Diagnostic and Comparative Therapeutic Study on Treatment of Gastroenteritis in Dogs Without and With Histamine H2 Receptor Antagonist

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1. Abstract

This study was applied to investigate the effect of Antodine® (Famotidine, 40 mg PO BID/~25 kg dog twice daily) supplement for 5 days in dogs suffering from gastro-enteritis. Twenty seven dogs enrolled in this study, their ages ranged between 6-8 month and their bodyweight ranged between 20-27 kg. Dogs divided into two groups, first group (Gp) included nine (n=9) clinically healthy dogs considered as control group, second group (Gp 2) included eighteen (n=18) dogs suffering from gastro-enteritis, kept in Dog Kennel and divided into two subgroups: (Gp2 A) included 9 dogs given the traditional regimen of treatment (GIT protectant, Anti-emetic, and fluid therapy); and (Gp 2 B) included 9 dogs treated with same regimen plus the addition of famotidine. Whole blood examined for changes in CBC and serum for selected biochemical constituents levels. Abdominal ultrasonography applied to detect changes in stomach and duodenum which revealed that gastritis, can produce a diffuse, mild to moderate thickening of wall with preservation of the wall layering. Early recovery and return of appetite, vital signs to normal occur at 3-5 days in dogs treated with famotidine while cases treated without famotidine recovery gained at 5-7 days of treatment.

Key words: *Dog, Gastroenteritis, Famotidine, Hematology, Ultrasonography*.

2. Introduction

Because that application of two well-known histamine H_1 antagonists (triprolidine or mepyramine) impaired the ability of posterior hypothalamus explants to protect the hippocampus from kintic acid (KA)-induced cell death, histamine appears to have considerable neuroprotective effects. It is thus possible that the increased histamine level and histamine release observed in both ischemic conditions and hibernation represent a relevant physiological response to neuronal stress and anoxia, opening up the possibility of the therapeutic use of histamine and/or histamine receptor ligands to treat related clinical conditions [1].

The most significant component in the treatment and prevention of stomach ulcers is acid suppression. For acid suppression, there are two main medication types now in use in veterinary medicine. Cimetidine, ranitidine, and famotidine are histamine-2 (H_2) receptor antagonists that reduce gastric acid secretion by binding to the H2 receptors of stomach parietal cells, blocking the secretion of both hydrochloric

acid and pepsin. The H+ –K+ ATPase proton pump, which is the final stage of stomach acid secretion, is blocked by proton pump inhibitors like omeprazole [5],[22].

While proton pump inhibitors are considerably more potent antacids than H2 blockers, the realities of dosing should be considered in drug selection. Unlike proton pump inhibitors, H_2 antagonists have good oral bioavailability when administered with food, andtherefore, need not be administered on an empty stomach as is the case with omeprazole [21], [22].

This study aimed to investigate the effect of oral administration of Famotidine supplement for 5 days in dogs suffering from gastro-enteritis.

3. Materials and Methods

Animals

All procedures performed in this study were in accordance with the ethical standards. The study was conducted on 27 dogs admitted to small animal clinic, Department of Medicine and Infectious Diseases, Faculty of Veterinary Medicine, Cairo University. Their ages ranged between 6-8 month and their bodyweight ranged between { 20-27 kg }.

Dog's complete history from its owner, including its health background, diet, eating/chewing habits, access to garbage and household chemicals, free-roaming activities and whether it is on any oral medications. Owners complain was estimated.

Study design

Dogs were divided into two groups, first group (Gp 1) included 9 clinically healthy considered as control group, second group (Gp 2) included 18 dogs suffering from gastro-enteritis, kept in the clinic's dog Kennel (Gp 2) and divided into two subgroups: (Gp2 A) included 9 dogs administered traditional regimen of treatment: Gastrointestinal protectants (sucralfate), Anti-emetic or anti-vomiting (metoclopramide), and fluid therapy (normal saline and dextrose saline 5%) and (Gp 2 B) included 9 dogs treated with the same regimen applied in group 2A in addition to famotidine (40 mg PO BID/~25 kg dog twice daily).

All cases exposed to complete comprehensive clinical and laboratory examination to exclude parasitic external and internal infestation and confirming obtaining of vaccination regimens.

Samples

Blood samples were collected by puncture of cephalic vein, first portion collected on EDTA containing tube for estimation of CBC using the methods described by Douglas and Wardrop [6].

Second portion collected on plain tube for serum separation for estimation of total protein, albumin, globulin level and (A/G) ratio.

Ultrasound examination

Ultrasonography was applied on healthy, diseased cases and after treatment [12].

Statistical analysis

Results were monitored in healthy and diseased dogs and after treatment in both Gp2 A and Gp2 B andstatistical analysis of obtained data was carried out by SPSS program version-21 using one-way ANOVA results were expressed as mean ± standard error at P value ≤ 0.05.

4. Results and Discussion :

Clinical findings :

Most consistent clinical signs recorded in the diseased group (Gp 2) were sudden onset of profuse vomiting with straining and abdominal pain, these signs were reported to be associated with gastritis [15]. Dehydration, lethargy or depression, increased thirst, blood in the vomit or feces, and abdominal pain are all possible symptoms [18].

Reduced appetite was detected in all examined diseased dogs, these findings came in agreement with Hinchcliff [9] who reported that any ailment that diminishes a canine's hunger or makes them hesitant to eat or drink or promotes (vomiting/regurgitation) for (inst-ance gastritis– can-promote dehydration and loss of condition.

Hemato-biochemical Findings

Results of hemato-biochemical alterations are shown in Table1, 2, 3. For hematology of group 2 (diseased dogs), there were significant decrease in RBCs count and PCV% which agree with previous study reported reduction in total erythrocyte count (TEC), packed cell volume (PCV) in dogs suffering from gastroenteritis compared to healthy dogs [16].

Decreased levels of total erythrocyte count and packed cell volume were also noticed according to [10], [2] .

Observed decrease in RBCs count might be due to anemia in hemorrhagic gastroenteritis [14], massive sloughing of intestinal epithelial cells [11] and damage of capillaries of villi in the intestine leading to hemorrhages [19].

An improvement in hematological indices in the form of significant increase in RBCs count and PCV% in both treatment groups (GP2 A, GP2 B) compared to diseased group (GP 2). No significant change in platelets number and HB in GP2 (diseased) compared to GP1 (healthy). MCV and lymphocyte count increased significantly in dogs suffering from gastro-enteritis [16].

Neutropenia was observed in most of the diseased dogs. The demand for WBC, particularly neutrophils, is high in the inflamed gastrointestinal tract, but due to hematopoietic cell destruction of leukocytes

in lympho-proliferative organs like the bone marrow.

There is an inadequate supply of leukocytes leading to several other hematological changes [7].

Neutropenia may occur due to marked inflammation of gastric mucosa associated with nonbacterial infectious disease like parvovirus infection [3].

Significant reduction in total proteins and decrease in albumin were observed in diseased dogs (gp 2) compared to healthy dogs (gp 1).

This decreased level of protein is attributed to its seepage through damaged capillaries of the villi of intestine as well as poor nutrition uptake ,so hypoproteinemia and hypoalbuminemia occur in dogs suffered with acute gastritis & Decrease in Albumin in gastroenteritis infected dogs might be due to severe protein losing enteropathy due to intestinal villi damage or intestinal hemorrhage [8], [16].

An improvement in protein profile was registered in both treatment groups compared with diseased state.

Ultrasonographical findings:

Ultrasonography examination of dog suffered from acute vomiting & Anorexia showed symmetric and extensive increase in gastric wall thickness of stomach body ranging from (5.1 mm to 1 cm) in 5 dogs with retained identification of wall layering, increased pyloric antrum wall thickness wasidentified in 2 dogs

(8.33 mm & 6.55 mm), and in one case pyloric sphincter increased in wall thickness (9.18 mm) was showed with luminal stenosis (Fig.1, 2, 3), These findings coinciding with previous research [13].

Early recovery and return of appetite, vital signs to normal occurs at 3-5 days in dogs treated with famotidine while cases treated without famotidine recovery gained at 5-7 days of treatment. Famotidine was reported to significantly decreased the severity score of exercise-induced gastric affections[21]. Famotidine was reported to have a similar potency of ranitidine but without the prokinetic or lower esophageal sphincter effect [20].

However, in one randomized control trial that study and compared high dose famotidine versus omeprazole in preventing “exercise-induced gastritis” in race dogs, omeprazole showed superior results compared with famotidine in prevention of the condition, albeit the later showed some benefits too [22].

Addition of famotidine to therapeutic protocol of gastritis in dogs showed some benefit in improving clinical recovery of the examined dogs.

5. Conclusion

This study aimed to investigate the effect of administration of Famotidine for 5 days in dogs suffering from gastro-enteritis. Early recovery and return of appetite, vital signs to normal occur at 3-5 days in dogs treated with famotidine while cases treated without famotidine recovery gained at 5-7 days of treatment.

6. References

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Table (1) Complete blood picture of healthy, gastro-enteritis and treated dogs

Parameters/Units	Group 1 (9)	Group 2 (18)	Group 2 A (9)	Group 2 B (9)
RBCs ($\times 10^6$ /ul)	$4.93^{a}\pm0.21$	$3.82^{b}\pm0.26$	$5.04^{a}\pm0.25$	**$5.24^{a}\pm0.25$**
Heamoglobin (mg/dl)	$10.20^{a}\pm0.32$	$9.11^{a}\pm0.41$	$9.84^{a}\pm0.45$	**$10.14^{a}\pm0.46$**
PCV (%)	$33.13^{a}\pm1.97$	$28.75^{b}\pm1.39$	$37.30^{a}\pm1.20$	**$37.00^{a}\pm1.20$**
Platelets (10^3)	$123^{a}\pm12.57$	$118^{a}\pm7.95$	$190^{a}\pm33.16$	**$192^{a}\pm36.84$**
MCV (fl)	$66.88^{b}\pm1.44$	$75.98^{a}\pm1.80$	$73.84^{a}\pm1.61$	**$73.14^{a}\pm1.04$**
MCH (pg)	$20.83^{b}\pm1.14$	$24.04^{a}\pm0.63$	$19.64^{b}\pm1.23$	**$19.51^{b}\pm1.19$**
MCHC (mg/dl)	$30.33^{ab}\pm1.73$	$31.69^{a}\pm0.42$	$26.74^{b}\pm1.47$	**$29.36^{ab}\pm1.18$**

Values have the similar symbol or symbols within the same raw are not significantly different at $P\leq0.05$.
Gp 1: control group
Gp 2: gastro-enteritis group
Gp2 A: administered traditional regimen of treatment
Gp 2 B: treated with addition of famotidine

Table (2) Differential leukocytes of healthy, gastro-enteritis and treated dogs

Parameters/Units	Group 1 (9)	Group 2 (18)	Group 2 A (9)	Group 2 B (9)
WBCs ($\times 10^3$/ ul)	$13.80^{a}\pm1.276$	$13.2^{a}\pm2.16$	$13.40^{a}\pm1.27$	$13.50^{a}\pm1.182$
Basophile (%)	$0.00^{a}\pm0.0$	$0.00^{a}\pm0.0$	$0.00^{a}\pm0.0$	$0.00^{a}\pm0.0$
Esinophile (%)	$2.50^{b}\pm0.33$	$6.75^{a}\pm2.27$	$7.25^{a}\pm0.92$	$6.85^{a}\pm0.78$
Staff (%)	$6.00^{a}\pm0.65$	$6.00^{a}\pm0.85$	$4.25^{b}\pm0.25$	$4.25^{b}\pm0.25$
Sigmented (%)	$60.25^{a}\pm2.02$	$47.25^{b}\pm4.24$	$47.50^{b}\pm3.48$	$46.50^{b}\pm1.91$
Lymphocyte (%)	$25.50^{b}\pm2.58$	$36.75^{a}\pm1.92$	$38.00^{a}\pm3.78$	$38.59^{a}\pm3.61$
Monocyte (%)	$5.75^{a}\pm1.03$	$3.50^{b}\pm0.33$	$3.00^{b}\pm0.38$	$4.00^{ab}\pm0.65$

Table (3) Selected Serum biochemical constituents of healthy, gastro-enteritis and treated dogs

Parameters/Units	Group 1 (9)	Group 2 (18)	Group 2 A (9)	Group 2 B (9)
Total protein (g/dl)	$5.59^{a}\pm0.22$	$4.25^{b}\pm0.16$	$4.53^{b}\pm0.15$	$5.21^{a}\pm0.27$
Albumin (g/dl)	$2.91^{ab}\pm0.12$	$2.53^{b}\pm0.14$	$2.68^{ab}\pm0.19$	$3.13^{a}\pm0.14$
Globulin (g/dl)	2.68±0.10	1.72±0.02	1.85±0.04	2.08±0.13
A/G Ratio	1.085±1.2	1.471±7	1.448±4.75	1.505±1.077

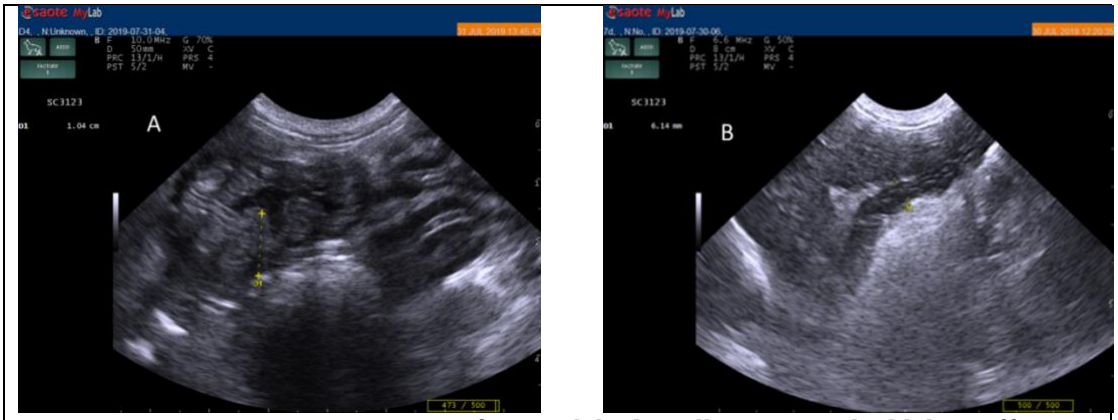


Figure 1: (A) Transverse axis view of stomach body wall in a 8 month old dog suffering from acute vomiting showing increased thickness of gastric wall (1.04 cm) with retained wall layering identification and hyperechoic mucosa.
(B) Transverse axis view of stomach body wall in a 1 year old dog suffering from acute vomiting showing increased gastric wall thickness (6.14 mm) with retained wall layering identification and hyperechoic luminal content with dirty shadowing artifact indicative for gaseous content .

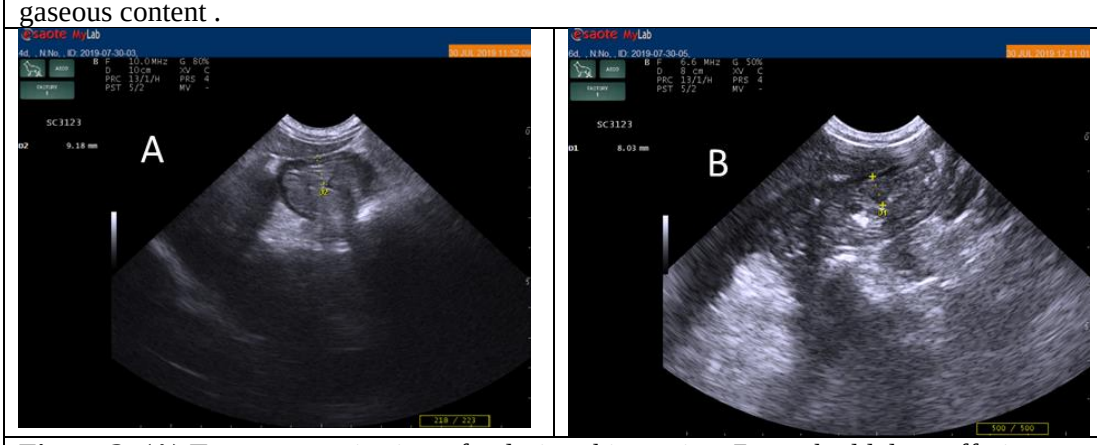
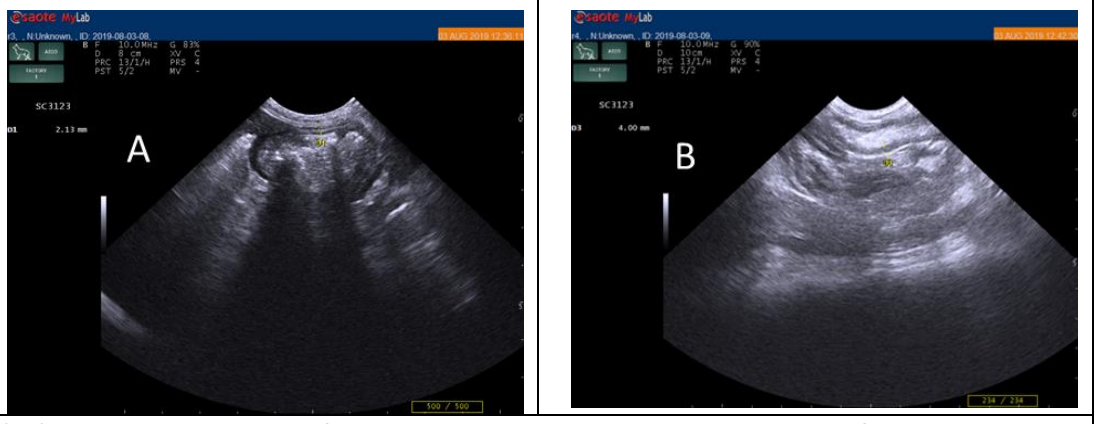


Figure 2: (A) Transverse axis view of pyloric sphincter in a 7 month old dog suffering from acute vomiting showing uniform increased wall thickness (9.18 mm) with luminal stenosis .
(B) Transverse axis view of pyloric antrum in a 8 months old dog suffering from acute vomiting showing uniform increased wall thickness (8.03 mm)



(A) Transverse axis view of stomach body wall in an one year old dog after treatment showing regression in gastric wall thickness (2.13 mm) .
(B) Transverse axis view of pyloric antrum in a 9 months old dog after treatment showing decrease in wall thickness (4 mm) .