Advanced Glycation End Products (AGEs), their receptors RAGE and AGER-1 and their association with insulin resistance and inflammation in obese and non-obese young subjects

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INTRODUCTION

In obesity the combination of differents effects like increase food consumption, oxidative stress and inflammation could increase the levels of advanced glycation end products (AGEs) and the action of their receptors.

OBJETIVE

To study circulating levels of AGEs, soluble RAGE and AGER-1 and their association with insulin resistance and inflammation in young subjects with obesity and normal weight

MATERIAL AND METHODS

We conducted a clinical, comparative and cross-sectional study in obese (n=80) and non-obese (n=80) young subjects from Leon Guanajuato, México. The project was approved by the Institutional Ethics Committee and all participants received an information letter and they had to sign informed consent. We calculated the body mass index according to Cole at al, and the consumption of AGEs in the diet (dAGEs) with the tables of Uribarri et al. We asked about the time physical activity practiced by the minute-week. We measured glucose, lipid profile, insulin, HOMA-IR, TNF-a, IL-6, serum AGEs (CML) and sRAGE. In a subsample of 27 subjects with normal weight and 21 subject with obesity we also measured the expression of RAGE and AGER1 by qPCR.
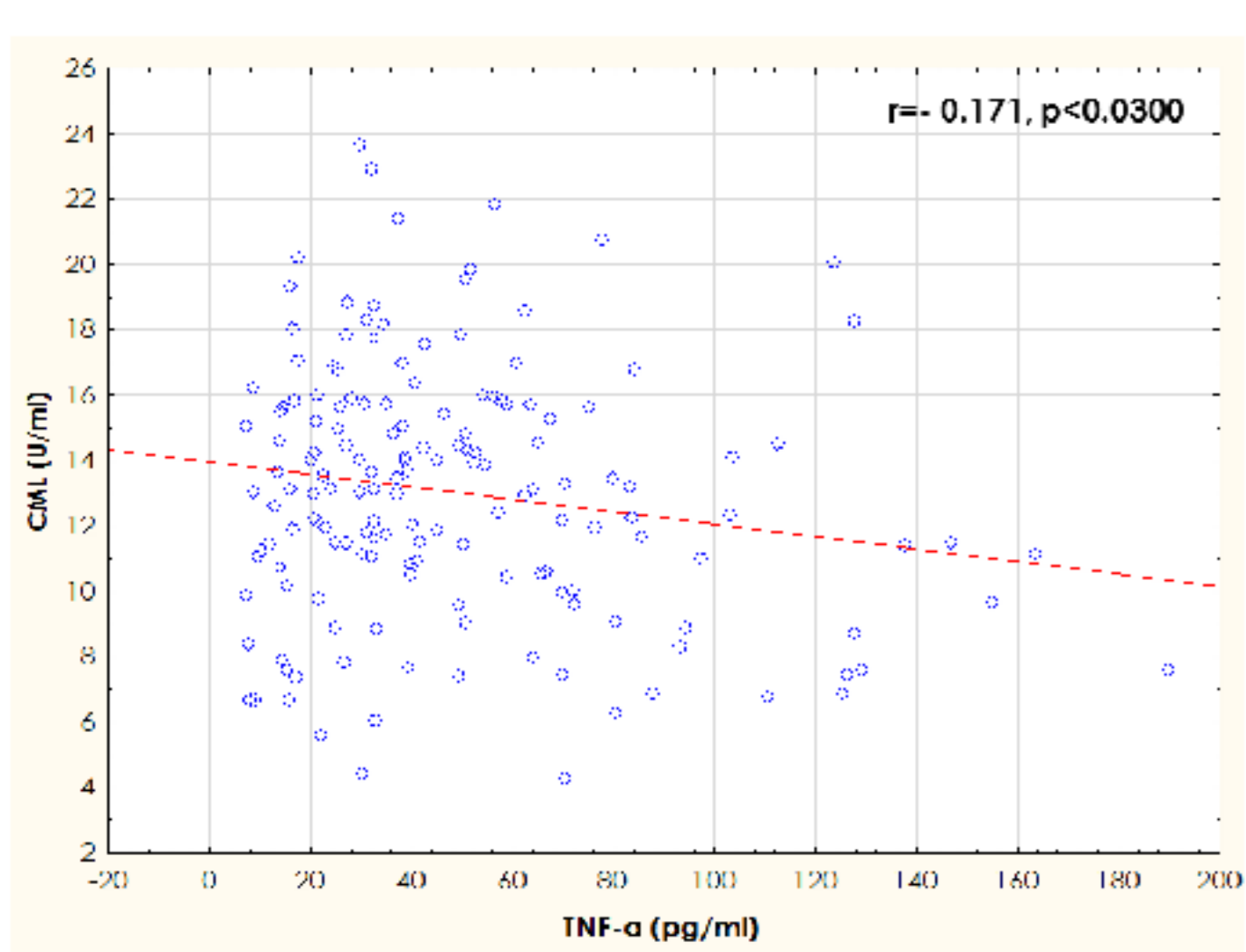
Figure 1. Association between levels of CML and TNF-α

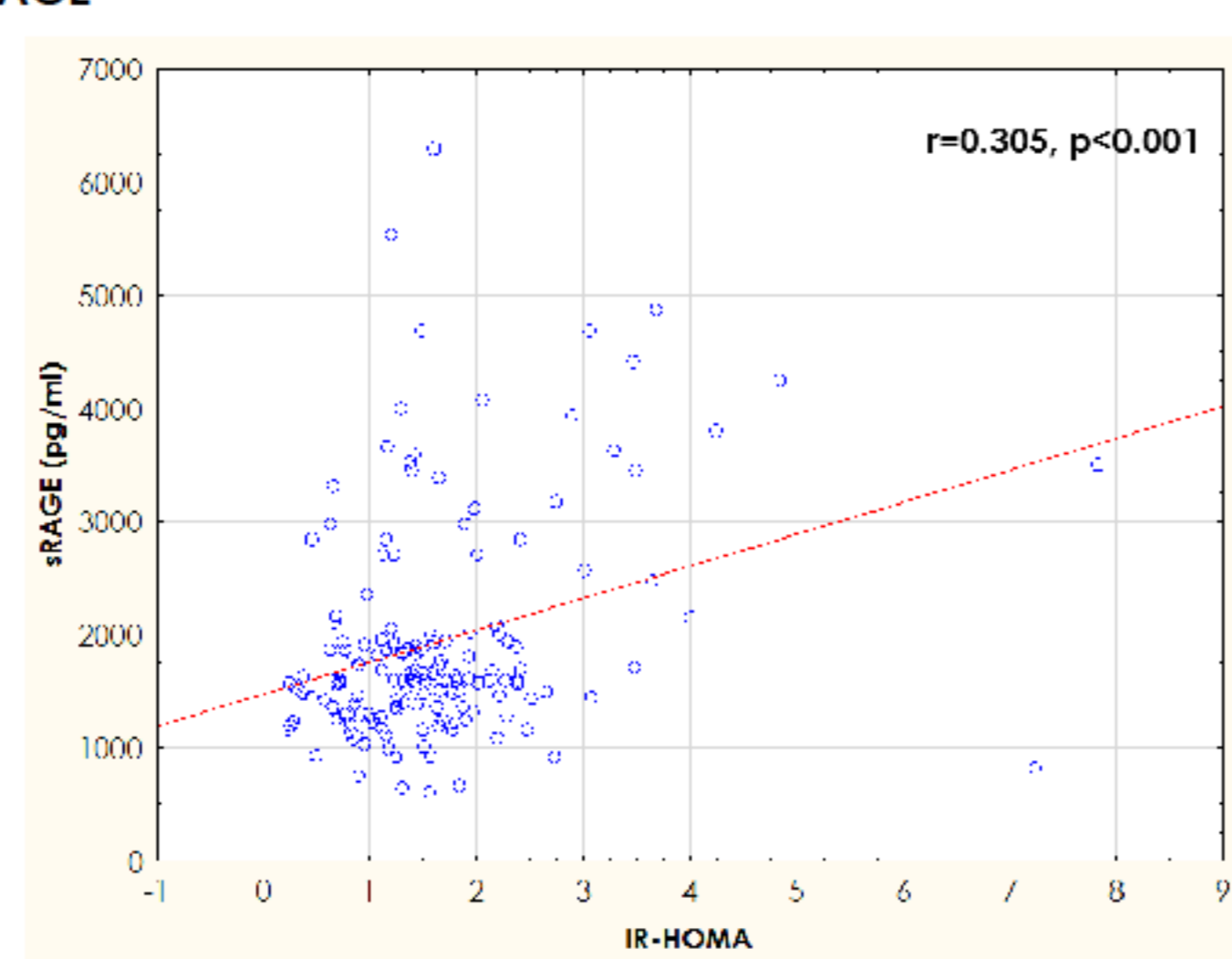Figure 2. Association between HOMA-IR and serum levels sRAGE

Table 2. Expression of AGEs receptors: RAGE and AGER1

AGEs Receptors				
	Non-obese n=27	Obese n=21	z/t	p
RAGE (AU)*	26.9±2.4	28.0±2.2	-0.64	0.519
AGER1(AU)	27.12.2	28.0±1.1	-1.70	0.024

RESULTADOS

We studied 160 subjects (16±1 years old), 55% females and 45% males. Table 1 shows the comparison between normal weight group and obese group. We found statistically significant difference in the group with obesity in triglycerides (z=-2.92, p<0.003), VLDL (z=-2.96, p<0.003), HOMA-IR (z=-4.62, p<0.001), TNF-α (z=-2.05, p<0.040) and IL-6 (z=-2.95, p<0.003). The normal weight group physical activity weekly was higher (z = -6.30, p <0.001). In Table 2 we show the expression of different transmembrane receptors, in the group with obesity, we found difference in expression AGER1 (t = -1.70, p <0.024). Serum levels of CML are associated with TNF-α (r=-0,172, p <0.030) and HOMA-IR (r = 0.244, p <0.026) Figure 1. HOMA-IR was associated with serum levels of sRAGE, Figure 2.

Table 1. Anthropometric, biochemical, dietary and physical activity characteristics between groups

Variables n=160	Non-obese n=80	Obese n=80	t/z	p
Anthropometric Variables				
Age (years)*	16.3±0.7	16.3±0.9	-0.21	0.829
Weight (kg)*	56.9±7.7	76.0±12	-8.82	0.001
Height (cm)*	163.9±0.08	163.1±0.07	-1.02	0.305
Waist (cm)*	78.5±9.9	84.4±11.3	-3.20	0.001
BMI (Kg/m²)*	21.1±1.9	28.4±4.0	-10.15	0.001
Biochemical Variables				
Glucose (mg/dl)	86.4±8.6	90.2±7.4	1.64	0.201
Cholesterol (mg/dl)	150.8±26	146.7±27.7	0.17	0.675
Triglycerides(mg/dl)*	97.7±34.2	112.1±33.9	-2.92	0.003
HDL-C (mg/dl)	65.3±6.9	63.5±8.1	0.02	0.881
LDL-C(mg/dl)*	65.4±20	69.7±21.3	-0.71	0.477
VLDL-C(mg/dl)*	19.3±6.7	22.3±6.7	-2.96	0.003
Insulin (µU/ml)*	5.7±2.5	8.9±5.9	-4.16	0.001
HOMA-IR *	1.2±0.5	1.9±1.1	-4.62	0.001
IL-6 (pg/ml)*	0.7±0.4	1.0±0.7	-2.95	0.003
TNF-α (pg/ml)*	44.8±35.7	52.5±34.2	-2.05	0.040
sRAGE (pg/ml)*	1839.7±932.9	2016.1±1042.4	-1.08	0.277
CML(u/ml)	12.9±4.0	13.0±3.7	0.38	0.536
Dietary and Physical Activity Variables				
Physical Activity (min/sem) *	154.6±76.2	72.6±60.8	-6.30	0.001
Energy Intake (cal/d)*	3343.8±1062.5	3384±1244.6	-0.31	0.975
Carbohydrates Intake(g/d) *	484.7±156.9	507.1±175.4	-0.63	0.529
Proteins intake(g/d)*	107.3±45.0	105.9±44.7	-0.06	0.951
Fats Intake(g/d)*	102.0±40.5	98.7±49.0	-1.12	0.259
dAGEs Intake (KU/d)*	8987.8±4721	8627.9±3205	-0.50	0.611
Diet-AGE density* (KU/cal)	94.6±21	93.5±13	-0.08	0.929

* U de Mann Whitney, Diet-AGE density, daily AGE intake/daily caloric intake;

CONCLUSIONS

The results show higher insulin resistance and inflammation in the subjects with obesity, one association of CML with insulin resistance and TNF-α; and higher expression of AGER1 in the obesity group.

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