

Translocation of Bacteria From the Gastrointestinal Tract: Protection Afforded by Lisofylline

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IMPAIRED MUCOSAL barrier function with resultant bacterial translocation (BT) are closely associated with infectious complications found in the intensive care unit and in transplanted patients. Lisofylline [(R)-1-(5-hydroxyhexyl)-3,7-dimethylxanthine] (LSF) selectively inhibits generation of phosphatidic acid,¹ which is a common second messenger to several pro-inflammatory mediators such as interleukin-1, tumor necrosis factor and LPS² that are involved in the pathogenesis of BT and are mediators of the systemic inflammatory response syndrome.³ The goal of our study was to evaluate the protective effect of LSF in a well-established model of BT.

MATERIALS AND METHODS

Male ACI rats weighing 200 to 250 g (Harlan Sprague Dawley) were used for the study. The small bowel (SB) was rendered ischemic by aseptically clamping the superior mesenteric artery for 30 and 45 minutes while the animals were kept euthermic (37°C). The SB was reperfused and the abdomen was sutured. Blood, mesenteric lymph nodes (MLN), spleen, liver, lung, and pancreas specimens were collected 24 hours after surgery for quantitative and qualitative microbiologic analysis. Peritoneal swab cultures were performed at the time of laparotomy (control), at the end of surgery before abdominal closure (contamination control), and at sacrifice. LSF (25 mg/kg) was administered intravenously (IV) in the study groups before and after the insult while control animals received equal volume of sterile saline. Translocation of fluorescent latex microspheres, administered to the rats 24 hours before experimentation in drinking water, was used to confirm the intestinal origin of translocating particles and was assessed by fluorescent-activated cell sorter on peritoneal lavages. SB mucosal changes were also assessed by histopathological analysis. Sham untreated animals were used as controls ($n = 6$). The effect of LSF alone was tested on unclamped animals ($n = 4$) while the effect of 30 and 45 minutes of intestinal ischemia on BT was evaluated between untreated ($n = 6$; $n = 10$, respectively) and LSF-treated rats ($n = 6$; $n = 9$, respectively). Fisher Exact Test was used to

compare the proportions of positive cultures and a P value of less than .05 was considered statistically significant.

RESULTS

The data summarized in Table 1 is expressed as a percentage of animals with positive organ cultures for *Erischeria-coli* and/or *enterococcus* ($>1 \times 10^4$ bacteria) or peritoneal swabs with more than 300 colonies ($P < .05$).

Intestinal ischemia/reperfusion injury was followed by significant translocation of bacteria to peritoneal cavity, MLN, liver, spleen, lung, and pancreas after 24 hours. Short treatment with IV LSF significantly decreased BT to liver, spleen, and lung. The sterility of the technique was ascertained by sterile post-clamping peritoneal swabs in 100% of study animals. Translocation of bacteria in this model did not occur during the ischemic phase (ie, during clamping). BT did not occur in neither untreated nor LSF-treated animals when exposed to only 30 minutes of intestinal ischemia. LSF treatment did not affect BT in unclamped controls. Histopathological evaluation of the SB did not show morphological significant differences between untreated and LSF-treated clamped groups.

DISCUSSION AND CONCLUSIONS

These data confirm that a significant BT occurs after a prolonged ischemic insult of the SB. A short course of IV LSF treatment significantly reduced BT to the liver, spleen, and lung when compared to untreated animals exposed to the same ischemic insult. The high morbidity and mortality associated with infective and septic complications in the

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Table 1. Results

	Peritoneum	Blood	Mesenteric Lymph Nodes	Liver	Spleen	Lung	Pancreas
I/R-45'	30	0	50	50	50	40	14
I/R-45' LSF	25	0	55	33*	22*	22*	16

$P < .5$.

early post-transplant period emphasize the importance of a treatment directed to reduce BT in this condition. These observations suggest a potential beneficial role of LSF in reducing the rate of BT in critical care of post-transplant patients.

REFERENCES

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