

Ischemia/Reperfusion Injury Induces Chronic Changes in the Small Bowel

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ISCHEMIA/REPERFUSION (I/R) injury is a common corollary of organ preservation, transplantation, and acute cellular rejection of intestinal allografts.¹⁻³ Long-term studies have been precluded by the prevailing notion that in the small bowel (SB), the changes induced by I/R injury resolve within a few days postoccurrence. However, having recently documented that a protracted deleterious effect of a single episode of I/R injury of kidneys,^{4,5} we proceeded to ascertain if a similar outcome is also witnessed in the SB.

MATERIALS AND METHODS

I/R injury in the SB of male ACI rats was induced by clamping in euthermic (37°C) conditions the superior mesenteric artery (SMA) for 45 minutes. While sham operated animals were used as controls (group IV; $n = 6$), SMA in the study group ($n = 6$ per group) was clamped either once (group I), twice (group II), or three times (group III) at 7-day interval. For the determination of chronic intestinal damage (CID), morphohistopathologic examination of the SB was performed at day ninety post-I/R. Macrophage (M ϕ) infiltration was ascertained by immunohistostaining with α -ED-2-mAb, apoptosis was quantified by TUNEL and RT-PCR was used to evaluate expression of ICAM-1, TGF- β , IGF, and IGF-R (receptor). Parametric tests were used for statistical analysis.

RESULTS AND DISCUSSION

As compared to animals in group IV, a single episode of I/R injury (group I) induced mild CID changes characterized by patchy degeneration of crypts. These changes were accentuated in animals in groups II and III in whom widespread degeneration of crypts with accompanying endothelial damage of the microvasculature was discerned. Additionally, in rats in the latter groups, there was also evidence for matrix degeneration, loss of germinal center, and heightened lymphocyte degeneration within the Payer's patches. Interestingly, as compared to sham-treated controls, a signifi-

cantly higher number of apoptotic cells ($P < .001$) and a prominent M ϕ infiltration ($P < .05$) was witnessed in the SB of group I animals, a finding accentuated in rats in groups II and III. Moreover a statistically significant altered expression of ICAM-1, TGF- β , and IGF-R was observed in the study animals compared to sham controls.

Unlike the prevailing conviction, these data demonstrates that transient I/R injury of the SB results in CID. We believe that the changes observed in the Payer's patches may contribute in facilitating bacterial translocation, which could explain the high rate of infections seen after intestinal transplantation. The altered structure of the intestinal mucosa observed, could also be responsible for the altered absorptive function of SB grafts that are subject to prolonged preservation or are affected by numerous episodes of acute rejection. The use of this novel model for a more comprehensive study of I/R injury related CID should be entertained.

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