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Evaluation of the effect of pantoprazole administration on the transit time of barium sulphate contrast medium in mixed breed dogs

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Abstract

Contrast-enhanced radiography is a diagnostic imaging technique that provides high-resolution images of the gastrointestinal tract and plays a prominent role in demonstrating the gastrointestinal motility and transit time in small animals. This study aimed to investigate the effect of pantoprazole on the gastric transit time of liquid barium sulfate contrast medium in mixed-breed dogs under a crossover experimental design. Ten clinically healthy mixed-breed dogs were randomly selected from a shelter in Ahvaz, Khuzestan province, Iran. Each dog served as its own control in the first period, where the contrast radiography was done without pantoprazole administration and one-week later, pantoprazole was administered followed by contrast radiography. Initial gastric emptying time (IGET) and complete gastric emptying time (CGET) were noted and data were analyzed. These results demonstrate that CGET was significantly ($P<0.05$) longer in the dogs treated with Pantoprazole (294±44.3 min) compared to control (240±56.6 min). However, IGET did not differ significantly between the two time periods. Moreover, sex had no significant impact on the gastric emptying times, since considerable variation was not evident even between the male and female subjects. In conclusion, a single dose of pantoprazole significantly delays the complete gastric emptying of a liquid contrast medium in dogs, suggesting the need for caution when interpreting gastrointestinal contrast studies, as pharmacologically induced delay might be mistaken for pathological motility disorders in patients.

1. Introduction

Food digestion is highly dependent on gastrointestinal motility, which is regulated in a coordinated fashion by hormonal and neuronal signals. Any disturbances in this process result in a range of clinical signs, including abdominal pain, inappetence, vomiting, nausea, regurgitation, diarrhea, and constipation. These signs not only compromise animal welfare but also contribute greatly to morbidity in critically ill animals (Bielefeldt et al. 2016; Neiger and Salavati 2020). Among the digestive system motility disorders, delayed gastric emptying (gastric stasis) is one of the most common gastrointestinal disorders in both humans and small animals (Whitehead et al. 2016). However, a significant deficiency exists in understanding the exact influence of commonly used acid suppressant medications, such as pantoprazole, on gastrointestinal motility, particularly in the context of delayed gastric emptying. Gastric motility can be influenced by several factors, including mechanical obstructions, gastric ulceration, and systemic disorders like electrolyte imbalance, metabolic diseases, traumatic brain injury, and several infectious or inflammatory diseases (Kurt et al. 2011; Neiger and Salavati 2020). This wide ranges of potential causes make diagnosing the primary cause challenging, which generally requires clinical examination and serial contrast radiography (Manzoor and Rasool 2024). While radiographic techniques such as barium studies are commonly used and widely available for qualitative assessment of gastrointestinal transit, they do not have the sensitivity to detect subtle motility disorders in critically ill patients reliably (Kurt et al. 2011; Manzoor and Rasool 2024).

Diagnostic interpretation is further complicated by the administration of medication, particularly acid suppressant drugs (ASDs) such as histamine H_2 receptor antagonists and proton pump inhibitors (PPIs) for the prevention or treatment of gastric ulceration (Litou et al. 2019; Manzoor and Rasool 2024). Among ASDs, PPIs are considered the most effective due to their favorable efficacy and safety profile (Netzer et al. 2001; Bardou and Martin 2008). However, in contrast to the histamine H_2 receptor antagonists, whose prokinetic effects are well documented, there is a relative dearth of information about the effects of PPIs on gastrointestinal motility. Because of this, the clinician cannot accurately distinguish between a harmless, pharmacologically induced delay in contrast transit and true pathological conditions, such as partial gastrointestinal obstruction. Such ambiguity could lead to unnecessary invasive procedures or delays in the appropriate treatment of life-threatening conditions (Bardou and Martin 2008; Whitehead et al. 2016). Moreover, in patients with pre-existing motility problems, administering a drug that could affect their gastrointestinal function might exacerbate the condition or

obscure its underlying pathology (Bielefeldt et al. 2016; Neiger and Salavati 2020). While PPIs such as pantoprazole have a significant effect on gastric pH, their impact on upper gastrointestinal motility is unclear based on conflicting reports in the literature (Netzer et al. 2001; Whitehead et al. 2016). Veterinary clinicians often use pantoprazole because of its favourable pharmacokinetic properties and plasma concentration-time profile. Given the widespread use of pantoprazole by clinicians, this study aimed to determine whether pantoprazole alters gastric emptying of a liquid barium sulfate contrast medium in healthy mixed-breed dogs undergoing upper gastrointestinal radiography. It was hypothesized that a single dose of pantoprazole would delay complete gastric emptying compared with the untreated control condition.

2. Materials and Methods

The study was conducted in Ahvaz city, Khuzestan province, Iran. Clinically healthy mixed-breed dogs, aged between 1 and 1.5 years, and weighing between 20 to 30 kg were included in this study. Ten dogs (five males and five females) were sampled randomly from a local dog shelter. After selection, all dogs were clinically examined to ensure the absence of systemic or gastrointestinal abnormalities, including normal body temperature, heart rate, respiratory rate, and the absence of clinical signs such as diarrhoea, vomiting, or anorexia. All animals were kept in similar kennel conditions throughout the study period. Standard management conditions involved daily feeding with commercial dry dog food, freshwater *ad libitum*, routine anthelmintic treatment, and vaccination with canine 8-in-1 vaccine (protecting against distemper, parainfluenza, parvovirus, leptospirosis, and infectious hepatitis). Before each experimental protocol, dogs were fasted for 24 hours, with free access to water, to prepare the gastrointestinal tract for contrast administration.

A randomized, two-period crossover design was employed to eliminate between-individual physiological variation among the dogs, with each dog serving as its own control. The study was divided into two experimental periods separated by a washout period of one week. The first protocol during the first period (control group) consisted of slow administration of 5 to 7 ml/kg barium sulfate suspension as a contrast medium via syringe dripping into the buccal fold of each dog. Immediately following administration, the dog was gently rolled to ensure the complete coating of the gastric mucosa by the contrast medium. The second protocol during the second period involved the administration of a single dose of 20 mg pantoprazole per dog (1.0 mg/kg) 120 minutes prior to barium sulfate administration to the same dogs.

Radiographs were obtained using conventional radiography. Radiographs were evaluated by one experienced observer. The observer was blinded to treatment period (pantoprazole vs control). For each dog, right lateral, left lateral, ventrodorsally (VD), and dorsoventral (DV) views were taken immediately following barium sulfate administration and subsequently after 10, 20, 40, and 60 minutes (Fig. 1a, 1b). Then, radiographs were taken at hourly intervals until complete gastric emptying of the contrast medium was observed. For subsequent time points, only the left lateral and ventrodorsally (VD) views were consistently taken to monitor gastric emptying. Initial gastric emptying time (IGET) and complete gastric emptying time (CGET) were assessed during the study. IGET was defined as the time point when the first recognizable portion of barium sulfate was observed to enter the duodenum, and CGET as the time point when no barium sulfate residue was visible in the stomach on both the lateral and VD radiographic projections.

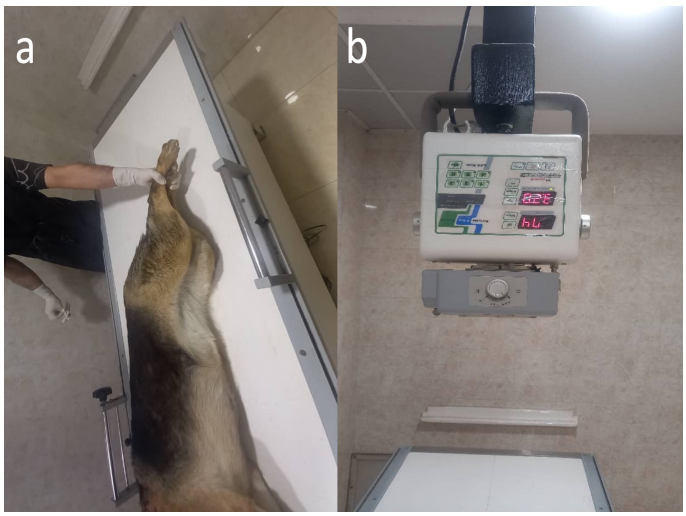

Fig. 1a. *Proper restraint and positioning of a mixed-breed dog for contrast radiographic imaging*
1b. *Radiography unit used for image acquisition throughout the study at various time points*

For statistical analysis, SPSS (Version 26) was used for descriptive statistics of both groups. Normality of the differences between paired measurements (pantoprazole vs control) was assessed using the Shapiro–Wilk test. Because data were normally distributed, paired t-tests were used to compare IGET and CGET between the two periods. Sex-based comparisons were exploratory and descriptive. For this pilot study, no formal a priori sample size calculation was performed; the study was designed to generate preliminary data and effect size estimates for future trials. Statistical significance was set at $P<0.05$.

3. Results and Discussion

The gastric emptying indices were summarized as mean and standard deviation (SD). The mean IGET was higher in the pantoprazole-treated group (9±7.5 min) compared to the control condition (5±3.5). CGET ranged from 180 to 360 minutes in the control period (240±56.6 min), whereas it was 294±44.3 min for the pantoprazole-treated group (Table 1). Sex-based descriptive statistics were performed for all ten dogs for the assessment of gastric emptying. The average minutes of initial gastric emptying were 48.0±73.2 and 36.0±112.20, respectively, for males and females. The mean minutes of complete gastric emptying were 240±56.6 and 294±44.3, for control and treated group, respectively. When analyzed by sex, the values remained within these clinical ranges, with no statistically significant difference observed between

Table 1. Summary statistics for gastric emptying indices in minutes

Indices	Minimum	Maximum	Mean ± SD
IGET in control group	0	10	5±3.5
IGET in the pantoprazole-treated group	0	20	9±7.5
CGET in control group	180	360	240±56.6
CGET in the pantoprazole-treated group	240	360	294±44.3

IGET: Initial Gastric Emptying Time; CGET: Complete Gastric Emptying Time; SD: Standard deviation

Table 2. Comparison of gastric emptying times between experimental groups

Parameter	Paired difference Mean ± SD	95% Confidence interval	T statistic	Degree of freedom	Significance
Initial Gastric Emptying Time	-4.00±2.66	[-10.03, 2.03]	-1.50	9	0.168
Complete Gastric Emptying Time	-54.00±18.86	[-96.68, -11.31]	-2.86	9	**0.019***

The negative mean difference indicates that the time was longer in the treated group (Treated - Control < 0).
* Significant (P<0.05)

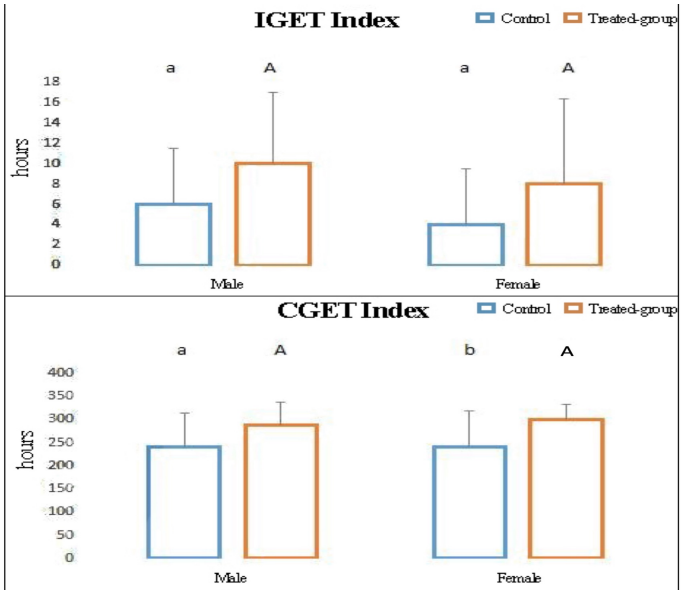

Fig. 2. Mean changes in IGET and CGET (hours) in study dogs of both sexes

male and female subjects (*P*>0.05) **(Table 2).** Comparative analysis revealed a significant mean paired difference of -54.00±18.86 between the control and pantoprazole-treated conditions (P<0.05). In other words, CGET in the pantoprazole-treated group (294±44.3 min) was significantly higher than the control group (240±56.6 min). However, IGET was not significantly different between the two study periods (P = 0.168) (Table 2). The comparative analysis ofthese indices in both male and female dogs showed there was no statistically significant difference between sexes (*P*>0.05) (Fig. 2).

A plain lateral abdominal radiograph at time zero (Fig. 3a) serves as a baseline radiograph to confirm proper positioning and contrast delivery. Fifteen minutes post-administration, the contrast medium predominantly filled the stomach, a key visual event for determining IGET (Fig. 3b). At 60 minutes, radiographs represent an intermediate phase and show the contrast medium moving through the small intestine and residual barium still present in the stomach, which is essential for tracking CGET (Fig. 3c). Abnormal gastric emptying plays a significant pathophysiological role in several acid-related and functional gastrointestinal disorders and Proton pump inhibitors (PPIs) are frequently used to treat conditions such as functional dyspepsia, peptic ulcer disease, and gastroesophageal reflux disease (Koziolek et al. 2019). Despite their extensive clinical use, the influence of PPIs on gastrointestinal motility remains incompletely understood, particularly in veterinary medicine. The current study showed that the administration of pantoprazole significantly delayed gastric emptying in dogs, with a mean CGET of 294±43 minutes compared to 240±56.6 minutes under un-treated conditions.

Understanding the impact of gastrointestinal medicines on normal digestive physiology and the mechanism involved supports successful drug management (Litou et al. 2019). The present study indicates that, in addition to its established role as an acid suppressant, pantoprazole may exert modulatory effects on gastrointestinal motility and alter the passage of ingested material. Only a few studies have assessed the effects of acid-suppressing drugs on gastric emptying in dogs, and the results from studies in humans are inconsistent. Such inconsistencies are largely due to methodological differences, including fasting status of subjects and whether gastric emptying of solids or liquids was

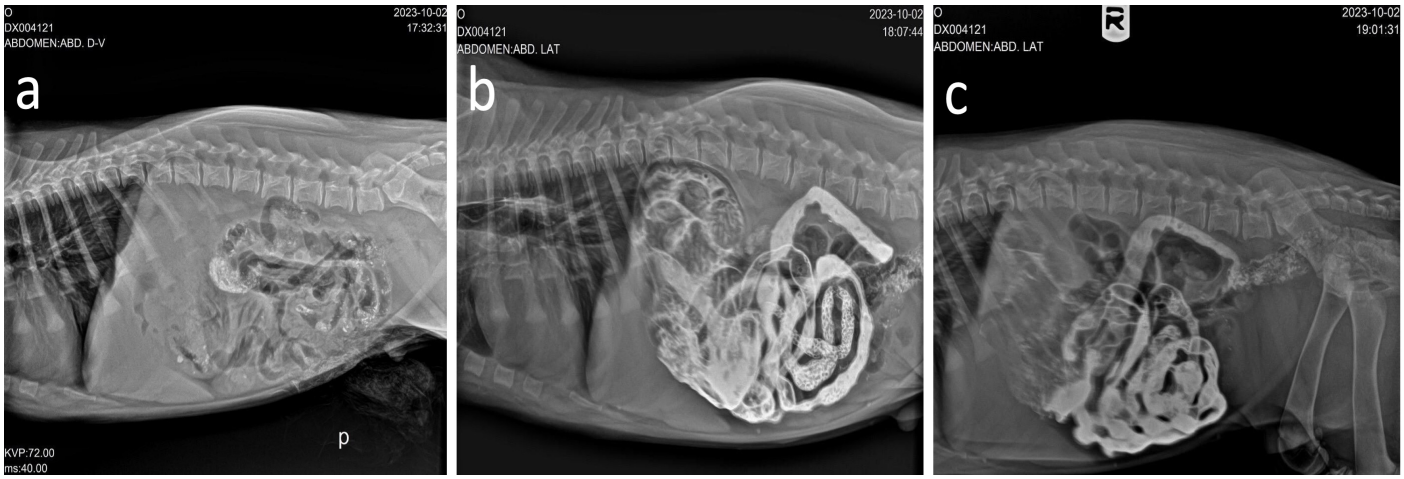

Fig. 3a. Plain lateral abdominal radiograph obtained at Time Zero
3b. Lateral abdominal radiograph obtained at 15 minutes following the oral administration of Barium Sulfate contrast medium
3c. Lateral abdominal radiograph obtained at 60 minutes following the oral administration of Barium Sulfate contrast medium

measured. It has been reported that PPIs can delay solid meal emptying by impairing acid-dependent hydrolytic digestion, whereas their effects on liquid emptying are less predictable (Koziolek et al. 2019). Parkman et al. (1998) demonstrated differential effect of PPIs under fed and fasted states. They recorded delayed gastric emptying of an egg sandwich meal following a week-long course of esomeprazole (20 mg daily). Interestingly, they also found an increased postprandial antral pressure activity and an increased fasting migratory motor complexes (Camilleri et al. 1998), highlighting the complex and sometimes paradoxical effects of PPIs on gut motility. However, no consensus has been established regarding the effect of PPIs on liquid emptying. It is hypothesized that PPIs variably alter the volume and energy density of the gastric content by the reduction in gastric fluid secretion and hence liquid emptying becomes unpredictable (Michalek et al. 2011; Koziolek et al. 2019). In the current study, dogs were fasted and gastric emptying was measured using a liquid suspension of barium sulfate. The delay in gastric emptying observed following pantoprazole administration is consistent with previous studies with omeprazole (Rasmussen et al. 1997). Sankara et al. (2007) proposed a potential explanation, suggesting that rabeprazole enhances distension-induced accommodation, resulting in delayed gastric emptying of a large volume of water, potentially due to decreased endoluminal pressure (Rasmussen et al. 1997; Sanaka et al. 2007; Sanaka et al. 2010). This mechanism appears to underlie the delayed gastric emptying observed in the present study. However, the effects of acid-suppressing agents appear to be drug class and dose-dependent. Treatment with famotidine, a histamine H_2 receptor antagonist, has been shown to slightly decreased gastric transit time, whereas nizatidine has been more consistently associated with gastroprokinetic effects in rodents and humans, accelerating solid-phase gastric emptying in dog models as potently as cisapride (Hare et al. 2000; Koziolek et al. 2019). This indicates that acid-suppressing agents with prokinetic properties may exert effects on gastrointestinal motility that differ from those of PPIs, which may influence drug pharmacokinetics, thereby affecting drug interactions and consequent therapeutic decision-making, particularly in patients with suspected bowel obstruction, abnormal gut motility, or other similar conditions (Tolbert et al. 2015; Koziolek et al. 2019; Duxbury et al. 2022).

Clinically, delayed gastric emptying has implications for both diagnosis and therapy. In diagnostic imaging, prolonged gastric retention of the contrast medium can reduce the diagnostic efficiency and mimic pathological motility disorders. Therapeutically, this delay could be beneficial in conditions requiring prolonged gastric retention of medication or protective coating agents. However, it may be detrimental in patients predisposed to vomiting, regurgitation, or aspiration, particularly those recovering from digestive system surgery (Whitehead et al. 2016; Neiger and Salavati 2020). Further studies are needed to elucidate the mechanisms of pantoprazole in delaying gastric emptying. Dose dependency, chronic vs acute administration, and possible interaction with diet or concurrent medication need to be further explored. Comparative trials with other PPIs and prokinetic agents would help determine whether this is a class effect or a drug-specific phenomenon of pantoprazole (Litou et al. 2019; Neiger and Salavati 2020). Because this two-period crossover study used a fixed sequence and a small sample size, we were unable to formally assess period or carryover effects, which is an additional limitation.

4. Conclusions

Pantoprazole significantly delays complete gastric emptying of a liquid contrast medium in dogs, indicating a modulatory effect on gastric motility beyond its well-documented role of acid suppression. This finding underscores the need for caution while interpreting gastrointestinal contrast studies and highlights the importance of further research to determine the underlying mechanisms and whether this effect is shared across the proton pump inhibitor class.

Declarations

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