

**ANTRAL MYOELECTRIC ACTIVITY IN SHEEP: THE EFFECT OF FEEDING AND  
ANTICHOLINERGIC DRUG ADMINISTRATION DURING VARIOUS PHASES OF MIGRATING  
MYOELECTRIC COMPLEX**

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*In six adult rams, chronic experiments were performed to assess the role of fasting, feeding, phase of migrating myoelectric complex (MMC) and anticholinergic drugs in antral myoelectric activity. Accordingly, animals underwent surgical implantation of five bipolar electrodes in to the antrum, duodenum and jejunum for continuous myoelectric activity recordings. Normal control spike burst amplitude in non-fasted sheep during phase 2b MMC and during feeding was  $103 \pm 19$  vs.  $155 \pm 10 \mu V$  ( $p < 0.01$ ) whereas spike burst duration was  $2.8 \pm 0.12$  vs.  $3.0 \pm 0.09$  s (N.S.), respectively. Feeding increased significantly the percentage of antral spike burst mean amplitudes while slow intravenous administration of graded doses of atropine and pirenzepine as well as of hexamethonium, alone and in combinations, usually depressed the antral spike bursts. Complete inhibition was observed occasionally. In non-fasted sheep equivalent values obtained during phase 2b MMC were  $84 \pm 8$ ,  $71 \pm 3$ ,  $74 \pm 3$  (control) and  $18 \pm 6$ ,  $17 \pm 2$ ,  $28 \pm 2$  ( $p < 0.001$ , moderate drug doses), respectively. These change were more pronounced during feeding and when the drugs were given during phase 2b or phase 3 of MMC. Further increase of the cholinergic blocking drug doses evoked relatively lower inhibition. It is concluded that the cholinergic system is important in the control of antral myoelectric activity in sheep. Moreover, it appears that during various MMC phases, different mechanisms can be activated.*

*Key words: anticholinergic drugs, antrum, feeding, sheep, spike burst*

**INTRODUCTION**

In the distal part of the multicompartamental stomach the digesta flow is almost continuous; hence antral motility is intensive (Ruckebusch, 1989). Therefore, normal motility in this region is important for efficient gastroduodenal coordination and undisturbed digesta flow. This, in turn, is related to digestion and secretory processes in distal regions of the gastrointestinal tract. Therefore, antral

motility is a rate-limiting event for the transport of luminal content practically in the entire gastrointestinal tract distal to the stomach.

Basic control mechanisms of the pyloric antrum still require further studies. Feeding is known to stimulate antral motility in sheep (Gregory *et al.*, 1985). However, other reports indicate that this effect may be dependent on food composition or exhibit an inhibitory character (Bolton *et al.*, 1976, Malbert and Ruckebusch, 1988).

As can be concluded from previous studies on man and dog (Dent *et al.*, 1983, Thor *et al.*, 1990), different control mechanisms can operate during various phases of the migrating myoelectric complex (MMC). Ovine antral motility is also coordinated with duodenal motility in relation to the MMC (Ruckebusch, 1976, Ruckebusch, 1988). However, these data are incomplete since antral patterns have not been fully recognized; basically the occurrence of MMC in this region is regarded as uncertain (Bueno & Fioramonti, 1980). Furthermore, no systematic studies have been performed so far.

Moreover the role of the cholinergic system in the control of antral spike bursts in sheep has not been thoroughly described. While bethanechol and pilocarpine were able to stimulate the gastroduodenal area, their effect on duodenal motility was stronger than on that of the stomach (Ruckebusch & Merritt, 1985). Vagal cooling or anticholinergic drugs inhibited ovine antral motility but there is some controversy about whether the inhibition was partial or complete as well as concerning the exact pattern of antral motility under these conditions (Bueno & Ruckebusch, 1978, Ruckebusch *et al.*, 1987, Malbert & Ruckebusch, 1989). Practically nothing is known concerning the role of muscarinic receptors subtypes in the control of antral spike bursts in sheep.

Thus, it was decided to assess the antral spike burst activity in fasted and non-fasted sheep, before, during and after feeding, along with anticholinergic drug administration during phase 1 - 2a, 2b or 3 of MMC. The aim of the study was to provide more precise data concerning the role of cholinergic muscarinic receptors (M, unspecific), M1 receptor subtype and cholinergic nicotinic receptors in the control of antral spike bursts in sheep, in various feeding conditions and in relation to the small-intestinal cyclic motility pattern.

#### MATERIALS AND METHODS

A total of 510 chronic experiments were performed on six adult rams, weighing 38 - 43 kg. The animals were fed on hay, 1 kg per day per animal, and a standard grain mixture, 3-5 g/kg of body weight (b.w.) daily. Drinking water was not limited.

##### *Animal preparation*

A right-side laparotomy was performed in 24 h fasted animals under general and local anaesthesia and bipolar platinum electrodes embedded in Teflon coat to diminish tissue reaction and facilitate long-term work (Romanski & Kuryszko, 1995), were implanted in the pyloric antrum (one electrode) and the small intestine (four electrodes) in order to obtain faultless MMC identification. The antral electrode was attached 4 cm before the pyloric ring and small-intestinal electrodes were attached to the: duodenal bulb (one electrode), 10 cm from the

antral electrode; distal duodenum (one electrode), 50 cm from the bulbar electrode; jejunum (two electrodes), 200 and 300 cm from the duodenal electrode. Marked wires were exteriorized and connected to the recorder. The gastrointestinal distances were measured during the surgery. At least 7-10 days were allowed for recovery. During this period, increasing rates of hay and grain mixture were given to reach the amount consumed before surgery and drinking water was not limited.

### Experiments

The following series of experiments were performed in all animals studied (Table 1):

Table 1. Types of experiments conducted in sheep with or without intravenous administration of 0.15 M NaCl or anticholinergic drugs. The myoelectric recordings (panel A) and measurements of blood pressure in coccygeal artery (panel B). All the recordings were performed both in fasted and non-fasted animals. Blood pressure measurements were performed in non-fasted, non-fed sheep

#### PANEL A:

1. control recording	2. control recording	0.15 M NaCl ↓	3. control feeding recording	↓
4. control modified sham recording	↓	feeding	5. control recording	↓
			drug alone	
			6. control recording	↓
			drug combinat.	

#### PANEL B:

7. control recording	0.15 M NaCl ↓	8. control recording	drug (H) ↓ alone
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↔ 30 min

1) non-fasted, non-fed sheep: a) controls, b) i.v. anticholinergic drug administration, during duodenal phase 1-2a MMC, c) anticholinergic drugs given i.v. during duodenal phase 2b MMC, d) anticholinergic drugs given i.v. during duodenal phase 3 MMC,

2) 48 h fasted, non-fed sheep: a) controls, b) and c), as in non-fasted sheep,

3) non-fasted, fed sheep: a) controls (feeding alone, "sham feeding"), b) and c), as in non-fasted, non-fed sheep; drugs given during feeding,

4) fasted and fed sheep, a) controls (feeding alone), b) and c), as in non-fasted, fed sheep.

During control experiments, 0.15 M NaCl was injected slowly (rate 2 ml/min, during 1 - 5 min) into a jugular vein through the indwelling catheter inserted before the experiment. In non-fasted animals the effect of modified "sham feeding" (demonstration of food without eating) was also tested. Anticholinergics were given in a similar manner as NaCl, alone and in different combinations. The following drugs were given alone (Table 2): atropine sulfate (A, Polfa), 0.002 (atropine, first - lowest dose, A1); 0.02 (A2); 0.1 (A3); 0.5 (A4) and 1.5 mg/kg b.w.; pirenzepine dihydrochloride (P, Sigma) 0.02 (P1); 0.1 (P2); 0.5 (P3) and 2.5 (P4) mg/kg bw; hexamethonium bromide (H, Sigma) 1.0 (H1); 2.0 (H2); 5.0 (H3) mg/kg. The drug combinations were (Table II): A3+H2 and P2+H2. No drug combinations given during phase 3 MMC were tested. The highest doses of drugs were used only in non-fasted sheep during phase 2b MMC. The myoelectric activity was continuously recorded throughout the experiment lasting 4-5 h (2-3 h control and 2-3 h after the given procedure) using the multichannel electroencephalograph (Reega Duplex TR XVI, Alvar Electronic) with paper speed 2.5 mm/s and time constant 0.01 s. In three of these sheep, the blood pressure in the coccygeal artery was measured before and after 0.15 M NaCl or H1, H2 and H3 administration. Cyclical activity (MMCs) was identified according to the criteria proposed by Code and Marlett (1975). Phase 2 of MMC was divided into phase 2a and 2b (Dent *et al.*, 1983). During the control period at least one full normal MMC cycle was recorded.

Experiments were performed in random order. Anticholinergic drugs were given only once during the day of the experiment and there was at least a two day interval (at least three days after the higher dose of H) between two consecutive experiments.

#### Calculations

The mean amplitudes of all considered spike bursts were calculated as the average amplitude of every detectable spike within a given spike burst. Two-minute representative periods just before and one-minute representative periods during feeding or just after NaCl or drug administration were selected for calculations. The median values of spike burst amplitude were determined for the given two-minute control period. Then, the mean value of medians of the amplitudes of all spike bursts was calculated and presented as the percentage of maximal spike burst median amplitude (treated as 100 %) for the same period. For the given one-minute period, the mean value of median amplitudes of all spike bursts was calculated and presented as the percentage of the maximal spike burst median of amplitude (treated as 100 %) selected in the control period. Duration of the period with decreased antral spike burst amplitude (i.e. between anticholinergic drug administration and rebound effect or returning antral spike burst amplitude to the control value) was usually longer than the selected calculation period. In non-fasted animals it lasted 3-7 min following H2, 6-11 min following A3 and 7-12 min following P2 administration. The percentage of slow waves with spikes was also assessed but the value of this parameter was negligible in the stomach since the suppression of spike bursts following anticholinergic drug administration was usually not complete. The duration of spike bursts was also taken into consideration although the calculated results were insignificant. The number of data presented has been reduced to the minimum and the non-significant data are not shown (Table 2).

Table 2. Recordings of ovine myoelectric activity. List of drugs and doses (in mg/kg) given during various phases of MMC. Results of experiments included in this paper indicated by \*

	MMC phase	No drug <sup>x</sup>	Hexamethonium	Atropine	Pirenzepine	H + A	H + P
NO FAST, FED	1-2a	*					
	2b	*	*	*	*	*	*
	3						
NO FAST, NOT FED	1-2a	*	*	*	*	*	*
	2b	*	*	*	*	*	*
	3	*		*	*	*	*
FAST, FED	1-2a	*		*	*	*	*
	2b	*	*	*	*	*	*
	3						
FAST, NOT FED	1-2a	*	*	*	*	*	*
	2b	*	*	*	*	*	*
	3						
SHAM FEEDING <sup>xx</sup>	1-2a	*	*	*	*	*	*
	2b	*	*	*	*	*	*
	3						

<sup>x</sup>control recording performed before each experiment; <sup>xx</sup>in non-fasted animals

The results underwent statistical analyses and are expressed as means " S.E.M. Statistical significances of experimental results vs. relevant control values were calculated by means of Student's t-test for paired data followed by analysis of variance. The minimal level of probability (p) at which statistical significance was indicated was 0.05. The n value was equal to 5-12 since most experiments were repeated on the same animal.

## RESULTS

Feeding increased calculated spike burst mean amplitude whereas the effects of the anticholinergic drugs given during feeding exhibited an inhibitory character (Table 3). As an example of primary, non-transformed data, normal control spike burst mean amplitude (mean amplitude of all spikes within a given spike burst) in non-fasted sheep during duodenal phase 2b MMC, before and during feeding was  $103 \pm 19$  and  $155 \pm 10$   $\mu$ V ( $p < 0.01$ ), respectively.

Table 3. Changes in antral spike bursts (in %) two minutes before (control) and one minute after anticholinergic drugs (treatment) given during feeding (F) in fasted (FAS) or non-fasted (NFAS) sheep. Feeding was started during phase (ph.) 1-2a or 2b MMC

F alone		ph.	ph.	A2	A3	P1	P2	P3	H2	A3+H2	P2+H2
		1-2a	2b	ph. 2b	ph. 2b	ph. 2b	ph. 2b	ph. 2b	ph. 2b	ph. 2b	ph. 2b
FAS, control:	mean	65	61	83	91	71	84	81	84	87	84
	fl S.E.M.	8	4	6	3	6	4	4	4	4	4
FAS, treatm.:	mean	96 <sup>a</sup>	91 <sup>b</sup>	64 <sup>a</sup>	25 <sup>c</sup>	59 <sup>n</sup>	35 <sup>c</sup>	51 <sup>b</sup>	46 <sup>c</sup>	39 <sup>c</sup>	38 <sup>c</sup>
	fl S.E.M.	2	2	5	4	4	6	5	5	3	3
NFAS, control:	mean	54	72	89	88	94	92	89	88	78	79
	fl S.E.M.	4	2	5	2	3	3	6	4	4	3
NFAS, treatm.:	mean	84 <sup>b</sup>	93 <sup>a</sup>	45 <sup>c</sup>	27 <sup>c</sup>	62 <sup>b</sup>	27 <sup>c</sup>	30 <sup>c</sup>	29 <sup>c</sup>	20 <sup>c</sup>	23 <sup>c</sup>
	fl S.E.M.	4	1	5	4	4	6	8	4	4	3

Statistical significance: <sup>a</sup>p<0.05; <sup>b</sup>p<0.01; <sup>c</sup>p<0.001; <sup>n</sup>not significant.

Other explanations, see section Materials and Methods

Normal duration of a spike burst in non-fasted sheep during duodenal phase 2b MMC, before and during feeding was  $2.8 \pm 0.12$  and  $3.0 \pm 0.09$  s (N.S.), respectively. Following anticholinergic drug administration, the antral spike burst

amplitude values were significantly different from controls only after the higher doses of the drugs given during feeding except H2. The effects of A and P were usually more pronounced in non-fasted animals than in fasted animals (Table 3). The effect of "sham feeding" on spike burst amplitude was similar to the effect of feeding (control  $48 \pm 4$  %, "sham feeding"  $81 \pm 3$  %,  $p < 0.001$ ). Duration of spike bursts was insignificantly longer during feeding (about 0.3 - 1.2 s) compared with the pre-feeding period. In other experiments these alterations were even less apparent and as insignificant they could be neglected. Thus, these data were not included.

In non-fasted, non-fed sheep, the anticholinergic drugs significantly lowered antral spike burst mean amplitude for 3 - 12 minutes, except the smallest doses of A (Table 4, Fig. 1). However, the effects of drugs injected during phase 1 or 2a MMC were much less marked (lower degree of significance or insignificant) than the effects of drugs given during phase 2b MMC (Table 4). Interestingly, the effect of a moderate dose of A was greater than that of the high A dose. The

Table 4. Changes in antral spike bursts (in %) two minutes before (control) and one minute after administration of increasing doses of atropine (A), pirenzepine (P) or after hexamethonium (H) given alone and in different combinations (treatment), during phase 1-2a or 2b MMC in non-fasted, non-fed sheep

		A1	A2	A3	A4	P1	P2	P3	H2	A3+H2	P2+H2
Control:											
ph. 1-2a	mean	50	63	55	83	47	58	60	55	50	53
	fI.S.E.M.	6	5	8	5	7	6	3	7	4	4
Treatment:											
ph. 1-2	mean	43 <sup>n</sup>	22 <sup>c</sup>	23 <sup>a</sup>	49 <sup>b</sup>	30 <sup>n</sup>	27 <sup>a</sup>	23 <sup>b</sup>	37 <sup>n</sup>	33 <sup>a</sup>	38 <sup>a</sup>
	fI.S.E.M.	5	3	3	5	6	3	2	3	4	7
Control:											
ph. 2b	mean	57	84	62	93	56	71	64	74	56	79
	fI.S.E.M.	5	8	3	4	3	3	4	3	5	5
Treatment:											
ph. 2b	mean	41 <sup>n</sup>	18 <sup>c</sup>	21 <sup>c</sup>	62 <sup>b</sup>	32 <sup>a</sup>	17 <sup>c</sup>	12 <sup>c</sup>	28 <sup>c</sup>	28 <sup>b</sup>	38 <sup>c</sup>
	fI.S.E.M.	5	6	3	7	4	2	3	2	3	3

Other explanations as in Table 3

administration of cholinergic blocking drugs during the duodenal phase 3 in non-fasted, non-fed sheep was as follows (Table 2): A1- $79 \pm 5$  vs.  $27 \pm 2$ ,  $p < 0.001$ ; P1 -  $62 \pm 6$  vs.  $54 \pm 7$ , N.S.; P3 -  $72 \pm 6$  vs.  $33 \pm 5$  %,  $p < 0.001$ , control vs. treatment, respectively.

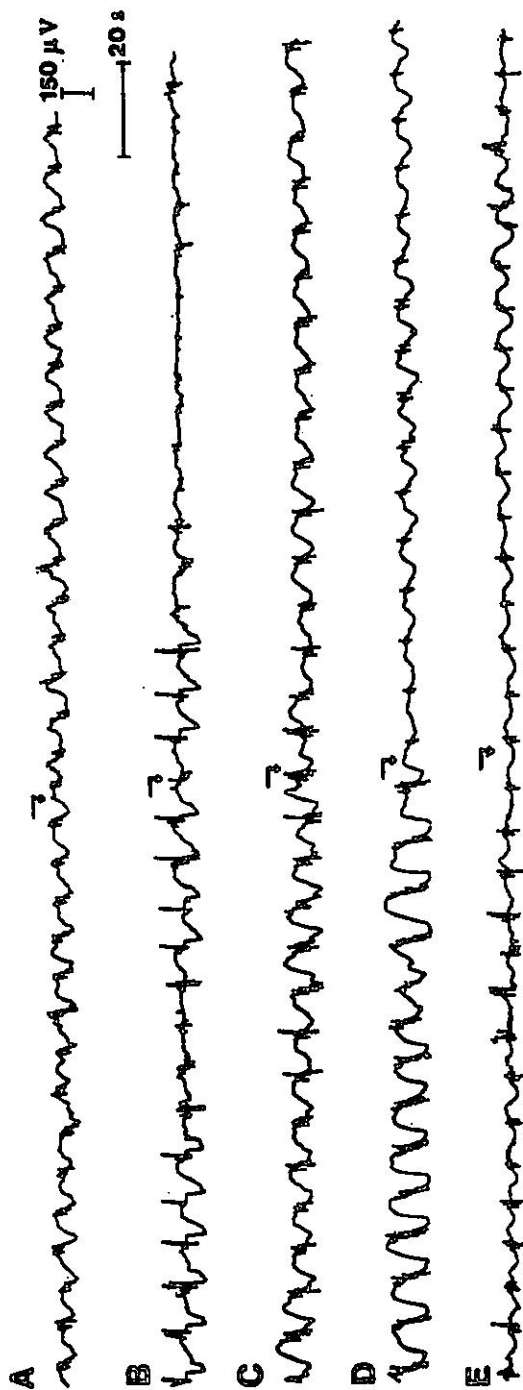


Figure 1. Antral myoelectric activity in non-fasted, non-fed sheep – 5-minute recordings of five different experiments performed in the same animal. Panel A - pirenzepine administration at 0.02 mg/kg i.v. during phase 1 of duodenal MMC. Panel B - pirenzepine administration at 0.02 mg/kg i.v. during phase 2b of duodenal MMC. Panel C - pirenzepine administration at 0.5 mg/kg i.v. during phase 1 of duodenal MMC. Panel D - pirenzepine administration at 0.5 mg/kg i.v. during phase 2b of duodenal MMC. Panel E - pirenzepine administration at 2.5 mg/kg i.v. during phase 2b of duodenal MMC. Arrows indicate end of slow injection of the drug. Calibration: 150  $\mu$ V, time bar: 20 seconds



Other results were similar to those obtained following drug administration during phase 2b MMC and are not shown (Table 2). When the drugs were administered in fasted, non-fed animals during phase 1 or 2a, the inhibition of spike burst mean amplitude was less marked (non-significant) than in non-fasted sheep. An example concerning various doses of P is shown on Fig. 1 (panels A-E). Only A4 and drug combinations exerted significant effects (Table 5).

Administration of drugs during phase 2b MMC (also of smaller doses) decreased antral spike burst amplitude significantly (Table 5). The moderate dose of A exerted a greater effect than the high dose.

The highest doses of cholinergic receptor-blocking drugs did not evoke the most pronounced response; this response was often weaker than the response to the moderate doses applied (Fig. 1, panel E). However, complete inhibition of antral spike bursts was more frequent than after smaller doses of anticholinergic substances.

Hexamethonium also exerted a systemic effect. The blood pressure values just before and 2, 5, 10 and 15 min after the drug administration decreased with all doses of Hx. Values before and after H1 were  $9.6 \pm 0.1$  (control);  $8.8 \pm 0.1$  ( $p < 0.05$ );  $8.5 \pm 0.1$  ( $p < 0.05$ );  $8.3 \pm 0.2$  ( $p < 0.01$ ) and  $8.4 \pm 0.1$  kPa ( $p < 0.01$ ), respectively. Values before and after H2 were  $10.8 \pm 0.1$ ;  $10.0 \pm 0.1$  ( $p < 0.05$ );  $9.5 \pm 0.1$  ( $p < 0.001$ );  $9.0 \pm 0.2$  ( $p < 0.01$ ) and  $8.9 \pm 0.1$  kPa ( $p < 0.001$ ).

Table 5. Changes in antral spike bursts (in %) two minutes before (control) and one minute after administration of anticholinergic drugs (treatment) during phase 1-2a or 2b MMC in fasted, non-fed sheep

		A2	A3	A4	P1	P2	P3	H2	A3+H2	P2+H2
<b>Control:</b>										
ph. 1-2a	mean	56	51	34	42	49	45	58	53	48
	f(S.E.M.)	4	4	2	3	4	4	4	3	4
<b>Treatment:</b>										
ph. 1-2a	mean	39 <sup>n</sup>	32 <sup>n</sup>	20 <sup>a</sup>	35 <sup>n</sup>	34 <sup>n</sup>	37 <sup>n</sup>	44 <sup>n</sup>	26 <sup>c</sup>	30 <sup>a</sup>
	f(S.E.M.)	7	4	2	5	3	4	5	3	4
<b>Control:</b>										
ph. 2b	mean	73	68	72	82	74	70	64	74	72
	f(S.E.M.)	8	2	3	5	5	4	4	5	3
<b>Treatment:</b>										
ph. 2b	mean	39 <sup>c</sup>	26 <sup>c</sup>	40 <sup>b</sup>	61 <sup>n</sup>	28 <sup>c</sup>	31 <sup>c</sup>	31 <sup>b</sup>	36 <sup>c</sup>	25 <sup>c</sup>
	f(S.E.M.)	5	4	6	8	4	3	4	3	2

Other explanations as in Table 3

Values before and after H3 were  $10.4 \pm 0.1$ ;  $10.0 \pm 0.2$  (N.S.);  $8.8 \pm 0.5$  ( $p < 0.05$ );  $8.8 \pm 0.3$  ( $p < 0.01$ );  $8.4 \pm 0.1$  kPa ( $p < 0.001$ ). Thirty min following H3 the blood pressure value was 8.40.1 kPa ( $p < 0.001$ ). The injection of 5 ml of 0.15 M NaCl during the control experiment did not change blood pressure significantly (data not shown).

#### DISCUSSION

Previous studies showed that feeding usually increases gastric myoelectric and motor activity in monogastric animals (Ruckebusch & Bueno, 1976, Hall *et al.*, 1996, Levanon *et al.*, 1998). Similar observations were reported in sheep (Gregory *et al.* 1985, Plaza *et al.* 1996) although other reports remain in contrast with these findings (Bolton *et al.*, 1976, Malbert & Ruckebusch, 1988, Lester & Bolton, 1994). In the presented investigations, feeding stimulated spike bursts in all the groups studied, independently of the duration of fasting period and of MMC phase. It was also demonstrated that anticholinergic drugs administered during feeding exerted a profound inhibitory effect on antral spike bursts. Since feeding exerts a similar effect as acetylcholine (Ruckebusch and Merritt, 1985, Wong and McLeay, 1988) and this effect is efficiently hampered by anticholinergic drugs, it appears, that stimulation of cholinergic mechanisms by feeding is an important part of this response.

The effects of anticholinergic drug administration to fasted or non-fasted sheep on antral spike burst amplitude were not much different. Due to the relatively large rumen volume and continuous flow of digesta a marked interdigestive period is lacking in ruminants and about three days of fasting are necessary to empty the rumen efficiently (Ruckebusch, 1989). Thus, even the 48 h fasting period employed in the present study would be insufficient to empty the stomach completely and hamper the continuous flow of gastric content.

Newertheless when the duration of the fasting period exceeded 38-40 h, typical hunger symptoms of fasted animal behavior were observed. Thus, the fasting period seemed to be sufficient. However, the continuous flow of contents was still not markedly inhibited which can explain the lack of regular differences between the groups of experiments performed on fasted and non-fasted animals. As reported by Malbert and Ruckebusch (1988), digesta flow is an important regulator of motor activity in the ovine stomach.

The drugs administered during phase 1-2a MMC evoked a less pronounced effect than that of the drugs given during phase 2b or phase 3 MMC. From several studies performed on man and dog (Dent *et al.*, 1983, Thor *et al.*, 1990, Medhus *et al.*, 2000) it can be concluded that during various phases of MMC, different control mechanisms can be triggered.

It has also been described that the refractory period during phase 1 - 2a may depress the motility response to drugs or other stimulants (Sarna and Daniel, 1974). Thus, it can be expected that the outcome of distinct experimental procedures might be dependent upon MMC phase thus producing miscellaneous effects. The presented results are in agreement with this suggestion. Thus, when nutritional and pharmacological procedures are applied during the motility studies, the planned experimental procedure should be initiated during a given phase of MMC.

Although various doses of drugs, especially atropine and pirenzepine, were applied, there were no typical dose-response effects and sometimes high doses evoked a weaker response than a low dose. A similar observation was reported by Kay and Smith (1956). It is well known that cholinergic drugs may exert a motor response through different pathways: acting on excitatory receptors localized on smooth muscles, via excitatory neural receptors in cholinergic and noradrenergic inhibitory neurons, via inhibitory receptors on sympathetic nerves and via receptors present on other neurons, including opioid pathways (Daniel, 1982). Pirenzepine is deprived of central action; thus only local influences can be considered. The possibility of enhancement of acetylcholine release by pirenzepine due to the blockade of M1 and M2 autoreceptors was recently suggested (Ogishima *et al.*, 2000). *Since this drug can act through different muscarinic receptor subtypes, it might be expected that the effect of pirenzepine may vary depending on the dose employed (Schiavone et al., 1989).* Thus, a higher dose of the blocking drug may trigger stronger counteraction and the final effect will be attenuated or even reversed.

The effect of atropine, as a non-specific muscarinic blocking substance, was not always dose-dependent. Similar results were obtained previously (Bueno & Ruckebusch, 1978). However, in another study antral motility was inhibited by atropine in a dose-response manner in this species (Ruckebusch *et al.*, 1987). *This controversy can be explained by differences in experimental conditions, by the distinct role of muscarinic receptor subtypes in the control of gastrointestinal motility as well as by different receptor density and localization (Caulfield & Birdsall, 1998).*

In the present study, hexamethonium was also efficient in decreasing the antral spike bursts and, as in the case of antimuscarinic drugs, this inhibition was not complete. Analyzing the results of other studies, it can be expected that the response to hexamethonium may be partial (Okamoto *et al.*, 1986, Nakazato *et al.*, 1987). Similar results were reported in sheep by other authors (Ruckebusch *et al.*, 1987). *In man, transdermal nicotine delivery did not affect gastric emptying of liquids and solids implying the absence of a motility-inhibitory effect (Wong et al., 1999).* Kohagen *et al.* (1996) observed antral hypomotility in nonsmokers and smokers. Thus, the results are controversial and may depend upon the route of hexamethonium administration. Since nicotinic receptors seem to be localized on both cholinergic and noradrenergic neurons (Daniel, 1982), these data indicate that there can be different pathways of nicotinic or antinicotinic drug action on antral motility. However, in the present study the antinicotinic and, perhaps also, antimuscarinic action of hexamethonium (Eglen *et al.*, 1989) were the reasons for significant depression of antral spike bursts. Lowering of the blood pressure by hexamethonium, although significant, was not marked and probably did not affect motor function directly since only substantial disruption in intramural circulation may evoke meaningful motor dysfunction (Chou, 1989).

The administration of antimuscarinic and antinicotinic drugs in combination did not evoke an additive effect on ovine antral spike bursts. Another report concerning the effect of atropine plus hexamethonium on gastric motility in man (Kay & Smith, 1956) indicated that the combination of drugs generally exhibited effective action but additive effects were not evident. It is possible that central and peripheral actions of these drugs may evoke an additive effect. Localization of nicotinic and muscarinic receptors in one regulatory pathway (from vagal efferent

fibers through intramural ganglia to the smooth muscle cell) rather excludes the possibility of occurrence of additive effects of anticholinergic drugs acting via different receptor subtypes, although the presence of cholinergic receptors on other regulatory neurohormonal pathways suggests that the occurrence of additive effects might be possible.

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**ANTRALNA MIOELEKTRIČNA AKTIVNOST KOD OVCE: EFEKTI OBROKA I  
ANTIHOLINERGIČNIH SUPSTANCI U RAZLIČITIM FAZAMA MIGRIRAJUĆEG  
MIOELEKTRIČNOG KOMPLEKSA**

ROMANSKI KW

SADRŽAJ

Ova ispitivanja su imala za cilj utvrđivanje uticaja ishrane, gladovanja i antiholinergičnih supstanci na faze migrirajućeg mioelektričnog kompleksa i antralnu mioelektričnu aktivnost. Ogledi su izvedeni na šest ovnova kojima su bile ugrađene bipolarne elektrode u predelu antruma želuca, duodenuma i jejunuma. Postignuti rezultati ukazuju da kod ovaca holinergični sistem ima značajnu ulogu u kontroli mioelektrične aktivnosti antruma i da se za vreme nastanka migrirajućeg mioelektričnog kompleksa aktiviraju različiti kontrolni mehanizmi.