABP and omentin levels in response to hyperinsulinemia at LD and HD. FABP decreased from 9.5±3.2 (BL) to 7.8±2.6 (LD) and to 7.7±2.6 (HD) ng/mL.

Omentin decreased from 484±161 (BL) to 421±140 (LD) and to 372±124 (HD) ng/mL. While omentin levels decreased significantly from LD to HD, the difference in FABP between LD and HD was less robust. Reductions in FABP and omentin were reproducible between clamp procedures (r^2 from 0.88 to 0.58).

Our results show for the first time that hyperinsulinemia reproducibly suppresses omentin and FABP in healthy humans, suggesting a potential role for insulin in regulating omentin and FABP. This may have implications for the regulation of these adipokines in IR.

INTRODUCTION

- Obesity is known to be associated with insulin resistance and increased cardiovascular disease
- FABP-4 and omentin are adipokines that have been reported to be altered in insulin resistance and are possibly associated with increased atherosclerosis
- There is limited knowledge on the role of insulin in the regulation of FABP-4 and omentin
- Understanding the effects of insulin on these adipokines may offer insight into their role in insulin resistance

METHODS

- Following an overnight fast, participants underwent a hyperinsulinemic euglycemic clamp (target glucose 90mg/dL), at LD insulin infusion of 10mU/m2/min for 0-180 min, followed by HD insulin infusion of 40mU/m2/min for 180-360 min
- Participants underwent serial sampling for glucose, insulin, C-peptide, omentin and FABP-4 at baseline and during steady state of the LD and HD infusion periods. Participants underwent a second identical procedure after 14 days to assess reproducibility of the methodology
- Omentin and FABP-4 were measured using ELISA kits (BioVendor, USA) and insulin was measured by RIA
- Changes in omentin and FABP-4 at HD and LD steady state were compared to that at baseline using paired-t tests
- Results are expressed as mean ± Standard Error of the Mean (SEM) or Standard Deviation (SD)

BASELINE DEMOGRAPHICS

	Parameter	Mean ± SD	Parameter	Period 1	Period 2
, by	Age (years)	27 ± 4	Glucose (mg/dL)		
ants.	Gender	6M, 9F		LD: 88.8 ± 0.5	LD: 89.6 ± 0.4
	Ethnicity	4 Non-Hispanic White, 11 Hispanic White		HD: 90.7 ± 1.2	HD:89.4 ± 1.0
	BMI (kg/m²)	22.0 ± 1.8	GIR (mg/kg/min)		
	Fasting Glucose (mg/dL)	86.5 ± 4.4		LD: 2.9 ± 0.3	LD: 2.7 ± 0.3
ow	Fasting Insulin (uU/mL)	6.9 ± 2.3		HD: 10.5 ± 0.7	HD: 10.1 ± 0.6
	Fasting C-Peptide (ng/mL)	1.2 ± .046			
(BL)	Total Cholesterol (mg/dL)	161.1 ± 25.2	C-Peptide (ng/mL)	LD: 0.81 ± 0.08	LD: 0.91 ± 0.0.09
	Systolic BP (mmHg)	112 ± 11		HD: 0.85 ± 0.1	HD: 0.87 ± 0.1
	Diastolic BP (mmHg)	60 ± 7			



STEADY STATE PLASMA INSULIN LEVELS (PERIOD 1 AND 2 POPULATION MEANS)



- Circulating omentin and FABP-4 levels decreased significantly in response to insulin in healthy humans Basal insulin and C-peptide levels, but not BMI, correlated significantly with basal omentin and FABP-4 levels
- FABP-4 correlated significantly with GIR during both LD and HD insulin infusion Changes in omentin and FABP-4 were reproducible and reductions in FABP-4 in response to hyperinsulinemia may be dose-dependent

STEADY STATE EXPERIMENTAL CONDITIONS

STEADY STATE PLASMA OMENTIN LEVELS (PERIOD 1 AND 2 POPULATION MEANS)



STEADY STATE GLUCOSE INFUSION RATES (GIR) (PERIOD 1 AND 2 POPULATION MEANS)







CORRELATIONAL ANALYSES

- Correlation between FABP-4 levels and basal insulin or C-peptide: r^2 = 0.45 and r^2 = 0.41 respectively
- Correlation between omentin levels and basal insulin or C-peptide: $r^2 = 0.32$ and $r^2 = 0.38$ respectively
- Correlation between FABP-4 levels and GIR: $r^2 = 0.46$ during LD and $r^2 = 0.48$ during HD insulin infusion
- Correlation between omentin levels and GIR: r² = 0.28 during HD insulin infusion
- Correlation of FABP-4 levels between Period 1 and Period 2: $r^2 = 0.51$ during LD and $r^2 = 0.46$ during HD insulin infusion
- Correlation of omentin levels between Period 1 and Period 2: $r^2 = 0.56$ during LD and $r^2 = 0.81$ during HD insulin infusion
- Correlation of insulin levels between Period 1 and Period 2: r= 0.98, $r^2= 0.96$
- Correlation of glucose infusion rates during LD insulin between Period 1 and Period 2: r=0.82 $r^2 = 0.6$
- Correlation of glucose infusion rates during HD insulin between Period 1 and Period 2: r=0.85 $r^2 = 0.72$

SUMMARY

Basal omentin correlated significantly with GIR during the HD insulin infusion and basal

CONCLUSION

Our results show for the first time that hyperinsulinemia reproducibly suppresses omentin and FABP-4 in healthy humans, suggesting a potential role for insulin in regulating omentin and FABP-4. Furthermore, omentin and FABP-4 are negatively associated with insulin action suggesting a potential role in insulin resistance and possibly atherosclerosis.

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