Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Time course study of intestinal epithelial barrier disruption in acute mesenteric venous thrombosis

*Shuofei Yang, MD, PhD, Jiaquan Chen, MD, Qihong Ni, MD, PhD, Haozhe Qi, MD, Xiangjiang Guo, MD, PhD, Lan Zhang, MD, PhD, and Guanhua Xue, MD, PhD**

Department of Vascular Surgery, Renji Hospital, School of Medicine, Shanghai Jiaotong University, Shanghai, China

ARTICLE INFO

Article history:
Received 23 May 2017
Received in revised form
29 October 2017
Accepted 13 December 2017
Available online 5 January 2018

Keywords::
Mesenteric venous thrombosis
Intestinal epithelial barrier
Acute ischemic injury
Therapeutic time window

ABSTRACT

Background: Acute superior mesenteric venous thrombosis (ASMVT) is an abdominal vascular condition. Early recanalization is essential to successful treatment. The aim of the study was to establish rabbit models of ASMVT and assess the time course of intestinal epithelial barrier disruption.

Methods: After surgical exposure of superior mesenteric vein (Sham group), large-vessel (L-group) and small-vessel (S-group) models were established by endothelium damage, stenosis creation, and thrombin injection. At baseline, 6, 9, and 12 h, hemodynamic and serum parameters were tested. Serum from ASMVT patients diagnosed at 24, 36, 48, and 60 h from symptom onset was collected. Intestinal barrier disruption was assessed by tight junction (TJ) protein expression, morphology changes, and bacterial translocation. Mesenteric arteriospasm was measured by flow velocity and intestinal wet/dry weight ratio. The serum level of intestinal fatty acid–binding protein and endotoxin in patients was also measured as an indicator for intestinal barrier function.

Results: Severe acidosis and lacticemia were observed in both the groups. The L-group experienced greater hemodynamic alteration than the S-group. Intestinal barrier disruption was detected by significantly decreased TJ protein expression, histology and ultrastructure injury of TJ, increased permeability, and bacterial translocation, at 9 h in the S-group and 12 h in the L-group. Secondary mesenteric arteriospasm occurred at the same time of complete intestinal barrier disruption and could be a significant cause of bowel necrosis. Significant increased level of intestinal fatty acid–binding protein and endotoxin was found in patients at 48 h in the S-group type and 60 h in the L-group type.

Conclusions: The ASMVT animal models of both the types were first established. The loss of intestinal barrier function occurred at 6 h in the S-group model and 9 h in the L-group model. For clinical patients, the time window extended to 36 h in the S-group type and 48 h in the L-group type.

© 2017 Elsevier Inc. All rights reserved.

* *Corresponding author*. Department of Vascular Surgery, Renji Hospital, School of Medicine, Shanghai Jiaotong University, Dongfang Road 1630, Shanghai 200127, China. Tel.: +86 13585785270; fax: +86 021-68383375.
E-mail address: guanhuaxue@yeah.net (G. Xue).

0022-4804/$ – see front matter © 2017 Elsevier Inc. All rights reserved.
https://doi.org/10.1016/j.jss.2017.12.022

Introduction

Acute mesenteric ischemia (AMI) is a catastrophic abdominal vascular disease with a daunting mortality of over 50%.[1] The ischemia-induced tissue hypoxia and inflammation can result in disruption of the intestinal epithelial barrier which is composed of a single layer of columnar epithelial cells bound together by interepithelial junctions.[2] Then intestinal bacteria translocate into the circulation and trigger the systemic inflammatory response.[3] Interaction between aggressive inflammation and hypoxia can promote a vicious cycle that ultimately develops to transmural bowel necrosis, sepsis, and multiple-organ dysfunction syndrome.[4]

Mesenteric vein thrombosis (MVT) is the least common form, accounting for 6%-9%, of AMI and typically involves the superior mesenteric vein (SMV).[5] Increased incidence of acute superior mesenteric venous thrombosis (ASMVT) has been detected worldwide because of raised awareness and wide use of contrast-enhanced computed tomography. Underlying thrombophilia often leads to small-vessel (S-group) MVT beginning from intramural venula, vasa recta, and venous arcades. Large-vessel (L-group) MVT involving the SMV trunk is more related to local inflammation. Patients of the S-group MVT are at greater risk of bowel infarction, whereas the L-group MVT may require endoscopic surveillance for esophageal varices.[6]

Once intestinal infarction occurs from venous engorgement and sequent arterial impedance, there are few options to relieve the mesenteric congestion.[7] Although the standard treatment for ASMVT is systemic anticoagulation and supportive measures, endovascular therapy has shown significant advantages in early mesenteric recanalization.[8,9] However, the indications and vascular access of endovascular techniques for different types of ASMVT are all undetermined.

The intestinal epithelium forms a barrier between the body and the gastrointestinal lumen, and shedding poses a threat to the integrity of intestinal barrier.[10] The opening of tight junction (TJ) is primarily dependent on the composition and organization of the TJ proteins (i.e., occludin [OCLN], zona occludens-1 [ZO-1], and claudin [CLDN]) which are responsible for the barrier function.[11] Intestinal fatty acid–binding protein (I-FABP), a low-molecular-weight protein specifically located in the intestinal epithelial cells, is reported as a biomarker for early diagnosis of AMI in recent studies.[12] It can be rapidly released into the circulation after irreversible injury of intestinal mucosal barrier function during AMI.[13] Appropriate maintenance of the intestinal epithelial barrier plays an indispensable role in the treatment of intestinal ischemia.[14] Despite mesenteric ischemia contributes to a multitude of intestinal disease, advances in this field remain modest with inability to translate any research findings to clinical practice. It may not only be related to the complex disease process but also to result from inappropriate research animal models. None of the models (e.g., temporary vascular occlusion [using atraumatic vascular clamps] or permanent vascular occlusion [using ligation] of the superior mesenteric artery [SMA] in rodent animals, original low-flow ischemia models in cats, and segmental mesenteric vascular occlusion models in pigs) can perfectly recapitulate the natural onset and complex progression of human disease.[3] In addition, no animal models of ASMVT are available for any translational research of intestinal barrier protection and recanalization treatment. The aim was to study the time course of intestinal epithelial barrier disruption in rabbit models of ASMVT to provide more information for early recanalization. Serous data of human patients were also analyzed in this study.

Materials and methods

This study was approved by the institutional animal care and use committee. Experiments were performed according to the National Institutes of Health Guidelines on the use of laboratory animals. The study of human blood samples was reviewed and approved by the institutional review board. Before the study began, the written informed consent form and authorization document that listed all the study procedures and risks were given to the participants. The consent procedure was approved by the institutional review board.

Animal preparation

New Zealand white rabbits (3-4 kg, 4-5 mo old) of either sex were provided by the Center of Comparative Medicine and Translational Research. All animals were housed at 21°C-24°C on a 12-h light and 12-h dark cycle and given free access to water and standard rabbit food. After an overnight fast, the rabbits were anesthetized with an intramuscular injection of 40-mg/kg ketamine (Shuanghe Pharmaceuticals, Beijing, China) and 6-mg/kg xylazine (Beijing Shuanghe Pharmaceuticals, China). The rabbits were intubated and ventilated on low level of isoflurane (2%) with oxygen during the procedure. Small incision was made in the neck to place an intra-arterial sheath into the right carotid artery. A 5-cm intravenous sheath was placed into the vena cava anterior through the right jugular vein. Using an angiocatheter, hemodynamic parameters (e.g., mean arterial pressure, heart rate, and central venous pressure [CVP]) were measured using a transducer (P231D; Gould Statham, Oxnard, CA) connected to an Electronic Medicine Recorder (Honeywell Inc, Morris Plains, NJ).

Experimental protocols

The timeline for the experiment is described in Figure S1. After instrumentation, animals were equilibrated for a period of 10 min, and baseline measurements were obtained.

Through a midline laparotomy, a neurosurgical vascular clip was applied to the SMV for 15 s twice, 30 s apart, to damage the endothelium. A 14-G needle was placed longitudinally along the ventral surface, and a 4-0 silk suture was tied around the SMV and the needle together at the point just below the confluence of portal vein and splenic vein. The needle was then removed leaving a 20% stenosis. A vessel clamp was placed at the stenosis section, and another clamp

Download English Version:

https://daneshyari.com/en/article/8835721

Download Persian Version:

https://daneshyari.com/article/8835721

Daneshyari.com