Small Bowel Myoelectric Activity in Peritonitis

Constantine T. Frantzides, MD, PhD, Carlos Mathias, MD, Kirk A. Ludwig, MD, Charles E. Edmiston, PhD, Robert E. Condon, MD, MS, Milwaukee, Wisconsin

Reprinted from the June issue.

The American Journal of Surgery

A Yorke Medical Journal
Published by Cahners Publishing Company
a Division of Reed Publishing USA
249 West 17th St., New York, N.Y., 10011

Small Bowel Myoelectric Activity in Peritonitis

Constantine T. Frantzides, MD, PhD, Carlos Mathias, MD, Kirk A. Ludwig, MD, Charles E. Edmiston, PhD, Robert E. Condon, MD, MS, Milwaukee, Wisconsin

Peritonitis is associated clinically with paralytic ileus, but the physiologic mechanisms of the effects of peritonitis on bowel myoelectric activity have not been explored. Bipolar electrodes were inserted into the rats, and myoelectric control recordings were obtained for 4 h/d for 5 consecutive days. Peritonitis was then induced, and myoelectric recordings were again obtained. Each animal served as its own control. Prior to induction of peritonitis (control), phase I, II, and III myoelectric activity was present in all recordings. The cycle duration of the migrating myoelectric complex was 17.17 ± 0.39 minutes, and the migration velocity of phase III was 0.61 ± 0.02 cm/min. The most striking feature during peritonitis was the complete inhibition of phase II activity. Phase III activity, however, was present with a cycle duration of 16.69 ± 0.42 minutes. This study shows that some features of intestinal myoelectric activity (phase III) are preserved during episodes of peritonitis, and others are changed (phase I) or lost (phase II). Disappearance of phase II activity in this type of ileus emphasizes its importance in normal small bowel motility.

Bacterial peritonitis continues to be a major infectious problem [1]. In the clinical setting, peritonitis is associated with ileus as evidenced by the inability to tolerate oral intake, the presence of abdominal distension, and altered bowel habits [2]. In fact, the presence of ileus, in the proper clinical setting, is sometimes the first clue to the existence of an intra-abdominal infectious process [3]. Experimental and clinical studies of peritonitis have focused attention primarily on the bacteriologic and systemic septic manifestations of the disease process. No studies to date have examined the small bowel myoelectric patterns that occur during episodes of peritonitis.

Standard peritonitis models do not lend themselves well to the study of motility patterns. Cecal ligation and puncture is a reliable and popular peritonitis model [4]. Unfortunately, the laparotomy used to create the peritonitis has profound effects on small bowel myoelectric activity apart from the peritonitis. Another reproducible model of peritoneal infection and abscess formation utilizes a precise quantitative challenge of bacteria incorporated into autoclaved rat colonic contents (50% vol/vol) and barium sulphate (10% wt/vol) inserted into a gelatin capsule for intraperitoneal implantation [5]. Again, the process of implanting the capsule affects myoelectric bowel activity, making the model inappropriate for our investigation.

To avoid laparotomy in producing peritonitis, some investigators have inoculated pure or mixed cultures into the peritoneal cavity. Intraperitoneal injection of feces is a poor model since it may produce only a local inflammatory process with no systemic manifestations of intra-abdominal infection. In addition, this method lacks both qualitative and quantitative characteristics that make it reproducible. Injection of pure bacterial cultures has been found by some investigators to produce a low mortality rate [6].

For our purposes, we needed a peritonitis model with unique features. The model had to be quantitatively and qualitatively reproducible, laparotomy for creation of the intra-abdominal infection had to be avoided, and the adjuvant substances used with the bacterial inoculum could not induce motility changes in and of themselves. In addition, the model had to allow survival through the period of recording. The aim of our investigation was to define the myoelectric small bowel motility patterns observed during diffuse bacterial peritonitis using such a model.

MATERIALS AND METHODS

Thirteen male Sprague-Dawley rats weighing 250 to 300 g were used. They were housed in metal cages, two rats per cage, and provided food (Ralston Purina Rodent Chow 5001) and water. They were kept in a room with a 22-hour dark photoperiod at 72°F and 45% humidity. During postoperative recovery and after induction of

From the Department of Surgery and the Surgical Microbiology Research Laboratory, Medical College of Wisconsin, Milwaukee, Wisconsin.

Requests for reprints should be addressed to Constantine T. Frantzides, MD, PhD, Department of Surgery, Medical College of Wisconsin, 9200 West Wisconsin Avenue, Milwaukee, Wisconsin 53226.

Presented as a poster paper at the 33rd Annual Meeting of the Society for Surgery of the Alimentary Tract, San Francisco, California, May 11–13, 1992.

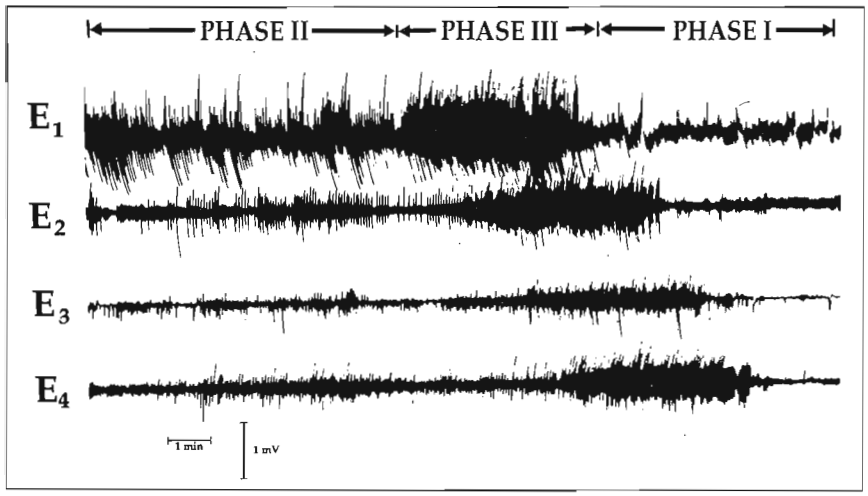

Figure 1. Typical myoelectric recording obtained during baseline period. Normal migrating myoelectric complex demonstrating phase I, II, and III activity. E = electrode.

TABLE I
Myoelectric Recording Results (mean ± SEM)

	MMC Cycle Duration (min)	Phase III Migration Velocity (cm/min)
Group A (n = 10)		
Baseline	17.17 ± 0.39	0.61 ± 0.02
Peritonitis	16.69 ± 0.42	0.56 ± 0.01
Group B (n = 3)		
Baseline	14.83 ± 0.74	0.74 ± 0.05
Peritonitis vehicle	13.40 ± 0.65	0.77 ± 0.04

peritonitis, rats were housed singly in their cages. The protocol for this study was approved by the Animal Welfare Committee of the Medical College of Wisconsin.

After the rats were fasted overnight, four bipolar electrodes were implanted into the small bowel. All operations were performed using sterile technique and under general thiopental anesthesia. A midline laparotomy incision was used, and electrodes were placed 3 cm apart on the small bowel starting 5 cm from the ligament of Treitz. The electrodes were sewn to the bowel using 6-0 monofilament polypropylene suture. The bipolar electrodes consisted of two 0.2-mm diameter silver wires, spaced 2 mm apart, connected separately to Teflon-insulated leads through soldered joints sealed with epoxy and embedded in a silicon rubber casing. The exposed tips of the silver wires extended 0.5 mm from the silicone backing. The assembly was sewn to the small bowel so that the exposed silver tips were oriented along the longitudinal axis of the gut. The electrode tips were pushed gently into the smooth muscle. The location and distance between the units were precisely recorded.

The leads from the electrodes were brought out through the abdominal wall and guided subcutaneously to the interscapular area where they exited from the hide. They were protected in the pocket of a jacket. Laparotomy wounds were closed in one layer.

Animals were allowed to recover for 2 weeks after instrumentation. Then, after an overnight fast, baseline myoelectric recordings were made for 4 h/d for 5 days. Myoelectric signals were recorded using a polygraph (Grass model 7) equipped with model P122 amplifiers (Grass Inst., Quincy, MA).

Group A (peritonitis group): After instrumentation and baseline recordings were completed, peritonitis was induced in 10 rats. The challenge inoculum containing defibrinated blood (2 mL) and barium sulfate (200 mg) was adjusted to a concentration of approximately 8.8 $\log_{10}$ colony-forming units (CFU)/mL for *Escherichia coli* and *Bacteroides fragilis*. By using a 30-gauge needle, 0.25 mL of this suspension was injected intraperitoneally into each abdominal quadrant. Myoelectric recordings were resumed 12 hours after induction of peritonitis and were performed for 4 h/d in the fasted state for 5 consecutive days.

Group B (peritonitis vehicle group): After instrumentation and baseline recordings were completed, three rats underwent intraperitoneal injection of the peritonitis suspension minus the bacterial inoculum (defibrinated blood and barium sulphate only). Myoelectric recordings were made as in group A.

Both group A and B animals were killed on the sixth day after injection. The abdominal cavity was carefully examined for evidence of peritonitis and abscess formation. Aerobic and anaerobic cultures of the peritoneal cavity and any abscesses were obtained.

Myoelectric parameters evaluated for the control and test periods were the migrating myoelectric complex (MMC) cycle duration and the MMC phase III migration velocity (distance traveled by phase III divided by time). The distance used was that between electrode 1 and electrode 4. The duration of the MMC cycle was determined by calculating the time interval between the appearance of two consecutive phase III activities at the same electrode site. MMC morphology was also evaluated (presence or absence of phases of MMC cycle). Each rat acted as its own control. Data from the baseline and the test periods were compared using the paired *t*-test.

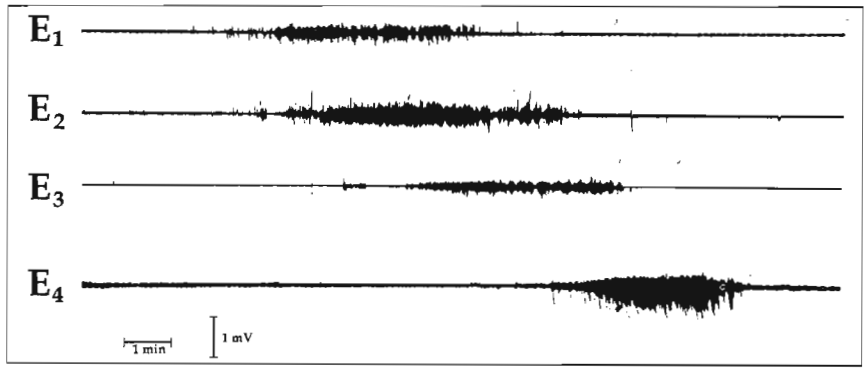

Figure 2. Myoelectric recording from group A rat made during peritonitis period. Small bowel myoelectric activity seems to be cycling normally but, on close examination, phase II activity is not present (compare with Figure 1). E = electrode.

RESULTS

Group A (peritonitis group): Prior to induction of peritonitis (baseline), all recordings obtained demonstrated phase I, II, and III myoelectric activity (**Figure 1**). The mean MMC cycle duration was 17.17 ± 0.39 minutes, and the mean migration velocity was 0.61 ± 0.02 cm/min.

Signs of peritonitis appeared within 48 hours in all animals injected with the challenge inoculum. After induction of peritonitis, the mean MMC cycle duration was 16.69 ± 0.42 minutes, and the mean migration velocity was 0.56 ± 0.01 cm/min (**Table I**). Neither the cycling periodicity nor the migration velocity changed significantly. Examination of the MMC morphology revealed changes. Whereas phase III cycled normally during peritonitis, phase I (quiescent period) became prolonged, and phase II disappeared. Loss of phase II of the MMC was the most striking feature observed during episodes of peritonitis (**Figure 2**).

Six days after the induction of peritonitis, rats were killed, and the abdomen re-entered under sterile conditions through the previous midline incision. Diffuse intra-abdominal infection was present in all rats. Along with numerous intra-abdominal adhesions, hyperemic peritoneal surfaces and multiple small abscesses were found in each rat. Aerobic and anaerobic culture results for the peritoneal cavity and dominant abscesses are shown in **Table II.** *E. coli* and *B. fragilis* were recovered from all abscesses. Cultures of the peritoneal cavity apart from the abscesses were negative at the time of sacrifice in all but one rat.

Group B (peritonitis vehicle group): Baseline myoelectric recordings obtained from group B rats demonstrated normal phase I, II, and III activity. MMC cycle duration was 14.83 ± 0.74 minutes, and the migration velocity was 0.74 ± 0.05 cm/min.

These rats did not appear toxic after injection of the peritonitis vehicle. They ate and defecated normally. No signs of peritonitis developed. MMC cycle duration and migration velocity did not change significantly during the test period (Table I). Examination of the MMC morphology also revealed no changes.

Six days after injection with the peritonitis vehicle, these rats were killed, and the abdomen was re-entered through the previous midline incision. Examination of the abdomen revealed small sterile granulomas, most prominent at the injection sites, numerous intra-abdominal adhesions, and only mildly hyperemic peritoneal surfaces. No abscesses were found. The granulomas and the peritoneal surfaces were sterile in all three rats (Table II).

TABLE II
Bacteriologic Data

	No. of Abscesses	Abscess Cultures		Peritoneal Cultures
		E. coli	*B. fragilis*	
Group A				
Rat 1	2	+	+	–
2	6	+	+	–
3	2	+	+	–
4	4	+	+	–
5	5	+	+	–
6	6	+	+	–
7	5	+	+	–
8	2	+	+	–
9	3	+	+	–
10	2	+	+	+*
Group B				
Rat 1	0	–	–	–
2	0	–	–	–
3	0	–	–	–

**E. coli, B. fragilis, Proteus* species, *S. aureus.*

COMMENTS

Peritonitis is clinically associated with paralytic ileus. It has been assumed that the clinical symptoms of intra-abdominal sepsis, namely, inability to eat, abdominal distention, and altered bowel habits, reflect myoelectric quiescence of the gastrointestinal tract. In 1899, Bayliss and Starling [7] showed that excitation of peritoneal receptors can reflexly inhibit intestinal smooth muscle. Scratching the parietal peritoneum or instillation of peritoneal irritants resulted in reflex inhibition of jejunal movement. Inhibition was unaffected by bilateral vagotomy but was eliminated by complete splanchnic section [8]. Ochsner *et al* [9] reported that spinal and splanchnic anesthesia eliminated the ileus seen with peritoneal irritation.

Landman and Longmire [*10*], using intraluminal pressure transducers, studied the effects of acute peritoneal irritation on extrinsically denervated jejunal loops in dogs. They proposed that a hormonal factor may be involved in paralytic ileus secondary to peritonitis. Mishra and coworkers [*11*] also studied the effects of various intraperitoneal injuries on the motility of canine small intestine. Using an intraluminal catheter to monitor both electrical and mechanical activity, they concluded that the small intestine of the dog is extremely resistant to paralytic ileus even when subjected to severe intra-abdominal irritation. No study, to date, has examined in detail the myoelectric activity of the small bowel during peritonitis.

Our peritonitis model reliably produced intra-abdominal sepsis. As seen in Table II, all rats developed intra-abdominal abscesses, and, at necropsy, the peritoneal cavity was grossly inflamed. One rat in group A also grew *E. coli*, *B. fragilis*, *Proteus* species, and *Staphlococcus aureus* from peritoneal cultures. The significance of this finding is unclear since infectious bacteria are usually walled off into abscesses by this time in experimental peritonitis [*5*]. The unexpected bacteria may have represented contaminants, the bowel may have been injured during injection, or translocation through the serosal surface of the bowel may have occurred. Neither of the adjuvant agents alone, or in combination, induces abscess formation [*12,13*]. In our study, injection of the adjuvants alone (the peritonitis vehicle) produced no toxic effects, and only a mild degree of intra-abdominal inflammation was noted at necropsy.

Disappearance of phase II activity during periods of ileus has been observed previously. The significance of this finding has received little attention. We have observed that in dogs undergoing intra-abdominal operations, phase III of the MMC returns within 4 to 6 hours after operation. However, during approximately the first 24 hours, the normally cycling MMCs lack phase II activity (unpublished data). Waldhausen and Schirmer [*14*] have also reported that phase II activity was often absent from small bowel MMCs in humans during the early postoperative period in humans. Recently, Ducerf and colleagues [*15*] also emphasized that the jejunal MMC lacks phase II activity in the early postoperative period.

The disappearance of phase II activity of the MMC during episodes of peritonitis can be interpreted in a variety of ways. Our hypothesis is based on other experimental observations regarding the generation of phase I and phase II of the MMC, which we have made in dogs [*16*]. Examination of the relations between phase I duration, phase II duration, phase III migration time, and phase III cycling period using simple linear-regression methods revealed that only the phase I duration was highly correlated with the phase III migration time and that only the phase II duration was highly correlated with the phase III cycling period. These findings led us to conclude that only phase III of the MMC migrates and that phase I activity may be controlled by phase III activity at distal sites. In addition, rather than being an integral part of the MMC cycle, phase II activity may simply represent background activity whose limits are determined by the occurrence of phase III.

If one accepts this hypothesis, then it is not difficult to conceive that during times of sympathetic hyperactivity (such as the postoperative period and episodes of peritonitis), the background activity of the small bowel (phase II) is suppressed. The fact that the peritonitis vehicle did not disrupt phase II activity is consistent with this hypothesis, since the vehicle would induce a lesser degree of peritoneal irritation, causing a lesser degree of sympathetic discharge, resulting in less suppression of normal background small bowel activity.

The assumption that peritonitis induces a total paralytic ileus is not supported by our findings. Although we did not study mechanical propulsion, we can say that, myoelectrically, there is no paralysis. The fact that MMCs cycle normally during a time when there is obvious gastrointestinal dysfunction emphasizes the importance not only of phase II for normal motility but the importance of a coordinated complete (phase I, II, and III) complex.

The MMC has been referred to for years as the intestinal "housekeeper" [*17*]. Scott and Cahall [*18*] have shown that in rats the interdigestive myoelectric complex is an important regulator of bacterial growth in the small intestine. Vantrappen and associates [*19*] have shown that MMC activity is absent in some patients with bacterial overgrowth. Recently, we have proposed that small bowel bacterial overgrowth seen in diabetic rat and dog models may be, at least partially, due to disordered small bowel motility patterns [*20–22*]. The concept of disordered small bowel motility patterns leading to small bowel bacterial overgrowth is intriguing, especially as we become more aware of the gut as a source of systemic disease and intestinal sepsis as a factor in the morbidity of multiple system organ failure.

In summary, although bacterial peritonitis alters gastrointestinal motor activity, it does not inhibit MMC cycling. Some features of small bowel myoelectric activity (phase III) are preserved during peritonitis, and others are changed (phase I) or lost (phase II). Disappearance of phase II activity in this type of ileus emphasizes the importance of this activity for normal small bowel motility.

REFERENCES

1. Wittman DH. Intraabdominal infections—introduction. World J Surg 1990; 14: 145–7.
2. Walker AP, Condon RE. Peritonitis and intraabdominal abscesses. In: Schwartz SL, Shires GT, Spencer FC, editors. Principles of surgery, 5th ed. New York: McGraw-Hill, 1989: 1459–89.
3. Shuck JM. Newer concepts in intra-abdominal infection. Am Surg 1985; 51: 304–8.
4. Clowes GH, Zuschneid W, Turner M, *et al.* Observations on the pneumonitis associated with severe infection in other parts of the body. Ann Surg 1968; 167: 630–50.
5. Weinstein KA, Onderdonk AB, Bartlett JG, Gorbach SL. Ex-

perimental intra-abdominal abscesses in rats: development of an experimental model. Infect Immunol 1974; 10: 1250–5.
6. Brown MK, Leslie GB. Animal models of peritonitis. Surg Gynecol Obstet 1976; 143: 738–40.
7. Bayliss WM, Starling EH. The movements and innervation of the small intestine. J Physiol (Lond) 1899; 24: 99–143.
8. Youmans WB. Nervous and neurohumoral regulation of intestinal motility. New York: Yence Publishers, Inc, 1949.
9. Ochsner A, Gage IM, Cutting RA. Comparative value of splanchnic and spinal anesthesia in treatment of experimental ileus. Arch Surg 1930; 20: 802–31.
10. Landman MD, Longmire WP. Neural and hormonal influences of peritonitis on paralytic ileus. Am Surg 1967; 33: 756–62.
11. Mishra NK, Appert HE, Howard JM. Studies of paralytic ileus: effects of intraperitoneal injury on motility of the canine small intestine. Am J Surg 1975; 129: 559–63.
12. Simmons RL, Diggs JW, Sleeman HK. Pathogenesis of peritonitis. III. Local adjuvant action of hemoglobin in experimental *E. coli* peritonitis. Surgery 1968; 63: 810–5.
13. Onderdonk AB, Bartlett JG, Louie T, Sullivan-Seigler N, Gorbach SL. Microbial synergy in experimental intraabdominal abscess. Infect Immunol 1976; 13: 22–6.
14. Waldhausen JHT, Schirmer BD. The effects of tube feeding on postoperative ileus. Presented at the Association for Academic Surgery, Louisville, Kentucky, November 1989.
15. Ducerf C, Duchamp C, Pouyet M. Postoperative electromyographic profile in human jejunum. Ann Surg 1992; 215: 237–43.
16. Lang IM, Sarna SK, Condon RE. Generation of phases I and II of migrating myoelectric complex in the dog. Am J Physiol 1986; 251: G201–7.
17. Szurszewski JH. A migrating electric complex of the canine small intestine. Am J Physiol 1969; 217: 1757–63.
18. Scott LD, Cahall DL. Influence of the interdigestive myoelectric complex on enteric flora in the rat. Gastroenterology 1982; 82: 737–45.
19. Vantrappen G, Janssens J, Hellemans J, Ghoos Y. The interdigestive motor complex of normal subjects and patients with bacterial overgrowth of the small intestine. J Clin Invest 1977; 59: 1158–66.
20. Frantzides CT, Nowak T, Edmiston CE, Roza AM, Lianos E. Effects of diabetes on the migrating myoelectric complex [abstract]. Gastroenterology 1990; 99: 1213.
21. Roza AM, Edmiston CE, Frantzides CT, *et al.* Untreated diabetes mellitus promotes intestinal microbial overgrowth. Am J Surg 1992; 163: 417–21.
22. Frantzides CT, Edmiston CE, Walker AP, Nowak T. The diabetic gut: a risk factor in postoperative infection. Surg Res Comm 1992; 12: 33–42.