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The role of chemerin and vaspin in Egyptian patients with viral hepatitis C

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ABSTRACT

Introduction: Noninvasive markers of fibrosis developed as an alternative to the staging of fibrosis by means of liver biopsy which is invasive, painful and with limitations in diagnostic use and accuracy. Adipokine profile appears to assume a unique role in the pathogenesis of chronic hepatitis C (CHC). Chemerin and vaspin are adipokines with the potential to regulate the inflammatory response.

The aim of this study is to evaluate and determine the role of serum levels of some adipokines as chemerin and vaspin as useful markers in prognosis and monitoring fibrosis in chronic hepatitis C among Egyptian patients.

Subjects and methods: Ninety individuals; with ages ranged between 19 and 60; were included in this retrospective study and divided into two groups; group I: twenty healthy control group and group II: seventy patients with chronic viral hepatitis C. Chronic viral hepatitis C patients were classified into five sub groups according to their stages of fibrosis; group I: included 14 patients without fibrosis: F0, group II: included 14 patients with portal fibrosis stage: F1, group III: included 14 patients with periportal fibrosis stage: F2, group IV: included 14 patients with abundant bridging fibrosis stage: F3, group V: included 14 patients with cirrhosis stage: F4. Chemerin and Vaspin levels were evaluated in all the subjects' sera by Enzyme- linked immunosorbent assay (ELISA).

Results: The serum chemerin level in CHC patients was significantly increased as compared with controls. Also, there was a positive correlation between the chemerin level and the stage of fibrosis. As the stage of fibrosis increases, the serum chemerin level increases. Serum vaspin decreased in CHC patients compared to controls and was positively correlated with fibrosis stage. Serum vaspin levels were significantly higher in patients with periportal fibrosis (F2), abundant bridging fibrosis (F3) and cirrhosis (F4) compared to portal fibrosis (F1) or without fibrosis (F0).

Conclusion: This study investigated and demonstrated that there is correlation between serum chemerin and vaspin levels and stages of fibrosis compared to controls, where the serum chemerin level increases in chronic hepatitis C patients compared to controls and increases with progression of stage of fibrosis. Whereas the serum vaspin level decreases in chronic hepatitis C patients compared to controls and increases with progression of stage of fibrosis to become near the serum levels in controls.

1. Introduction

Hepatitis C virus (HCV) is a major global health burden representing around 170 million chronic infections worldwide (Abdel-Hamid et al., 2018). It is estimated that, among the people who are living with chronic HCV infection globally, 10%–20% will develop complications of chronic liver disease and 1%–5% will develop liver cancer (Abdel-Hamid et al., 2015). Hepatitis C is often asymptomatic infectious disease, but chronic infection can lead to different prognosis, like fibrosis and cirrhosis which are scarring of the liver and advanced scarring over many years, respectively (Jung and Yim, 2017). When fibrosis progresses to cirrhosis there is a great risk of many hepatic- related

Abbreviations: HCC, Hepatocellular carcinoma; CHC, Chronic viral hepatitis C patients; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; T.BIL, Total bilirubin; ALP, alkaline phosphatase; ANOVA, analysis of variance; ROC curve, Receiver-operating characteristics; AUC, area under the curve; PV+, positive predictive value; PV−, negative predictive value; AUC, area under the curve; TGF, fibrogenic agent-transforming growth factor; ELISA, Enzyme- linked immunosorbent assay; BMI, body mass index; TAG, TriAcylglycerol; SPSS, Statistical Package for Social Science.

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complications like hepatocellular carcinoma (HCC) and even mortality. Thus, it's very important to monitor chronic liver disease to identify its progression, begin specific treatments, and also decide whether more invasive measures like liver transplantation are needed or not (Pinter et al., 2016).

Despite being the most common and depended method of staging the liver fibrosis, Liver biopsy is an invasive technique with an availability of errors during the sampling process (De Lucca Schiavon et al., 2014).

Chemerin is a newly discovered hormone that is basically expressed by fat-tissue and the liver (Xie et al., 2014). Chemerin is a new adipokine. Its expression has been found in a number of tissues including those of the liver, pancreas and lungs, as well as in adipose tissue. It has been shown to be associated with body mass index (BMI), plasma triacylglyceol (TAG), blood pressure (Buechler, 2014). While, Vaspin is a visceral adipose tissue and it is a derivative of serpin, 395 amino acid (45.2 kDa) adipokine exhibiting nearly 40% homology with alpha1-antitrypsin (Kukla et al., 2017). Vaspin is expressed in the number of tissues of the body, especially in white adipose tissue/fat cells that affect the liver and skeletal muscle (Tuemmler et al., 2015).

2. Subjects and method

2.1. Study subjects

Ninety individuals; with ages ranged between 19 and 60; were included in this retrospective study and divided into two groups; group I: twenty healthy control group and group II: seventy patients with chronic viral hepatitis C. Chronic viral hepatitis C patients (CHC) were classified into five sub groups according to their stages of fibrosis; sub group a: included 14 patients without fibrosis: F0, sub group b: included 14 patients with portal fibrosis stage: F1, sub group c: included 14 patients with periportal fibrosis stage: F2, sub group d: included 14 patients with abundant bridging fibrosis stage: F3, sub group e: included 14 patients with cirrhosis stage: F4. Patients were compared to 20 healthy control subjects, had no recognizable diseases and clinically free from any abnormality. They were not receiving any medication. Tissue samples were obtained by transurethral resection of the liver collected and dissected under stringent sterile conditions and immediately frozen in liquid nitrogen. Body mass index, was recorded. All patients were selected from Abbasseya Fever Hospital and samples were collected after their approval. Written, informed consent was obtained from each patient before enrolment into the study.

2.2. Patients inclusion criteria

Patients that participated in the study fulfilled the inclusion criteria included: age ranged between 19 and 60 years, positive HCV antibodies, detectable HCV-RNA, HCV genotype 4, liver biopsy showing histological evidence of chronic hepatitis C. All patients had liver biopsies performed using the TNM staging system by the seventh edition of the American Joint Committee on Cancer (AJCC) (Edge et al., 2010) as part of the diagnostic routine, and accordingly standard treatment protocols and follow-up schedules based on published guidelines were selected (NCCN V.2. 2016). Toxicity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTC, 2006). Histopathological features were assessed according to Scheuers (inflammatory activity, fibrosis) and Brunts (steatosis) scales.

2.3. Patients exclusion criteria

Thyroid dysfunction, psychological disorders, autoimmune diseases, uncontrolled diabetes, other co-morbid conditions (e.g.: ischemic heart disease, renal failure, cerebrovascular disorders), organ transplantation, cytopenias, smoking, and obesity.

2.4. Biochemical tests

Briefly, 5 ml of peripheral blood were drawn from every one subjects; they were collected into serum vacuum tubes with clot activator, instantly centrifuged in 3000 rpm for 10 min to separate serum. The serum partitioned into aliquots then stored at −80 °C till the time of assay. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (T.BIL), alkaline phosphatase (ALP) were measured directly after the separation of serum, while visceral adipose-specific serine protease inhibitor (Vaspin) and Chemerin were measured ELISA after being stored at −80 °C till the collection of all the control and patients' sera.

2.5. Statistical analysis

Data were analyzed by SPSS program (Statistical Package for Social Science; SPSS Inc., Chicago. IL, USA version 21). The tests used were: mean, SD standard deviation, the biological variables were compared with one-way analysis of variance (ANOVA) test then by student's test and their values were reported as mean ± SD, Pearson correlation coefficient test (r): to test for linear relation between two numeric variables. Receiver-operating characteristics curves (ROC) were constructed to assess the diagnostic performance of the serum markers in discriminating HCC from other groups. Sensitivity, specificity what's more diagnostic accuracy were calculated in accordance with standard methods. $P < 0.05$ for a two-tailed test might have been considered statistically significant. A probability value (P value) under 0.05 was considered statistically significant.

Table 1
Comparison between statistics of the clinical and laboratory data of the F0 group, F1 group, F2 group, F3 group, F4 group and the control groups.

Variables	Control Gp. N = 20	F0 Group N = 14	F1 Group N = 14	F2 Group N = 14	F3 Group N = 14	F4 Group N = 14
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
AST (IU/l)	26.55 ± 11.02	28.50 ± 9.12	55.79 ± 12.85[a,b]	54.5 ± 20.41[a,b]	55.57 ± 13.43[a,b]	55.79 ± 12.24[a,b]
ALT (IU/l)	11.45 ± 4.01	31.07 ± 5.84[a]	67.36 ± 7.38[a,b]	48.86 ± 8.59[a,b,c]	56.00 ± 7.57[a,b,c,d]	68.79 ± 7.09[a,b,d,e]
ALP (IU/l)	60.85 ± 12.88	55.92 ± 5.29	69.57 ± 11.83[b]	83.07 ± 12.49[a,b,c]	162.21 ± 20.65[a,b,c,d]	159.50 ± 20.59[a,b,c,d]
T.BIL (mg/dl)	0.56 ± 0.19	0.53 ± 0.12	0.67 ± 0.17[b]	1.46 ± 0.15[a,b,c]	2.59 ± 1.16[a,b,c,d]	3.77 ± 1.03[a,b,c,d,e]
Chemerin (ng/ml)	4.55 ± 1.22	6.52 ± 0.72[a]	14.11 ± 1.13[a,b]	17.14 ± 0.91[a,b,c]	20.39 ± 0.49[a,b,c,d]	23.15 ± 0.55[a,b,c,d,e]
Vaspin (ng/ml)	2.19 ± 0.29	0.87 ± 0.06[a]	0.61 ± 0.06[a,b]	1.66 ± 0.20[a,b,c]	1.99 ± 0.19[a,b,c,d]	2.16 ± 0.22[b,c,d]

[a] Significant from control at $p < 0.05$.
[b] Significant from F0 stage at $p < 0.05$.
[c] Significant from F1 stage at $p < 0.05$.
[d] Significant from F2 stage at $p < 0.05$.
[e] Significant from F3 stage at $p < 0.05$.