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Role of Endosialin/CD248 and Cytoglobin in Liver Fibrosis

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Abstract

Background: Chronic liver diseases are a major global health burden. Cytoglobin (Cygb), Human IV globin is abundantly expressed in CSCs between hepatocytes. CYGB can bind oxygen and nitric oxide and is said to protect hepatic stellate cells (HSCs) from reactive oxygen species (ROS).

Aim: To estimate role of CD248 and Cygb in the process of liver fibrosis.

Patients and methods: This study was conducted on 44 Egyptian patients with hepatic stenosis detected by ultrasound, and 40 healthy volunteers as control group.

Results: Our results showed statistically significant (P value < 0.001) increased CD248 in patients group (189.03 ± 66.6) when compared with control group (138.7 ± 36.5), decreased Cygb in the patients group (1.62 ± 0.35) when compared with the control group (1.93 ± 0.26).

Conclusion: Our study identified Cygb and CD248 as a novel therapeutic-targets in liver-fibrosis.

Keywords: CD248, Chronic liver disease, Cygb, Fibrosis

1. Introduction

Chronic liver disease symbolized as a major global health problem with mortality rate 2 million death worldwide each-year.1

Risk factors of chronic liver disease were included, hepatitis C-Virus, hepatitis B-Virus, Alcoholic and NonAlcoholic seato-hepatistis, autoimmune and genetic diseases.2

Liver fibrosis recognized with the chronic inflammatory disease with mortality rate 45% all-over the world.3

Clinically, the treatment of liver cirrhosis emerged with antiviral therapies for viral-hepatitis, change lifestyle, and bariatric surgeries.4

Cytoglobin (CYGB) is the human fourth globin antifibrotic target factor which is expressed by hepatocytes.5

CD248 is an endo-thelial tumor marker expressed on endo-thelial cells with several types of cancers, such as; the brain and colon. As perprevious studies attempted to apply CD248 markers were expressed in chronic liver injury and highly expressed with liver fibrosis.6

Therefore; This study aims to evaluate the role of CD248 and Cygb in the liver fibrosis process and the development of antifibrotic therapies.

2. Patients and methods

In this cross-sectional-study at the Internal Medicine Department, Assiut Faculty of Medicine, Al-Azhar University. 44 Egyptian patients with chronic liver disease were enrolled. 40 patients were divided into two groups; Chronic-liver-disease group: including 44 patients with chronic liver disease. The diagnosis were based on clinical picture, ultrasound, and laboratory investigations. Healthy control group: including 40 age and sex matched healthy volunteers who were normal by clinical, laboratory and radiologic investigations.
Patients proved as having chronic liver diseases and Age greater than 18 years old were included. Patients who less than 18 years old, end-stage liver disease, other fibrotic diseases and systemic sclerosis, malignancy and Noncompliant patients were excluded.

History and clinical examination: Complete history taking, Full clinical examination include assessment of general condition, vital signs. Abdominal, chest and heart examination were assessed with focus on manifestations of chronic-liver-disease were collected from all patients. Blood pressure equal or more than 140/90 mmHg defined as hypertension. Laboratory Investigations: Complete blood picture (CBC), Liver profile, Renal function tests, Lipid profile and Quantitative detection of Cygb and CD248 in serum.

7 ml of venous-blood was collected from each patient. The collected-sample was allowed to clot for half an hour in a water bath at 37 °C, and then it was centrifuged for 15 min at 3000 revolutions/minute for separation of serum by means of a clean dry Pasteur pipette. 2 ml of blood was put on EDTA (1 mg/ml blood) and mixed thoroughly to perform CBC.

Quantitative detection of CYGB in serum was measured in all patients by enzyme-linked immune-sorbent assay (ELISA) commercial kit (Human Cytoglobin, CYGB ELISA Kit, Chongqing Biospes Co., Ltd, China). This kit was based on standard sandwich enzyme-linked immune-sorbent assay technology. The purified anti-CYGB antibody was precoated onto 96-well plates.

Quantitative detection of CD248 in serum was measured in all patients by enzyme-linked immune-sorbent assay (ELISA) commercial kit. The purified antiEndosialin/CD248 antibody was precoated onto 96-well plates.

Assessment of the liver for its size in both midline and mid-clavicular line, surface of the liver and echogenicity.7

The study was approved by Committee of Internal Medicine Department and Committee of Faculty of Medicine and then by the Ethical Committee at Al-Azhar University.

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. Quantitative data were expressed as mean±SD. Qualitative data were expressed as frequency and percentage.

3. Results

Highly statistically significant ($P$ value < 0.001) increased CD248 in patients group (189.03 ± 66.6) when compared with control group (138.7 ± 36.5).
**Table 5. Comparison between studied groups studied laboratory data.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (N = 44)</th>
<th>Control (N = 40)</th>
<th>MW</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBG (mg/dl)</td>
<td>156.7 ± 88.2</td>
<td>100.1 ± 5.1</td>
<td>538</td>
<td>&lt;0.001 S</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>174.4 ± 58.4</td>
<td>157.9 ± 11.6</td>
<td>724</td>
<td>0.162 NS</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>144.8 ± 73.9</td>
<td>117.4 ± 10.3</td>
<td>792</td>
<td>0.430 NS</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.86 ± 0.4</td>
<td>0.83 ± 0.2</td>
<td>778</td>
<td>0.356 NS</td>
</tr>
</tbody>
</table>

**Table 6. Description of Sonar results in patient’s group.**

<table>
<thead>
<tr>
<th>Patient’s group (N = 44)</th>
<th>Cirrhotic liver</th>
<th>Fatty liver</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>75%</td>
<td>25%</td>
</tr>
</tbody>
</table>

**Table 7. Relation between Sonar results and liver function tests.**

<table>
<thead>
<tr>
<th>Sonar results</th>
<th>N</th>
<th>ALT</th>
<th>AST</th>
<th>Bilirubin</th>
<th>ALP</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhotic</td>
<td></td>
<td>25</td>
<td>8</td>
<td>13</td>
<td>17</td>
<td>3.2 0.071 NS</td>
</tr>
<tr>
<td>Fatty</td>
<td></td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>11</td>
<td>3.5 0.062 NS</td>
</tr>
</tbody>
</table>

**Table 9. Relation between Sonar results and laboratory data.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>MW</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBG (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhotic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 10. Relation between Sonar results and studied markers.**

<table>
<thead>
<tr>
<th>Sonar results</th>
<th>CD248 (pg/ml)</th>
<th>Cygb (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhotic</td>
<td>193.1 ± 65.4</td>
<td>135</td>
</tr>
<tr>
<td>Fatty</td>
<td>176.7 ± 71.9</td>
<td>216.8 ± 0.4</td>
</tr>
</tbody>
</table>

**Table 11. Correlation study between Endosialin, Cygb and other studied data in patient’s group.**

**4. Discussion**

Chronic liver diseases are a major global health burden and account for ~2 million deaths/year worldwide Wilhelm and colleagues.\(^8\) Therefore; this study was aimed to obtain the role of CD248 and Cygb-markers in liver-fibrosis that targeted the development of antifibrotic-therapies.

Our review results showed no significant-difference between concentrated on group as respect age,
sex, liver capability tests and Cholesterol, fatty substances and serum creatinine. There were 11 (25%) males and 33 (75%) females in patients group while there were 12 (30%) males and 28 (70%) females in control bunch.

In any case, our review observed that measurable critical expanded glucose in patients-group (156.7 ± 88.2) when contrasted and control group (100.1 ± 5.1). As to; realistic discoveries there were 33 (75%) patients with cirrhotic liver and 11 (25%) patients with greasy liver in the concentrated on patients.

In spite of the fact that, our outcomes showed measurable critical (p-estimate <0.001) expanded serum levels of CD248 in patients group (189.03 ± 66.6) when contrasted and control group (138.7 ± 36.5). In concentrate by Wilhelm and colleagues, CD248 articulation was concentrated by immunostaining and quantitative PCR in both ordinary and unhealthy human and murine liver tissue and separated hepatic stellate cells (HSCs). Comparative outcomes were accounted for by Mogler and colleagues, who distinguished the HSC marker CD248 as a basic equilibrium of liver fibrogenesis and regenerative hepatocyte expansion. In accordance with these perceptions, Lin and colleagues analyzed CD248 articulation in the liver tissue of patients with hepatic cirrhosis and in carbon tetrachloride (CCl4)-actuated liver tissue of patients with hepatic cirrhosis and in carbon tetrachloride (CCl4)-actuated liver fibrosis. In the meantime, the reasonability of rodent hepatic stellate cell line T6 (HSC-T6) cells was restrained by Cygb and the apoptosis prompted by Cygb in HSC-T6 cells was recognized by Annexin V/PI twofold staining.

In one more review led by Nishi and colleagues, kidney ischemia-reperfusion expanded the quantity of Cygb-positive cells per region and up-managed Cygb mRNA and protein articulation in kidney cortex tissues. Hypoxia up-managed Cygb articulation in refined rodent kidney fibroblasts. The organic capability of Cygb in vivo was assessed in Cygb-overexpressing transgenic rodents. Utilizing both transgenic rodents and refined kidney fibroblasts, it was shown that Cygb articulation presents cell security through a cancer prevention agent component and that heme in Cygb is significant as a result of its antioxidative capacity.

4.1. Conclusion

We found expanding in CD248 in patients-group when contrasted and control-group and diminishing Cygb in patients-group when contrasted and control-group. Cygb and CD248 recognized as a novel therapeutic targeting liver-fibrosis.
Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

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Conflicts of interest

Conflict of interest statement: The authors declared that there were No conflicts of Interest.

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