

A Pilot Study on the Clinical Effects of Forans Nutri-Gard® for relief of Gastric Ulcers in Horses

R. van den Hoven, S. Wlaschitz, S. Leinker, C. Uray, Clinical Department of Small Animals and Horses, Clinic of Internal Medicine and Infectious Diseases, Veterinary University of Vienna, Veterinärplatz 1, A-1210 Vienna, Austria.

Introduction

Since 3 meter endoscopes have become routinely available for equine diagnostic purposes, equine gastrology has come to its full potential. Among many other clinical investigators, it was especially Murray and his co-operators who gave equine gastrology an upsurge. It is now commonly known that gastric ulcers are recognised problems in thoroughbred and standard bred race horses. The prevalence in horses stabled at race tracks or at training yards is estimated between 66 and 90% (Hammond et al. 1986, Murray 1994). Even in leisure horses the prevalence is about 37% (Murray et al. 1989). Most lesions in the living horse can be found endoscopically in the epithelium of the pars cutanea, especially near the margo plicatus. In horses kept at pasture the condition is rather uncommon (Murray 1994). It is presumed that the squamous epithelial lining of the pars cutanea of the horse stomach has a limited resistance to peptic injury similar to the oesophageal mucosa of man (Orlando 1991). When horses are not eating, the equine gastric mucosa becomes exposed periodically to highly acidic conditions (Murray and Schusser 1993). This condition may occur in stabled horses that are fed oats or pellets 2 or 3 times daily in combination with limited amounts of roughage. Horses at pasture continuously fill their stomachs with food, thereby continuously buffering the gastric acid production and gastric ulcers will develop less likely. The term "Equine Gastric Ulcer Syndrome" (EGUS) has been adopted in reference to a number of specifically unique problems that can manifest as mucosal erosion and ulceration within either the oesophagus, stomach or upper duodenum, or some combination thereof (Orsini, 2000). In the majority of cases only the stomach is affected. Gastric ulceration in mature horses may be suspected from subjective clinical signs such as mild to severe colic, poor appetite, poor body condition, dullness and attitude changes, poor performance and other behavioural changes (Murray et al. 1989, Orsini 2000). As could be expected from the vague clinical symptoms, Murray et al (1989) reported that the correlation between clinical signs and severity of ulceration appears quite variable.

The therapeutic strategies for ulcer healing include 3 basic approaches. The first approach is to keep the intragastric pH > 4, which can be achieved with HCl buffering compounds such as Al/Mg hydroxide, or alternatively with histamine H₂-antagonists (H₂-antagonists) such as cimetidine or ranitidine (Furr and Murray 1989). Both drugs must be given 3 times daily. There is still doubt on the efficacy of H₂-antagonists on ulcer healing (Nieto et al. 2001). A more efficient drug, the proton pump inhibitor omeprazole, only needs to be given once daily (MacAllister et al, 1999) and was highly effective in a large field trial (Johnson et al, 2001). The second approach may be the

coating of the ulcer by a polysulfated sugar such as sucralfate. This substance possibly also induces the mucosal production of the protective prostaglandin E₂ (PGE₂), which is also the main goal of the third therapeutic approach according to Merritt (2003). Feeding corn oil also may increase mucosal PGE₂ synthesis (Merritt, 2003). A combination of sucralfate and H₂-antagonists is also given to horses. If this is a rational combination remains questionable, since in man sucralfate is only used to treat ulcers in the pars glandularis and in the duodenum and not for oesophageal ulcers. Orsini (2000) believes that this fact may be the explanation for the apparent lack of efficacy of sucralfate in horses, since most equine ulcers are not located in the pars glandularis.

The bioavailability of H₂-antagonists for the horse is less than in man (Orsini 2000), which complicates treatment. However proton pump inhibitors appear to pose more potential (Papoch 1993, Sangiah et al, 1989). Treatment of race and sport horses with drugs like omeprazole, ranitidine and cimetidine may cause problems in doping control. Recently FEI allowed competition horses to be treated with omeprazole and ranitidine, but other racing and equestrian organisations still prohibit the presence of any foreign substance in the body of the horse and its excreta. Apart from doping rules and side effects, the other drawback of these pharmacological substances is their high price.

Alternatives to buffer intragastric pH or protect the ulcers may be pectin-lecithin based product (Pronutin®). Venner et al. (1999) described favourable effects on ulcer healing by this product. Another plant based product is Nutri-Gard®. It contains a concentrated level of potato cell wall fibre. The product has a very high water binding capacity with 90% absorbed in less than one minute. Furthermore it contains lecithin, inulin, galactose, yeast and magnesium.

The purpose of this study was to investigate the protective and healing effect on EGUS of Nutri-Gard® in competition horses. The study was an explorative clinical study using routine clinical endoscopy techniques for evaluation of treatment and did not need ethical approval

Materials and Methods

Clinical cases and treatment

Thirteen patients with clinical and/or endoscopic symptoms of gastric ulcer disease, comprising racing animals and saddle horses, were used. The distribution of age, gender and use are given in Table I.

Table I

Name	Age (years)	Gender	Use
Jubiola	12	Mare	Dressage
Märchenprinz BV	4	Gelding	Racing
Dustin Qui	6	Gelding	Racing
Wooly	21	Gelding	Pleasure Riding
Britt Stollberg	3	Mare	Racing
Destiny	12	Mare	Pleasure Riding
Maximum Risk S	4	Gelding	Racing
Rambo Venus	5	Gelding	Racing
Kaoma	11	Mare	Dressage
Manza Goldstar	9	Gelding	Racing
Dufle	8	Gelding	Racing
Lady Cotton	4	Mare	Racing
Einstein D.K.	6	Gelding	Racing

At the start of the treatment, the clinical histories of the animals were taken in order to find out if animals had been medically treated within the last 4 weeks. Horses that had been treated less than 4 weeks before presentation with cimetidine, ranitidine or omeprazole were not included in the trial.

The horses were stabled in the facilities of the clinic of internal medicine for about 18 hours. After endoscopy and initiation of therapy, animal were sent home and received their regular feed which comprised pasture hay and commercial horse pellets, oats or muesli. Pasture hay was of moderate quality. Nutri-Gard® was mixed with the pellets and or oats. No other medication or feed supplement was given to the horses during the conduct of the trial. The management of the majority of the horses could be supervised by personnel of the clinic of internal medicine, since most of the horses were housed on yards that were frequently visited for other reasons too. After 14 days and after 28 days animals returned to the clinic for their second and third gastroscopic examination.

Study design

The study was set up as a longitudinal self controlled study. Gastric ulcer scores before and after Nutri-Gard® treatment were compared case by case over a one month observation period. The trial was executed from December 2003 till February 2004.

Procedures

After over night fasting, the animals underwent gastroscopy under standing conditions in stocks. If deemed necessary, a sedative mixture of detomidine (Domosedan®) and butorphanol (Butomidor®) was administered intravenously.

Lesions were scored immediately by the endoscopist according to the practitioner's simplified scoring system (Andrews et al, 1997; Orsini, 2000) on a scale from 0 to 3 (0 -intact mucosa, can have mild reddening and/or mild hyperkeratosis; 1 - small single or multiple ulcers; 2 -big solitary or multiple ulcers; 3 - extended, confluent ulcers with regions with deep ulceration). All observations were recorded and photographs were taken from abnormal parts of the stomach.

After initial analysis, an alternative scorings system was used to semi-quantify lesion number and severity of blinded randomised endoscopic photographs of the abnormal gastric areas of the cases. Two experienced endoscopists who were in ignorance of the case information, scored the randomly ordered pictures according to the system (Table II) of MacAllister et al. (1997).

Table II: No./Severity score according to MacAllister et al. (1997)

Number score	Clinical description
Grade 0	No lesions
Grade 1	1-2 localised lesions
Grade 2	3-5 localised lesions
Grade 3	6-10 localised lesions
Grade 4	>10 lesions

Severity score	
Grade 0	No lesions
Grade 1	Appears superficial
Grade 2	Deeper structures involved (depth Grade 1)
Grade 3	Multiple lesions & variable severity (Grade 1,2 and/or 4)
Grade 4	Same as Grade 2 but with active (hyperaemic and/or darkened crater)
Grade 5	Same as Grade 4 plus active haemorrhage & adherent blood clot

The data were analysed with Friedman test using SPSS 11.5 for Windows. Kendall correlation was used for comparison of scoring systems.

Results

Thirteen horses entered the study. All horses underwent a first and a second gastroscopic examination. Two horses that were already healed on Day 14 were allowed to omit the final examination on 28 Days. One horse that had not shown improvement by the 14-day examination did not report for its 28-day examination appointment. This horse was considered as a treatment failure.

A treatment effect was already seen after 14 days of supplementing the feed with Nutri-Gard® in 38% (5 out of 13) of the cases. At 28 days after start of treatment the success rate had increased to 69% (8 out of 13). The body weight changes are given in Table III.

Table III. Mean, minimum, maximum and standard deviation of body weight and ulcer score before (day 0), after 14 days of treatment (day 14) and at 28 days of treatment (day 28).

	n	min	max	mean	standard deviation
Body weight Day 0	13	406	608	484	64
Body weight Day 14	13	411	610	485	66
Body weight Day 28	10	404	564	470	51
Ulcer score Day 14	13	1	3	2.4	0.9
Ulcer score Day 14	13	0	3	1.8	1.4
Ulcer score Day 28	10	0	3	1.7	1.2

A quantification of the effect using the EGUS score was performed and the results are given in Table IV.

Table IV. Median and 95%-confidence intervals for each scoring system

	Pre treatment	14 Days	28 Days
EGUS	3 1.9-2.9	3 1.0-2.7	2 1.2-2.4
Numbers Score	3.5 2.4-3.8	2.5 1.1-3.3	2.0 1.2-3.2
Severity Score	3.5 2.3-3.8	2.5 0.9-3.0	2.0 1.1-3.0

An example of the endoscopic appearance of a healed case is given in Fig.1.

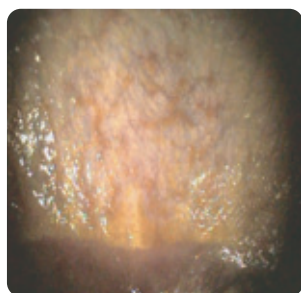


Fig.1.

The mean body weight first increased and later decreased, however the changes were not significant ($p=0.097$). The EGUS score had improved by 1 scoring unit after one month, this difference was not statistically significant ($p=0.095$).

The EGUS Scores obtained by the unblinded observers and the Severity (SC) and the Number Scores (NS) obtained by blinded endoscopist were moderately correlated (EGUS with NS: $r_2 = 0.66 - 0.81$, EGUS with SC: $r_2 = 0.65 - 0.81$). The median scores and their 95%-confidence intervals are given in Table IV.

The total numbers of ulcers had decreased by treatment as was showed by the 1.5 unit decrease in score, but this reduction in NS was not statistically significant ($p=0.128$). The ulcers had decreased in severity in the opinion of unblinded endoscopists. The SC had improved by 1.5 units, but this difference was also statistically not significant ($p=0.203$).

Discussion

The trial was set up as a self-controlled study. This design type is suitable for initial investigations of new treatments (Louis et al, 1986). We performed this study to get an impression whether its worth to further study the effects of the product. The first ulcer scoring system that was used by the endoscopists during the examination of the horses was the practitioner's simplified scoring system (Andrews et al, 1997; Orsini 2000), also known as EGUS score. Andrews et al (1997) used this scoring system to evaluate the effects of omeprazole treatment in a dose confirmation trial. Using the EGUS score, we could show that Nutri-Gard® improved or healed gastric ulcers in 69% of the treated horses. Although 39% of the horses already showed improvement after 14 days, most of the cases needed 28 days to show a clear treatment effect. Andrews et al (1999) reported that spontaneous improvement or healing of ulcers was found in 32% of their cases, while treatment with 4 mg/kg omeprazole daily for 1 month resulted in improvement or healing of 92% of the cases. The average pre-treatment score in that study was 2.2, which is slightly less than the mean EGUS score of 2.4 in our study. Taking a spontaneous healing percentage of 32%, the observed healing of 69% in our study analysed by Chi2-test on proportional data was significantly different ($p=0.05$). Since the clinical success rate after Nutri-Gard® treatment was significantly greater than that what could have occurred after spontaneous improvement or healing, we concluded that Nutri-Gard® treatment has a beneficial activity on the healing of gastric ulcer syndrome in the horse. Compared to the omeprazole healing rate, Nutri-Gard® under our testing conditions appeared less potent. The healing based on improvement of scores in our study could not be proven by statistically significant differences.

In an explorative trial, Venner et al (1999) reported ulcer healing after a 14 day treatment period with a pectin-lectin based product. In contrast to this, Murray and Grady (2002) could not find a preventive effect of this pectin-lectin complex on gastric mucosal lesions in a feed deprivation model in ponies, although in 2 of 8 ponies showed some protective effect could be seen.

Conclusion

The conclusion of our study was that we could show that Forans Nutri-Gard® was better than spontaneous healing and that clinical ulcer scores improved after a one-month treatment period, however this trend was not statistically significant. These initial findings support further studies with the product in larger groups of horses using more advanced study designs.

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