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CYTOKINE IMBALANCE AND METABOLIC DISTURBANCES IN PATIENTS WITH INSULIN RESISTANCE SYNDROME

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Abstract: This study examined the relationship between inflammatory cytokines and metabolic abnormalities in patients with insulin resistance syndrome. Forty-five patients with metabolic syndrome and 30 healthy individuals were evaluated for anthropometric, metabolic, and immunological parameters. Patients demonstrated increased insulin levels and reduced Caro index, confirming impaired insulin sensitivity. Serum TNF-α increased to 136.55±35.6 pg/ml, whereas IL-4 decreased to 4.3±0.15 pg/ml compared with controls. Significant associations were identified between TNF-α, IFN-γ, and Caro index, indicating a relationship between inflammatory activation and metabolic dysfunction.

Keywords: insulin resistance; metabolic syndrome; TNF-α; IFN-γ; IL-4.

ДИСБАЛАНС ЦИТОКИНОВ И МЕТАБОЛИЧЕСКИЕ НАРУШЕНИЯ У БОЛЬНЫХ С СИНДРОМОМ ИНСУЛИНОРЕЗИСТЕНТНОСТИ

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Аннотация: Целью исследования было изучение взаимосвязи провоспалительных цитокинов с метаболическими нарушениями у пациентов с синдромом инсулинорезистентности. Обследованы 45 пациентов с метаболическим синдромом и 30 практически здоровых лиц с оценкой антропометрических, метаболических и иммунологических показателей. У пациентов выявлено повышение уровня инсулина и снижение индекса Caro, что характеризовало нарушение чувствительности к инсулину. Концентрация TNF-α достигала 136,55±35,6 пг/мл, тогда как уровень IL-4 снижался до 4,3±0,15 пг/мл по сравнению с контролем. Установлены статистически

значимые взаимосвязи TNF-α и IFN-γ с индексом Caro, что указывает на связь провоспалительной активации с нарушениями метаболической регуляции.

Ключевые слова: инсулинорезистентность; метаболический синдром; TNF-α; IFN-γ; IL-4.

Introduction: Metabolic syndrome is a complex condition in which abdominal obesity, insulin resistance, arterial hypertension, and metabolic abnormalities develop together. Metabolic stress can influence immune regulation through oxidative stress, altered adipose tissue activity, and chronic inflammatory signaling. Cytokines produced by adipose tissue and immune cells may participate in the transition from metabolic imbalance to sustained low-grade inflammation. Tumor necrosis factor alpha is particularly important because increased production may accompany insulin resistance and interfere with normal insulin signaling. Interferon gamma reflects cellular immune activity and may interact with inflammatory mediators during metabolic dysfunction. In contrast, interleukin-4 has anti-inflammatory properties and contributes to humoral immune regulation. Simultaneous assessment of proinflammatory and anti-inflammatory cytokines may therefore characterize immune changes associated with metabolic syndrome. The relationship between cytokine concentrations and insulin sensitivity is clinically relevant because metabolic abnormalities may precede overt diabetes mellitus. The source investigation evaluated patients with metabolic syndrome and healthy controls, focusing on anthropometric parameters, carbohydrate metabolism, insulin sensitivity, lipid profile, cytokine concentrations, and anticardiolipin antibodies. Particular attention was given to the Caro index as an indicator of insulin resistance. Correlation analysis examined associations between immune and metabolic variables. This approach may clarify whether inflammatory activation accompanies impaired insulin sensitivity and whether selected cytokines can serve as potential indicators of metabolic deterioration.

Aim of the study: To determine the relationship between inflammatory cytokines and metabolic abnormalities in patients with metabolic syndrome, with particular

attention to insulin resistance and associations between TNF-alpha, IFN-gamma, IL-4, and the Caro index.

Materials and methods. The study included 45 patients with metabolic syndrome and 30 healthy individuals as controls. Mean age was 60.9±3.7 years in the metabolic syndrome group and 59.5±4.5 years in controls. The metabolic syndrome group comprised 7 men and 38 women, whereas controls included 4 men and 26 women. Anthropometric assessment included body mass index and waist-to-hip ratio. Metabolic syndrome was defined according to World Health Organization criteria, with insulin resistance, abdominal obesity, body mass index above 30 kg/m2, and arterial hypertension as inclusion characteristics. Insulin resistance was assessed using the Caro index calculated from fasting plasma glucose and insulin; a value below 0.33 indicated insulin resistance. Plasma glucose was measured by the glucose oxidase method, and glycated hemoglobin by affinity chromatography. Total cholesterol and triglycerides were measured enzymatically, while low-density lipoprotein cholesterol was calculated using the Friedewald formula. Immunoreactive insulin was measured by one-step sandwich enzyme-linked immunosorbent assay. Serum TNF-alpha was determined by solid-phase enzyme-linked immunosorbent assay, while IFN-gamma and IL-4 were measured using sandwich enzyme-linked immunosorbent assays. Anticardiolipin antibodies of IgG, IgM, and IgA classes were determined by indirect solid-phase enzyme immunoassay. STATISTICA version 6 software was used. Between-group differences were assessed with Student's t-test, while associations were examined using Spearman rank correlation. Statistical significance was accepted at $p<0.05$.

Results. Mean body mass index was 36.6±0.8 kg/m2, corresponding to grade II obesity, and differed significantly from controls ($p<0.0001$). Waist circumference was 107±1.6 cm and waist-to-hip ratio was 0.92±0.01 ($p<0.0001$). Blood pressure was 145.73±2.9/90.00±1.59 mmHg and differed significantly from controls ($p<0.0001$). HbA1c increased from 4.70±0.18% to 5.7±0.11% ($p<0.0001$), whereas glucose did not differ significantly. Insulin increased from 9.10±1.1 to 19.6±2.2 microU/ml ($p<0.001$), while Caro index decreased from 0.55±0.03 to 0.33±0.04

($p<0.001$). TNF-alpha increased from 10±2.3 to 136.55±35.6 pg/ml ($p<0.01$), while IL-4 decreased from 7.4±1.07 to 4.3±0.15 pg/ml ($p<0.01$). IFN-gamma showed no significant difference: 31.4±6.4 versus 37.2±8.4 pg/ml. Anticardiolipin antibodies also showed no significant differences. TNF-alpha correlated positively with HDL cholesterol ($r=0.53$) and strongly with IFN-gamma ($r=0.86$). Positive associations were also found between TNF-alpha and Caro index ($r=0.48$), IFN-gamma and Caro index ($r=0.77$), and anticardiolipin antibodies and Caro index ($r=0.56$). These findings indicate significant relationships between inflammatory mediators and metabolic regulation.

Conclusions: Metabolic syndrome was characterized by abdominal obesity, insulin resistance, hyperinsulinemia, and increased inflammatory activity. Patients had higher body mass index, blood pressure, HbA1c, and insulin, while Caro index was reduced. TNF-alpha increased markedly, whereas IL-4 decreased significantly. IFN-gamma showed no significant group difference but correlated strongly with TNF-alpha and Caro index. These associations support a link between cytokine activity and impaired insulin sensitivity. The findings suggest that inflammatory activation accompanies metabolic dysfunction in insulin resistance. Cytokine profiling may provide useful information about metabolic dysfunction and immune imbalance. Such markers could complement conventional metabolic assessment in clinical studies in future research.

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