The Potential Hepatoprotective Effect of Metformin in HCV-Infected Pediatric Patients with Beta Thalassemia Major

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Introduction

Beta thalassemia major (β-TM) is a genetic blood disorder characterized by severe anemia that requires lifelong supportive care.

It’s highly prevalent among Mediterranean peoples with carrier rate between 5.3 and ≥ 9% in Egypt.

Iron overload-induced oxidative stress and transfusion-acquired hepatitis C virus (HCV) infection are the main lineament of liver damage in β-TM patients.

Beyond diabetes, hepatoprotective effect of metformin in some liver diseases has been demonstrated and proven by different studies.

Objectives

The aim of our study was to investigate the safety and the potential hepatoprotective effect of metformin in HCV-infected β-TM pediatric patients focusing on its effects on liver biochemical profile, oxidative stress status and fibrosis severity.

Methods

This was a prospective, randomized, parallel, controlled, open label study.

60 out of 225 screened β-TM pediatric patients, infected with HCV aged between 11-18 years; were selected and randomly assigned to control group or treatment group in 1:1 allocation; (n = 31, n = 29 respectively).

Both groups were receiving regular packed red blood cells transfusions, iron chelators and other supportive medications: metformin (500 mg, twice daily) was added to the regimen of the treatment group only.

Patients were followed-up for six months with assessment of liver biochemical profile (liver enzymes, total bilirubin, albumin and international normalized ratio (INR)), oxidative stress markers (total antioxidant capacity (TAC) and malondialdehyde (MDA)), liver fibrosis by FibroScan, clinical symptoms improvement and metformin’s adverse effects.

Results

Change in TAC and MDA serum levels indicated significantly improved oxidative stress status in the treatment group compared to significant deterioration in the control group (P < 0.001).

Fibrosis grade improvement was observed in 14 patients in the treatment group over 6-months period versus one improved case in the control group.

There was a significant decrease over time in aspartate aminotransferase (AST) serum level in the treatment group only (P= 0.013). Although the non-significant difference between groups, improvement in ALT and AST serum levels was higher in the metformin group than in the control group.

No adverse effects due to metformin administration were reported except for some GIT upset which resolved before the end of the first week of treatment.

Change in ALT and AST Serum levels within Both Groups over the Study Period Expressed as Mean ± SD.

Fibrosis Improvement Status

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group (N = 30)</th>
<th>Metformin-treated group (N = 27)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT (U/L)</td>
<td>Baseline</td>
<td>3rd month</td>
<td>6th month</td>
</tr>
<tr>
<td></td>
<td>107.30 ± 20.96</td>
<td>98.51 ± 18.30</td>
<td>94.47 ± 17.04</td>
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<tr>
<td></td>
<td>107.81 ± 20.96</td>
<td>90.48 ± 19.15</td>
<td>88.58 ± 17.26</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>Baseline</td>
<td>3rd month</td>
<td>6th month</td>
</tr>
<tr>
<td></td>
<td>254.89 ± 43.74</td>
<td>239.39 ± 33.64</td>
<td>248.05 ± 36.61</td>
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<tr>
<td></td>
<td>255.81 ± 43.74</td>
<td>231.73 ± 34.06</td>
<td>229.41 ± 35.76</td>
</tr>
</tbody>
</table>

*Mixed repeated measure ANOVA (time*group interaction) at P < 0.05

References