

Background

Chronic positive caloric balance due to excessive food intake or physical inactivity in the appropriate genetic background leads to obesity, increased visceral fat, insulin resistance, hypertension and atherogenic dyslipidaemia, which collectively has been referred to as metabolic syndrome. Emerging evidence has drawn attention towards the role of cell dysfunction (lipotoxicity) and lipid-induced programmed cell death (lipoapoptosis) in the pathogenesis of these abnormalities. As other adipokynes, leptin may have a pivotal role in these mechanisms by affecting food intake, insulin sensitivity, glucose and lipid metabolism. It has been proposed that lack of leptin action may result in overnutrition, reduced glucose and fat oxidation, ectopic lipid accumulation and insulin resistance [1, 2].

Objectives

- To evaluate the association of absolute serum levels of leptin and leptin concentrations adjusted to the amount of fat mass with risk factors for metabolic syndrome in adult non-diabetic obese subjects
- To identify a critical leptin level that may distinguish obese patients with and without risk factors for metabolic syndrome

Patients and Methods

We have studied 51 adult non-diabetic obese subjects (42 women; age 36.7±10 yrs; BMI 46.2±10 Kg/m²) who were classified according to risk factors for metabolic syndrome using IDF criteria* [3]:

Group I (n=13): none or 1 risk factor

Group II (n=21): 2 risk factors

Group III (n=17): 3 or more risk factors

*Central obesity associated with at least of two of the following parameters:

1) Triglycerides ≥ 150 mg/dl;

2) HDL-cholesterol < 40 mg/dl (men) or < 50 mg/dl (women);

3) Blood pressure ≥ 130/85 mmHg;

4) Fasting glycemia ≥ 100 mg/dl or previous diagnosis of type 2 diabetes

Exclusion criteria: obesity related to genetic, endocrine or metabolic diseases; pregnancy; type 2 diabetes; use of corticosteroids or any medication known to promote weight gain; unstable weight in the last 3 months.

Total body fat (BF) was measured by bioimpedance (Biodynamics 310).

Leptin was determined by RIA (Linco Research Inc., St Charles, MO)

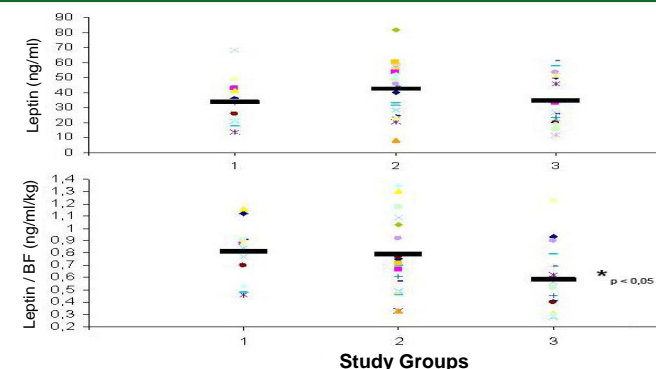
Results

	Group 1 (n=13)	Group 2 (n=21)	Group 3 (n=17)
Age (yrs)	37.7 ± 8.6	35.8 ± 12.1	36.9 ± 8.5
Weight (kg)	97.0 ± 22.1	119.1 ± 21.8	135.2 ± 29.0 ^a
BMI (kg/m ²)	39.3 ± 8.6	46.8 ± 10.2	50.6 ± 8.2 ^a
Waist (cm)	114.9 ± 19.1	124.0 ± 16.7	134.3 ± 16.4 ^a
Systolic BP (mmHg)	120.6 ± 11.9	127.1 ± 13.1	131.8 ± 9.5 ^a
Diastolic BP (mmHg)	77.7 ± 4.4	83.8 ± 5.9	84.1 ± 7.1 ^a
Glucose (mg/dL)	88.7 ± 5.2	105.2 ± 19.6 ^b	124.3 ± 27.8 ^{a,c}
Insulin (μUI/mL)	13.1 ± 5.6	22.0 ± 8.4 ^b	31.7 ± 14.8 ^a
HOMA-IR	2.85 ± 1.20	5.75 ± 2.48	10.36 ± 7.37 ^a
Triglycerides (mg/dL)	100.4 ± 34.9	152.0 ± 111.1	220.8 ± 48.2 ^{a,c}
HDL (mg/dL)	220.8 ± 48.2	50.1 ± 13.0	40.6 ± 8.4
LDL (mg/dL)	104.1 ± 23.1	115.1 ± 29.8	119.2 ± 28.0
TSH (μUI/mL)	2.18 ± 1.53	2.38 ± 1.60	2.61 ± 1.59
Free T4 (ng/dL)	1.23 ± 0.21	1.19 ± 0.22	1.23 ± 0.26

p < 0,05: ^a group 3 vs group 1; ^b group 2 vs group 1; ^c group 3 vs group 2

	Group 1 (n=13)	Group 2 (n=21)	Group 3 (n=17)
Leptin (ng/ml)	33.6 ± 14.8	42.4 ± 17.6	34.5 ± 17.0
Body fat (kg)	41.3 ± 16.1	53.9 ± 14.6	60.2 ± 14.9 ^a
Leptin / Body Fat (ng/ml/kg)	0.81 ± 0.22	0.79 ± 0.31	0.58 ± 0.27 ^b

p < 0,05: ^a group 3 vs group 1; ^b group 3 vs group 1 and group 2



	Blood Pressure		Glycemia		Triglycerides		HDL cholesterol	
	Normal (n= 15)	Altered (n= 36)	Normal (n= 24)	Altered (n= 27)	Normal (n= 25)	Altered (n= 26)	Normal (n= 24)	Altered (n= 27)
Leptin (ng/ml)	40.17 (16.27)	36.42 (17.28)	35.35 (13.46)	39.46 (19.54)	40.40 (16.51)	34.76 (17.16)	36.59 (18.59)	38.35 (15.59)
Leptin/BF (ng/ml/kg)	0.78 (0.23)	0.70 (0.31)	0.79 (0.24)	0.68 (0.32)	0.83 (0.26)	0.63 (0.28)*	0.77 (0.32)	0.69 (0.26)

* p = 0,01

Conclusions

- Obese subjects with 3 or more risk factors for metabolic syndrome had lower values of leptin per body fat, suggesting that the development of metabolic syndrome might be associated with a progressive decline of leptin production by the adipose tissue
- No absolute level of leptin or leptin per body fat was accurate to discriminate obese with and without metabolic syndrome; obese subjects with hypertriglyceridemia had lower values of leptin per body fat

References

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- UNGER, Trends Endocrinol Metab 2003;14:398-403
- ALBERTI et al., Diabet Med 2006;23:469-480