Prophylactic Effect of Vitamin C on Cyclosporine A-induced Liver Toxicity

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ABSTRACT

Background: Cyclosporine A (CsA) is an important immunosuppressive agent; however, its clinical use is limited by several side effects such as hepatotoxicity. Vitamin C (ascorbic acid) is a very important and powerful antioxidant and protects membranes against oxidation.

Objectives: The aim of this study was to study protective role of vitamin C against CSA-induced hepatotoxicity.

Materials and Methods: Thirty male Wister strain rats weighting 210-260g were randomly divided into 3 groups (n = 10): group A was the control group and received placebo (Normal Saline), group B was the CSA-treated group and received 15mg/kg/day CsA for 21 days, group C was the CsA + vitamin C group and was received 200mg/kg/day vitamin C orally 3 hours before receiving 15mg/kg/day CsA. On 22th day rats serum obtained for measuring biochemical factors including bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride, alkaline phosphatase (ALP) and lactate dehydrogenase (LDH), total protein, and albumin.

Results: Bilirubin, ALT, AST, triglyceride, ALP, and LDH levels were lower in CsA + ascorbic acid group than that of CsA group (P < 0.05) while plasma total protein and albumin were significantly higher in CsA + ascorbic acid group than that of CsA group (P < 0.05).

Conclusions: In conclusion, we have shown that vitamin C administration provides protection against CSA-induced injury in rat liver function and may have hepatoprotective role in the patients experiencing CSA treatment.

Implication for health policy/practice/research/medical education: To reduce CsA-induced hepatotoxicity.

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1. Background

Cyclosporine A (CsA) is an important immunosuppressive agent which is an essential part of drug regimen in transplant patients and in the treatment of diseases involving immune system (1). However, its clinical and experimental use is limited by several side effects such as...
as nephrotoxicity, cardiotoxicity, hypertension and hepatotoxicity (2). Different authors suggest that reactive oxygen species (ROS) production, oxidative stress, depletion of hepatic antioxidant system, and increase in malondialdehyde (MDA) be possible mechanisms of CsA hepatotoxicity (3-6). Fortunately, there are several antioxidant mechanisms that can neutralize free radicals in living organisms. Antioxidant defense mechanisms can be grouped by enzymatic antioxidants (mainly superoxide dismutase, glutathione peroxidase and catalase) and non-enzymatic antioxidants (e.g. tocopherols, carotenoids, ascorbic acid and others) that can neutralize free radicals (7). From non-enzymatic antioxidants, vitamin C (ascorbic acid) is a very important, and powerful, antioxidant, and protects membranes against oxidation. (8).

Recent in vitro and ex vivo studies have revealed that vitamin C in plasma increases dose-dependent resistance to lipid peroxidation (9). Majority of in vivo studies have showed reduction in markers of oxidative DNA, lipid and protein damage after supplementation with vitamin C (10).

2. Objectives

The aim of this study was to study protective role of vitamin C against CsA-induced hepatotoxicity through studying changes in some plasma biochemical factors.

3. Materials and Methods

Thirty male Wister strain rats weighting 230-260g were randomly divided in to 3 groups (n=10); besides, they were kept in accordance with the “Principles of Laboratory Animal Care and the Guide for the Care and Use of Laboratory Animals”. They had free access to commercial rat food and water. The CsA (Sigma-Aldrich Corp. St. Louis, MO, U.S.A.) oral solution (100 mg/ml15mg/kg/day) was given orally by gavage. Vitamin C (Osveh, Tehran, IR Iran) (100mg/mL, 200mg/kg/day) was delivered by oral gavage. Vitamin C (ascorbic acid) is a very important, and powerful, antioxidant, and protects membranes against oxidation. (8).

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Table 1. Serum levels of bilirubin, Total protein, Albumin, ALT, AST, Triglyceride, ALP, and LDM in control, CsA and CsA + Vit C groups. Results expressed as mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>CsA</th>
<th>CsA + Vit C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>0.120 ± 0.008</td>
<td>0.179 ± 0.144</td>
<td>0.154 ± 0.014</td>
</tr>
<tr>
<td>LDH (IU/L)</td>
<td>1156.700 ± 27.252</td>
<td>1750.00 ± 37.392</td>
<td>1521.20 ± 33.891</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>33.523 ± 3.046</td>
<td>43.770 ± 3.391</td>
<td>33.523 ± 3.046</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>25.460 ± 3.312</td>
<td>43.770 ± 3.391</td>
<td>33.523 ± 3.046</td>
</tr>
<tr>
<td>Total protein (g/dL)</td>
<td>7.114 ± 0.154</td>
<td>5.334 ± 0.254</td>
<td>5.334 ± 0.254</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.264 ± 0.251</td>
<td>3.012 ± 0.181</td>
<td>3.546 ± 0.234</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>71.314 ± 4.516</td>
<td>199.900 ± 6.279</td>
<td>91.266 ± 5.046</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; ALP, Alkaline Phosphatase; CsA, Cyclosporine A; LDH, Lactate Dehydrogenase
have shown that vitamin C administration provides protection against CsA-induced injury in rat liver function and it may have hepatoprotective role in patients experiencing CSA treatment.

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References