Migrating motor complex changes after side-to-side ileal bypass in mouse ileum ex-vivo: mechanism underlying the blind loop syndrome?

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Purpose: This study was intended to investigate the migrating motor complex (MMC) changes after ileal bypass in ex-vivo mouse models. Methods: Partial (side-to-side) and total bypass (occlusion of proximal part of bypassed loop) were performed on ileums of female Institute of Cancer Research mice. After 2 and 4 weeks, the bypassed segments were harvested and MMCs were recorded at 4 different sites ex-vivo. Amplitude, duration, interval, direction of propagation, and the area under the curve (AUC) of MMCs were measured and compared to those of the controls. Results: In control mice (n = 7), most MMCs propagated aborally (91.1%). After 2 weeks of partial bypass (n = 4), there was a significant decrease in both amplitude and AUC, and orally-propagating MMCs increased significantly (45%, P = 0.002). Bidirectional MMCs (originating in the bypassed loop and propagating in both directions) were also observed (10%). The amplitude of the MMCs remained decreased at 4 weeks after partial bypass (n = 4), and neither the AUC nor the direction of propagation showed significant changes compared to 2 weeks. Similarly, in the total bypass model, both the amplitude and AUC of the MMCs decreased significantly compared to controls. In contrast to partial bypass, 95% of the MMCs within the bypassed loop propagated aborally after 2 weeks (n = 6), which was similar to the control state. After 4 weeks (n = 5), however, MMCs either lost their temporal relationship or completely disappeared. Conclusion: The changes in propagation direction of the MMCs in the partially bypassed loop may contribute to stagnation of bowel contents and the development of blind loop syndrome.

Key Words: Myoelectric complex, Migrating, Mice, Ileum, Jejunoileal bypass

INTRODUCTION

In surgical practice, small to small or small to large bowel bypass is performed for various settings such as radiation enteritis or Crohn’s disease. However, blind loop syndrome is a well-documented complication following the side-to-side anastomosis of the intestine. Stagnation of the intestinal contents and subsequent bacterial overgrowth in the bypassed loop has been known to be the cause [1]. Re-entry of the intestinal contents through the lateral anastomosis into the bypass loop might be related to the stagnation [2]. Clinically, some surgeons used proximal
loop ligation during the loop esophago-jejunostomy to prevent this phenomenon with some success [3]. However, no clear mechanism for development of blind loop syndrome or beneficial role of proximal loop ligation during the intestinal bypass procedure has been demonstrated.

Migrating motor complex (MMC) describes organized groups of contractions periodically migrating down both the small and large intestine, and has been observed in a variety of animals, including humans [4,5]. MMC is one of the key elements in gastrointestinal motility, and has been known to act as an intestinal house-keeper; periodically cleansing the bowel in preparation for the next meal. Ever since Wood [6] first described the MMC in the isolated mouse colon and Bush et al. [7] described the MMC in the isolated mouse ileum, MMC has been most intensively studied in the mouse model ex-vivo.

We hypothesized that the mechanism underlying the stagnation of the intestinal contents in the blind loop syndrome might be related to changes in MMC, and so we measured the MMCs after creating a side-to-side ileal bypass anastomosis in a mouse and extrapolated the mechanism of the stagnation through the ex-vivo experiments.

METHODS

Animal treatment

Female Institute of Cancer Research mice, aged 8 weeks, were used for the ileal side-to-side anastomosis. The animals were purchased from specific pathogen free laboratory animal company (Koatech, Pyeongtaek, Korea). We did not restrict diet and no bowel preparation was performed pre-operatively. The mice were anesthetized with a single i.p. dose of tiletamine/zolazepam (Zoletil, Virbac Laboratories, Carros, France) 40 mg/kg. Single s.c. dose of atropine (Daihan Pharm Co., Seoul, Korea) 0.04 mg/kg was administered to decrease the tracheal secretion to prevent asphyxia and single i.p. dose of cefmetazole (Daewoong Co., Seoul, Korea) 50 mg/kg was administered. When the absence of a hindlimb pinch-withdrawal reflex was verified, a median laparotomy was performed. After identifying the appendix and ileo-cecal junction, the ileum was traced proximally to locate 4 cm and 8 cm from ileo-cecal junction. After opening the antimesenteric border about 3 mm, side-to-side anastomosis was performed using 10-0 monofilament suture (Ethilon, Ethicon Inc., Sommerville, NJ, USA) under magnifying (x5) surgical loupe. The anterior and the posterior rows were sutured in an interrupted manner for five stitches, respectively (partial bypass model; Fig. 1A). For a total bypass model, the proximal portion of the bypass loop was doubly ligated to create obstruction with the same suture material, without compromising the mesenteric vascular arcade (Fig. 1B). After completion of the anastomosis, the intestine was replaced within the abdomen and the abdomen was closed with 5-0 silk suture. The animals were allowed to recover post-operatively on a heated blanket. Throughout the surgery and recovery the animals were intermittently oxygenated with a 97% O2-3% CO2 mixture. Operated animals were sacrificed by CO2 inhalation fol-