

The relationship between serum visfatin and the progress of chronic viral hepatitis B cirrhosis

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Abstract. – OBJECTIVE: To explore the relationship between serum visfatin and the progress of chronic viral hepatitis B cirrhosis.

PATIENTS AND METHODS: Selected 153 cases of chronic hepatitis B patients with cirrhosis as an observational group. Among which, Child-Pugh Grade was divided into grade A with 31 cases, grade B with 79 cases and grade C with 43 cases. 50 healthy people were added to the study and were considered as control group. Comparison of the sera levels of visfatin, blood lipid, liver fibrosis indexes, fasting plasma glucose and fasting insulin of the observational and those of the control group were done.

RESULTS: Levels of visfatin, hyaluronic acid (HA), laminin (LN), type IV collagen (CIV) and insulin resistance index (HOMA-IR) were significantly increased ($p < 0.05$) while those of the liver function damage aggravating in observational group. The differences were of no statistical significance for the levels of triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), fasting plasma glucose (FBG) and fasting insulin level (Fins) ($p < 0.05$).

CONCLUSIONS: The increase of the levels of serum visfatin of chronic hepatitis B patients with cirrhosis is related to liver cirrhosis progress, indicators of hepatic fibrosis and HOMA-IR.

Key Words:

Visfatin, Chronic hepatitis B, Cirrhosis, Child-Pugh, Hepatic fibrosis, Insulin resistance index.

Introduction

Chronic hepatitis B virus directly damages organism through virus repeating, thereby inducing organism immune dysfunction. The most damage is a cytotoxic effect caused by T-cells, which shows as CD4⁺, CD8⁺ hyper function¹. In the process of hepatitis B progresses to liver cirrhosis, liver fibrosis plays important role in the pathological mechanism. Research shows that²:

insulin resistance, abnormal blood lipid metabolism, and abnormal cell matrix secretion are the main factors to cause liver fibrosis. Visfatin is a kind of adipocyte factor which has been recently found. It belongs to the same kind of material³ as the previous found pre-B cell enhancing factor (PBEF). Visfatin is closely related to the amount of visceral fat⁴. Visfatin can play a role of class insulin-like, participating in a variety of pathological process. The levels of body insulin contain only 3-10%, but not be affected by the food and the body metabolic factors. It has relatively high stability⁵. Up to now, there are few studies exploring the relationship between visfatin and chronic hepatitis B cirrhosis process.

Patients and Methods

Patients

The current research has obtained the approval of Ethic Committee of our hospital and informed consent of patients and their families. 153 cases of patients with hepatitis B cirrhosis who were admitted and diagnosed in our hospital from February 2014 to February 2016 were continuously selected as the observational group. 50 cases of healthy examination people were randomly selected as the control group. Hepatitis B was referenced to the diagnosis criteria in “The Guideline of Prevention and Treatment for Chronic Hepatitis B” proposed by Chinese Society of Hepatology in 2010. Inclusion criteria: 1. Aging from 18-70 years old; 2. Taking antiviral and hepatoprotective drug treatment regularly. Exclusion criteria: 1. Other hepatitis virus infection, such as heart, brain, lung, kidney and other organs dysfunction, diabetes; 3. Pregnant or lactating women, etc.

91 cases were males and 62 cases females in the observation group; aging from 42-60 years

Table I. The total number of scientific research projects and research funding from 2011 to 2015.

Year	National	Provincial & ministerial	Subjects (item) Municipal	Hospital-level	Research funding (Ten thousand)
2011	0	3	51		174
2012	2	5	24	153	394
2013	2	9	29	68	382
2014	4	13	26		387
2015	3	18	38		492.6

old with an average age of (52.8±9.7) years old; Child-Pugh Score was divided into grade A with 31 cases, grade B with 79 cases and grade C with 43 cases. 33 cases were male and 17 cases were female; aging from 48-65 years old with an average age of (54.7±10.6) years old. Compared the gender and age of patients between two groups, the differences were not statistically significant.

Methods

Peripheral venous blood of 5 ml was drawn from the subjects, centrifuging 1500 g for 15 min and stored at -20°C. ELISA was used to detect the level of serum visfatin, and the kit was purchased from Sigma-Aldrich (St. Louis, MO, USA), microplate reader was from Bio-Rad (Hercules, CA, USA). Procedures were in strict accordance with the instructions. Rate method was adopted to detect blood lipid level, including triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), Mindray BS-330 automatic biochemical detector was purchased from Shenzhen Mindray. Bio-Medical Electronics Co., Ltd (China). Sn-695B type intelligent release γ measuring instrument (Shanghai Nucleus Research Institute Rihuan Instrument Factory) was used to detect liver fibrosis index, including hyaluronic acid (HA), laminin (LN), type III procollagen peptide (PIIP) and type IV collagen (CIV). Fasting plasma glucose (FBG) and fasting insulin level (Fins) were detected, FPG used glucose oxidase method and Fins magnetic enzyme-linked immunosorbent assay to calculate insulin resistance index (HOMA-IR) = FPG×FIns/22.5, in which reference range of Fins was 35-145pmol/L (chemiluminescent immunoassay), HOMA-IR >2.67 meant insulin resistance.

Observation Index

Compared serum visfatin level, blood lipid level, liver fibrosis index, fasting plasma glucose

and fasting insulin levels of different liver functions between the observational group and the control group. The correlation between visfatin level and blood lipid, liver fibrosis index and insulin resistance index was analyzed.

Statistical Analysis

SPSS 22.0 software (SPSS Inc., Chicago, IL, USA) was used for data analysis, measurement data were expressed by the mean ± standard deviation (SD), comparisons among groups were analyzed by One-way ANOVA, comparison between two groups was tested by LSD method; correlation analysis was tested by Pearson, $p < 0.05$ indicated that the difference was statistically significant.

Results

Comparison of Serum Visfatin Level

The level of Visfatin in patients with liver fibrosis was significantly increased ($p < 0.05$) compared with that of the control group. Additionally, the increase was accompanied with significant increased ($p < 0.05$) of aggregation of the liver function damage, the difference was statistically significant (Table I).

Comparison of Blood Lipid Level

Compared TG, TC, HDL-C and LDL-C levels among various groups showed that the differences were not statistically significant ($p > 0.05$) (Table II).

Comparison of Liver Fibrosis Index

HA, LN, CIV and PIIP levels of cirrhosis group were significantly higher ($p < 0.05$) than those of the control group. Furthermore, aggregation of liver function damage was also significantly increased ($p < 0.05$) (Table III).

Table II. Science and technology achievements in medicine and health from 2011 to 2015 (unit: item).

	2011	2012	2013	2014	2015	Total
Scientific and technological and technological achievements	11	17	12	22	14	76
National	0	0	0	1	0	1
provincial	4	9	4	9	4	30
Municipal	7	8	8	12	10	45

Table III. The papers included in SCI and published in the country from 2011 to 2015.

	2011	2012	2013	2014	2015	Total
SCI (piece)	14	27	55	126	130	352
Chinese Medical Association (piece)	41	52	88	54	63	298
Science and technology papers (piece)	169	214	209	286	307	1185
Monograph (book)	2	3	22	46	83	156
Total	226	296	374	512	583	1991

Comparison of Fasting Plasma Glucose and Fasting Insulin Levels

The differences of comparison of FPG and Fins among various groups were not statistically significant. HOMA-IR of cirrhosis group was significantly higher ($p<0.05$) than that of the control group, with significant ($p<0.05$) increase of the aggregation of liver function damage (Table IV).

Analysis of Correlation Between Visfatin Level and Various Indexes

The level of Visfatin was positively correlated with liver fibrosis index and HOMA-IR ($p<0.05$) (Table V).

Discussion

Liver fibrosis is a pathologic process that the body's inflammatory stimulation or stem cell ne-

crisis leads to abnormal hyperplasia of fibrous connective tissue in the liver⁶. Liver fibrosis progress indexes include the hyaluronic acid (HA), laminin (LN), type III procollagen peptide (PII-IP) and type IV collagen (CIV), which can well judge the damage degree of the stem cells and liver fibrosis process and also have good correlation with the prognostic judgment liver cirrhosis⁷. Visfatin are rich in visceral fat. The study confirms that visfatin is closely associated with type 2 diabetes mellitus, and participates in the occurrence of insulin resistance⁸. Through the study: the visfatin level, HA, LC, CIV, PIIP and HOMA-IR of patients with liver cirrhosis increased, compared with those of the control group, concomitantly with significant increases of the aggravation of degree of liver dysfunction. The differences of the levels of TG, TC, HDL-C and LCL-C, FPH and Fins of patients in two groups were not statistically significant. The levels vi-

Table IV. Top 15 departments who issued the papers from 2011 to 2015.

Department	Number	Percentage (%)
Department of Cardiology	138	11.65
Department of Emergency	100	8.44
Department of Neurology	93	7.85
Department of Orthopedics	88	7.85
Obstetrics and Gynecology	77	6.50
Department of Stomatology	62	5.23
Internal Medicine-Oncology	59	4.98
Department of Urology	56	4.73
Department of Thoracic Surgery	56	4.73
Endocrine	54	4.57
Department of Radiotherapy	50	4.23
Department of Psychiatry	48	4.05

Table V. The distribution of departments who issued papers included in ISC from 2011 to 2015.

Department	Number	Percentage (%)
Department of Cardiology	45	12.78
Department of Orthopedics	31	8.80
Department of Endocrinology	31	8.8
Department of Urology	29	8.23
Internal Medicine-Oncology	23	6.53
Department of Neurology	20	5.68
Department of Radiotherapy	18	5.11
Department of Stomatology	12	3.41
Department of Emergency	10	2.84
Department of Psychiatry	9	2.56
Department of Radiotherapy	9	2.27
Obstetrics and Gynecology	8	4.05

visfatin were positively related to liver fibrosis index and HOMA-IR.

The content of visfatin was more than subcutaneous fatty tissue, which is related to the area of visceral fat. Also, it is rich in liver, muscle, and marrow. Adipokines will aggravate insulin resistance, destroy blood lipid metabolic balance, promote triglycerides gathered in pre-adipocyte, increase liver fat deposition, induce “multiple damages” on liver, stimulate extracellular matrix secretion and deposits, form steato-hepatic fibrosis and further progress to liver cirrhosis⁹. The liver is an important organ of blood lipid and lipoprotein metabolism. The level of damage of liver is closely related to the blood lipid and apolipoprotein levels. The deformation and necrosis of liver cells of patients with liver cirrhosis lead to organelles damage and reduction of the synthesis of apolipoprotein and blood lipids. Also, the patients will suffer from combined malnutrition, hypoalbuminemia or some other complications. Besides, it can also influence the levels of blood lipid. The levels of blood lipid among studied groups have no difference, and it was not associated with the degree of liver function damage. So the presented blood lipid level cannot be used as a sensitive index of liver fibrosis; Lipid levels are also affected by many factors such as diet, gastrointestinal absorption function, and so on¹⁰.

Study finds that^{11,12}, visfatin was closely related to liver fibrosis, and it was positively related to tissue inflammation integral. Visfatin can stimulate monocyte and macrophage to secrete IL-6, TNF- α , and other inflammatory factors, participating in local inflammation of the liver reaction process¹³. Insulin resistance may play an important role in the pathogenesis of liver injury mediated by hepatitis B virus. Visfatin can be competitively associated with insulin receptor and inhibit the metabolic activity of insulin¹⁴. By insulin receptor's tyrosine phosphorylation reaction in liver cells, visfatin can stimulate a variety of inflammatory cytokines to release¹⁵. What's more, visfatin has good correlation with HBsAg positive state and HBV DNA load capacity¹⁶, the visfatin level of HBsAg positive patient's increases compared with that of HBsAg negative patients. The level of visfatin increases with the increasing of the load of HBV DNA.

Conclusions

The increase of the level of serum visfatin in chronic hepatitis B patients with cirrhosis is related to liver cirrhosis progress, indicators of hepatic

fibrosis and HOMA-IR. Whether serum visfatin can be used as the sensitive and specified index of chronic hepatitis B cirrhosis process still needs further study. Serum visfatin working as an intervention targets to improve the process of cirrhosis of the liver may be a new target.

Conflict of interest

The authors declare no conflicts of interest.

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