Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

Peritoneal lavage with povidone-iodine solution in colorectal cancer–induced rats

Hua-Li Song, MM,[a] *Dong-Mei Zhang, PhD,*[b,*] *Heng Wen, MM,*[c] *Meng Wang, MM,*[b] *Na Zhao, MM,*[b] *Yu-Hua Gao, MM,*[b] *and Ni Ding, MM*[a]

[a] *Department of Anesthesiology, Ningxia Medical University, Yinchuan, Ningxia, China*
[b] *Department of Anesthesiology, General Hospital of Ningxia Medical University, Yinchuan, Ningxia, China*
[c] *Department of Anesthesiology, The Second Affiliated Hospital of Zhejiang Chinese Medical University, Hangzhou, Zhejiang, China*

ARTICLE INFO

Article history:
Received 6 November 2017
Received in revised form
3 February 2018
Accepted 27 February 2018
Available online xxx

Keywords:
Peritoneal lavage
Povidone-iodine
Intestinal mucosa barrier
Shock

ABSTRACT

Background: Although peritoneal lavage with povidone-iodine (PVPI) is frequently performed after surgery on the gastrointestinal tract, the effects of PVPI on the intestinal epithelial barrier are unknown. The purpose of this study was to investigate the effects of abdominal irrigation with PVPI on the intestinal epithelial barrier in a colorectal cancer (CRC)–induced rat model.

Materials and methods: The CRC model was induced in rats with azoxymethane and dextran sodium sulfate. Next, a total of 24 male CRC-induced rats were randomly divided into three groups ($n = 8$): (1) a sham-operated group, (2) an NS group (peritoneal lavage 0.9% NaCl), and (3) a PVPI group (peritoneal lavage with 0.45%-0.55% PVPI). The mean arterial pressure was continuously monitored throughout the experiment. The levels of plasma endotoxin and D-lactate, blood gases, and protein concentration were measured. The ultrastructural changes of the epithelial tight junctions were observed by transmission electron microscopy.

Results: The mean arterial pressure after peritoneal lavage was lower in the PVPI group than that in the NS group. The protein concentration and levels of endotoxin and D-lactate were higher in the PVPI group than they were in the PVPI group. In addition, PVPI treatment resulted in a markedly severe metabolic acidosis and intestinal mucosal injury compared with NS rats.

Conclusions: Peritoneal lavage with PVPI dramatically compromises the integrity of the intestinal mucosa barrier and causes endotoxin shock in CRC rats. It is unsafe for clinical applications to include peritoneal lavage with PVPI in colorectal operations.

Introduction

Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer death worldwide. The main cornerstone of treatment for CRC is surgery.[1] Peritoneal lavage is frequently performed after the surgeries of the gastrointestinal tract.[2,3] Povidone-iodine (PVPI) is a polymer of iodine complexed with polyvinylpyrrolidone (PVP) and exhibits antiseptic and tumoricidal benefits.[4] PVPI is the most common iodophor and is available globally. PVP can

* *Corresponding author*. Department of Anesthesiology, General Hospital of Ningxia Medical University, Yinchuan Shengli Road #1160, Yinchuan 750004, Ningxia, China. Tel.: +86 13995086686; fax: +86 09514073090.
E-mail address: zdm_ych@hotmail.com (D.-M. Zhang).
0022-4804/$ – see front matter
https://doi.org/10.1016/j.jss.2018.02.055

form stable complexes with iodine, which is slowly released to the environment as free iodine with concomitant bactericidal activity.[5] In addition, a previous study demonstrated that PVPI had an antitumoral effect on colon cancer cells,[6] and this effect is associated with the superoxide dismutase activity that is caused by the oxidizing effects of its free iodine.[7] For these reasons, PVPI has been widely popularized for clinical use as a therapeutic agent for the purpose of minimizing postoperative septic complications and reducing cancer recurrence.[8] Although PVPI possesses a broad spectrum microbicide against bacteria and is lethal to CRC cells, concern about its potential toxicity still remains. Peritoneal fibrosis has been reported after intraperitoneal lavage with PVPI in clinical practice.[9] However, if PVPI is administered after the inducement of appendicitis-peritonitis, the survival of dogs is absolutely shortened.[10] Moreover, other experimental studies have demonstrated that PVPI solution results in high mortality and causes serious peritoneal damage.[11,12] We hypothesized that peritoneal lavage with PVPI may compromise the integrity of intestinal mucosal barrier. However, until now the effects of PVPI on the intestinal epithelial barrier have rarely been investigated. Therefore, the aim of the present study was to determine the effects of abdominal irrigation with PVPI on the intestinal epithelial barrier in a CRC-induced rat model.

Materials and methods

Rats

Five-wk-old male Sprague-Dawley rats were purchased from the Laboratory Animal Center of Ningxia Medical University (Yinchuan, China). The rats were maintained under controlled conditions of humidity (50 ± 10%), light (12 h light/12 h dark), and temperature (23 ± 2°C) according to the Institutional Animal Care Guidelines. All experiments were approved by the Animal Care and Use Committee of Ningxia Medical University.

Rat model of CRC and grouping

The rat model of CRC was created as previously described.[13,14] A total of 24 male Sprague-Dawley rats were subjected to a single intraperitoneal injection of azoxymethane (AOM) (15 mg/kg, Sigma–Aldrich Chemical Co, St. Louis, MO) at 5 wk of age. After the administration of the injection, the animals were exposed to three cycles of 3% dextran sodium sulfate (MP Biomedicals, Aurora, OH) in the drinking water for 7 d and normal drinking water for the subsequent 14 d (Fig. 1). All rats were randomly divided into three groups at week 16: (1) a sham group with no intraperitoneal lavage ($n = 8$), (2) an NS group with peritoneal lavage with 7 mL/kg of warm saline (0.9% NaCl, 37°C) solution ($n = 8$), (3) a PVPI group with peritoneal lavage with 7 mL/kg of warm 0.45%-0.55% PVPI (37°C; $n = 8$).[12]

Surgical procedures

At the end of week 16, rats were anesthetized with an intraperitoneal injection of 2% sodium pentobarbital (60 mg/kg). Ventilation was maintained with a ventilator ($V_T = 6.0$-7.0 mL, respiratory rate = 70 bpm, I:E = 1:2). After anesthesia, the caudal vein and the right carotid artery were isolated and cannulated with sterile polyethylene catheters (PE-50). All surgical procedures were performed under sterile conditions. The catheter was placed in the caudal vein for the drug administration and fluid supplement (4 mL/kg/h). The heart rate and mean arterial pressure (MAP) were continuously monitored by connecting the right carotid artery catheter to a pressure transducer and a computerized physiograph (BL-420S; Techman Soft, Chengdu, China). Then, a laparotomy was performed through a 2.0 cm midline incision followed by peritoneal lavage for 3 min. The irrigant solution was dispersed into the abdominal cavity after abdominal massage for 30 s as previously described. Subsequently, the irrigant fluid was suctioned out, and the wound was then aseptically covered with gauze. The irrigant fluid and blood samples were collected for biochemical analyses before the peritoneal lavage and at 30 min after the peritoneal lavage.

Blood gas analysis

Arterial blood samples were collected at the baseline and 30 min after the peritoneal lavage. Approximately 200 μL of carotid blood was used for the measurement of potential of hydrogen (pH), the base excess (BE), HCO_3^-, and the blood lactate level (i-STAT 300 G Blood Gas Analyzer; Abbott, Denver, CO).

Protein concentration measurement

Protein concentration was determined with a BCA protein assay kit (KeyGen Biotech, Nanjing, China) using bovine plasma albumin as the standard. Before irrigation and 30 min

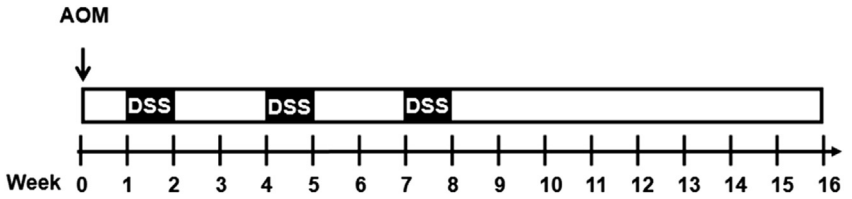

Fig. 1 – Experimental schedule. Rats at 5 wk of age were given a subcutaneous injection of AOM at 15 mg/kg body weight (black arrow). One wk after the AOM injection they were given three cycles of 3% dextran sodium sulfate (black box) in drinking water for 1 wk and normal drinking water for 2 wk.