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Peritoneal lavage using chlorhexidine gluconate at the end of colon surgery reduces postoperative intra-abdominal infection in mice

Wael E. Shams, MD,[a,*] Gregory A. Hanley, DVM, PhD,[b] Andrea Orvik, MD,[c] Nicole Lewis, PhD,[d] and M. Salah Shurbaji, MD[c]

[a] James H. Quillen Veterans Affairs Medical Center, and Department of Internal Medicine, Division of Infectious Diseases, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee
[b] Division of Laboratory Animal Resources, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee
[c] Department of Pathology, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, Tennessee
[d] Department of Mathematics and Statistics, College of Arts and Sciences, East Tennessee State University, Johnson City, Tennessee

ARTICLE INFO

Article history:
Received 19 November 2014
Received in revised form
13 January 2015
Accepted 16 January 2015
Available online 22 January 2015

Keywords:
Chlorhexidine gluconate
Peritoneal
Lavage
Colon surgery
Mice

ABSTRACT

Background: The use of peritoneal lavage with antiseptic solutions after bowel surgery remains controversial. This study compared peritoneal lavage using chlorhexidine gluconate at low concentrations and normal saline in mice with cecal ligation and perforation.

Methods: A total of 180 mice were randomized to six groups. Groups A, B, and C received one-time intraperitoneal injections of normal saline, chlorhexidine gluconate 0.05%, and chlorhexidine gluconate 0.025%, respectively. Groups D, E, and F were all subject to cecal ligation and perforation, then underwent partial cecectomy and peritoneal lavage with normal saline only, chlorhexidine gluconate 0.05% followed by normal saline, and chlorhexidine gluconate 0.025% followed by normal saline, respectively. Animals were followed postoperatively then sacrificed and examined at necropsy for occurrence of intra-abdominal abscesses, adhesions, or other pathology.

Results: A total of 48 mice (26.7%) developed postoperative intra-abdominal abscesses. Group E mice that had chlorhexidine gluconate 0.05% lavage had significantly lower incidence of postoperative intra-abdominal abscesses compared with that of group D mice that had saline lavage only ($P = 0.0113$). There was no significant difference in occurrence of macroscopic adhesions among mice groups that had or did not have surgery. ($P = 1$ and $P = 0.3728$). Microscopic peritoneal fibrosis occurred significantly more among group E mice that had chlorhexidine gluconate 0.05% lavage compared with group D mice that had saline lavage only ($P = <0.005$). There was no significant difference in postoperative mortality between surgical groups ($P = 0.8714$).

* *Corresponding author*. Division of Infectious Diseases, Department of Internal Medicine, James H. Quillen College of Medicine, East Tennessee State University, Box 70622, Johnson City, TN 37614. Tel.: +1 423 439 6380; fax: +1 423 439 7010.
E-mail address: shams@etsu.edu (W.E. Shams).
0022-4804/$ – see front matter
http://dx.doi.org/10.1016/j.jss.2015.01.030

Conclusions: Chlorhexidine gluconate 0.05% peritoneal lavage after partial colectomy (cecectomy) in mice reduces postoperative intra-abdominal infection without significant macroscopic adhesion formation.

1. Introduction

Postoperative surgical site infections (SSIs) continue to be a major cause for morbidity and mortality in spite of aggressive infection control measures and preoperative antimicrobial prophylaxis. In addition, SSIs increase postoperative length of hospital stay with cumbersome healthcare costs that may be quadrupled in case of colorectal surgery complicated with SSI [1–3]. The Centers for Disease Control and Prevention define SSIs as infections occurring within 30 d after a surgical operation, and affecting either the incision, superficially or deeply, or organs, or body spaces at the site of operation [4]. Colorectal surgeries are more prone to be complicated with SSIs given the high risk of bacterial contamination from large bowel flora during operation. Even with adequate perioperative antimicrobial prophylaxis, SSI rates may top 25%, with more likely need for intensive care unit admission and doubled risk of death [5,6].

Chlorhexidine gluconate is a cationic-chlorinated biguanide antiseptic agent that disrupts cytoplasmic membranes, resulting in both immediate and persistent antimicrobial activity that may last up to 24 h. It has good activity against wide range of gram-positive, gram-negative bacteria, yeast, molds, and enveloped viruses. Chlorhexidine gluconate has also been shown to be safe for the cleaning and disinfecting of the skin and oral mucous membranes [7–9]. The food and drug administration approved the use of chlorhexidine gluconate 0.05% (IrriSept O.R.; IRRIMAX, Inc, Lawrenceville, GA) for cleaning and final irrigation of various wounds [10].

Although chlorhexidine gluconate compounds are currently approved as antiseptics for skin, soft tissue, and mucous membrane, their use for abdominal washout in gastrointestinal surgeries that involve opening the peritoneum with possible bowel contents spillage and contamination has not been adequately tested or approved. This may have been, in part, secondary to long, and known history of using repetitive, and prolonged exposure of higher chlorhexidine gluconate concentrations (classically dissolved in high concentrations of ethanol) to induce peritoneal sclerosis and fibrosis in experimental laboratory animal models [11,12]. Peritoneal fibrosis and sclerosis have been also described to complicate prolonged use of chlorhexidine gluconate in alcohol in the connection procedure for continuous ambulatory peritoneal dialysis in human patients [13]. However, the outcome of transient contact of low concentration chlorhexidine gluconate without excipients, such as alcohol, surfactants, soaps, sudsing agents, perfumes, and dyes, to animal or human peritoneum remains to be investigated given its potential and beneficial antiseptic effects that may reduce postoperative SSIs.

This study was done to test the hypothesis that peritoneal lavage with chlorhexidine gluconate at 0.05% or 0.025% concentration toward the end of colon surgery may reduce postoperative intra-abdominal infection in mice with experimental cecal perforation and peritoneal contamination. It also tested whether a single peritoneal exposure to chlorhexidine gluconate at 0.05% or 0.025% concentration when injected intraperitoneally or used for peritoneal lavage at the end of bowel surgery may or may not result in peritoneal fibrosis or sclerosis at 6 wk postoperatively.

2. Materials and methods

2.1. Experimental model

One hundred and eighty male Imprinting Control Region (ICR) mice at 6–8-wk-old (body weight, 25 ± 3 g) were randomized to six groups A–F included in this study. Animals were purchased from Harlan Laboratories, Tampa, FL and received in four shipments of 30, 50, 50, and 50 mice, respectively. Animals were allowed to acclimate for at least 5 d before the start of the study at East Tennessee State University Animal Laboratory. The care of these animals was in compliance with the *Guide for the Care and Use of Laboratory Animals* from the National Council, National Academy press, Washington, D.C. 2011. All animal procedures were approved by East Tennessee State University Animal Care and Use Committee. All animals were group-housed and provided with water and 8604 Teklad Rodent Diet (Harlan Laboratories, Tampa, FL) *ad libitum*.

2.2. Animal laboratory procedures

All interventions were performed under aseptic conditions. The anterior abdominal wall was clipped using a surgical hair clipper. No perioperative antibiotics were used in any of the groups to allow accurate evaluation of the effects of chlorhexidine gluconate 0.05% and 0.025% use.

2.3. One-time intraperitoneal injection of normal saline and low concentrations chlorhexidine gluconate 0.05% and 0.025% for groups A, B, and C

Groups A, B, and C each included 10 mice that were not subject to surgery and received one-time, 1.0 mL intraperitoneal injections of normal saline, chlorhexidine gluconate 0.05% (IrriSept O.R.), and chlorhexidine gluconate 0.025 (IrriSept O.R. diluted with equal amount of sterile water), respectively, through the left lower abdominal quadrant into the peritoneal cavity.

2.4. Surgical procedures for groups D, E, and F

Groups D, E, and F each included 50 mice that were all subject to cecal ligation and perforation of cecal tip with spillage of cecal contents and contamination of the peritoneum. The