The Evaluation of Oxidative Stress Levels in Obesity

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The World Health Organization defines overweight as a body mass index (BMI) of 25.0 to 29.9 kg/m² and obesity
as BMI of >30 kg/m² (first class obesity - BMI of 30.0 to 34.9 kg/m², second class obesity - BMI of 35.0 to 39.9 kg/
m² and third class obesity - BMI >40kg/m²). Recent studies revealed that obesity-related factors depend not
on the excess body weight, but rather on the regional distribution of the adipose tissue. Thus, abdominal fat
accumulation stimulates inflammation and entertains a pro-oxidant state, becoming an important risk factor
for obesity-related disorders [4]. Abdominal obesity is undoubtedly the most dangerous form of obesity. Several
studies revealed a linear association between T2DM and BMI, distribution of fat, and the relative proportions of lipids
in insulin-sensitive tissues: liver, skeletal muscle and adipose tissue. Waist circumference has emerged as an
excellent predictor of the risk to develop T2DM [6-9].

The association between elevated values of reactive oxygen species and a decreased antioxidant capacity
defines oxidative stress. Oxidative stress involvement is blamed in many diseases, including obesity. We
evaluated oxidative stress levels by FORT (Free Oxygen Radical Testing – reactive oxygen species levels)
and FORD (Free Oxygen Radical Defence – antioxidant capacity assay) values in obese subjects vs. controls.
FORT values were high and FORD values were low in obese patients vs. controls, notably in obese subjects
with comorbidities (diabetes, hypertension, dyslipidaemia, coronary heart disease, anaemia, hepatic
steatosis). We found positive correlations between FORT values and total cholesterol, uric acid, triglycerides,
LDL, body mass index, HDL/total cholesterol ratio, and negative correlations between FORT and age, HDL.
FORD levels correlated oppositely to FORT. Our results suggest that obesity and oxidative stress are linked.

Keywords: Oxidative Stress, Obesity, Reactive Oxygen Species, Antioxidants, Comorbidities

Obesity is a complex metabolic disorder characterized
by an excessive accumulation of adipose tissue. There is a
clear link between obesity and the development of
metabolic syndrome, type 2 diabetes mellitus (T2DM),
cardiovascular and liver disorders, possibly explained by
a common putative element: oxidative stress [1-3].

The Experimental part

We enrolled 20 healthy controls and 54 obese patients.
Informed consent was obtained from all subjects prior to
study inclusion. Patients were diagnosed with obesity
based on BMI values. Hypertension, T2DM, dyslipidaemia,
anæmia, coronary heart disease (CHD) and hepatic
steatosis were assessed as comorbidities. Blood tests
(complete blood count, lipid profile, uric acid etc) were
run. OxS levels were evaluated using the Free Oxygen
Radical Testing assay (FORT; normal range: ≤ 2.3 mmol/
L H2O2). Antioxidant status was measured using the Free
Oxygen Radical Defence (FORD; normal range: 1.07 -1.53
mmol/L Trolox) test. The methods are described in detail
elsewhere [18]. The study was approved by the Ethics
Committee of the University of Medicine and Pharmacy
of Craiova, Craiova, Romania (approval no. 40/27.03.2018).
All procedures and experiments were carried out taking
into consideration the ethical standards requested by the
Helsinki Declaration of 1975, as revised in 2008(5), as well
as the national law.

Results and discussions

The study group (62.63 ± 8.57 years, range 41-82 years
vs. 64.1 ± 2.26 years, range 61-69 years in controls)
included 44 women (81.48%) and 10 men (18.52%). 30
patients (55.56%) resided in rural areas and 24 patients
(44.44%) in urban areas. Mean BMI was 37.01 ± 3.77 kg/

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m², range 31.83-47.93 (obesity class I: 18 patients, 33.30%; class II: 25 patients, 46.30%; class III: 11 patients, 20.40%) (fig. 1). We registered the following comorbidities: dyslipidaemia (53 patients, 98.15%), hypertension (35 patients, 64.81%), anaemia (24 patients, 44.44%), T2DM (20 patients, 37.04%), CHD (16 patients, 29.63%) and hepatic steatosis (7 patients, 12.96%) (fig. 2).

FORT values were increased in obese patients vs. controls (3.19 ± 0.40 mmol/L vs. 2.16 ± 0.38 mmol/L; p-value<0.001). FORD values were increased in controls vs. obese patients (1.41 ± 0.44 mmol/L vs. 0.66 ± 0.16 mmol/L; p-value<0.001). FORT values were increased and FORD values were decreased in obese patients with comorbidities vs. controls (p-value<0.001): T2DM (3.33 ± 0.31 mmol/L vs. 2.16 ± 0.38 mmol/L; 0.60 ± 0.10 mmol/L vs. 1.41 ± 0.44 mmol/L), hypertension (3.30 ± 0.41 mmol/L vs. 2.16 ± 0.38 mmol/L vs. 0.62 ± 0.16 mmol/L vs. 1.41 ± 0.44 mmol/L), CHD (3.29 ± 0.80 mmol/L vs. 2.16 ± 0.38 mmol/L vs. 0.61 ± 0.14 mmol/L vs. 1.41 ± 0.44 mmol/L), anaemia (3.18 ± 0.33 mmol/L vs. 2.16 ± 0.38 mmol/L vs. 0.66 ± 0.13 mmol/L vs. 1.41 ± 0.44 mmol/L) and hepatic steatosis (3.11 ± 0.30 mmol/L vs. 2.16 ± 0.39 mmol/L vs. 0.65 ± 0.12 mmol/L vs. 1.41 ± 0.44 mmol/L). No significant differences were seen between obese patients with/without comorbidities.

Positive correlations were recorded between: FORT-total cholesterol (r=0.31; fig. 3), FORT-uric acid (r=0.25), FORD-HDL (r=0.14), FORT-LDL (r=0.24), FORT-TG (r=0.10), FORT-HDL/cholesterol ratio (r=0.24), FORD-age (r=0.08) and FORT-BMI (r=0.43; fig. 4). Negative correlations were recorded between: FORT-total cholesterol (r=-0.27; fig. 5), FORD-uric acid (r=-0.30), FORD-HDL (r=-0.09), FORD-LDL (r=-0.15), FORT-TG (r=-0.12), FORT-HDL/cholesterol ratio (r=-0.26), FORD-age (r=-0.13) and FORD-BMI (r=-0.35; fig. 6).

Obesity is associated with hyperglycaemia and insulin resistance. Hyperglycaemia and circulating free fatty acids increase ROS production and promote insulin resistance, reduce insulin gene expression and insulin secretion, probably via post-translational repression of some transcriptional factors such as musculo-aponeurotic fibrosarcoma protein A and pancreatic duodenal homeobox-1 which bind to the promoter region of the insulin gene [13]. On the other hand, the FoxO family of Forkhead transcription factor regulates gluconeogenesis, adipocyte differentiation, β-cell proliferation and antioxidant response [19]. Advanced glycation end products and the protein...
kinase C pathway stimulate the production of ROS by activating NOX enzymes and NF-κB [20-21]. ROS activate the c-jun-N-terminal kinase, a stress-sensitive serine/threonine kinase, causing phosphorylation of the insulin receptor substrate at serine residues and thus attenuating the c-jun-N-terminal kinase, a stress-sensitive serine/activating NOX enzymes and NF-κB [20-21]. ROS activate crosstalk between oxidative stress, obesity, low-grade inflammation, also found in obese patients [38-39]. Further studies should be conducted to explore the crosstalk between oxidative stress, obesity, low-grade chronic inflammation and carcinogenesis.

Conclusions

Our results show that obesity and oxidative stress are linked. Elevated levels of reactive oxygen species and decreased levels of antioxidants were registered in obese patients vs. controls, and in obese patients with comorbidities vs. controls. No statistically significant differences were registered in obese patients with comorbidities vs. obese patients without comorbidities. Free oxygen radicals values correlated positively with high lipid values, BMI, uric acid, and negatively with age. Antioxidant levels evolved oppositely.

References


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