pHyloGASTRO® IN THE TREATMENT OF EQUINE GASTRIC ULCER LESIONS

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Highlights

1. Equine Gastric Ulcer Syndrome (EGUS) is the most common disease of the equine stomach with a high prevalence.
2. Nutraceutical compounds have been shown to have a positive effect on preventing or healing naturally occurring gastric ulcers.
3. pHyloGASTRO® is a herbal feed composed of medical herbs that act on restoring the acid-base balance.
4. pHyloGASTRO® seems to be an effective feed additive for the improvement of gastric lesions.
5. We believe that the 6-week treatment period, recommended by the manufacture, is too short, since often gastric mucosal lesions did not completely heal in our treated group.

Abstract

Equine Gastric Ulcer Syndrome (EGUS) is the most common disease of the equine stomach with high prevalence of both squamous and glandular disease reported in various populations.

The aim of this study was to evaluate the effectiveness of a phytotherapic compound (pHhyloGASTRO®) in the therapy of EGUS.

Materials and methods. The study was performed as a randomised double-blinded single centre study. The study population was composed of 19 equids which were submitted to gastroscopy before and after a six-week treatment with feed additive (10/19) (pHyloGASTRO®, [4]Union B.I.O. srl, Italy) or a placebo (9/19). Severity grade was evaluated on a scale from 0-4. The variables of interest were gastric lesion score and improvement grade. Changes and comparisons of variables were performed by contingency table analyses. P level of significance was set at 0.05 in all analyses.

Results. In terms of gastric lesion scores, the treated group improved significantly compared to the placebo group.

Discussion and conclusions. pHyloGASTRO® seems to be effective in the treatment of EGUS. Further studies are needed to verify whether prolonged administration of pHyloGASTRO® could be more effective in completely healing gastric lesions.

Key words

Equids, EGUS, treatment, nutraceutical compounds, pHyloGASTRO®

1. **Introduction**

Gastric ulceration is the most common disease of the equine stomach with a high prevalence of both squamous and glandular disease reported in various populations [1-3]. The term Equine Gastric Ulcer Syndrome (EGUS) was first adopted by the EGUS Council in 1999 and includes a complex of pathological conditions characterized by the presence of ulcers in the terminal portion of the oesophagus, in the proximal (squamous) and distal (glandular) parts of the stomach, and in the proximal part of the duodenum of equids [4]. Recently various authors [5-7] and the European College of Equine Internal Medicine (ECEIM) Consensus Statement [8] have provided a new nomenclature of EGUS and proposed updated guidelines regarding pathophysiology, diagnosis, and treatment [5,8].

Many drugs have been investigated and are available for the treatment and management of EGUS [8-11]. The proton pump inhibitor omeprazole has been found to be very efficient in both treating and preventing gastric ulcers in horses [8]. Other drugs such as histamine$_2$ antagonists or gastric mucosal protectors have shown less efficacy than omeprazole in the treatment of EGUS [8,11,12].

Along with pharmacological therapies, nutraceutical compounds appear to have a positive effect on preventing or healing naturally occurring gastric ulcers [13-20]. Thus, interest in more natural products has been growing. The purpose of this study was to evaluate the effect of the feed additive pHyloGASTRO® (Union B.I.O. srl, Italy) on the treatment of spontaneously occurring gastric ulcers of the squamous mucosa in a population of equids.

2. Methods

2.1 Materials

The study population was composed of 19 equids (ten Standardbred trotting horses and nine Amiata donkeys). The equids were equal regarding distribution of gender and breed. None of the animals showed clinical signs of EGUS, were athletes and were used for reproduction. Inclusion criteria: 1) all the equids were affected by gastric ulcers at gastroscopy; no changes in the feeding and environment during the study period were made.

2.2 Study design

The study was performed as a randomised double-blinded single centre study and the protocol was approved by the Ethical Committee of the University of Pisa [no. 9069/2014]. Group allocation and blinding: once enrolled into the study, horses were randomly allocated to a dose group by pulling their names out of a hat. One investigator (F.B.) was

responsible for randomisation while another investigator (S.B.) remained blinded to the group allocation until scoring was completed and recorded.

Ulcers were diagnosed by gastroscopy performed under sedation after 12 hours of fasting and 4 hours of water deprivation as reported in the literature [21]. Severity grade was evaluated on a scale from 0-4 as proposed by others [4]. Gastroscopy was always performed by the same operator (S.B.), as indicated by others [22]. For the examination, a 300 cm scope (Karl Storz, Germany) and a portable processor (Gastropack, Karl Storz, Germany) were used. The images were stored on a DVD recorder. The stomach was insufflated with air through an air-flow system attached to the biopsy channel of the scope until the internal stomach folds appeared flattened. Feed material adhering to the non-glandular mucosa was flushed away with sterile water in order to visualize the entire non-glandular portion of the stomach, including the greater curvature, the lesser curvature, and the dorsal fundus. The number and degree of ulcers were recorded in accordance with the Equine Gastric Ulcer Council (EGUC) recommendations [4].

Equids were divided in two groups: the “placebo group” was composed of 9/19 animals (median age 10 years); the “treated group” was composed of 10/19 animals (median age 8 years). The two treatment groups were clinically equal regarding distribution of gender and breed. The “treated group” was treated with pHyloGASTRO® (Union B.I.O. srl, Italy) at a dose of 60 ml per equid BID PO for 6 weeks, while the “placebo group” was treated BID with a similar-looking same-volume placebo for 6 weeks. Both pHyloGASTRO® and placebo were administered using a feeding device. The administration was always performed by the same operator (C.G.). pHyloGASTRO® is composed of medical herbs (*Althaea officinalis, Aloe barbadensis, Hoedeum vulgar, Malva sylvestris, Glycyrrhiza glabra, Echinacea angustifolia, calendula officinalis, Clay ventilated*) powered by *Matrix UB*® (the aqueous extract of *Olea europaea*, a phyto-active enhancer). The medical herbs previously reported showed antinflammatory, cytoprotective, antioxidant, mucus healing, and acid-base balance restoring activities (table 1) [23-38]. A clinical examination was carried out daily for each animal to monitor gastro-intestinal side effect. All the equids were submitted to a gastroscopy after the 6-week treatment.

2.3 Statistical analysis

The variables of interest were gastric lesion score and improvement grade. Changes and comparisons on variables were performed by contingency table analyses. Significance was set at 0.05 in all analyses. All the analyses were performed using a GraphPad Prism 6.0 (USA).

3. Results

All the equids in the study were affected by gastric ulcers in the non-glandular mucosa (Equine Squamous Gastric Disease, ESGD) [5,8]. No health problems or side effects (diarrhoea, stipsis, disorexia or anorexia, colic) related to treatment with pHyloGASTRO® were observed during the all study period. The feed additive was readily accepted by all the pHyloGASTRO®-treated horses in the same manner as the placebo.

Before treatment, the “treated group” equids showed 2/10 grade 1, 6/10 grade 2, 1/10 grade 3, while no equids showed grade 4; the “placebo group” equids showed 3/9 grade 1, 3/9 grade 2, 3/9 grade 3, while no equids showed grade 4. The pre-treatment distribution of gastric lesion scores was not significantly different between the two groups.

After 6 weeks of treatment, the “treated group” showed 2/10 equids with grade 0, 7/10 with grade 1, 1/10 with grade 3, while no animals showed grades 2 and 4; the “placebo group” showed 2/9 with grade 0, 2/9 with grade 1, 3/9 with grade 2, and 2/9 with grade 3, while no animals showed grade 4. Outcomes for both “placebo” and “treated” groups are reported in table 2.

The “treated group” improved significantly compared to the “placebo group” ($p=0.04$). Concerning the improvement score of the gastric lesions, equids treated with pHyloGASTRO® showed a significantly ($p=0.0001$) higher improvement than equids treated with the placebo (Table 3).

No differences were found between the two groups considering complete healing of gastric lesions vs improvement.

4. Discussion

EGUS is a complex disease, which for nearly 30 years has been recognized as a highly prevalent condition both in training and at rest horses [5,8,11]. A new nomenclature of EGUS along with updated guidelines regarding pathophysiology, diagnosis, and treatment have recently been proposed [5-8]. In particular, the European College of Equine Internal Medicine (ECEIM) committee recognizes that the terminology for EGUS needed clarification and proposes the nomenclature of Equine Squamous Gastric Disease (ESGD) amd Equine Glandular Gastric Disease (EGGD) [15].

The pharmacology products most commonly used for the treatment of gastric ulcers in horses focus on blocking gastric acid secretion and increasing stomach pH, which creates a permissive environment for physiological ulcer healing [8,10-11]. However, the research

for methods to treat or prevent gastric ulcers effectively without requiring the continued administration of costly pharmaceutical agents together with issues regarding withdrawal times or side effects is a new trend not only in human medicine, but also in veterinary medicine.

In order to meet this growing need for more natural products, this study aimed to evaluate the effectiveness of pHyloGASTRO® in the treatment of EGUS in adult equids. Our results showed an easy administration and ingestion of pHyloGASTRO® by the treated horses, with no health problems or side effects related to the treatment. A total of 44.4% of the "placebo" horses and 80% of the "treated" horses showed an improvement or a complete healing of the ulcers.

The improvement in the degree of ulceration score in the "placebo" group was similar compared to previous studies [17]. An improvement in placebo-treated patients has been reported in humans [39-41] and some studies have been published in veterinary medicine [42-43].

Also the improvement in the degree of ulcerations in the "treated" group is in line with a previous study [17], which investigated the effect of a nutraceutical compound and found an improvement of 77.8% of the horses treated.

Comparing the two groups, statistical calculations revealed a significant reduction in gastric mucosal lesions in the "treated" horses compared to the "placebo" group after six weeks of administration of the nutraceutical feed. This is in line with findings reported in previous papers where different nutraceutical compounds were tested [14-15,17,19-20].

Concerning the gastric lesion scores, equids treated with pHyloGASTRO® improved more significantly ($p=0.0001$) than equids treated with the placebo. Our results are in line findings reported in the literature [17,19-20].

5. Conclusions

pHyloGASTRO® seems to be an effective feed additive for the improvement of gastric lesions. However, the treatment period of six weeks, recommended by the manufacture, seems too short, since the gastric mucosal lesions had often not completely healed in the treated group. Thus, further studies are needed to verify whether a prolonged administration of pHyloGASTRO® could be more effective in obtaining a complete healing of gastric lesions. A limitation of the study could be the lack of a group treated only with the

Matrice UB® solution. The addition of this group could lead to understanding whether the improvement to EGUS lesions was due to medical herbs, to *Matrice UB*® or both.

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Medical herbs	**Mechanism of action**	**Literature**
Althaea officinalis	Antinflammatory, cytoprotective	[23,24]
Aloe barbadensis	Antinflammatory, cytoprotective, mucus healing	[23]
Hordeum vulgare	Cytoprotective, mucus healing, acid-base restoring	[25]
Malva sylvestris	Anti ulcerogenic activity	[26-28]
Glycyrrhiza glabra	Gastric healing	[29-31]
Echinacea angustifolia	Oxidant-antioxidant balance	[32]
Calendula officinalis	Antiulcer, antinflammatory effect	[33]
Clay ventilated	Ulcer healing	[34]
Olea europea	Gastroprotective agent, antioxidant activity	[35-38]

310 Table 1 – Mechanism of action of medical herbs that are compounds of
311 pHyloGASTRO® (Union B.I.O. srl, Italy).

312

PLACEBO GROUP	
Pre-treatment lesion score	**Post-treatment lesion score**
3	3
1	0
2	2
3	3
1	0
1	1
2	1
3	2
2	2
TREATED GROUP	
Pre-treatment lesion score	Post-treatment lesion score
3	3
1	1
3	1
2	1
1	0
2	0
2	1
2	1
2	1
2	1

Table 2 – Pre and post treatment lesion score outcome in “placebo” and “treated” groups.

		Improved			No change	P
		-3	-2	-1	0	
Start vs 6 weeks	Control group	0	0	4/9	5/9	0.0001
Start vs 6 weeks	Treated group	0	2/10	6/10	0/10	

Table 3 – Change in gastric lesion scores before and after 6-week period between "control" and "treated" groups.