Sutton, D.G.M., Preston, T. , Christley, R.M., Cohen, N.D., Love, S. , and Roussel, A.J. (2002) *The effects of xylazine, detomidine, acepromazine and butorphanol on equine solid phase gastric emptying rate*. Equine Veterinary Journal, 34 (5). pp. 486-492. ISSN 0425-1644

<http://eprints.gla.ac.uk/471/>

Deposited on: 29th October 2004

The effects of xylazine, detomidine, acepromazine and butorphanol on equine solid phase gastric emptying rate

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Keywords: horse; sedative; gastric emptying; ¹³C-octanoic acid; breath test

Summary

The aim of this study was to measure the effects of specific commonly used sedative protocols on equine solid phase gastric emptying rate, using the ¹³C-octanoic acid breath test (¹³C-OABT). The gastric emptying of a standard ¹³C-labelled test meal was measured once weekly in 8 mature horses over two 4 week treatment periods. Each horse acted as its own control. In treatment *Period 1*, saline (2 ml i.v.), xylazine (0.5 mg/kg i.v.), detomidine (0.01 mg/kg i.v.) or detomidine/butorphanol combination (0.01/0.02 mg/kg i.v.) was administered in randomised order after ingestion of the test meal. During treatment *Period 2*, test meal consumption was followed by saline, xylazine (1.0 mg/kg i.v.), or detomidine (0.03 mg/kg i.v.) administration, or preceded by acepromazine (0.05 mg/kg i.m.) in randomised order. The ¹³C:¹²C ratio of sequential expiratory breath samples was determined by isotope ratio mass spectrometry, and used to measure the gastric half-emptying time, $t_{1/2}$, and duration of the lag phase, t_{lag} , for each of the 64 tests.

In treatment *Period 1*, detomidine/butorphanol prolonged both $t_{1/2}$ and t_{lag} with respect to xylazine 0.5 mg/kg and the saline control ($P < 0.05$). In *Period 2*, detomidine 0.03 mg/kg delayed each parameter with respect to saline, acepromazine and xylazine 1.0 mg/kg ($P < 0.001$). Xylazine 1.0 mg/kg also lengthened t_{lag} relative to the saline control ($P = 0.0004$), but did not cause a significant change in $t_{1/2}$. Comparison of treatment periods showed that the inhibitory effect of detomidine on gastric emptying rate was dose related ($P < 0.05$). These findings may have clinical significance for case selection when these agents are used for purposes of sedation and/or analgesia.

Introduction

Although the cardiopulmonary, metabolic and analgesic effects of many equine sedative protocols have been reported widely, there is little knowledge of their effect *in vivo* on specific regions of the gastrointestinal tract. This may have important implications for their clinical use, particularly when used for the sedation of cases presenting with colic, as inappropriate sedative treatment could

exacerbate the underlying gastrointestinal disturbance. The paucity of published information on pharmacological modulation of equine gastric emptying rate is due in part to the inherent technical difficulties previously involved in the measurement of this parameter.

The aim of this study was to measure the effect of specific commonly used sedative regimens on equine solid phase gastric emptying rate, using the ¹³C-octanoic acid breath test (¹³C-OABT). This stable isotope breath test has been validated against radioscintigraphy for the measurement of solid phase gastric emptying in horses with both normal and delayed gastric emptying (Sutton *et al.* 2002a,b). Principal methods of assessing drug effects on gastrointestinal motility *in vivo* have previously included electromyenterography (Roger and Ruckebusch 1987; Merritt *et al.* 1989a), strain gauge transduction (Hunt and Gerring 1986; Clarke *et al.* 1988), duodenal manometry (Merritt *et al.* 1998) and both gastric (Ringger *et al.* 1996) and caecal (Lester *et al.* 1998) radioscintigraphy. When compared to electromechanical techniques, the ¹³C-OABT offers the advantage to clinicians of providing a quantitative measurement of the gastric emptying rate of labelled ingesta itself, rather than of contractile activity alone. The test is also noninvasive, avoids the use of radioisotopes and is simple to perform, with minimal equipment requirements. The combination of these factors made the ¹³C-OABT an ideal choice for the pharmacological studies on solid phase gastric emptying reported here, which involved over 64 individual tests of emptying rate.

The effect of certain sedative agents on equine liquid phase gastric emptying has been reported previously (Doherty *et al.* 1999), using the recently validated acetaminophen absorption test (Lohmann *et al.* 2002). However, while the control mechanisms of liquid emptying are intimately involved with those of solids (Houghton *et al.* 1988), many of the controlling factors differ (Read and Houghton 1989) and the effect of sedative agents on solid phase emptying of a voluntarily ingested meal is likely to bear greater clinical relevance. In this study, the effects of randomised xylazine, detomidine, acepromazine and butorphanol administration on equine gastric emptying rate were determined, using the ¹³C-octanoic acid breath test. To our knowledge, the effect of these agents on equine solid phase gastric emptying has not previously been reported.

Materials and methods

Study design

The study was divided into two 4 week treatment periods. During each period, the gastric emptying (GE) of a standard test meal was measured once weekly in each of 8 horses, using the ^{13}C -OABT. In *Period 1*, ingestion of the test meal was followed by randomised i.v. treatment with saline (2 ml control), xylazine (Rompun 100 mg/ml injectable)¹ (0.5 mg/kg), detomidine (Dormosedan)² (0.01 mg/kg) or detomidine/butorphanol (Torbugesic)³ combination (0.01/0.02 mg/kg). In *Period 2*, test meal consumption was followed by randomised treatment with either saline (2 ml control), xylazine (Rompun 100 mg/ml injectable)¹ (1.0 mg/kg) or detomidine (Dormosedan)² (0.03 mg/kg) or preceded by 5 min with acepromazine (Promace)³ (0.05 mg/kg i.m.), in line with current sedation protocols. Treatments were randomised for week and individual, and each horse was its own control. Seven of the 8 horses used in *Period 1* were also used in *Period 2*, and 64 breath tests were performed in total. In addition to allowing measurement of the relative effect of different sedative protocols on GE rate, the study was designed to investigate dose-related effects with minimal loss of statistical power. The study was approved by the Texas A&M University Laboratory Animal Care Committee (Animal Use Protocol 2001-60).

Subjects

Nine healthy mature horses (6 Quarter Horses and 3 Thoroughbreds) of median age 12.0 years (mean 12.3 years, range 9–17 years) and weight 518.5 kg (mean 497.5, range 422.7–530.7 kg) were used in the study. Each horse had haematological and biochemical parameters within the reference range, and no history of gastrointestinal disease. From 2 weeks before and throughout the study, the horses were maintained outdoors on a low ^{13}C diet of *ad libitum* alfalfa hay, to ensure a constant basal metabolic production of $^{13}\text{CO}_2$.

^{13}C -octanoic acid breath test protocol

The ^{13}C -OABT was performed as has been detailed previously (Sutton *et al.* 2002a). Food was withheld for 12–14 h to ensure an empty stomach, before voluntary ingestion of a labelled test meal (150 g crimped oats, 100 g bran, 200 ml water) containing 1 mg/kg octanoic acid-1- ^{13}C , of minimum 99 atom % $^{13}\text{C}^5$ in 2 baked egg yolks. Two expiratory breath samples were collected, prior to test meal ingestion, and thereafter samples were collected in duplicate at 15 min intervals for 6 h, then at 30 min intervals for 3 h, using a modified Aeromask⁵ and 250 ml breath collection bag⁶. Breath samples were stored in 10 ml Exetainer⁷ tubes until analysed. Food and exercise were prohibited for the duration of the test to minimise basal fluctuations in $\dot{V}\text{CO}_2$ and $^{13}\text{CO}_2$ production, but there was free access to water.

Expiratory breath $^{13}\text{CO}_2$ measurement: Total CO_2 content and $^{13}\text{C}:^{12}\text{C}$ ratio of each sample were analysed by continuous flow isotope ratio mass spectrometry (PDZ Europa ABCA⁸) using a calibrant 5% CO_2 in nitrogen standard gas⁹. As detailed previously (Sutton *et al.* 2002a), the $^{13}\text{C}:^{12}\text{C}$ ratio of each sample was measured, relative to that of the international limestone standard, and expressed as the $\delta^{13}\text{C}$ value. Analytical accuracy was maintained below an acceptable s.d. of 0.2 per run for quality

control $\delta^{13}\text{C}$ values. After subtraction of the average ^{13}C -abundance of the baseline (predose) breath samples, the $\delta^{13}\text{C}$ ratio of each sample was converted to S.I. units (parts per million excess ^{13}C). Data were then expressed as percentage dose recovery (PDR) of the administered isotope per hour using the method of Sutton *et al.* (2002b).

Calculation of gastric emptying indices

Equine solid phase gastric emptying data have been demonstrated previously to fit modelling functions developed in human gastroenterology (Wyse *et al.* 2001; Sutton *et al.* 2002a), and indices of gastric emptying were derived using the modelled function developed by Ghooos *et al.* (1993):

$$(1) \quad y = at^be^{-ct}$$

where y is the percentage of the ^{13}C dose recovered in breaths/h; t is time (h); and a , b and c are regression constants. Curve fitting and calculation of constants was performed by nonlinear least squares regression analysis using the Microsoft Excel Solver¹⁰ function. The point under this curve at which half the total ^{13}C cumulative dose recovery has occurred is equivalent to the gastric half-emptying time, $t_{1/2}$, and was calculated using the function:

$$(2) \quad t_{1/2} = \text{Gammainv}(0.5; b + 1; 1/c)$$

Using the formula developed by Ghooos, the gastric lag phase (t_{lag}) prior to the time of maximal emptying rate, was calculated from the division of the 2 constants: b/c . To facilitate comparison with published data, the gastric emptying coefficient (GEC) was also calculated for each test from the value: $\ln a$.

Statistical analysis

A general linear model ANOVA and Tukey pairwise 95% simultaneous confidence interval 2-tailed tests were used to determine the effect of the different sedatives on gastric emptying parameters within each period of treatment, relative to the saline control. This analysis was performed using computer software¹¹. Wilcoxon signed rank tests were used to determine whether or not significant differences existed between treatment periods for both saline control values and different doses of the α_2 -adrenergic agonists.

TABLE 1: Effects of saline, xylazine (0.5 mg/kg), detomidine (0.01 mg/kg) and detomidine/butorphanol (0.01/0.02 mg/kg) on mean gastric emptying indices in 8 horses (*Period 1*). Tests were performed in random order at weekly intervals

Treatment (mg/kg)	n	Mean s.d. $t_{1/2}$ (h)	Mean s.d. t_{lag} (h)	Mean s.d. GEC
Saline	8	^a 2.58 (0.46)	^{c,d} 1.24 (0.63)	^g 2.81 (0.40)
Xylazine 0.5	8	^b 2.53 (0.41)	^{e,f} 1.74 (0.27)	^h 3.13 (0.39)
Detomidine 0.01	8	3.02 (0.35)	^{c,e} 2.50 (0.48)	2.58 (0.49)
Detomidine 0.01/ butorphanol 0.02	8	^{a,b} 3.44 (0.62)	^{d,f} 3.01 (0.68)	^{g,h} 1.62 (1.31)

$t_{1/2}$ = gastric half-emptying time; t_{lag} = duration of lag phase prior to maximal rate of gastric emptying; GEC = gastric emptying coefficient. Matching superscript letters denote a significant difference between treatments ($P < 0.05$).

Fig 1a: The modelled mean % dose recovery curves of the ^{13}C tracer in the breath of 8 horses after a ^{13}C -OABT, followed by immediate treatment with saline, xylazine (0.5 mg/kg), detomidine (0.01 mg/kg) or detomidine (0.01 mg/kg) and butorphanol (0.02 mg/kg) combination in random order, at weekly intervals.

Fig 1b: The modelled mean % dose recovery curves of the ^{13}C tracer in Period 2. A ^{13}C -OABT was performed in 8 horses on 4 occasions, accompanied by randomised treatment with either saline, acepromazine (0.05 mg/kg), xylazine (1.0 mg/kg) or detomidine (0.03 mg/kg). Tests were performed at weekly intervals. Seven of the 8 horses used in Period 2 were also used in Period 1 (Fig 1a). A total of 32 breath tests were performed in each 4 week period.

Results

Of the 64 solid phase gastric emptying tests performed, 61 were successful. Data from 3 tests in Period 2 were not included in the analysis due to incomplete ingestion of the test meal.

Period 1

Mean % dose recovery/h of the ^{13}C tracer in the breath of 8 horses was calculated for every time point of each treatment and modelled using the given formula of Ghooes *et al.* (1993). These modelled dose recovery curves are shown in Figure 1a. The shape of the modelled curves varies for each treatment. Compared to the saline control, xylazine 0.5 mg/kg (XYL 0.5) had little effect on the time of maximal emptying rate (t_{lag}), which was delayed by detomidine 0.01 mg/kg (DET 0.01) and further still by the detomidine/butorphanol (DET/BUT) combination. XYL 0.5

Fig 2: The mean % dose recovery of the ^{13}C label in the breath of 8 horses after a ^{13}C -OABT, followed by i.v. treatment with xylazine 0.5 mg/kg. The s.d. is shown at each point. The actual data produce a curve that is more exponential in shape than the best fit curve produced by the modelling function. The modelled curve leads to slight over-estimation of duration of the gastric lag phase (t_{lag}).

tended to produce a characteristic exponential peak for isotope recovery, with a rapid early recovery of isotope, which was underestimated by the modelling function, as shown in Figure 2.

Mean values for $t_{1/2}$, t_{lag} and GEC in the 8 horses after treatment with the saline control or the different sedative agents are shown in Table 1. Mean gastric $t_{1/2}$ after saline was 2.58 h, which was within the range previously reported in healthy horses using this technique (Sutton *et al.* 2002a). The effect of each treatment on $t_{1/2}$ was consistent, with low coefficients of variation (CV%; (s.d./mean) $\times$ 100) ranging from 11.5% after DET 0.01 to 18.0% after DET/BUT.

DET/BUT produced a significant delay in $t_{1/2}$ compared to both saline ($P = 0.0082$) and XYL 0.5 ($P = 0.0018$). Following XYL 0.5, $t_{1/2}$ was marginally faster than that following saline. When considering t_{lag} , both DET 0.01 and DET/BUT delayed this parameter with respect to both saline ($P < 0.0001$) and xylazine ($P = 0.0023$; $P < 0.0001$). Boxplots have been used to summarise the effect of the treatment protocols on both $t_{1/2}$ (Fig 3a) and t_{lag} (Fig 3b). Mean GEC mapped the changes in the initial rate of isotope recovery caused by the different treatments, with DET/BUT causing a significant change relative to saline and XYL 0.5.

Period 2

The modelled curves for mean % dose recovery/h of the ^{13}C tracer in 8 horses after the treatments administered in this period are shown in Figure 1b. It is seen that the dose recovery curves following both saline and acepromazine 0.05 mg/kg (ACP 0.05) administration are similar, while recovery of the ^{13}C isotope (and hence gastric emptying) is delayed following xylazine 1.0 mg/kg (XYL 1.0) and dramatically so, following detomidine 0.03 mg/kg (DET 0.03). The mean values for $t_{1/2}$, t_{lag} and GEC for the 8 horses after the treatments administered in this period are shown in Table 2. In this period, the $t_{1/2}$ inter-individual CV% for saline, ACP 0.05, XYL 1.0 and DET 0.03 were 25.8%, 16.1%, 12.9% and 14.6%, respectively.

Gastric emptying parameters after ACP 0.05 were not different to those of saline in any category. DET 0.03 delayed both $t_{1/2}$ and t_{lag} with respect to saline, ACP 0.05 and XYL 1.0 (in each

Fig 3a: Boxplots demonstrating the effect of different treatments on gastric half-emptying time ($t_{1/2}$) of a standard test meal as measured by the ^{13}C -OABT. Each treatment was given to 8 horses in randomised order over a 4 week period (Period 1). Total number of tests = 32. *Denotes an outlying value.

Fig 3b: Boxplots demonstrating the effect of Period 1 treatments on gastric lag phase (t_{lag}) in 8 horses as measured by the ^{13}C -OABT. Total number of tests = 32.

case, $P < 0.001$). Mean $t_{1/2}$ after XYL 1.0 was not significantly different to that following saline or ACP 0.05 treatment. However, XYL 1.0 delayed t_{lag} relative to both saline ($P = 0.0004$) and ACP 0.05 ($P = 0.0027$). As expected, DET 0.03 also changed GEC with respect to saline, ACP 0.05 and XYL 1.0 ($P < 0.0001$). Boxplots are presented to highlight the effect of treatments on $t_{1/2}$ (Fig 4a) and t_{lag} (Fig 4b) in this period.

Interperiod comparison

There was a tendency in Period 2 for gastric $t_{1/2}$ after saline to be longer than that of Period 1, but this was not significant ($P < 0.1$). In order to determine the effect of α_2 -agonist dose on GE, the mean difference in $t_{1/2}$ between saline and XYL 0.5/XYL 1.0, and saline and DET 0.01/DET 0.03 was calculated for each treatment period. This procedure served to control for temporal effects on GE in the study animals. The significance of interperiod differences in these data sets was examined using Wilcoxon signed rank tests. Mean $t_{1/2}$ following XYL 1.0 was not significantly different compared to XYL 0.5, but the delay in mean $t_{1/2}$ caused by DET 0.03 was significantly greater than that caused by DET 0.01 ($P < 0.05$).

TABLE 2: Effects of saline, xylazine (1.0 mg/kg), detomidine (0.03 mg/kg) and acepromazine (0.05 mg/kg) on mean gastric emptying indices in 8 horses (Period 2). A ^{13}C -OABT followed by randomised treatment was performed 4 times in each individual at weekly intervals

Treatment (mg/kg)	n	Mean s.d. $t_{1/2}$ (h)	Mean s.d. t_{lag} (h)	Mean s.d. GEC
Saline	6	^a 3.14 (0.81)	^{d,e} 1.91 (0.50)	ⁱ 2.70 (0.43)
Acepromazine 0.05	7	^c 3.24 (0.52)	^{f,g} 2.00 (0.67)	^j 2.39 (0.43)
Xylazine 1.0	8	^b 3.71 (0.48)	^{d,g,h} 3.19 (0.61)	^k 1.35 (1.07)
Detomidine 0.03	8	^{a,b,c} 5.28 (0.77)	^{e,f,h} 4.87 (0.75)	^{i,j,k} 3.01 (2.33)

$t_{1/2}$ = gastric half-emptying time; t_{lag} = duration of gastric lag phase; GEC = gastric emptying coefficient. Matching superscript letters denote a significant difference between treatments for that parameter ($P < 0.05$). Data from 3/32 tests were not included due to incomplete ingestion of test meal.

Discussion

The results of this study suggest that apparent equipotent sedative doses of xylazine (0.5 mg/kg) and detomidine (0.01 mg/kg) (England *et al.* 1992) differ in their effect on solid phase GE rate in healthy horses. XYL 0.5 tended to promote early initial GE, without affecting $t_{1/2}$, whereas DET 0.01 delayed both $t_{1/2}$ and t_{lag} . When the common clinical combination of detomidine/butorphanol (0.01/0.02 mg/kg) was used (Clarke and Paton 1988; Taylor *et al.* 1988), gastric $t_{1/2}$ and t_{lag} were delayed significantly. In addition, detomidine produced a marked dose-dependent slowing of GE rate, which was not seen with xylazine. Based on the results presented, DET 0.03 is likely to have a clinically significant effect on equine solid phase GE rate. By contrast, acepromazine used at a standard premedicant dose of 0.05 mg/kg i.m. (Marntell and Nyman 1996), had an insignificant effect on equine gastric transit time.

The effect of sedative agents on equine solid phase GE has not, to our knowledge, been previously investigated. In the United States, where the study was performed, xylazine¹ and detomidine² are both licensed for equine analgesia and sedation at i.v. dosages of 1.1 mg/kg and 0.02 or 0.04 mg/kg respectively, and the marked difference on GE observed between the agents within these dose ranges was greater than expected. The effect of lower doses of the agents on GE was investigated in Period 1, as these are the doses frequently used in clinical practice for sedation (Muir and Mason 1993; Bueno *et al.* 1999) and/or treatment of abdominal pain (Clarke and Paton 1988; Hamm *et al.* 1995). Once again, there was a marked difference in effect between XYL 0.5 and DET 0.01, which was augmented by the addition of butorphanol 0.02 mg/kg to the detomidine.

Xylazine and detomidine cause sedation by depression of the locus coeruleus neurons in the pons of the lower brainstem (England and Clarke 1996). Their antinociceptive action is mediated by inhibition of presynaptic pain modulating noradrenergic neurones in the brainstem via α_2 adrenoceptors (Virtanen, 1986). However, these agents also affect postsynaptic CNS α_2 receptors (Virtanen and MacDonald 1985) and at higher concentrations are partial agonists at α_1 receptors (Virtanen and Nyman 1985), reducing pain responses at the spinal level. *In vitro* experiments have shown consistently that detomidine has a greater potency at α_2 receptors than xylazine (Virtanen and Nyman 1985),

Fig 4a: Boxplots demonstrating the effect of different treatments on gastric $t_{1/2}$ in Period 2, as measured by the ^{13}C -OABT. Four randomised treatments were given to each of 8 individuals at weekly intervals. Data from 3/32 tests were not included due to incomplete consumption of test meal. *denotes outlying value.

Fig 4b: Boxplots demonstrating the relative effects of different treatments on gastric lag phase duration, t_{lag} , in 8 individuals in Period 2. Treatments were administered at weekly intervals in randomised order. Data from 3/32 tests were not included due to incomplete consumption of test meal.

and this is matched by its superior visceral analgesia in both clinical cases (Jochle *et al.* 1989) and experimental models (Lowe *et al.* 1986) of equine colic. Detomidine at 0.02 mg/kg provided good equine visceral analgesia for about 40 min (Lowe *et al.* 1986; Jochle 1989), which was approximately equivalent to xylazine 1.1 mg/kg in depth (Jochle and Hamm 1986). The lower doses of xylazine (Jochle *et al.* 1989) and detomidine (Lowe *et al.* 1986) used in Period 1 of this present study both provide lesser, dose-dependent visceral analgesia. However, in light of the results of this study, it should be remembered that augmenting detomidine dosage above 0.02 mg/kg principally increases duration rather than depth of analgesia (Jochle *et al.* 1989; Hamm *et al.* 1995).

The inhibition of gastric emptying seen in this study following detomidine administration probably resulted from peripheral presynaptic inhibition of α_2 receptors, causing decreased release of noradrenaline and consequent reduction in acetylcholine release from the enteric plexi (Gerring and Hunt 1986; Rang *et al.* 1999). Central noradrenergic inhibition also probably affected gastric motility (Virtanen 1986). In the dog, it has been

demonstrated that both xylazine and medetomidine decrease gastrin release after ingestion (Nakamura *et al.* 1997). Potentially, altered gastrin release may be a further mechanism in the horse leading to reduced gastric motility after α_2 agonist administration, but this has not been proven. Finally, the dose dependent effect of detomidine on equine GE may be mediated by action at α_1 receptors at higher doses, or at a specific α_2 subtype (Rang *et al.* 1999). Further GE studies in the presence of selective antagonists would be required to investigate this further.

In this study, butorphanol acted synergistically with detomidine to delay gastric emptying further. Butorphanol produces sedation and analgesia via partial agonism at μ and κ opioid receptors. In isolation, minimum doses of 0.1 mg/kg are usually required for visceral analgesia (Kalpravidh *et al.* 1984; Muir and Robertson 1985; Becht 1986; Stout and Priest 1986). However, the addition of low doses of butorphanol to α_2 agonists has been reported to enhance sedation and analgesia while minimising cardiopulmonary depression (Taylor *et al.* 1988; Thurmon *et al.* 1996). While its inhibitory effects at higher doses (0.1 mg/kg) on equine jejunal and large intestinal motility have been documented (Sojka *et al.* 1986), the additive effect of butorphanol 0.02 mg/kg on GE was greater than expected. Using electromyenterography, Merritt *et al.* (1989b) reported that butorphanol 0.05 mg/kg caused a 'resetting' of the activity of the gastric antrum and duodenum, with minimal disruption to periodicity. The results of this study may therefore suggest genuine synergistic inhibition of butorphanol and detomidine on equine GE.

Acepromazine is a potent neuroleptanalgesic (Thurmon *et al.* 1996). It is most frequently administered i.m. prior to anaesthesia to potentiate the effects of anaesthetic agents (Becht 1986). Acepromazine also inhibits α_2 agonist-induced bradycardia (Marntell and Nyman 1996) in addition to decreasing the required minimum alveolar concentration of inhalation agents (Doherty *et al.* 1997). Indeed, epidemiological evidence suggests that acepromazine administration prior to general anaesthesia may reduce the incidence of anaesthetic-related fatalities (Johnston *et al.* 1995). Previous equine work has suggested that acepromazine may decrease the electrical activity of jejunal Thiry-Vella loops (Davies and Gerring 1983) and also delay liquid phase emptying (Doherty *et al.* 1999). However, in accordance with the results of canine studies (Zontine 1973; Voges *et al.* 1995), the results outlined here suggest that premedication doses of acepromazine have insignificant effect on equine solid phase GE rate.

The results of this study document both the comparative and dose-related effects of specific sedative agents on equine solid phase gastric emptying, using a new diagnostic technique (Wyse *et al.* 2001; Sutton *et al.* 2002a,b). However, although GE is a rate-determining step in small bowel transit, extrapolations should not be made to the entire gastrointestinal tract as regional differences exist, particularly in response to specific autonomic transmitters (Hunt and Gerring 1986). In general terms, results of electromechanical studies have suggested that the left dorsal colon, left ventral colon and caecum have greater sensitivity than particularly the jejunum, to α_2 agonists (Adams *et al.* 1984; Sasaki *et al.* 2000), with most potent inhibition by detomidine (Lowe *et al.* 1986). It is relevant to note that while xylazine 0.5 mg/kg has been reported to have negligible (Merritt *et al.* 1989a) or temporary (Merritt *et al.* 1998) inhibitory effect on duodenal motility, the same dose has also been reported to reduce the spike burst duration of the ileum, right ventral colon, small colon and to

decrease caecal emptying rate of radiolabelled markers (Lester *et al.* 1998). Xylazine may also produce a dose dependent inhibition of both caecal mechanical activity (Hunt and Gerring 1986) and blood flow (Clarke *et al.* 1988; Rutkowski *et al.* 1991).

Hence, it is emphasised that the results of this study specifically document the effect of these sedative agents on gastric motility alone. In our opinion, detomidine at doses of 0.03 mg/kg or greater is likely to have detrimental effect on GE rate of solids. This effect may be more marked if given in combination with even low doses of butorphanol. Furthermore, in conditions such as endotoxaemia, where there is enhanced sympathetic neurotransmitter release (Eades and Moore 1993) or postoperative ileus, which is associated with reflex adrenergic stimulation (Glise *et al.* 1980; Gerring and Hunt 1986), the effect of α_2 agonists on equine GE may be further enhanced. Hence, high doses of detomidine should perhaps be avoided in cases likely to have delayed gastric emptying. In cases presenting with nasogastric reflux or gastric impaction, low doses of xylazine would be recommended to facilitate diagnostic procedures. In addition, the results of this study suggest that the preanaesthetic administration of acepromazine to colic cases presenting without cardiovascular compromise would be unlikely to compromise gastric emptying rate.

Manufacturers' addresses

- ¹Bayer Corporation, Shawnee Mission, Kansas, USA.
- ²Animal Health (Pfizer Inc.), Exton, Pennsylvania, USA.
- ³Fort Dodge Laboratories Inc., Fort Dodge, Iowa, USA.
- ⁴Benner Road, Miamisburg, Ohio, USA.
- ⁵Trudell Medical International, London, Ontario, Canada.
- ⁶QuinTron Instrument Company, Milwaukee, Wisconsin, USA.
- ⁷Labco Ltd., High Wycombe, Buckinghamshire, UK.
- ⁸PDZ Europa Ltd, Sandbach, Cheshire, UK.
- ⁹Praxair, inc., Danbury, Connecticut, USA.
- ¹⁰Microsoft Corporation, One Microsoft Way, Redmond, USA.
- ¹¹Minitab Inc., State College, Pennsylvania, USA.

Acknowledgements

The authors thank Professors David Williams and William Moyer for the generous provision of facilities at Texas A&M University College of Veterinary Medicine, and acknowledge Drs Anne Bahr, Sheila Robertson and Jörg Steiner plus Sheila Gumming, Elizabeth Stewart and Sam Wigington for expert technical assistance and advice. Financial support for this study was gratefully received from the Link Equine Colic Research Fund at Texas A & M University College of Veterinary Medicine. David Sutton is funded by a Horserace Betting Levy Board research training scholarship.

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Received for publication: 2.4.02

Accepted: 6.6.02