Protective effect of ticagrelor on liver damage induced by ischemia-reperfusion

Yusufhan Yazir1, Melda Yardımoğlu Yılmaz1, Selenay Furat Rencber1, Kübra Kavram1, Göktuğ Şirin2
1Department of Histology and Embryology, Kocaeli University Faculty of Medicine, Turkey
2Department of Gastroenterology, Kocaeli University Faculty of Medicine, Turkey

Introduction & OBJECTIVES: Ischemia-reperfusion injury (IRI) occurs after different surgical treatments and may have an effect in remote organs, causing multiple organ dysfunction syndrome and death. The aim of this study is to evaluate the protective effect of ticagrelor on liver histology in ischemia-reperfusion model.

Materials & METHODS: Thirty-five Sprague-Dawley rats were divided into 5 groups: In group 1, only laparatomy was performed. In all groups except for the sham group (group 1), IRI was induced by clamping the aorta with atraumatic vascular clamp infrarenally for two hours, followed by 4 hours of reperfusion. In group 2-5, animals were treated with 0.1 ml saline, dose of 7.5 mg/kg, 15 mg/kg and 25 mg/kg ticagrelor, respectively. At the end of the experiment, livers were removed, processed and embedded in paraffin blocks and cut into 4-5 μm sections. Histologic evaluation was performed H&E-stained sections. Liver injury was scored from 'mild' to 'severe. Hepatic IRI were classified as follows: Grade 0, no damage; Grade 1, mild damage with cytoplasmic vacuolization and nuclear pycnosis; Grade 2, moderate damage with expanded nuclear pycnosis, increase of cytoplasmic eosinophilia and loss of intercellular borders; Grade 3, severe damage with hemorrhage, neutrophil infiltration and severe necrosis. TUNEL protocol was applied and apoptotic index was calculated. All sections were examined by light microscope.

RESULTS: In sham group (group 1), microscopic architecture and cellular arrangement of liver were normal. Grade 3 injury was seen in group 2 and 3. Cytoplasmic vacuoles in hepatocytes, numerous leucocytes in sinusoids, vena centralis and portal area, hemorrhage, and necrosis were observed in these groups. In group 4 and 5, grade 1 and grade 2 injuries were seen such as moderate leucocytes and sinusoidal dilatation. The number of apoptotic cells in group 2 was more than group 4 and 5. There was a significant difference between group 1 and 2, group 1 and 3, group 2 and 3.

CONCLUSIONS: Our results suggest that ticagrelor plays a protective role against ischemia-reperfusion induced histological impairments and apoptosis. Although future clinical trials are required, the effective dose of ticagrelor may be used in ischemia-reperfusion induced liver damage.

Keywords: Ischemia-reperfusion, ticagrelor, liver, apoptosis.

TUNEL staining photomicrographs of all groups
TUNEL staining photomicrographs are seen of the liver in dose of 7.5 mg/kg (A, B), 15 mg/kg (C, D) and 25 mg/kg (E, F) of treatment groups, respectively.
<table>
<thead>
<tr>
<th>Abstract Category/Topic</th>
<th>Pathology and clinical medicine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language</td>
<td>English</td>
</tr>
<tr>
<td>Saved:</td>
<td>01.02.2017 20:50:44</td>
</tr>
<tr>
<td>Submit:</td>
<td>01.02.2017 23:54:16</td>
</tr>
</tbody>
</table>

Confidential to Author and Editor

Presenter : Yusufhan Yazir (yusufhanyazir@yahoo.com)