Does ticagrelor have a protective effect on intestinal injury induced by ischemia/reperfusion?

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Ischemia-reperfusion injury (IRI) occurs after different surgical treatments and may have an effect in remote organs, causing multiple organ dysfunction syndrome and death (1, 2). Several studies consistently showed that ticagrelor inhibits the cellular uptake of adenosine, in addition to antagonizing the P2Y12 receptor (3, 4). The platelet inhibitor ticagrelor is strongly recommended during 12 months post-acute coronary syndrome in European guidelines (5). The aim of this study is to evaluate the protective effect of ticagrelor on intestine in ischemia-reperfusion model. Thirty five Spraque-Dawley rats were divided into 5 groups: In group 1, only laparotomy was performed. In all groups except for the sham-operation (group 1) group, IRI was induced by clamping the aorta with atraumatic vascular clamp infrarenally for 2 hours, followed by 4 hours of reperfusion. In groups 2 to 5, animals were treated with 0.1 ml saline, doses of 7.5 mg/kg, 15 mg/kg and 25 mg/kg ticagrelor, respectively. At the end of the experiment, for histological examination, intestines were taken 60 min after reperfusion. The tissues were fixed in 10% formaldehyde for 48 h at room temperature, dehydrated by graded ethanol, and embedded in paraffin. 4-5 μm thick paraffin sections were stained with H&E. Apoptosis was performed by use of the TUNEL technique (ApopTag Plus Peroxidase In Situ Apoptosis Detection Kit, S7101; EMD Millipore Corp., Temeculla, CA) according to the manufacturer’s instructions, and then studied
using light microscopy. Intestinal histological damage was evaluated according to the Park Score as previously described (6) in stained with H&E.

The histological structure of intestinal mucosae was intact and clearly visible in group 1; histological impairments were observed in groups 2-5 with inflammatory cells compared with the group 1. In groups 4-5, histological damage decreased, mucosal impairment was determined milder than that in groups 2-3. In group 2 and 3, apoptotic cells were seen more than other groups (Figure 1).

In the present study, we conclude that ticagrelor has a prophylactic effect against intestinal damage induced by IRI for local mucosal protection, and increase in vascular dialatation, inflammation. Ticagrelor may have a protective role against mucosal histopathology and apoptosis induced by IRI. Although future clinical trials are required, the effective dose of ticagrelor may be used in IRI-induced intestine damage.

Keywords: Ticagrelor, ischemia-reperfusion, intestine, apoptosis

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