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Lazaroid U74006F for Canine Small Bowel Preservation

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LAZAROIDS are a new group of synthetic 21-amino-steroids that inhibit iron-dependent lipid peroxidation without steroid action.[1] It has been known that lazaroids protect various organs from ischemic and reperfusion injury.[2-4] The aim of this study was to determine if one of the lazaroid compounds, U74006F, is effective for canine small bowel preservation.

MATERIALS AND METHODS

Adults mongrel dogs, weighing from 18 to 24 kg, were used. The entire small bowel was procured and flushed with cold lactated Ringer's solution containing heparin through the superior mesenteric artery. The intestinal lumen was also irrigated with the same solution. After the graft was preserved in the cold lactated Ringer's solution for 24 hours, it was transplanted orthotopically into the same animal. The U74006F was intravenously administered at a dose of 0 mg/kg (Laz(0)), 5 mg/kg (Laz(5)), 10 mg/kg (Laz(10)), or 15 mg/kg (Laz(15)) 30 minutes before graft removal and 30 minutes before graft reperfusion. Five animals were randomly tested at each group. For histological examination and biochemical determinations including maltase, malondialdehyde (MDA), myeloperoxidase (MPO), phospholipids (PL), and energy charge (EC), short segments of the ileum were collected before procurement, immediately after vascular flushing, at the end of 24-hour preservation, and 15 minutes and 1 hour after graft reperfusion.

RESULTS

Compared to the no-treatment group, lazaroid U74006F treatment suppressed the loss of maltase (Fig 1A), MDA production (Fig 1B), MPO activity (Fig 1C), and PL degradation (Fig 1D), and regained significantly higher EC after graft reperfusion. Structural alterations developed in the ileal mucosa after graft reperfusion, including denudation or sloughing of the mucosa, hemorrhage, neutrophil accumulation, and deep crypt cell necrosis. These changes were more evident with the no-treatment group than the groups treated by lazaroids.

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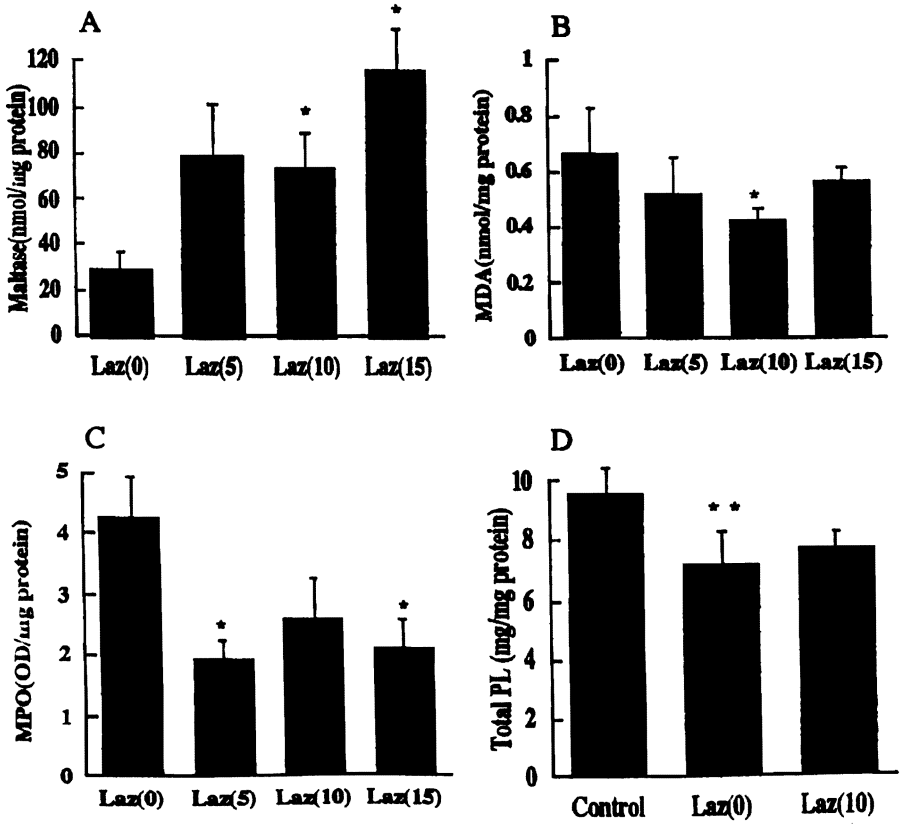

Fig 1. Changes of maltase activity **(A)**, MDA **(B)**, MPO **(C)**, and total PL **(D)** in the indicated groups at 1 hour after reperfusion. Values are expressed means ± SEM. $^{*}P < .05$ vs Laz(0); $^{**}P < .05$ vs control.

CONCLUSION

Lazaroids are potent inhibitors of iron-dependent lipid peroxidation and have been shown to be beneficial in a various organs for ischemic reperfusion injury.[2–4] In this study, after small bowel reperfusion, lazaroid U74006F was found to ameliorate villus enzyme loss (Maltase), to inhibit lipid peroxidation (MDA), to decrease neutrophil infiltration (MPO), to reduce phospholipid degradation, and to enhance energy charge. Lazaroid U74006F treatment also demonstrated the less histological damage than did the no-treatment group. Thus, our study confirms that lazaroid U74006F is effective for protection of the canine small bowel from preservation and reperfusion injury.

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