Trichinella spiralis Infection Alters Small Bowel Motor Activity in the Fed State

VERNE E. COWLES and SUSHIL K. SARNA
Departments of Surgery and Physiology and Digestive Disease Research Center, Medical College of Wisconsin, and Zablocki Veterans Administration Medical Center, Milwaukee, Wisconsin

The effect of Trichinella spiralis infection on small intestinal transit and motor activity in the fed state during the intestinal phase of infection was studied. Contractions were recorded by strain gauge transducers, and mean transit time was measured by marker dilution technique. The mean amplitude and area of individual phasic contractions decreased, but no change occurred in their mean duration during trichinosis. The total amplitude and area of phasic contractions also decreased; this was caused by a decrease in the frequency of contractions as well as a decrease in the mean parameters. The reduction in the total duration was entirely caused by the decrease in frequency. The reduction in the total parameters of all contractions was the result of a reduction in the same parameters for both propagating and nonpropagating contractions. However, the decrease in the parameters of propagating contractions was much greater. Also, there was a decrease in the distance of propagation of phasic contractions. The transit time as a result of phasic contractions increased during Trichinella spiralis infection. Additionally, T. spiralis infection induced giant migrating contractions in the fed state that were never observed during control. Chyme was propelled very rapidly and effectively by giant migrating contractions. The findings of the present study suggest that during diarrhea induced by T. spiralis infection, the phasic contractions may act to decrease transit and, hence, allow more contact time for absorption of water and nutrients. However, this response may be counter-balanced by giant migrating contractions that rapidly propel chyme into the colon and compound the diarrhea associated with T. spiralis infection.

Trichinosis is caused by eating meat previously infected with Trichinella spiralis. Clinical symptoms of trichinosis, during the intestinal phase of the infection, include nausea, vomiting, abdominal cramps, and diarrhea (1,2). The intestinal phase of the infection is the period during which infective larvae develop into sexually mature worms. This phase is characterized by histological and functional changes of the intestine (1,2). The diarrhea observed during this phase of infection could be caused by two primary mechanisms: (a) decreased ability of the small intestine to digest and absorb nutrients and (b) abnormal motor patterns that may propel chyme and intestinal and pancreaticobiliary secretions too rapidly for absorption of water, nutrients, and electrolytes in the small intestine.

The decreased ability of the small intestine to digest and absorb during the inflammatory response to T. spiralis infection has been established previously (3,4). The effect of T. spiralis infection on motor activity and transit has been studied previously mostly in the fasted state. Castro et al. (5) reported that small intestinal transit in the fasted state was significantly increased in rats during trichinosis. Studies of Palmer et al. (6) with rats and Schanbacher et al. (7) with dogs showed that in the fasting state an intense burst of electrical response activity (ERA), also known as action potentials or spikes, migrated very rapidly in the aborad direction during the intestinal phase of trichinosis. This burst of ERA seems to be the electrical correlate of the giant migrating contraction (GMC), as reported by Sarna (8). Indeed, we reported recently that the incidence of GMCs originating in the proximal small intestine is increased dramatically in fasted dogs during the intestinal phase of trichinosis (9,10). The GMCs are highly propulsive (11), and in the fasted state they rapidly propel intestinal, pancreatic,
and biliary secretions into the colon. This may contribute to diarrhea.

The effect of *T. spiralis* infection on postprandial motor activity and transit has received little attention, although motor disturbances after a meal may be a major factor in producing diarrhea if undigested food is propelled into the colon. Schanbacher et al. (7) reported a decrease in the number of cycles of electrical control activity (ECA) that were accompanied by ERA in the fed state during the intestinal phase of trichinosis in dogs. Transit time was not measured, nor was any abnormal myoelectric activity reported in the fed state in their study.

Our hypothesis is that intestinal inflammation caused by *T. spiralis* infection results in significant changes in the spatial and temporal organization of contractions, such as their frequency and distance of propagation, in the fed state. These parameters determine the rate of transit. In addition, GMCs may also occur during trichinosis in the postprandial state, which would rapidly propel undigested food into the colon. Giant migrating contractions never occur postprandially under normal conditions (8,12,13). However, they have been reported to occur after a meal during radiation enteritis (12).

Our objective in this study was threefold: (a) to determine if postprandial transit time of the small intestine is decreased or increased during diarrhea induced by *T. spiralis*; (b) to determine what parameters of phasic contractions, such as amplitude, duration, area, frequency, propagation distance, and percentage of propagated contractions, change in response to *T. spiralis* infection; and (c) to determine if any abnormal motor patterns, such as GMCs, are present during the fed state, while the dogs have diarrhea.

Methods

Experiments were performed on six healthy conscious dogs of either sex, weighing 18–26 kg. This study was reviewed and approved by the Animal Care Committees of the Medical College of Wisconsin and Veterans Affairs Medical Center. Access to the abdominal cavity was obtained through a midventral laparotomy under sodium pentobarbital anesthesia (30 mg/kg IV). Two two-way cannulas were implanted in each dog, 25 and 105 cm aboral to the ligament of Treitz. The cannulas were designed so that during an experiment they allowed complete bypass of chyme coming from above. For the rest of the time, they allowed normal passage of luminal contents in the distal direction. An intraluminal silicone catheter (internal diameter, 2.6 mm; external diameter, 4.8 mm) was implanted distal to the first cannula, so that its tip rested 5 cm aboral to the cannula. The 75-cm distance between the tip of the catheter and the second cannula constituted the study segment. Contractions of the small intestine were recorded by quarter Wheatstone bridge strain gauge transducers as previously described (14). Each transducer was calibrated before implantation (15). The transducers were sutured to the seromuscular layer to record circular muscle contractions. Two transducers were placed proximal to the study segment, 10 and 20 cm oral to the first cannula; eight transducers were placed in the middle of the study segment at 4-cm intervals, and two were placed distal to the study segment, one 20 cm aboral to the second cannula and one 10 cm oral to the ileocolonic junction. The transducer lead wires were brought out through a stainless steel cannula in the abdominal wall, as previously described (16,17). The dogs were allowed 2–3 weeks to recover from surgery before experiments were begun.

The recordings were made on a 12-channel Grass recorder (model 7; Grass Instruments Co., Quincy, MA). The lower and upper cutoff frequencies were set at direct current and 15 Hz, respectively. The signals were simultaneously recorded by a magnetic FM tape recorder (model 3968A; Hewlett-Packard Co., San Diego, CA) for later playback at a different paper speed and computer analysis.

Male mice (C57-1) were used to maintain a stock infection of *T. spiralis*. The stock was maintained by oral administration of 500 larvae per mouse. Larvae were allowed to mature for at least 30 days before they were used to infect the dogs. The larvae were recovered from the mice by pepsin digestion of skeletal muscle, as previously described by Castro and Fairbairn (18).

Control recordings were made for 2 to 3 weeks before infection with *T. spiralis*. After an overnight fast, one complete MMC cycle was recorded at the most proximal strain gauge transducer; the dog was then fed a 1300-kcal canned dog food meal consisting of 1.5 kcal/g, 8.5% protein, 5% fat, and 16.5% carbohydrate (PED, Hill’s Pet Products Inc., Topeka, KS) at 20% of the next MMC cycle. After feeding, the proximal cannula was closed so that luminal contents would flow through the study segment. Mean transit time (MTT) was determined at the beginning of the second postprandial hour by standard marker dilution method using [14C]polyethylene glycol 4000 (PEG). A 1-mL bolus of [14C]PEG was injected through the catheter, and samples were collected at the distal cannula at 15–90-second intervals for 30 minutes. Each sample was about 2 mL. Two postprandial control experiments were completed on each animal.

Experiments with *T. spiralis* were completed as follows. On the day of infection with *T. spiralis*, one complete MMC cycle was recorded at the most proximal strain gauge transducer and then 2 × 107 larvae/kg were injected into the jejunal through the intraluminal catheter at 20% of the next MMC cycle. This dose of larvae has previously been reported to cause trichinosis in dogs by Schanbacher et al. (7). After an overnight fast, the dogs were fed a 1300-kcal solid meal, as above. As in control studies, MTT was determined at the beginning of the second postprandial hour. Two postprandial experiments with transit time measurement were completed for each animal. The feeding experiments were performed during the period when the dogs had diarrhea, 2–5 days after infection (10).

The samples for MTT determination were centrifuged at 5000 rpm for 20 minutes, and 0.5 mL of the supernate was used to determine 14C activity by liquid scintillation (Tri-Carb 1900CA, Packard Instruments Co., Downers Grove,
MTT determination. Individual phasic contractions in the time between two consecutive samples, and the study segment were low pass filtered at 1 Hz and digitized at 10 samples per second into individual computer files (Nova 4/X; Data General Corp., Westboro, MA) for the 30-minute period during which samples were taken for MTT determination. Individual phasic contractions in the computer files were identified as reported previously (13,15,21,22). After having identified all the phasic contractions in a file, the program determined the mean and total values for the contraction parameters of duration, amplitude, and area. The total value of a parameter represents the summation of that parameter for all contractions in the 30-minute period. The amplitude was determined in grams, duration in seconds, and area in gram-seconds.

Next, the program determined if a contraction propagated to an adjacent site (13,15,22). Contractions that propagated < 4 cm were called nonpropagated contractions; those that propagated ≥ 4 cm were called propagated contractions. We reported earlier that this definition effectively separates propagated contractions that are largely responsible for propulsion from the nonpropagating contractions that mainly mix and stir the chyme (15). A contraction that propagated over two or more recording sites was considered as one contraction, although it occurred at several sites. The mean distance of propagation was calculated as the average distance that propagating contractions traveled during the 30-minute period. All values are expressed as mean ± SEM. The mean values of each day’s experiment were used to determine a mean value for each dog during the control state and T. spiralis infection. Statistical analysis was performed with n equaling the number of dogs. Paired t test was used for statistical comparison of the data. A P value of ≤ 0.05 was considered to be statistically significant.

Results

Diarrhea developed in all dogs by the second day after infection with T. spiralis. The dogs were considered to have diarrhea when they produced liquid stools. As reported later, GMCs were recorded postprandially during T. spiralis infection. The GMCs can very rapidly propel intestinal contents (8,11).

Because one of our aims was to determine the effect of T. spiralis infection on individual phasic contractions, the transit time data were discarded if a GMC occurred during its measurement, and the experiment was repeated on a different day.

The MTT as a result of individual phasic contractions during the fed state increased significantly from 4.6 ± 0.5 minutes to 9.0 ± 0.3 minutes (Figure 1A) after T. spiralis infection. There was a significant reduction in the frequency (Figure 2G), mean amplitude (Figure 2B), and mean area (Figure 2A) of phasic contractions during T. spiralis infection, but there was no change in the mean duration (Figure 2C). The reduction in the mean area was, therefore, caused by a decrease in the mean amplitude, because the mean duration did not change.

Total area, total amplitude, and total duration of phasic contractions were all significantly reduced after T. spiralis infection (Figure 2D–F). The decrease in the total duration of contractions was caused by a significant reduction in the frequency of phasic contractions from 11.2 ± 0.4 to 5.8 ± 0.2 cycles/min (Figure 2G), because mean duration was not different during control and T. spiralis infection. By contrast, the decrease in total area and amplitude of phasic contractions was caused by the reduction in frequency as well as the mean area and amplitude.

The percentage of individual phasic contractions that propagated ≥ 4 cm as well as their mean distance of propagation were significantly decreased during T. spiralis infection from 59.1% ± 2.4% to 46.4% ± 2.9% and 12.4 ± 0.7 to 8.8 ± 0.5 cm, respectively (Figure 1B and C).

We reported recently that propagated contractions are mainly responsible for propulsion of intestinal contents and nonpropagated contractions for mixing and stirring (15). Therefore, we analyzed the changes in the parameters of propagated and nonpropagated contractions separately to see how small intestinal motor function may change during T. spiralis infection. There was a significant reduction in the frequency of both propagated and nonpropagated contractions (Figure 3A), but the decrease in the frequency of propagated contractions was much greater and
accounted for the greater part of the reduction in the frequency of all phasic contractions.

The results for total duration, total amplitude, and total area of propagated and nonpropagated phasic contractions were similar to that of frequency. Total duration, total amplitude, and total area of both propagated and nonpropagated phasic contractions were significantly reduced after *T. spiralis* infection (Figure 3B–D). Again, as with frequency, the reduction in total parameters of all contractions was the result of the decrease in the same parameters for both propagated and nonpropagated phasic contractions.

**Discussion**

Our findings show that *T. spiralis* infection has a major effect on postprandial small intestinal motor activity. The total duration, total amplitude, total area, and frequency of all contractions are reduced, and there is also a decrease in the mean amplitude and mean area of contractions. The decrease in the total parameters of all phasic contractions is caused by a decrease in the same parameters for both propagated and nonpropagated contractions separately. However, the decrease in the parameters of propagated contractions is the major factor. In contrast to the reduction in the parameters of phasic contractions, there is a dramatic increase in the incidence of GMCs in the postprandial state, with over a third of them originating in the proximal small intestine.

Recently, we reported that propagated contractions show a strong inverse correlation with MTT, whereas nonpropagated contractions are not related to transit (15). This finding supports the hypothesis that nonpropagated contractions may mainly mix and agitate luminal contents, whereas propagated contractions propel them (13,17,23–25). If so, the reduction in the parameters of nonpropagated contractions during *T. spiralis* infection may affect the ability of the jejunum to thoroughly mix the ingested meal with secretions and to expose it evenly to the mucosal surface for absorption. This together with a decrease in digestive enzymes and absorptive capacity during trichinosis (3,4,26) may result in reduced ability of the small intestine to break down complex carbohydrates, fats, and protein after a meal. By contrast, the decrease in the parameters of propagated contractions would slow transit through the small intestine. This would allow more time for digestive and absorptive processes to be accomplished. Because the relative inhibition of propagating phasic contractions was much greater than that of the nonpropagating ones, it is unlikely that postprandial phasic contractions contrib-
Figure 4. After infection with *T. spiralis*, a GMC originated 81 cm from the pylorus and migrated to the ileocolonic junction. The GMC occurred 75 minutes after feeding a 1300-kcal meal. Numbers on the left show the distance of corresponding strain gauge transducer from the pylorus. SG, strain gauge.

In the normal postprandial state, GMCs seldom occur after a meal (8,12,13). However, after *T. spiralis* infection GMCs originating in the proximal small intestine were induced during the postprandial period. A GMC is a large-amplitude and long-duration contraction that spasmodically contracts a 20–30 cm segment and can migrate over the entire length of the small intestine in 5–10 minutes. In doing so, these contractions are capable of emptying the bulk of intestinal contents into the colon in just a few minutes. Normally, it may take several hours to do the same with individual phasic contractions.

The rapid propulsion of the ingested meal by GMCs may be one of the major factors in producing diarrhea during trichinosis. If a GMC occurs in the postprandial state, the chyme will not have enough time to be digested and absorbed. In addition, the postprandial intestinal, pancreatic, gastric, and biliary tract secretions will also be rapidly propelled into the colon. Bacterial breakdown of partially digested food and secretions would increase the osmotic load on the colon and intensify the diarrhea caused by *T. spiralis* infection. Postprandial GMCs have also been reported during radiation enteritis (12).

Patients with trichinosis often complain of abdominal cramps and discomfort. Giant migrating contractions have previously been reported to be associated with abdominal pain in patients with the irritable bowel syndrome (27) and with whining and apparent discomfort in dogs (8,10,12). The GMCs may cause pain either by contracting the gut wall beyond its nociceptive threshold at the site of contraction or by distending the segment ahead of it as a result of rapid propulsion of a large bolus of luminal contents (23), especially in the postprandial state.

Cholera toxin and *T. spiralis* infection are both known to induce diarrhea. However, there are some basic differences in the secretory changes in the two cases. Small intestinal secretion is increased significantly during diarrhea induced by cholera toxin (28,29) but not during diarrhea induced by *T. spiralis* (10). Our present findings show that there are some similarities and some differences in the postprandial motor activity in the two types of diarrhea induced by these agents. The similarity is that transit time caused by individual phasic contractions is prolonged in both cases. This increased transit time in both conditions is caused by a reduction in the frequency of propagated contractions and the distance they propagate (13). The increase in transit time could be considered to be a beneficial response to both agents, because it would increase the time available for digestion and absorption. However, *T. spiralis* infection results in the initiation of GMCs in the postprandial state, whereas cholera toxin does not (13). Postprandial GMCs would rapidly propel undigested food into the colon amplifying the diarrhea associated with *T. spiralis* infection. Another difference between cholera toxin–induced diarrhea and that caused by *T. spiralis* infection is that the contractile parameters of nonpropagated contractions are not affected with cholera toxin (13), whereas *T. spiralis* infection results in a decrease in contractile parameters of nonpropagating contractions. Therefore, the mixing and agitating function of the small intestine would be compromised during *T. spiralis* infection but not affected during the secretory state induced by cholera toxin.
In conclusion, during the diarrheal state after infection with T. spiralis, the individual phasic contractions act to decrease jejunal transit and thus allow more contact time for absorption of water and nutrients postprandially. However, this effect may largely be overcome by the GMCs induced in the postprandial state that would rapidly propel the intestinal contents into the colon and compose the diarrhea associated with the intestinal phase of trichinosis.

References


Received June 26, 1990. Accepted January 15, 1991.

Address requests for reprints to: Sushil K. Sarna, Ph.D., Surgical Research 151, Zablocki Veterans Administration Medical Center, 5000 West National Avenue, Milwaukee, Wisconsin 53295.

Supported by grant DK32346 from National Institute of Diabetes and Digestive and Kidney Diseases and Department of Veterans Affairs Medical Research Service.

The authors thank Dr. Gilbert A. Castro for his advice and help in using the nematode T. spiralis. He supplied us with the initial stock of mice infected with T. spiralis.