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Role of Xanthine-Oxidase System in Mucosal Injury After Intestinal Preservation and Transplantation

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THE XANTHINE-OXIDASE (XO) system has been considered to be involved in warm ischemia-reperfusion injury of the small intestinal mucosa.[1] Briefly, during warm ischemia in the small intestine, xanthine dehydrogenase (XD) is converted to XO, which produces superoxide radicals in the presence of its substrate (hypoxanthine and xanthine) and oxygen.[2] Meanwhile, adenosine triphosphate (ATP) is degraded and its degradation product, hypoxanthine, accumulates in the mucosal tissue.[2] Upon reperfusion (rewarming and reoxygenation), the mucosal tissue is damaged by superoxide radicals produced by converted XO, oxygen, and accumulated hypoxanthine.[3] In order to examine whether the XO system is the cause of cold ischemia-reperfusion injury, mucosal XD, XO hypoxanthine, and maltase (MAL) (as an index of mucosal injury) were measured in an autotransplantation model of 24-hour preserved canine intestine.

MATERIALS AND METHODS

Operative procedures were essentially the same as those of Lillehei et al.[4] Twelve entire small intestines of mongrel dogs were harvested and 1 L and 2 L of cold lactated Ringer's (LR) solution was flushed through the superior mesenteric artery (SMA) and lumen, respectively. Six dogs were autotransplanted immediately by end-to-end anastomoses of the SMA and the superior mesenteric vein (group A). The other six dogs were autotransplanted after preserving the intestine for 24 hours in cold LR solution (group B). Mucosal tissues were taken before and 15, 30, 60, and 120 minutes after reperfusion, and immediately frozen in liquid nitrogen.

MAL activity of the mucosa was measured by the method of Dahlqvist.[5] Tissue hypoxanthine concentration was measured by the method of Wynants and Belle[6] by high-performance liquid chromatography (HPLC) equipped with a reverse phase column. Mucosal tissues of before and 1 hour after reperfusion were used for XD and XO measurements by the method of Wajner.[7]

RESULTS

MAL activity, which indicates the integrity of the mucosa, was maintained within normal range during cold preservation in both groups (group A = 221 and group B = 158 nmol/min/mg protein). However, MAL activity in group B animals decreased to 53.8 nmol/min/mg protein until 60 minutes after graft revascularization, whereas MAL activity of group A remained unchanged.

There was no conversion of XD to XO, even after 24-hour cold preservation (Fig 1). Perfusion of group A grafts caused no changes to XD and XO; however, XD and XO decreased 17% and 47%, respectively, in group B grafts, possibly by severe mucosal damage. Hypoxanthine concentration doubled immediately after cold flushing, and remained elevated during the 24-hour cold preservation period (Fig 1).

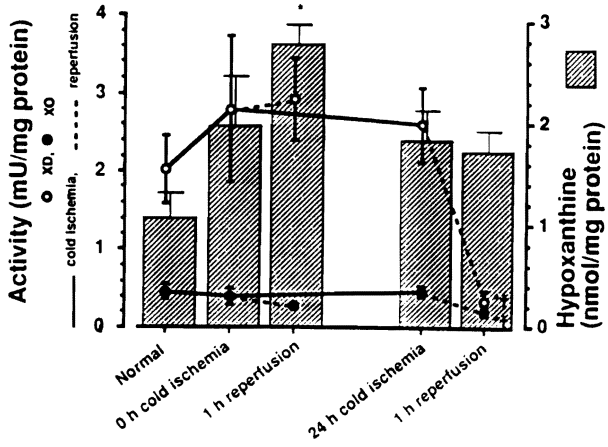

Fig 1. XD and XO, and hypoxanthine concentration, during 24-hour cold ischemia and 1-hour reperfusion. $^*P < .05$ vs normal control; $P < .05$ vs 0 hours.

SUMMARY

Preservation of grafts for 24 hours caused severe mucosal damage after reperfusion as demonstrated by the decrease of MAL activity. However, neither XD-to-XO conversion nor hypoxanthine accumulation was detected during 24-hour cold preservation. These results indicate that superoxide radicals from the XO system are not responsible for intestinal cold ischemia–reperfusion injury.

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