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Density of interstitial cells of Cajal of gastric tissue of equids with gastric ulcers: Interspecies comparative study

A.L. Medina-Bolívar, V.M. Usuga-Moreno and J.R. Martínez-Aranzales

Equine Medicine and Surgery Research Line, CENTAURO Research Group, School of Veterinary Medicine, Faculty of Agricultural Sciences, University of Antioquia, Medellin, Colombia

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Correspondence:
J.R. Martínez-Aranzales
jose.martinez@udea.edu.co

Abstract

The interstitial cells of Cajal (ICC) are essential for regulating gastrointestinal motility in equids, as they act as pacemakers that synchronize smooth muscle contractions of the digestive tract. This study aimed to determine and compare the distribution and population density of ICC in the gastric tissue of equids (horses, donkeys, and mules) with and without gastric ulcerative lesions to assess their role in the pathophysiology of equine gastric ulcer syndrome (EGUS) in these species. Sixty healthy and ulcerated stomachs whose lesions were identified in glandular and/or squamous mucosa were evaluated, and the ulcers were classified. In addition, histological and immunohistochemical techniques were used to assess the lesions and to determine the ICC. The results indicate that the ICC subtypes showed similar distributions in healthy and ulcerated conditions, as did all the equids studied. However, a significant decrease in the total number of ICC was observed in stomachs with ulcers compared with healthy animals. The squamous mucosa showed less immunoreactivity for ICC than did the glandular mucosa of the fundus and pyloric antrum. However, the number of ICC in the squamous mucosa was generally lower. Despite evidence of alterations in gastric ICC density between healthy and ulcerated patients, additional studies are needed to determine the association with EGUS; however, this is the first report on the associations between gastric pathologies and ICC behavior in equids.

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Introduction

The interstitial cells of Cajal (ICC) are considered pacemakers and mediators of neurotransmission in various parts of the gastrointestinal tract in humans and other species (1-3). Previous studies have identified and characterized ICC in the equine gastrointestinal tract (4,5). Still, most have focused on their distribution along the intestinal tract. Histological and immunohistochemical studies have described the behavior of ICC in cases associated with colic in horses (6), specifically in obstructive pictures of the large and small intestine (7), luminal distention of the small colon (8), inflammatory bowel diseases (9), and equine dysautonomia (grass sickness) (10). These alterations are characterized by disturbances in gastrointestinal motility. Studies on the distribution and characterization of ICC in equine gastric tissue layers are scarce. However, Hudson *et al.* (4) reported a similar pattern in the greater curvature and the pyloric canal region in healthy equines; therefore, the role they play in cases of gastric alterations remains unknown. ICC may be involved in gastric motility, as these cells are considered intermediaries between inhibitory and excitatory nerves that modulate the excitability of the circular muscle layer of the stomach (11,12). In this sense, ICC could play a role in cases of gastric lesions arising from or perpetuated by motility alterations. Equine Gastric Ulcer Syndrome (EGUS) comprises Equine Squamous Gastric Disease (ESGD) and Equine Glandular Gastric Disease (EGGD), is highly common in these specimens, and its multifactorial nature involves both exogenous factors and

management conditions, which are mostly studied (13), and endogenous, such as deficiency in gastroprotective mechanisms and motility and gastric emptying (13-17). Alterations in the ICC population related to motility may increase gastric emptying time and thereby increase the probability of a caustic effect on the gastric mucosa, especially the squamous mucosa, due to a poorer defence mechanism (14,18,19).

The objective of this study was to determine and compare the distribution and population density of the ICC of the gastric tissue of equids (horses, donkeys, and mules) with and without gastric ulcerative lesions to consider their participation in the pathophysiology of EGUS in each species.

Materials and methods

Ethical approval

All procedures were approved by the Ethics Committee for Experimentation with Animals of the University of Antioquia (No. 1472022) and carried out in accordance with the relevant laws and guidelines.

Gastric tissue sampling

A total of 60 stomachs of equids (horses, donkeys, and mules), 30 healthy and 30 ulcerated, from a slaughterhouse located in Rionegro city, Antioquia, Colombia, were obtained immediately after slaughtering. The equids of both sexes were, on average, 12 years old, as estimated through dental chronometry. The average weights were 350±20 kg for the horses, 230±15 kg for the donkeys, and 340±16 kg for the mules. Before identification of the stomach, a cut was made between the cardia and the pyloric antrum through the greater curvature to fully expose the gastric surface, and the contents were removed and flushed with abundant water. The entire gastric surface was then inspected to classify stomachs as having or not having ulcers. Stomachs with intact gastric surfaces, without evidence of inflammation, erosions, ulcers, or hyperkeratosis, were classified as healthy. Stomach ulcers were classified based on both gastric diseases, namely ESGD and EGGD. ESGD was classified by the number (0-4) and severity (0-5) of lesions, according to MacAllister *et al.* (20), and, for EGGD, the classification suggested by the European College of Internal Medicine was considered (21). In addition, all findings related to chronic and acute gastritis, hyperkeratosis, and gastric lumen abnormalities were recorded. After macroscopic inspection, three (3) samples were taken from the squamous gastric mucosa, the glandular gastric mucosa, and the pyloric antrum. The samples were obtained by dissecting both types of gastric mucosa, making incisions approximately 1 cm in length that extended through all the layers of the organ. The tissue was then preserved in 10% buffered formalin (22). The total stomachs were divided into two groups: Group 1 (30 stomachs), with gastric ulcers (10 equines, 10 donkeys, and 10 mules), and Group 2 (30 stomachs), without gastric ulcers or healthy (10 horses, 10 donkeys, and 10 mules).

Histological and immunohistochemical analysis

Complete samples of gastric tissue were analysed with conventional and routine paraffin embedding histological techniques, with a special orientation (longitudinally and transversely) so that the fibers of the circular muscle layer of the external muscle were parallel at the time of cutting, according to the technique used by Pavone and Mandara (5). The samples were subsequently cut into 0.5 cm thick sections approximately 1 cm in length to be subjected to a routine process, which included dehydration with ethyl alcohol, clearing with xylene, inclusion and blocking with paraffin, cutting by microtome, and H&E staining, and finally examined under a light microscope to evaluate the integrity of the tissue architecture and describe abnormalities of the gastric mucosa in the layers of the epithelial lamina, lamina propria and submucosa of the sampled regions. The findings were classified as mild, moderate, or severe.

For the immunohistochemical analysis of the ICC, anti-CD117 antibodies (c-Kit, Vitro Master Diagnostics®) (monoclonal rabbit anti-human antibodies, 1:200 dilution, Clone EP10) were used. After deparaffinization and rehydration, the antigens were recovered using a citrate buffer solution containing an anti-CD117 antibody (10 mmol/L Tris base, 1 mmol/L EDTA at pH 9.0, and 10x pH 6 citrate buffer (PT Module)), which was preheated for 20 minutes in a water bath. To deactivate the endogenous peroxidase, 6% hydrogen peroxide was applied for 5 min. Afterward, the slides were covered with the CD117 antibody (ready to use) for 1 hour in a humidified chamber. The immunoreactivity was detected using the "Master Polymer Plus Detection System" from Vitro Master Diagnostics®, Spain, EAN: 8435421235496; REF: MAD-000237QK-125 (1250 test); LOT: 237QK1250099. Finally, toluidine blue staining was used to confirm the presence of mast cells (4). For cell classification, 10 fields were used, corresponding to 2.37 mm^2 for each sample. The cells were classified morphologically as stellate, spindle, oval, or oval mastocytoid (4,5); their density/quantity was determined in each histological layer of the tissue, including the submucosa, myenteric plexus, and muscle layers. The cell morphology was determined based on the appearance of the cells as follows: stellate, those that had projections or irregular shapes; fusiform, those that had a spindle shape; oval, those that had a convex and rounded shape; and similar to the profile of an egg and oval mastocytes, those that were completely circular.

Statistical analysis

The results were analysed using descriptive statistics, including means, standard deviations, and percentage distribution of the number and types of ICC found in the various locations of each sample from the different equid

species. The Shapiro-Wilk test was used to assess the normality of the data. Data from cases that did not show normal distribution were used to compare the density of ICC between ulcerated and healthy animals. To determine statistically significant differences ($P<0.05$) between location, gastric zone, cell morphology, and equid species, and between healthy and ulcerated conditions, the Kruskal-Wallis and t-test were used.

Results

Macroscopic evaluation of the gastric surfaces made it possible to select stomachs without lesions in both the mucosa region and the *Margo plicatus* region, as well as to determine and classify the presence of ulcers on the entire gastric surface of the equids (Table 1 and Figure 1). In general, ESGD was the most common among equid species, with grades ranging between II and IV (80-90%, N=30), with donkeys and mules having the highest grades. Regarding EGGD, the percentage of presence was lower, oscillating between 10 and 90% (N=30) (II and IV), where lesions of greater degrees were observed in both donkeys and mules. Gastritis was detected only in the glandular mucosa, with a greater presence in horses.

Table 1: Classification of the degrees of ulcerative lesions in both the gastric mucosa of the selected equids

Grade	Glandular mucosa*			Squamous mucosa **		
	H	D	M	H	D	M
0	2	0	2	2	0	2
I	0	0	0	0	0	0
II	0	1	2	5	4	1
III	0	7	1	3	4	4
IV	1	1	5	0	2	3
Gastritis	7	1	2	0	0	0

H= Horses, D= Donkeys, M= Mules.

At the histopathological level, healthy individuals exhibited only a few inflammatory cells, with no lesions compatible with EGUS or signs of acute or chronic inflammation upon macroscopic inspection. The findings in the layers of each gastric region of the ulcerated horses, donkeys and mules are shown in tables 2-4, showing lesions such as parakeratotic hyperkeratosis, vascular congestion, epithelial hyperplasia, dysplasia, structures compatible with parasites, necrosis, cellular degeneration, fibrosis, hemorrhage and cellular infiltration by neutrophils, lymphocytes, plasma cells, and histiocytes and eosinophils, findings classified as mild, moderate, or severe (Figure 2).

The immunohistochemical evaluation revealed ICC immunoreactivity in the gastric regions of equids of both healthy and ulcerated groups, as shown in figures 3-5. In addition, the different cell morphologies observed in ulcerative individuals across the different gastric mucosa are shown in figure 6. The stellate and fusiform ICC were the most abundant in all layers of the regions of all equids, both healthy and ulcerated; there were no statistically significant differences. Meanwhile, those of the oval type, those of lesser quantity, and those in many layers were absent. A fourth cell type, mastocytoid oval, was observed in high numbers only in the submucosal areas and confirmed as mast cells by toluidine blue staining, which is why they were excluded from the analysis.

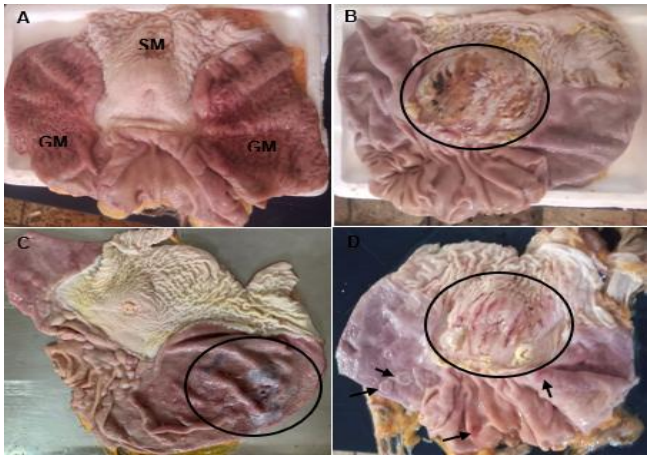

Figure 1: Macroscopic evaluation of equids' gastric mucosa. A. Healthy gastric mucosa of an equine (GM: Glandular Mucosa, SM: Squamous Mucosa). B. Ulcerative lesions in the squamous mucosa of a donkey (circle). C. Ulcerative lesions in the glandular mucosa of a mule (circle). D. Lesions in the glandular mucosa (arrows) and squamous mucosa (circle) of a mule.

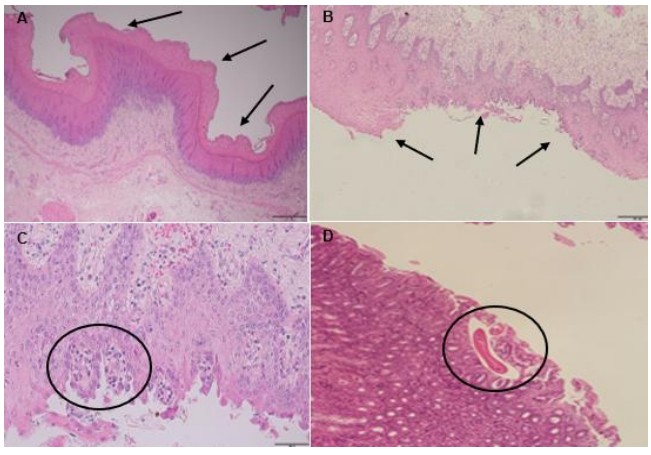

Figure 2: Histopathological findings (H&E staining) of equid gastric mucosa. 40X. A. Parakeratotic hyperkeratosis in a horse (arrows). B. Gastric ulcer in a donkey (arrows). C. Necrosis and inflammatory infiltrate in the gastric mucosa of a donkey (circle). D. Chronic gastritis with a parasite within the gastric mucosa of a mule (circle).

Table 2: Frequency of histopathological findings according to the degree of severity and location in the gastric region evaluated in the selected horses.

Location	Findings	Squamous M.			Glandular M.			Pyloric Antrum		
		Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
Epithelial layer	Parakeratotic hyperkeratosis	1	6	3	0	0	0	0	0	0
	Hyperplasia	1	3	3	6	0	0	1	3	0
	Exocytosis	1	0	0	1	1	0	3	1	0
	Cell degeneration	0	1	0	0	0	0	0	1	0
	Eosinophils	0	0	0	1	0	0	1	0	0
	Neutrophils	0	0	2	0	0	0	0	0	0
	Vascular congestion	0	0	0	1	0	0	0	0	0
	Dysplasia	0	0	0	1	0	0	0	0	0
	Parasite-compatible structures	0	0	0	0	1	0	0	0	0
	Ulcers	1	0	1	0	0	0	0	0	0
	Necrosis	1	0	1	0	0	0	0	0	0
	Fibrosis	2	0	0	0	0	0	0	0	0
Lamina propia	Vascular congestion	2	1	0	1	3	0	1	2	0
	Hyperplasia	0	0	0	3	0	0	0	0	0
	Neutrophils	0	0	0	1	0	0	4	1	0
	Lymphocytes	1	0	0	3	2	0	5	1	0
	Plasmocytes	0	0	0	1	1	0	3	1	0
	Eosinophils	0	0	0	2	1	0	3	0	0
Submucosa	Vascular congestion	1	2	0	1	2	1	2	1	0
	Neutrophils	1	0	0	0	0	0	0	0	0
	Lymphocytes	1	0	0	3	0	0	4	0	0
	Plasmocytes	0	0	0	1	0	0	1	0	0
	Eosinophils	1	0	0	1	0	0	1	0	0
	Hemorrhage	0	0	0	0	0	0	1	0	0

Mod: Moderate, Sev: Severe, M: Mucosa.

Table 3: Frequency of histopathological findings according to the degree of severity and location in the gastric region evaluated in the selected donkeys

Location	Findings	Squamous M.			Glandular M.			Pyloric Antrum		
		Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
Epithelial layer	Parakeratotic hyperkeratosis	1	1	8	0	0	0	0	0	0
	Hyperplasia	0	2	6	1	4	0	1	4	0
	Exocytosis	0	0	0	3	2	0	1	0	0
	Neutrophils	1	0	0	0	0	0	0	0	0
	Lymphocytes	0	0	0	0	0	0	2	0	1
	Histiocytes	0	0	0	0	0	0	0	0	1
	Parasite-compatible structures	0	0	0	0	0	2	0	0	1
	Vascular congestion	0	0	0	0	0	1	0	0	0
	Ulcers	1	1	0	0	0	0	0	0	0
	Cell degeneration	1	0	0	0	1	0	0	0	0
Lamina propria	Vascular congestion	0	5	0	1	3	2	2	3	1
	Hyperplasia	0	0	0	1	1	0	0	0	0
	Neutrophils	1	0	0	0	1	0	2	0	0
	Lymphocytes	1	2	0	2	3	0	5	2	2
	Plasmocytes	0	0	0	0	1	0	2	1	0
	Eosinophils	1	0	0	1	0	0	3	2	0
	Necrosis	0	0	0	0	0	0	0	0	1
	Fibrosis	0	0	0	0	0	0	1	0	0
	Parasite-compatible structures	0	0	0	0	0	2	0	0	1
Submucosa	Vascular congestion	1	5	0	0	5	0	0	4	0
	Lymphocytes	2	0	0	1	3	0	2	1	0
	Neutrophils	0	0	0	0	0	0	1	0	0
	Eosinophils	0	0	0	0	0	0	1	1	0
	Necrosis	0	0	0	0	0	0	0	0	1
	Fibrosis	0	0	0	0	0	0	1	0	0
	Hemorrhage	0	0	0	1	0	0	1	1	1

Mod: Moderate, Sev: Severe, M: Mucosa.

Table 4: Frequency of histopathological findings according to the degree of severity and location in the gastric region of the selected mules

Location	Findings	Squamous M.			Glandular M.			Pyloric Antrum		
		Mild	Mod	Sev	Mild	Mod	Sev	Mild	Mod	Sev
Epithelial layer	Parakeratotic hyperkeratosis	1	1	8	0	0	0	0	0	0
	Hyperplasia	0	2	6	1	4	0	1	4	0
	Exocytosis	0	0	0	3	2	0	1	0	0
	Neutrophils	1	0	0	0	0	0	0	0	0
	Lymphocytes	0	0	0	0	0	0	2	0	1
	Histiocytes	0	0	0	0	0	0	0	0	1
	Parasite-compatible structures	0	0	0	0	0	2	0	0	1
	Vascular congestion	0	0	0	0	0	1	0	0	0
	Ulcers	1	1	0	0	0	0	0	0	0
	Cell degeneration	1	0	0	0	1	0	0	0	0
Lamina propria	Vascular congestion	0	5	0	1	3	2	2	3	1
	Hyperplasia	0	0	0	1	1	0	0	0	0
	Neutrophils	1	0	0	0	1	0	2	0	0
	Lymphocytes	1	2	0	2	3	0	5	2	2
	Plasmocytes	0	0	0	0	1	0	2	1	0
	Eosinophils	1	0	0	1	0	0	3	2	0
	Necrosis	0	0	0	0	0	0	0	0	1
	Fibrosis	0	0	0	0	0	0	1	0	0
	Parasite-compatible structures	0	0	0	0	0	2	0	0	1
Submucosa	Vascular congestion	1	5	0	0	5	0	0	4	0
	Lymphocytes	2	0	0	1	3	0	2	1	0
	Neutrophils	0	0	0	0	0	0	1	0	0
	Eosinophils	0	0	0	0	0	0	1	1	0
	Necrosis	0	0	0	0	0	0	0	0	1
	Fibrosis	0	0	0	0	0	0	1	0	0
	Hemorrhage	0	0	0	1	0	0	1	1	1

Mod: Moderate, Sev: Severe, M: Mucosa.

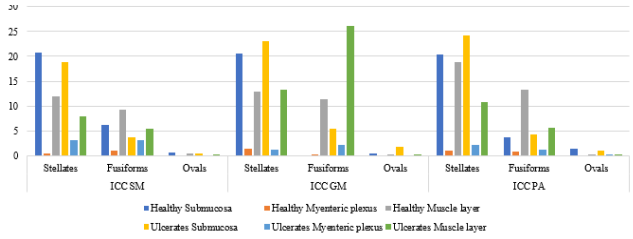

Figure 3: Total of Interstitial Cells of Cajal (ICC) according to morphology and location in the squamous mucosa (SM), glandular mucosa (GM), and pyloric antrum (PA) of healthy and ulcerated horses.

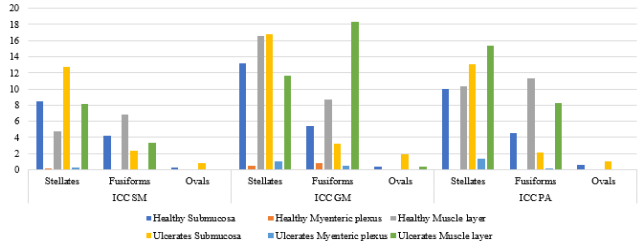

Figure 4: Total of Interstitial cells of Cajal (ICC) according to morphology and location in the squamous mucosa (SM), glandular mucosa (GM), and pyloric antrum (PA) of healthy and ulcerated donkeys.

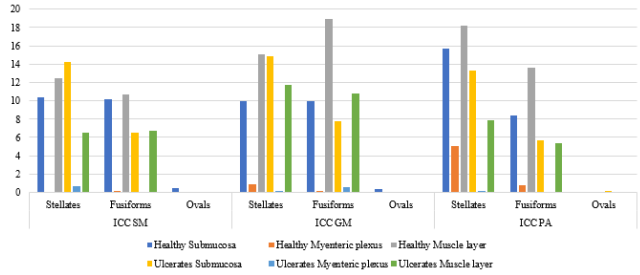

Figure 5: Total of interstitial cells of Cajal (ICC) according to morphology and location in the squamous mucosa (SM), glandular mucosa (GM), and pyloric antrum (PA) of healthy and ulcerated mules.

The number and distribution of ICC were variable across layers, being more pronounced in the muscular layer, with a greater number of cells and lower counts of the three species of ulcerated equids. The total count in the selected fields is presented in figure 7. The horses had a greater number of ICC than did the donkeys and mules; additionally, the latter two species showed a decrease in number between healthy and ulcerated conditions. The gastric regions with the highest density of ICC were the glandular mucosa of the fundus and pyloric antrum, specifically in the submucosal and muscular layers. However, the latter comprised the longitudinal and

internal circular muscles. However, all comparisons between variables within and between groups showed no significant statistical differences.

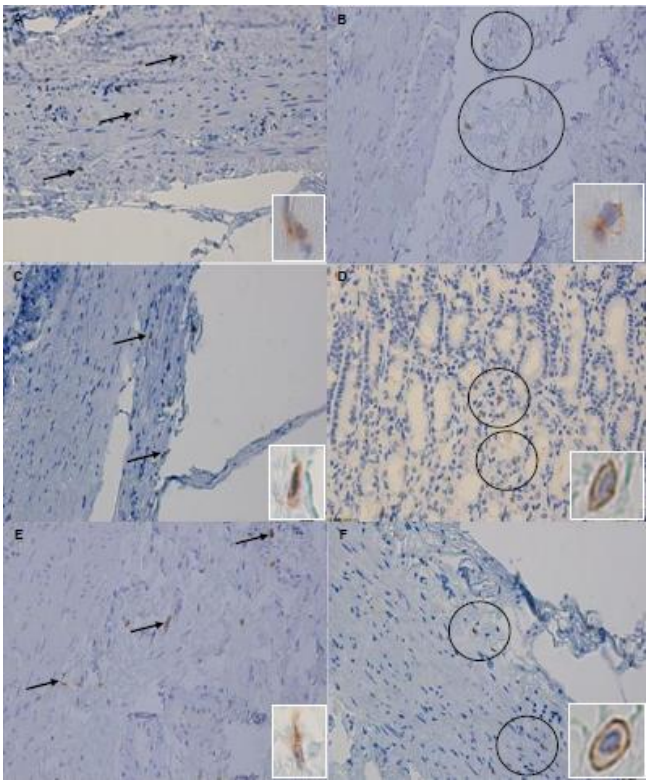

Figure 6: Immunolabeling of interstitial cells of Cajal (ICC) using CD117 antibodies, highlighting their morphologies in the gastric mucosa of ulcerated individuals. 40X. A: Stellate ICC in the glandular mucosa of an ulcerated donkey (arrows). Inset: Higher magnification of stellate ICC. B: Squamous mucous stellate ICC of an ulcerated horse (circles). Detail: Enlarged view of stellate ICC. C: Fusiform ICC in the glandular mucosa of ulcerated mules (arrows). Inset: Higher magnification of fusiform ICC. D: Oval ICC in the glandular mucosa of an ulcerated donkey (circles). Inset: Magnified view of oval ICC. E: Fusiform ICC in the squamous mucosa of an ulcerated horse (arrows). Detail: Enlarged view of fusiform ICC. F: Oval ICC in ulcerated mule glandular mucosa (circles). Inset: Higher magnification of oval ICC.

Discussion

Observations of the variability in the frequency of EGUS presentation, including both ESGD and EGGD, among individuals exposed to similar predisposing factors (23-25), even in species such as mules under extreme management conditions, which present low prevalence (26), have drawn attention to the multifactorial nature of the syndrome. The possible involvement of endogenous and inherent equid factors, shifting the perspective to consider the injury pathway not only from the gastric lumen to the epithelium, but also from the epithelium to the lumen. In this sense, ICC are related to gastrointestinal motility (2,4,5), which in turn is associated with gastric emptying and the caustic effect of hydrochloric acid as a function of time (14,27), which is why we sought to describe the changes in the ICC population in the stomachs of ulcerated equids and with inflammatory processes compared with healthy ones.

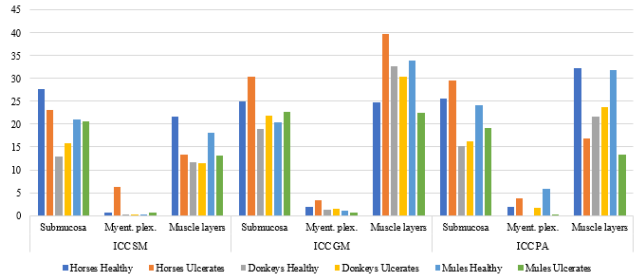

Figure 7: Total of interstitial cells of Cajal (ICC) according to location in each of the gastric regions studied in healthy and ulcerated equids (horses, donkeys, and mules). Squamous Mucosa (SM), Glandular Mucosa (GM), and pyloric antrum (PA).

Studies on the nature, development, distribution, and function of ICC have been carried out with an emphasis on the intestinal tracts of adult equines, neonates, and fetuses (4,5,28), where they are related to motility patterns (29,30). However, there is little information on the distribution and characteristics of ICC in equine stomachs, although one study partially described ICC in some gastric regions (4). In this regard, a recent survey described and characterized ICCs in the intestine and in rabbits, reinforcing prior reports on the limited literature on these cells in gastric tissue (31).

The involvement of ICC in intestinal motility patterns is well described. Likewise, they may be involved in gastric motility, since these cells are considered intermediaries of inhibitory and excitatory nerves that modulate the excitability of the circular muscle layer of the stomach (11,12). Moreover, certain high-density or high-concentration ICC regions, called pacemakers, are located in the gastric antrum (2,32,33). In contrast, others are located between the muscular layers and are referred to as mechanoreceptors (34,35). In the stomachs evaluated in both conditions (healthy and ulcerated), a greater number of ICC were observed in the muscular layers of the ventral fundus and the pyloric antrum covered by glandular mucosa, which agrees with previously described studies.

In addition to determining the presence of stellate, fusiform, and oval ICC, a distribution pattern in the submucosa, similar to that described in the intestinal segments and related to motility, was confirmed (4). Therefore, ICC may play a role in the gastric emptying

process, which is considered a gastroprotective mechanism (13-17), as it affects gastric pH gradients related to the caustic effect.

Structural changes and a reduction in the density of the ICC have been reported in humans with pathologies such as pyloric hypertrophic stenosis, ulcerative colitis, chronic and transient idiopathic intestinal pseudo-obstruction, Hirschsprung's disease, meconium impaction, anorectal malformations, megacolon, diabetic gastroparesis, inflammatory bowel disease, and constipation (11,36-40). In horses, several inflammatory and obstructive pathologies that compromise the intestinal tract have also been described; however, studies associating gastric pathologies with ICC behavior are lacking, which is why the present study was carried out.

When the ICC densities of healthy stomachs with ulcers and/or gastritis in each species of equids were compared, the decrease in the population of ICC in the ulcerated stomachs of mules, in contrast with the equines and donkeys, was apparent, indicating that the intensity of the inflammatory process or the degree of severity of EGUS possibly influences the number of ICC, since these mules presented the highest degrees of seriousness, even with the presence of parasites within the mucosa (41). Previous findings have been reported in humans and horses with inflammatory bowel disease (9,38), due to overregulation of inducible nitric oxide synthase and eicosanoid production, leading to decreased excitability of ICC and smooth muscle cells and reduced muscle contractility (42,43). Therefore, this is the first report of the association between gastric pathologies and ICC behavior in equids. However, no significant statistical differences were observed between the comparisons.

The fact that the equines and donkeys did not present the same ICC distribution behavior as the ulcerated mules, in addition to presenting less severe lesions, may also be due to other factors related to the exact lack of homogeneity of the place of collection and the number of samples per stomach. Between six and eight samples were considered representative of the gastric surfaces (44). However, the stomachs from equines presented the highest number of ICC regardless of the condition (healthy or ulcerated), suggesting an apparent difference in the patterns of distribution of ICC in the stomach compared with those in donkeys and mules. However, more studies are needed to explore these results, with a greater number of samples per stomach and the use of additional neuronal and enteroglial markers, to better understand the electrical activity of the equine stomach (9).

Despite the limited evidence of alterations in gastric ICC density between healthy and ulcerated patients, these findings should be interpreted with caution, as the stomachs of healthy animals differ from those of ulcerated patients and cannot account for individual factors, as some differences between mammals have been described (4). In addition, owing to the nature of the study, it was not possible to determine whether changes in the number of ICC were a cause or an effect of the presence of ulcerative and inflammatory lesions, as suggested by Fintl and Hudson (42). Studies on the alteration of these cells have contradicted the patterns of intestinal motility in the presence of some pathologies (45-47); however, there are no previous reports in gastric tissue regarding EGUS.

The ICC subtypes were similar under both conditions (healthy and ulcerated) and across all equids; apparently, only the number of ICC subtypes changed. On the other hand, the squamous mucosa showed immunoreactivity for ICC, although in lesser quantity than in the glandular mucosa of the fundus and pyloric antrum; however, this cannot be inferred to be a predisposing factor, given the degree of injury observed in this mucosa. Although gastric emptying is related to the presentation of EGUS, this process is complex. It involves mechanoreceptors in adjacent structures, hormones, nerves, chemical interactions, and lumen sensors, among others, that participate in muscle contraction (15,25,48), with the ICC overseeing orchestrating and interrelating the various components and phases so that gastric emptying occurs (11,31,33).

Finally, histopathological analyses were very similar among equids; however, in many cases, they did not reflect the severity of lesions observed macroscopically, possibly due to the low number of samples processed and their lack of representativeness of gastric surfaces (49). On the other hand, a relative relationship between macroscopic and histopathological evaluation has been described (50). Since gastric lesions can be multifocal, heterogeneous, and unevenly distributed, it is possible to miss alterations or findings outside the examined sections.

Conclusion

This is the first report on the associations between gastric pathologies and ICC behavior in equids. However, no substantial statistical differences were observed among the variables analyzed. The types of ICCs were similar in both healthy and ulcerated tissues and across all equid species; only their numbers varied.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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كثافة الخلايا الخلالية كاجال في أنسجة المعدة لدى الخيول المصابة بقرحة المعدة: دراسة مقارنة بين الأنواع

أنجي ميدينا بوليفار، فيفيانا أوسوجا مورينو، خوسيه مارتينيز أرانزاليس

خط أبحاث طب وجراحة الخيول، مجموعة أبحاث سنتاورو، الطب البيطري، كلية العلوم الزراعية، جامعة أنتيوكيا، ميديلين، كولومبيا

الخلاصة

تعتبر الخلايا الخلالية كاجال ضرورية لتنظيم حركية الجهاز الهضمي لدى الخيول، لأنها تعمل كأجهزة تنظيم ضربات القلب التي تعمل على مزامنة تقلصات العضلات الملساء في الجهاز الهضمي. تهدف هذه الدراسة إلى تحديد ومقارنة التوزيع والكثافة للخلايا الخلالية كاجال في أنسجة المعدة للخيول (الخيول والحمير والبغال) مع أو بدون آفات تقرح المعدة لتقييم دورها في الفيزيولوجيا المرضية لمتلازمة قرحة المعدة للخيول في هذه الأنواع. تم تقييم ستين معدة سليمة ومتقرحة تم تحديد آفاتها في الغشاء المخاطي الغدي و/أو الحرشفي، وتم تصنيف القرحات. بالإضافة إلى ذلك، تم استخدام التقنيات النسيجية والكيميائية المناعية لتقييم الآفات وتحديد المحكمة الجنائية الدولية. تشير النتائج إلى أن الأنواع الفرعية للخلايا الخلالية كاجال أظهرت توزيعات مماثلة في الحالات الصحية والمتقرحة، كما فعلت جميع الخيول التي تمت دراستها. ومع ذلك، لوحظ انخفاض كبير في العدد الإجمالي للخلايا الخلالية كاجال في المعدة المصابة بالقرحة مقارنة بالحيوانات السليمة. أظهر الغشاء المخاطي الحرشفي نشاطًا مناعيًا أقل للخلايا الخلالية كاجال مقارنة بالغشاء المخاطي الغدي لقاع العين والغار البواب. ومع ذلك، كان عدد الخلايا الخلالية كاجال في الغشاء المخاطي الحرشفي أقل بشكل عام. على الرغم من وجود أدلة على حدوث تغيرات في كثافة الخلايا الخلالية كاجال في المعدة بين الحيوانات السليمة والمصابة بالقرحة، إلا أن هناك حاجة إلى دراسات إضافية لتحديد الارتباط مع متلازمة قرحة المعدة للخيول؛ ومع ذلك، هذا هو التقرير الأول عن الارتباطات بين أمراض المعدة وسلوك الخلايا الخلالية كاجال في الخيول.