"Effect of obesity on growth-related oncogen factor-alpha, thrombopoietin and tissue inhibitor metalloproteinase-1 serum levels"

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ABSTRACT

BACKGROUND AND AIMS: We have recently identified several adipokines oversecreted by omental adipose tissue of obese subjects: two chemokines [Growth-Related Oncogen factor-α (GRO-α), Macrophage Inflammatory Protein-1β (MIP-1β)], a tissue inhibitor of metalloproteinase (TIMP-1), an interleukin (IL-7) and a growth factor (thrombopoietin; TPO). As these adipokines are already known to be involved in cardiovascular disease, insulin resistance and type 2 diabetes, they may link obesity to its cardiovascular or metabolic co-morbidities. The aims of the present study were: 1) to examine whether the increased production by adipose tissue in obesity was reflected by higher circulating levels and 2) to attempt to identify the potential responsible factors [...]
721

Effect of obesity on growth-related oncogene factor-a, thrombopoietin and tissue inhibitor metalloproteinase-1 serum levels

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Background and aims: We have recently identified several adipokines oversecreted by omental adipose tissue of obese subjects: two chemokines (Growth-Related Oncogene factor-a (GRO-a), Macrophage Inflammatory Protein 1β (MIP 1 β)), a tissue inhibitor of metalloproteinases (TIMP-1), an interleukin (IL-7) and a growth factor (thrombopoietin, TPO). As these adipokines are already known to be involved in cardiovascular disease, insulin resistance and type 2 diabetes, they may link obesity to its cardiovascular or metabolic co-morbidities. The aims of the present study were: 1) to examine whether the increased production by adipose tissue in obesity was reflected by higher circulating levels and 2) to attempt to identify the potential responsible factors.

Subjects and methods: Serum levels of GRO-a, MIP-1β, TIMP-1, IL-7 and TPO were measured by ELISA in 32 lean, 15 overweight, 11 obese and 17 morbid obese age-matched women. Other anthropometric, metabolic and hormonal parameters were also determined: body composition, blood pressure, serum levels of lipids, glucose, insulin, leptin and adiponectin. Insulin sensitivity was evaluated by the euglycemic-hyperinsulinemic glucose clamp. Energy expenditure and substrate oxidation were determined by indirect calorimetry.

Results: Obese and morbid obese women exhibited several clinical or laboratory features of the metabolic syndrome. When compared to age-matched controls, they were characterized by higher blood pressure, hyperinsulinemia and insulin resistance, abnormal lipid profile, increased serum leptin and decreased serum adiponectin concentrations. Out of the five adipokines studied, three exhibited higher circulating levels in obese and/or morbid obese women than in lean ones (5 ± 20%, 30% and 55% for TIMP-1, GRO-a and TPO, respectively, P<0.05 or less). Serum levels of these three adipokines did strongly positively correlate with BMI, fat mass and waist circumference (P<0.01). Serum levels of GRO-a, TIMP-1 and TPO did positively correlate with hyperinsulinemia and/or negatively with insulin sensitivity (P<0.05 or less). Serum levels of TIMP-1 did also positively correlate with leptin and blood pressure while TPO was negatively related to adiponectin but positively to circulating lipids levels (free fatty acids and triglycerides; P<0.05 or less). Multiple regression analysis showed that fat mass was a significant independent determinant of GRO-a, TIMP-1 and TPO levels. Insulinemia and glycaemia were two additional independent determinants of TPO.

Conclusion: As already shown for TIMP-1, we demonstrate that circulating levels of GRO-a and TPO were higher in obese and/or morbid obese women and related to adiposity. These higher systemic levels may, at least in part, reflect the exacerbated secretion of these adipokines previously described in omental adipose tissue in obesity. Hence, that adiposity per se was an independent determinant of these high systemic levels reinforces the concept that hypertrophied adipocytes and surrounding recruited macrophages are fundamental contributors to this "hyperadipokinemias". Because circulating levels of these adipokines did correlate with several features of the metabolic syndrome, these levels may link obesity to its cardiovascular and metabolic disorders.

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