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Serum Adipokine Levels as a Predictor of Liver Damage in Patients with Metabolic-Associated Fatty Liver Disease Pathogenetic Mechanisms of Acute Coronary Syndrome

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Abstract: Until recently, most authors believed that pathological changes in liver damage in patients with metabolic-associated fatty liver disease. Insulin resistance (IR) is considered one of the important mechanisms involved in the pathogenesis of metabolic liver dysfunction. It is widely known that the development of steatosis is associated with the accumulation of fat in the liver and insulin resistance (IR), and IR is considered to be the main pathogenetic cause of liver steatosis. It is widely recognized that the development of steatosis is associated with hepatic fat accumulation and insulin resistance (IR), with IR believed to be the main pathogenetic cause of hepatic steatosis.

Keywords: metabolic associated fatty liver disease, leptin, resistin, adiponectin and cytokines, insulin, IL-6 and FNO-a C-reactive protein.

Introduction

Insulin resistance is one of the major factors aggravating metabolic syndrome. As is known, all tissues with insulin receptors can become insulin resistant, but the tissues that primarily cause insulin resistance are the liver, skeletal muscle, and adipose tissue. Insulin resistance impairs glucose utilization leading to compensatory increased insulin production by beta cells and hyperinsulinemia.

Numerous studies have proven that Insulin resistance can be found even in normal weight adolescents, as shown in a number of publications [2,3], and is considered when developing diagnostic criteria for obesity, obesity obesity are just one of three diseases that a combination of hepatic steatosis allows the diagnosis of fatty liver disease [4]. Unfortunately, in this group of patients, fatty liver disease is often under-diagnosed because, by remaining asymptomatic for an extended period of time, it does not require screening in the general population.

The purpose of this study is to evaluate serum adipokines and cytokines as predictors of liver injury in patients with metabolic associated fatty liver disease.

Material and Methods

Under observation were 98 (98%) including 77 patients with fatty liver dystrophy in metabolic syndrome. Patient age ranged from 40 to 65 years (54.0±4.8). The control group included 21

non-MAFLD healthy volunteers of comparable age. In the MAFLD group, the proportion of males was significantly higher than that in the control group (72.6%). Exclusion criteria included patients with alcohol history alcohol intake >20 g/day, viral hepatitis, autoimmune liver disease, use of hepatotoxic drugs or other chronic diseases.

The study was conducted at the TMA Multidisciplinary Clinic Immunoenzymes (ELISA), clinical, biochemical studies and ultrasound study were conducted using automatic proprietary analyzers. Mindray and Human, BioChemMac diagnostics.

Results and Discussions

Fatty liver dystrophy was diagnosed qualitatively by liver ultrasonography (US) using standardized criteria. Ultrasound examination was performed in all patients using the same equipment (EUB-8500 scanner; Hitachi Medical Corporation, Tokyo, Japan) and by the same operator (Webb M), as previously described. The radiologist was unaware of the blood test results and clinical history of the participants, and the calculation of steatosis biomarkers was performed only after the radiological examination. During ultrasonography, graphical representation of echo intensity (bar graph) within the area of interest in the liver.

Hepatorenal ultrasound index (HRI) ≥ 1.50 indicated fatty liver dystrophy (parallel to steatosis >5%. Adiponectin is the most prevalent adipokine in serum red blood cells, which insulin sensitivity, tissue inflammation, endothelial function, and lipid metabolism.

Moreover, increasing data evidence that hypoadiponectinemia may play a significant role in the development of insulin resistance. However, little is known about the value of circulating adiponectin as a surrogate marker of obesity itself and the development of obesity-related phenotypes in the general population.

As can be seen from the presented results of the study (Table 1), the mean serum adiponectin concentration was reliably lower in patients with MAFLD than in the control group (5.18±0.43 vs. 9.67<0.0.05; Png/0.05).

Table-1. Serum concentrations of adipokines and insulin in the treated and control groups M±m

Indications	Main group n=77	Control group n=21
Leptin (ng/mL)	14,32±1,27*	8,89±0,79
Adiponectin (ng/mL)	5,18 ± 0,43*	9,67 ± 0,83
Resistin (ng/mL)	22,18 ± 2,32	26,53 ± 2,41
Insulin (IU/ml)	19,82 ± 1,84*	11,34 ± 1,15
TNF-α (pg/ml)	19,27 ± 1,63 *	8,34 ± 0,79
IL -6 (pg/ml)	7,34 ± 0,53*	4,05 ± 0,41
C-reactive protein (mg/L)	6,42 ± 0,58*	3,47 ± 0,36

*Note: * – P<0.05 compared with control.*

Because adipose tissue contains various cell types such as adipocytes, immune cells, endothelial cells, and fibroblasts, it produces and releases a variety of secretory proteins into the systemic bloodstream. Most adipokines exhibit pro-inflammatory activity

Leptin is known to activate monocytes and macrophages to produce pro-inflammatory IL-6, TNF-α and IL-12 and stimulate the production of CCL2 and vascular endothelial growth factor in stellate cells such as Hepatic TNFα signaling of human inflammation and LPS, stimulate the expression of leptin and the leptin receptor.

Leptin also enhances the production of pro-inflammatory Th1 cytokines while suppressing the production of anti-inflammatory Th2 cytokines such as IL-4 in CD4+T cells.

As can be seen from the presented results of the study the serum concentration of leptin in the basic group was reliably 1.6 times higher at 14.32±1.27ng/ml than the values of the control group at 8.89±0.7.ml. It should be noted that one important function of adipocyte peptide

(leptin) is triglyceride retention in adipocytes. Similar dynamics were observed and relative TNF-α concentration which in baseline group of 19.27 ± 1.63 pg/ml exceeded baseline values by 2.4 times relative to control group values of 0.79 ± 8.34 pg/m

Resistin also stimulates human peripheral mononuclear cells to produce IL-6 and TNF-α through the NF-κB signaling pathway, In turn, tumor necrosis factor-α represents a cytokine of pdeocytovirus, which on the insulin signaling cascade at the expense of enhancing free fatty acid release by adipocytes and decreasing adiponectin synthesis.

As indicated above, one function of leptin is that it activates monocytes and macrophages to produce pro-inflammatory IL-6. Studies have shown that serum IL-6 levels are 7.34 ± 0.53 pg/ml in adolescents with MAFLD exceeded control levels by 1.9-fold, indicating enhanced pro-inflammatory cytokine synthesis for enhanced reactive protein synthesis in the liver.

The present study focused on adipokines – bioactive proteins secreted by adipose tissue including leptin, resistin, adiponectin, tumor necrosis factor α and interleukin 6 in adolescents with MAFLD. Как известно, адипокины, в свою очередь, активируют печеночные иммунные механизмы, ведущие к образованию провоспалительных медиаторов, таких как С-реактивный белок (СРБ) и другие.

Obesity is commonly associated with insulin resistance and hyperinsulinemia and is frequently associated with high blood pressure and various metabolic disorders such as dyslipidemia and elevated glucose levels.

Recently, it has been established that inflammatory immune responses in adipose tissue are one of the main mechanisms conferring insulin resistance in rodents and humans, and dynamic co-immune alterations in adipose tissue regulate inflammatory responses. Innate immune responses mainly mediated by macrophages trigger a key inflammatory process in adipose tissue leading to insulin resistance Macrophages differentiate into two functionally distinct populations. Th1 cytokines, IFN-γ, activate the expression of nitric oxide synthase (NOS2) in in classically activated macrophages (M1), whereas Th2 cytokines such as IL-4 and IL-13 induce arginase-1 (ARG1) in alternatively activated macrophages (M2) and enlarge inflammatory macrophages (M1 inflammatory cytokines such as TNF-α, IL-6 and IL-1β.

Fat cells also play a critical role in obesity-induced inflammation and insulin resistance through the production of pro- and anti-inflammatory cytokines in adipose tissue.

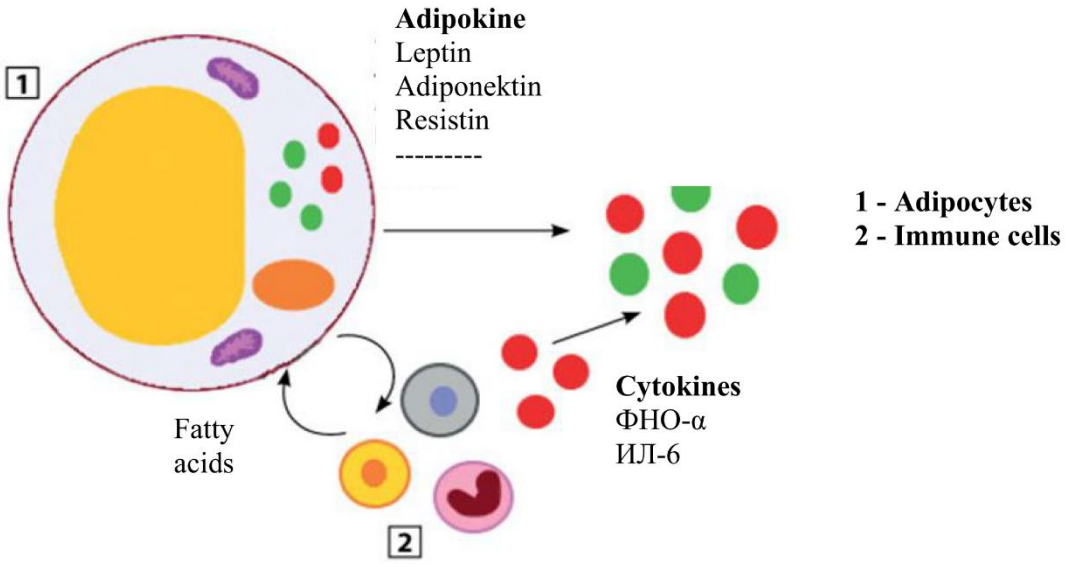

Figure 1. Interactions between adipocytes and immune cells in adipose tissue.

As can be seen in the figure, adiponectin is highly expressed by adipocytes and has potent anti-inflammatory properties.

Tumor necrosis factor- α is a cytokine that has a direct effect on the insulin signaling cascade by improving adipocyte free fatty acid release and reducing adiponectin synthesis.

In numerous models of obesity and diabetes, tumor necrosis factor- α is overexpressed in fat and muscle tissues, and tumor necrosis factor- α blocks the action of insulin in cultured cells. In humans, the factor tumor necrosis - α is also overexpressed in adipose and muscular tissues of obese and insulin resistant individuals.

Diad sayan impanaral, anengneng mi so negatibon siglaotan na adiponectin tan IL-6. Say lebel na adiponectin et mibabali ed lebel na TNF-α tan IL-6 ya onliliber, lapud parehon sarayan cytokine et mangaamper ed adiponectin messenger RNA ed adipose tissue. Diad kasunian, say adiponectin et mamapawala na anti-inflammatory ya kablian to diad pangisebel ed IL-6.Adiponectin has also been shown to inhibit the production and action of tumor necrosis factor-α.

Since hypoadiponectinemia can accelerate the tumor necrosis factor-α response, hypoadiponectinemia may cause insulin resistance. However, hyperinsulinemia suppresses adiponectin gene expression in adipocytes, and decreased adiponectin secretion in the insulin-resistant state may be caused by hyperinsulinemia.

Adiponectin has been shown to directly and indirectly influence insulin sensitivity through modulation of insulin signaling and molecules involved in glucose and lipid metabolism, while resistance to insulin may be the main determinants of hypoadiponectinemia in obesity. Therefore, we aimed to answer this question and identify potential links between circulating adiponectin concentrations and insulin resistance. Since adiponectin can reduce circulating fatty acid levels by increasing fatty acid oxidation and decreasing fatty acid synthesis, the hypoadiponectinemia we noted may Increase the risk of hypertension in obese individuals due to its adverse effects on lipid metabolism in patients with IR.

Based on this study, we suggest that changes in adipose hormone levels offer an additional tool for identifying MAFLD.

Our observation of elevated IL-6 levels in the study group indicated that IL-6 contributes to liver insulin resistance and steatosis by disrupting insulin signaling pathways. Our observed increase in blood CRP levels indicated Activation of IL-6 synthesis in the liver in response to IL-6 stimulation and also indicated systemic inflammation. It should be noted that CRP is not only a marker of liver inflammation but also an indicator of endothelial dysfunction.

In this situation, TNF-α, a key inflammatory cytokine produced by macrophages and adipocytes, plays a key role in liver fat accumulation and hepatocellular apoptosis. The elevated TNF-α levels in our study confirm it as a marker of liver inflammation and fibrogenesis in MAFLD patients.

Furthermore, TNF-α interferes with adiponectin signaling and promotes insulin resistance, further exacerbating lipid accumulation in the liver. The clinical implications of this study are significant, as they highlight the potential utility of IL-6, CRP, and TNF-α as diagnostic and prognostic indicators in individuals with obesity and risk of developing MAFLD.

Thus, patients with MAFLD exhibit significantly elevated levels of inflammatory biomarkers such as IL-6, CRP, and TNF-α, as well as adipokines, compared to patients without liver MAFLD. These results highlight the central role of systemic inflammation in the pathogenesis of MAFLD and highlight the potential of these markers as non-invasive indicators for early detection and risk assessment.

Thus, our data indicate a possible role for all of the aforementioned adipokines and cytokines in the pathogenesis and progression of MAFLD, and this is further supported by liver imaging studies.

Conclusion

Serum adipokine levels as a predictor of liver damage in patients with metabolic-associated fatty liver disease. In this setting, TNF-α, a key inflammatory cytokine produced by macrophages and adipocytes, plays a key role in liver fat accumulation and hepatocellular apoptosis. Elevated TNF-α levels in our study support it as a marker of liver inflammation and fibrogenesis in MAFLD patients.

Furthermore, TNF-α interferes with adiponectin signaling and promotes insulin resistance, further exacerbating lipid accumulation in the liver. The clinical implications of this study are significant, as they highlight the potential utility of IL-6. CRP and TNF-α as diagnostic and prognostic indicators in individuals with obesity and risk of developing MAFLD, which will ensure the earliest possible detection of disorders functional status in patients with metabolic-associated fatty liver disease and identification of groups of patients who are particularly in need of effective therapy.

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