Clinical Science

Effects of montelukast on the healing of ischemic colon anastomoses

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KEYWORDS:
Ischemia/reperfusion; Colon anastomoses; Montelukast

Abstract

BACKGROUND: The aim of this study was to examine whether treatment with montelukast, a selective leukotriene antagonist, would affect anastomotic healing in a reperfused colon rat model with remote ischemia/reperfusion injury.

METHODS: Rats (n = 12 per group) were intraperitoneally administered normal saline or 10 mg/kg montelukast sodium 60 minutes before and for 5 days after surgery. Ischemia was induced for 45 minutes through superior mesenteric artery occlusion. A left colon anastomosis was made. Blood and peri-anastomotic tissue samples were obtained on postoperative day 5.

RESULTS: Mean anastomotic bursting pressures of the control and montelukast groups were 159.17 ± 29.99 and 216.67 ± 26.40, respectively (P < .001). Compared with saline, montelukast treatment increased the mean tissue hydroxyproline level (2.46 ± .30 vs 3.61 ± .33 μmol/L) and decreased tissue caspase-3 activity (36.06 ± 5.72 vs 21.78 ± 3.87) and malondialdehyde levels (3.43 ± .34 vs 2.29 ± .34 nmol/g) (P < .001 for all). Other plasma markers of injury also showed differences.

CONCLUSIONS: Montelukast prevented ischemia/reperfusion-induced damage in a rat model of colonic anastomotic wound healing.

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Intestinal ischemia and reperfusion carry a significant risk for mortality and morbidity, associated with single-organ or multiple-organ dysfunctions. Reperfusion of ischemic intestines may lead to irreversible functional and morphologic changes of organs distant to the primary site of injury, such as the lung or liver.1–4 Leakage or dehiscence of intestinal anastomoses after colorectal or emergency surgery is another dangerous complication. Therefore, ischemia/reperfusion on the anastomotic line or whole bowel may impair the anastomotic healing process and crucially affect anastomotic leaking or dehiscence.5–8

Leukotrienes play a major role in ischemia/reperfusion injury, especially in ischemia/reperfusion-induced hepatic
injury. Arachidonate 5-lipoxygenase is an important enzyme in the production of leukotrienes from arachidonic acid. Antileukotriene agents, such as montelukast, have been shown to protect against injury in several inflammatory models in rats, such as ethanol-induced gastric mucosal damage,\textsuperscript{9} colitis,\textsuperscript{10,11} burn-induced and sepsis-induced multiple-organ damage,\textsuperscript{12,13} and renal ischemia/reperfusion injury.\textsuperscript{14} Montelukast is a selective reversible cysteinyl-leukotriene type 1 receptor antagonist that is commonly used in the treatment of allergic asthma.\textsuperscript{15,16} Experimental evidence suggests additional therapeutic roles for montelukast, such as protecting the liver and intestine from hepatic ischemia/reperfusion injury by reducing apoptosis and oxidative stress.\textsuperscript{17,18} However, to our knowledge, no previous study has examined the effects of montelukast in an ischemic colon anastomosis model.

The aim of the present study was to test whether treatment with montelukast would be protective for colon anastomotic healing under conditions of remote ischemia/reperfusion in a rat model. The primary outcomes of this study were the anastomotic bursting pressure, which reflects the mechanical strength of the anastomosis; and the perianastomotic tissue hydroxyproline concentration, which reflects collagen synthesis or accumulation around the anastomosis. Secondary outcomes included perianastomotic and serum levels of relevant biochemical markers of oxidative stress and tissue damage.

**Methods**

**Animal care and use**

This study included 24 adult male Wistar albino rats with a median weight of 210 g (range, 180 to 220 g). All animals were weighed daily and had free access to a standardized laboratory diet and water throughout the experiments. Rats were randomly assigned to 2 groups of 12 rats each. In the control group, rats were administered 1 cm\textsuperscript{3} of normal saline intraperitoneally as placebo before surgery. In the experimental group (montelukast group), rats were administered intraperitoneal 10 mg/kg montelukast sodium as pretreatment at 60 minutes before surgery. Treatments with saline (control) or montelukast sodium (experimental group) were repeated daily at the same dose for 5 postoperative days.

The animals were fed with standard rat chow and water postoperatively. On the 5th postoperative day, animals were killed with an overdose of ether anesthesia and were subjected to in vitro analytic procedures. No rats died during the experimental period or showed any sign of intestinal necrosis or gangrenous bowel segments at the end of the ischemia/reperfusion period.

Surgical procedures, anesthesia use, and animal care methods were in accordance with the guidelines of the National Institutes of Health’s *Guide for the Care and Use of Laboratory Animals* (publication no. 86-23, revised 1985). Approval for the study protocol (decision no. 2010/3) was obtained from the ethics committee of Namik Kemal University Medical Faculty Experimental Animals Laboratory before initiation of the experiments and pilot studies.

**Chemicals**

A commercially available form of montelukast (Clast; Nobel İlaç San, İstanbul, Turkey) was used to decrease leukotriene levels in the experiments. Montelukast was reconstituted and homogenized in 2% ethanol as described by Daglar et al.\textsuperscript{17} Ethanol use to reconstitute montelukast is not associated with a significant hepatotoxic effect in rats.\textsuperscript{19}

**Operative technique**

Rats were anesthetized using an intramuscular injection of ketamine 50 mg/kg (Ketalar; Parke-Davis, Eczacibasi, Istanbul, Turkey). All animals were allowed to breathe spontaneously during the experiments. All surgical procedures were performed by the same investigators (A.C. and E.E.). The abdominal skin of rats was disinfected with 10% povidone-iodine solution (Isosol; Merkez Lab İlaç San, İstanbul, Turkey). The body temperature was maintained at 37°C with a heating lamp. At the end of the surgery, 5 mL of saline solution was administered subcutaneously to prevent dehydration.

A 5-cm midline incision was performed in all animals. In both groups, after laparotomy, the superior mesenteric artery and collateral vessels were occluded immediately distal to the origin of the aorta with a microvascular clamp (S & T, Neuhausen am Rheinfall, Switzerland) to induce ischemia. Additionally, the collateral circulation was interrupted by clamping the ileal branches in the mesentry. After 45 minutes, clamps were removed and circulation was started to obtain reperfusion. After declamping, in all animals, pulsations were seen to return to the marginal vessels, and the bowels began to appear pinker and healthier in the intestines that were directly subjected to ischemia/reperfusion stress.

After completion of reperfusion, in all animals, a transection was made in the left colon at approximately 3 cm above the peritoneal reflection. Colonic feces was gently swabbed using a manual milking method. Anastomosis was performed with interrupted sutures of 6-0 monofilament polypropylene (Prolene; Ethicon, Edinburgh, United Kingdom). The abdominal wall and skin were closed with running sutures of 3-0 silk (Dogsan, İstanbul, Turkey).

**Measurement of anastomotic bursting pressure**

The anastomotic bursting pressure was measured in all rats as described by Kologlu et al.\textsuperscript{20} Briefly, a 6-cm colonic segment (including the anastomosis in the middle) was
carefully resected en bloc with adhered tissues (omentum, small bowel, or colon) to preserve anastomotic integrity. Bursting pressure measurements were obtained within 5 minutes of the rat’s being killed. The fecal content of the resected segment was cleared gently using physiologic saline. One end of this segment was closed with a ligature using 3-0 silk, and a catheter was secured to the other end. Inside a glass jar filled with water, air was pumped into the colon segment at a rate of 2 mL/min with an infusion pump. The intraluminal pressure was monitored while the air was being pumped. The intraluminal pressure at which air leakage from the anastomosis occurred was recorded as the bursting pressure. This parameter reflected the mechanical strength of the anastomosis. Bursting occurred at the anastomotic line in all samples.

**Tissue sampling**

After the anastomotic bursting pressure was measured, a 1-cm segment of the left colon containing the anastomotic suture line was resected, frozen in liquid nitrogen, and stored at −80°C for biochemical analyses.

**Blood sample collection**

Blood samples were drawn by intracardiac puncture from the subjects under anesthesia just before death on day 5 for the measurement of plasma levels of aspartate aminotransferase, alanine aminotransferase, tissue necrosis factor (TNF)–z, interleukin (IL)–6, nitric oxide, reduced glutathione, superoxide dismutase, and catalase activity. Plasma samples were obtained by centrifugation of whole blood and stored at −80°C until assay.

**Biochemical analyses**

Homogenization of tissue specimens and determination of protein concentrations were performed as described by Sier et al.21

**Hydroxyproline level in perianastomotic tissue.** Tissue samples were placed into hydrolysis tubes. Equal volumes of potassium phosphate buffer (50 mmol/L, pH 7.0) and concentrated hydrochloric acid were added to each tube, and the samples were hydrolyzed at 110°C for 16 hours. The pH of the samples was adjusted to 8.5 with diluted sodium hydroxide, and samples were oxidized at room temperature with chloramine-T solution. After 4 minutes, Ehrlic’s reagent was added to the tubes. The color was developed at 60°C for 25 minutes. The absorbency at 560 µm was determined by the method of Bergman and Luxely.22 The hydroxyproline concentration was calculated as micrograms per milligram of wet-tissue weight.

**Myeloperoxidase activity in perianastomotic tissue.** Myeloperoxidase activity was measured as described by Kruidener et al.23 Briefly, tissue homogenates were incubated with .5% hexadecyltrimethylammonium bromide in 50 mmol/L potassium phosphate buffer (pH 5.5), containing .026% o-dianisidine dihydrochloride substrate and .018% hydrogen peroxide. The reaction kinetics was monitored for 30 minutes at 450 nm in 96-well plates. The specificity of the reaction was checked with sodium azide (.1 mmol/L). All samples were analyzed in duplicate and standardized with a homogenate of pooled human neutrophils. The myeloperoxidase activity was expressed in arbitrary units.

**Malondialdehyde level in perianastomotic tissue.** Malondialdehyde levels were determined using the thiobarbituric acid method. Briefly, .2 mL of serum was mixed thoroughly with .8 mL of phosphate-buffered saline (pH 7.4) and 25 µL of butylated hydroxytoluene solution. A .5-mL aliquot of 30% trichloroacetic acid was added to the samples, which were placed on ice for 2 hours. The samples were centrifuged at 2,000 g at 25°C for 15 minutes. Subsequently, 1 mL of each supernatant was mixed with .075 mL of .1 mol/L ethylenediamine tetracetic acid and .25 mL of 1% thiobarbituric acid in .05-N sodium hydroxide. The supernatant of each sample was placed in boiling water for 15 minutes and then cooled to room temperature. The absorbance of thiobarbituric acid reactive substances was measured at 532 nm and expressed in millimdaltons using the molar extinction coefficient for malondialdehyde (1.56 × 105 cm−1 mol/L−1). The results were expressed in nanomoles per milliliter per milligram protein.

**Caspase-3 activity in perianastomotic tissue.** Caspase-3 enzyme activity (in picomoles aminomethylcoumarin per minute per milligram protein) was measured as described by Jonges et al.24

**Biochemical levels in plasma.** Serum erythrocyte catalase activity was measured using Goth’s25 spectrophotometric method. Serum nitric oxide levels were measured using the Griess reagent method. Briefly, nitrate was converted with nitrate reductase, and Griess reagent was added, which converted nitrite to a purple azo compound. Protein interference was avoided by treating the reacted samples with zinc sulfate and centrifuging them for 5 minutes at 10,000g. Azochromophor spectrophotometry was performed at 450 nm with sodium nitrate as the standard. Results were expressed in millimoles per liter.26

To measure reduced glutathione, 200 µL of serum was added to 250 µL of .6 mmol/L dithiobis nitrobenzoic acid to form a yellow compound, which was measured by quantitative colorimetry at 420 nm. The nitrite formation method was used to measure superoxide dismutase activity in serum samples. Inhibition of the chromogenic reaction was monitored at a wavelength of 560 nm.27

Serum levels of the cytokines TNF-z and IL-6 were measured using an immunoenzymatic enzyme-linked immunosorbent assay method (Quantikine High Sensitivity
Human; R&D Systems, San Diego, CA), according to the manufacturer’s protocol. The minimum detectable concentrations of TNF-α and IL-6 were .12 and .03 pg/mL, respectively, as specified by the manufacturer. Intra-assay (2.6 for TNF-α and 1.6 for IL-6) and interassay (14 for TNF-α and 6.4 for IL-6) precision performance was determined on 20 replicates from the laboratory quality control data. Serum alanine aminotransferase and aspartate aminotransferase activities were determined according to Reitman and Frankel.28

Statistical analyses

Results are expressed as mean ± SEM. Differences among the groups were evaluated using chi-square and Mann-Whitney U tests. Differences with P values <.05 were considered statistically significant. Data were analyzed using the SPSS for Windows version 16.0 (SPSS, Inc, Chicago, IL).

Results

Effects of montelukast on the bursting pressures of ischemic colon anastomoses

We compared the effect of the antileukotriene agent montelukast on the colonic anastomotic bursting pressure in rats subjected to anastomosis and ischemia/reperfusion injury. The mean anastomotic bursting pressure of the control group (159.17 ± 29.99) was lower than that of the montelukast-treated group (216.67 ± 26.40) (P < .001). In all animals, anastomotic rupture occurred at the anastomotic suture line.

Effects of montelukast on biochemical levels in colonic perianastomotic tissue and plasma

Table 1 shows the levels of relevant biochemical parameters in perianastomotic tissue and serum after colonic ischemia/reperfusion injury in rats without or with montelukast treatment. The mean anastomotic tissue concentration of hydroxyproline was lower in the control group than in the montelukast group (2.46 ± .30 vs 3.61 ± .33 μmol/L, P < .001), whereas the mean caspase-3 activity level was higher in the control group than in the montelukast group (36.06 ± 5.72 vs 21.78 ± 3.87, P < .001). No difference in perianastomotic tissue myeloperoxidase activity level was observed between the groups (P = .885). Compared with the control group, lipid peroxidation in the colonic anastomotic tissues was reduced by montelukast treatment, as indicated by the reduced malondialdehyde level of the experimental group (3.43 ± .34 vs 2.29 ± .34 nmol/g, P < .001). Compared with the control group, serum catalase, reduced glutathione, and superoxide dismutase levels were increased, whereas nitric oxide, TNF-α, IL-6, aspartate aminotransferase, and alanine aminotransferase levels were decreased in the montelukast group after ischemia/reperfusion injury (P < .001 for all).

Comments

In the present study, we used a rat model of colonic anastomosis in the setting of ischemia/reperfusion injury.

### Table 1

Biochemical levels in perianastomotic tissue and serum after colonic ischemia/reperfusion injury in rats without or with montelukast treatment

<table>
<thead>
<tr>
<th>Parameter in perianastomotic tissue</th>
<th>Group 1 (ischemia/reperfusion + saline treatment)</th>
<th>Group 2 (ischemia/reperfusion + montelukast treatment)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyproline (μmol/L)</td>
<td>2.46 ± .30</td>
<td>3.61 ± .33</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Myeloperoxidase (U/g)</td>
<td>.44 ± .04</td>
<td>.44 ± .03</td>
<td>.885</td>
</tr>
<tr>
<td>Malondialdehyde (nmol/g)</td>
<td>3.43 ± .34</td>
<td>2.29 ± .34</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Caspase-3 activity</td>
<td>36.06 ± 5.72</td>
<td>21.78 ± 3.87</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Parameter in plasma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Catalase (kU/gHb)</td>
<td>15.98 ± 3.04</td>
<td>24.76 ± 3.55 (†)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Nitric oxide (nmol/g)</td>
<td>127.00 ± 29.28</td>
<td>88.58 ± 9.75 (‡)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Reduced glutathione (μmol/g)</td>
<td>11.28 ± .56</td>
<td>18.88 ± 3.30 (†)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Superoxide dismutase (U/mL)</td>
<td>31.98 ± 7.80</td>
<td>49.32 ± 6.57 (†)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>TNF-α (pg/mL)</td>
<td>.43 ± .04</td>
<td>.31 ± .02 (‡)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>.52 ± .05</td>
<td>.27 ± .06 (‡)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>33.50 ± 5.30</td>
<td>22.83 ± 2.90 (‡)</td>
<td>&lt;.001*</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/L)</td>
<td>43.59 ± 3.55</td>
<td>32.77 ± 2.89 (‡)</td>
<td>&lt;.001*</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± SD.
IL = interleukin; TNF = tissue necrosis factor.
*Statistically significant.
We hypothesized that ischemia/reperfusion injury would be responsible for most of the anastomotic leaks and that montelukast could partially or mainly reverse the adverse effects and improve anastomotic healing. Treatment with montelukast improved the mean anastomotic bursting pressure and increased the hydroxyproline level compared with the untreated control group. These results suggest the ability of montelukast to prevent ischemia/reperfusion-induced damage in a rat model of colonic anastomotic wound healing.

Both systemic (remote) and local (colonic) ischemia have been shown to impair intestinal anastomotic healing by decreasing tissue collagen synthesis/accumulation around the anastomosis, as evidenced by reduced hydroxyproline levels and easier anastomotic rupture. Increased inflammation at the anastomotic periphery is reflected by increased tissue levels of oxidative enzymes and plasma levels of proinflammatory cytokynes. The inflammatory response to traumatic injury and foreign materials (eg, sutures) that occurs with anastomosis construction may be a normal part of the wound-healing process. However, exaggerated inflammation (eg, in the presence of intra-abdominal infection) may delay wound healing because of increased collagenolysis. Because anastomotic dehiscence is associated with severe outcomes, including a risk for local tumor recurrence, many studies have focused on improving anastomotic wound healing by using local and systemic approaches.

As an end product of lipid peroxidation, malondialdehyde is a well-known parameter for determining free radical formation in tissues. In this study, the elevated level of malondialdehyde was suppressed by montelukast, indicating that montelukast reduced lipid peroxidation and, thereby, supported the maintenance of cellular integrity in rat colon anastomoses. Consistent with the increases in toxic oxygen metabolites, the tissue malondialdehyde level was significantly increased after ischemia/reperfusion, indicating the presence of enhanced lipid peroxidation due to ischemia. However, montelukast treatment prevented the deleterious systemic effects of ischemia/reperfusion injury.

The reflow of oxygenated blood through the ischemic tissue induces the generation of proinflammatory mediators that recruit leukocytes to the reperfused tissue, ultimately leading to tissue injury. To control this acute inflammatory response, the body recruits mast cells to the reperfused tissue, which generate reactive oxygen species and incite the production of proinflammatory cytokynes, such as TNF-α and ILs. We observed increased plasma TNF-α and IL-6 levels in the control group, which were reduced with montelukast treatment. The control group also showed increased production of markers of ischemia and other cellular damage (eg, TNF-α, IL-6, nitric oxide, aspartate aminotransferase, alanine aminotransferase, and caspase-3 activity) in the perianastomotic tissue and plasma, as well as reduced plasma catalase activity, decreased reduced glutathione and superoxide dismutase levels, and unchanged colonic tissue myeloperoxidase levels. During ischemia/reperfusion, these endogenous antioxidative defenses are likely to be perturbed as a result of the overproduction of oxygen-derived radicals by cytosolic pro-oxidant enzymes, inactivation of detoxification systems, consumption of antioxidants, and failure to replenish antioxidants adequately.

The healing process is very vulnerable to ischemia/reperfusion-induced oxygen-derived free radicals, which cause oxidative damage to biomembranes, lipids, proteins, and deoxyribonucleic acid, leading to organ dysfunction and cell death. Specifically, leukotriene B4 is among the most potent chemoattractants for neutrophils. It is also involved in neutrophil activation. Pharmacologic inhibition of endogenous leukotriene biosynthesis could be protective against ischemia/reperfusion injury. Although many studies have focused on leukotrienes, only a few studies have investigated the effects of leukotriene inhibition on hepatic ischemia/reperfusion injury. Our findings suggest that montelukast may exert its beneficial effects through the reduction of nitric oxide–derived free radicals, resulting in decreased cell membrane damage. We examined the plasma level of nitric oxide, to estimate nitric oxide production after intestinal ischemia/reperfusion. We found that the plasma nitric oxide levels were significantly increased in the ischemia/reperfusion-subjected animals of both groups. However, montelukast treatment significantly reduced the plasma levels of nitric oxide.

To the best of our knowledge, montelukast has not been previously studied in an ischemic colon anastomosis model. Canbay et al investigated the effects of the oral and rectal administration of montelukast in a nons ischemic colon model, reporting that montelukast caused impairment of wound healing without altering the anastomotic bursting pressure and reversed the oxidative damage of colon anastomoses in rats. Although the findings of Canbay et al are largely different from ours, these differences likely originate from the diversity of the study models. Although both we and Canbay et al used the same surgical method to induce colon anastomosis, they did not induce ischemia/reperfusion injury before anastomosis. The effects of leukotriene antagonists on wound healing in the background of oxidative damage due to ischemia/reperfusion injury are expected to be different from those in the setting of uncomplicated wound healing. Furthermore, although both studies used a montelukast dosage of 10 mg/kg/d, the administration route of the drug was different between the 2 studies (oral/rectal in Canbay et al vs intraperitoneal in the present study). Previous experimental studies have demonstrated that the peritoneal route is preferable for the administration of drugs, including montelukast.

Our model was intended to be a model of gastrointestinal anastomotic wound healing in the setting of ischemia/reperfusion injury in the left colon as a remote organ. Ischemia/reperfusion injury is an important clinical problem that is associated with high morbidity and mortality in
surgery. In many vascular operations (e.g., abdominal aortic aneurysm repair, embolectomy for superior mesenteric artery occlusion, repair of traumatic vascular lacerations, treatment of hypovolemia due to bleeding, and organ transplantations), a concomitant gastrointestinal anastomosis may be necessary. The construction of a gastrointestinal anastomosis during these situations may be risky, in part because of the reperfusion of ischemic tissues.

Related to this issue, Kuzu et al. showed that reperfusion stress after superior mesenteric artery ischemia for 30 minutes caused a delay in the anastomotic healing process in the left colon. Similarly, Kologlu et al. showed that 60 minutes of segmental small intestinal, unilateral lower extremity, and renal ischemia/reperfusion significantly delayed anastomotic healing in the right colon. Consistent with these previous studies, we observed that after 45 minutes of superior mesenteric artery and collateral occlusion in control group rats, the ongoing reperfusion caused a significant delay in the wound-healing process of a left colonic anastomosis. However, treatment with montelukast recovered the determined parameters in perianastomotic tissue and plasma, with improved colonic bursting pressure.

This study had some limitations. The very small sample size of the study prohibited us from observing any clinically significant differences with montelukast treatment. The superior mesenteric artery occlusion model was used as a model of remote ischemia/reperfusion injury during anastomotic surgery. Additional studies would be needed to determine whether the findings are different under conditions of local (colonic) ischemia/reperfusion injury. Although our findings point to a potential mechanism by which montelukast may exert its effects, additional, robust studies are needed to verify our observations. The surgeon was not blinded to the study groups, which may have affected his performance of the anastomosis procedure. However, this model has been extensively used, and the results of the model are well known by the authors. For this reason, we preferred the surgeon to be unblinded to the groups in this study.

Most ischemia/reperfusion studies have included the use of a sham plus anastomosis group. In those studies, the results of the sham plus anastomosis group have been very similar to those of the montelukast treatment group. Therefore, to complete the study with a minimum number of subjects, we did not include a sham plus anastomosis group in the present study. This situation may be considered a limitation of this study. However, in our opinion, the omission of this group had no negative impact on our results, as has been clearly stated in previous reports.

Despite these limitations, our results clearly showed that montelukast had systemic preventative effects on ischemia/reperfusion injury during the wound-healing process in left colonic anastomosis in rats. These findings are promising in terms of the potential use of this drug in the treatment of patients undergoing intestinal anastomoses, under conditions in which remote ischemia may be a concern.

Conclusions

Although the remote effects of reperfusion injury after 45 minutes of superior mesenteric artery occlusion caused impairment in the anastomotic healing of the left colon with an intact blood supply, montelukast treatment significantly prevented the ischemia/reperfusion-induced damage in the colonic anastomotic wound healing. Montelukast, which has been exploited in the treatment of asthma, could find new use in the treatment of at-risk patients undergoing anastomosis. Reperfusion of acutely ischemic intestines is common under conditions of superior mesenteric artery occlusion, supraceliac aortic cross-clamping for repair of abdominal aortic aneurysms, or other aortic-vascular surgeries. The very small sample size of the present study was insufficient to reveal a difference from a clinical perspective. In addition, many questions remain regarding this possible application of montelukast. Although this study suggests a benefit of the use of montelukast, further testing will be needed. Well-designed clinical studies are needed to evaluate the effects of this drug on human subjects and to elucidate the specific mechanisms of activated protein C protection against ischemia/reperfusion-related organ injury.

References
