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Original Research

Advanced oxidation protein products are more related to metabolic syndrome components than biomarkers of lipid peroxidation

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ABSTRACT

Although advanced oxidation protein products (AOPPs) have been reported as the most appropriate parameter for determination of oxidative stress in patients with metabolic syndrome (MetS), a direct comparison between protein and lipid peroxidation has not been performed yet. The aim of this study was to compare protein peroxidation with lipid peroxidation measured by 2 different methodologies (*tert*-butyl hydroperoxide-initiated chemiluminescence and ferrous oxidation-xylenol orange assay). The hypothesis of this study was that AOPPs would be more related to MetS than to oxidative markers of lipid peroxidation. This cross-sectional study evaluated 76 patients with MetS and 20 healthy subjects. Prooxidant-antioxidant index (PAI) assessed as AOPP/total radical-trapping antioxidant parameter ratio progressively increased ($P < .05$) according to the number of MetS components, whereas AOPPs and total radical-trapping antioxidant parameter increased ($P < .05$) when 5 components were compared with 3 components. Spearman test showed a positive correlation between AOPPs and waist circumference ($r = 0.318$, $P < .01$), fasting glucose ($r = 0.250$, $P < .05$), homeostasis model assessment insulin resistance ($r = 0.043$, $P < .01$), triacylglycerol ($r = 0.713$, $P < .0001$), highly sensitive C-reactive protein ($r = 0.275$, $P < .05$), and uric acid ($r = 0.356$, $P < .01$), whereas there was an inverse correlation with high-density lipoprotein cholesterol ($r = –0.399$, $P < .001$). Prooxidant-antioxidant index demonstrated a positive correlation with waist circumference ($r = 0.386$, $P < .01$), fasting glucose ($r = 0.388$, $P < .01$), fasting insulin ($r = 0.344$, $P < .05$), homeostasis model assessment insulin resistance ($r = 0.519$, $P < .001$), triacylglycerol ($r = 0.687$, $P < .0001$), highly sensitive C-reactive protein ($r = 0.278$, $P < .05$), and uric acid ($r = 0.557$, $P < .0001$), whereas there was an inverse correlation with high-density lipoprotein cholesterol ($r = –0.480$, $P < .0001$). In conclusion, protein peroxidation determined by AOPPs, and especially by PAI, is more related to MetS components than lipid peroxidation. In addition, PAI progressively increased with the number of MetS components.

Abbreviations: AGEs, advanced glycation end-products; AOPPs, advanced oxidation protein products; BMI, body mass index; DBP, diastolic blood pressure; FOX, ferrous oxidation-xylenol orange; HDLc, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment insulin resistance; hsCRP, highly sensitive C-reactive protein; LDLc, low-density lipoprotein cholesterol; MetS, metabolic syndrome; NO_2^-, nitrite; NO_3^-, nitrate; PAI, prooxidant-antioxidant index; SBP, systolic blood pressure; TAC, total antioxidant capacity; TC, total cholesterol; TG, triacylglycerol; TRAP, total radical-trapping antioxidant parameter; WC, waist circumference.

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1. Introduction

Metabolic syndrome (MetS) comprises pathological conditions that include insulin resistance, arterial hypertension, visceral adiposity, and dyslipidemia, which favors the development of cardiovascular diseases and type 2 diabetes [1]. Existing evidence suggests that MetS is rising in developed countries and in developing countries [2]. Obesity and insulin resistance are considered the leading causes of MetS; however, many other pathophysiological mechanisms such as adipocytokines, hyperuricemia, nitric oxide, and oxidative stress may contribute to the potential cardiovascular risk factors related to the syndrome [3].

The imbalance between prooxidant and antioxidant mechanisms has been considered one of the most important pathophysiological mechanisms of chronic diseases, and there is consistent evidence in the literature to support the hypothesis that oxidative stress could be considered an early event in MetS pathophysiology rather than merely a consequence [4,5]. Advanced oxidation protein products (AOPPs) have been reported as the most appropriate parameter for determination of oxidative stress in MetS patients [6,7]. Advanced oxidation protein products are formed during oxidative stress by the action of chloraminated oxidants, mainly hypochlorous acid and chloramines, produced by myeloperoxidase in activated neutrophils [8,9]. They are structurally similar to advanced glycation end-products (AGEs) and exert similar biological activities to AGEs, that is, induction of proinflammatory cytokines and adhesion molecules [8]. In addition, it has been suggested to be an early marker of diabetes mellitus [10] and MetS [7].

Some reports have shown that AOPPs were more correlated than other oxidative markers with some MetS parameters and especially with glucose metabolism [7,10–12]. It is conceivable to suggest that AOPP is an excellent parameter to measure oxidative stress in MetS patients because both AOPPs and AGEs share the same origin, that is, hyperglycemia [11]. However, a direct comparison between protein and lipid peroxidation in MetS to determine which marker of oxidative stress is more related to MetS parameters has not been performed yet.

Although some studies have shown that AOPP levels increased progressively with the number of MetS components [4,7], we are not aware of any study that have reported the influence of the number of MetS components on protein oxidation and lipid peroxidation measured concomitantly. Bearing in mind the aforementioned reports, we hypothesized that protein oxidation would be more related to MetS and its components than lipid peroxidation.

Therefore, the main objectives of the present study were to compare protein oxidation measured by AOPPs with lipid peroxidation measured by 2 different methodologies, chemiluminescence and ferrous oxidation-xylenol orange (FOX) assay, and to verify which oxidative marker is more related to MetS patients. Our secondary aim was to verify the influence of the number of MetS components on oxidative stress measurements evaluated.

2. Methods and materials

2.1. Subjects

Seventy-six individuals (15 male and 61 female) aged 49 ± 9 years selected among Internal Medicine ambulatory patients of the University Hospital of Londrina, Paraná, Brazil, were chosen to participate in this cross-sectional study (Figure). Information on lifestyle factors and medical history was obtained through clinical evaluation. Metabolic syndrome was defined following the Adult Treatment Panel III criteria [13]. When 3 of 5 of the listed characteristics were verified, a diagnosis of MetS was performed: (1) abdominal obesity: waist circumference (WC) ≥102 cm in men and ≥88 cm in women, (2) hypertriglyceridemia ≥150 mg/dL (1.695 mmol/L), (3) low levels of high-density lipoprotein cholesterol (HDLc) of ≤40 mg/dL (1.036 mmol/L) in men and ≤50 mg/dL (1.295 mmol/L) in women, (4) high blood pressure of ≥130/85 mm Hg, (5) and high fasting glucose ≥100 mg/dL (5.6 mmol/L). The control group consisted of 20 healthy workers (1 male and 19 female) aged 48 ± 4.41 years of the University Hospital of Londrina, Paraná, Brazil. None of the participants of the study presented with thyroid, renal, hepatic, gastrointestinal, or oncologic disease, and none of the participants had a clinically evident infection or were receiving drugs for hyperglycemia or drugs known to affect lipoprotein and uric acid metabolism or antiinflammatory drugs, for at least 4 weeks before the study. All patients gave written informed consent, and the study protocol (CEP 258/08) was fully approved by the ethical committee of the University of Londrina (Paraná, Brazil).

2.2. Anthropometric and blood pressure measurements

Height and weight were measured in the morning with subjects wearing light clothing, but no shoes. After these, 2 blood pressure measurements, taken with a 10-minute interval between them after the subject had been seated, were recorded. The mean of these measurements was used in the analysis. We considered the current use of antihypertensive medication as an indication of high blood pressure. Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Waist circumference was measured with a soft tape on standing subjects midway between the lowest rib and the iliac crest.

2.3. Biochemical and inflammatory biomarkers measurements

After fasting for 12 hours, the subjects underwent the following laboratory blood analysis: glucose, total cholesterol (TC), HDLc, low-density lipoprotein cholesterol (LDLc), triacylglycerol (TG), and uric acid, which were evaluated by a biochemical autoanalyzer (Dimension Dade AR; Dade Behring, Deerfield, IL, USA), using Dade Behring kits; plasma insulin levels were determined by MEIA (AxSYM, Abbott Laboratory, Abbott Park, IL, USA), and serum highly sensitive C-reactive protein (hsCRP) was measured using a nephelometric assay (Behring Nephelometer II; Dade Behring, Marburg, Germany).

All samples were centrifuged at 3000*g* for 15 minutes, and plasma or serum aliquots were stored at –70°C until assayed.

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