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EFFECTS OF TETRACYCLINE ON RUMINAL ACTIVITY AND BLOOD CALCIUM IN SHEEP

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ABSTRACT

The objective of this study was to assess the effects of tetracycline administration on the frequency of ruminal contractions and serum calcium concentrations. Rumen contractions were monitored by auscultation in 23 sheep prior to the administration of oxytetracycline and recorded every 12 hours for 84 hours after the intramuscular injection of the antibiotic. The blood for calcium analyses was collected by venipuncture of the jugular vein before and at 24, 48, 72, and 96 hours after the administration of oxytetracycline. The serum calcium concentrations were determined by atomic absorption spectrophotometry. The analysis of variance (ANOVA) was used to analyse the time effect of tetracycline treatment on the rumen contractions and serum calcium concentrations. There was a significant decrease ($P < 0.01$) in ruminal contractions following the application of oxytetracycline, with a maximum decrease at 24 hours following oxytetracycline application and a return to the initial rumen contraction frequency by 60—72 hours following the oxytetracycline application. The oxytetracycline administration resulted in a serum calcium decrease from 2.42 mmol.l^{-1} to 2.26 mmol.l^{-1} 24 hours after the administration ($P < 0.01$). In conclusion, the administration of tetracycline in sheep can be associated with a decline in ruminal motility potentially causing production losses, particularly in lactating ewes. Despite the resulting transient production decreases, oxytetracycline remains the antibiotic drug of choice for the treatment of bacterial infections in small ruminants, including foot rot especially.

Key words: calcium; rumen activity; sheep; tetracycline

INTRODUCTION

Belonging to broad-spectrum antibiotics, the group of tetracyclines is composed of: tetracycline, oxytetracycline, doxycycline and minocycline. They are actively transported into prokaryotic cells and inhibit protein synthesis by competing with tRNA for the A site of the ribosome. They

have a bacteriostatic effect. Tetracyclines chelate metal ions such as calcium, magnesium, iron and aluminium, forming non-absorbable complexes. Therefore if given orally, the presence of milk, antacids or iron preparations can decrease their absorption. The undesirable effects of the drug include gastrointestinal disturbances due to direct irritation and modification of the normal gut flora, and vitamin B complex deficiency can occur as a consequence. Since they chelate with Ca^{2+} ions, tetracyclines are deposited in bones and teeth, causing staining and sometimes dental hypoplasia and bone deformities [9]. Rumen and abomasal motilities are reduced in hypocalcaemia due to the general effects of a depression of levels of ionised calcium on smooth muscle contractility and on neuromuscular transmission [6, 7].

Tetracyclines are widely used in the treatment of the foot rot in ruminants. In a study of 209 sheep farmers, those which treated sheep with foot rot using parenteral antibiotics and foot sprays had a peak prevalence of 2 %, as opposed to a peak prevalence of 9 % in farmers who treated foot rot by hoof trimming and topical spraying [14]. In another study, the treatment of foot rot with parenteral oxytetracycline reduced clinical lameness in sheep significantly [10].

The aim of this study was to assess the effects of long acting tetracycline administration on the number of ruminal contractions and serum calcium concentrations.

MATERIALS AND METHODS

Rumen contractions were monitored in 23 adult merino female sheep (mean body weight 49 kg) prior to the administration of oxytetracycline and recorded every 12 hours for 84 hours after the intramuscular injection of the antibiotic. The sheep were admitted to the clinic for treatment of foot rot. After the diagnosis of foot rot, patients were treated with a single intramuscular injection of a long acting oxytetracycline (Tetradur LA 300, 30 $mg.kg^{-1}$). The drug was administered into the neck muscles (5 ml). The feeding of the experimental animals consisted of 0.2 kg of concentrates, and free access to hay and water. The ruminal contractions were counted by placing a stethoscope in the para-lumbar fossa on the left side of the animal and counting the number of ruminal contractions over a 5 minute period. In addition, the intensity of the rumen contractions were assessed by auscultation at the same time. The blood was collected by venipuncture of the jugular vein before and 24, 48, 72, and 96 hours after the administration of oxytetracycline. The serum calcium concentrations were determined by flame AAS method (Perkin Elmer AAnalyst 100).

The analysis of variance (ANOVA) with the post hoc Bonferroni test (IBM SPSS Statistics 23, 2015) was used to analyse the time effect of tetracycline treatment on the rumen contractions and serum calcium concentrations.

RESULTS

The ANOVA revealed a significant decrease ($P < 0.01$) in ruminal contractions following the application of oxytetracycline, with a maximum decrease at 24 hours following the oxytetracycline application and a return to the initial rumen contraction frequency by 60—72 hours following the oxytetracycline application (Table 1). As well as a reduction in the frequency of ruminal contractions, there was a decrease in the intensity of the contractions. In general, the contractions became quieter and sometimes difficult to distinguish effectively. Typically around 24 hours after the antibiotic administration, the intensity was at its lowest, coinciding with the greatest decrease in frequency. The strength of contractions gradually returned to normal over the same time period as the contraction frequency.

The oxytetracycline administration resulted in a serum calcium decrease from 2.42 $mmol.l^{-1}$ to 2.26 $mmol.l^{-1}$

Table 1. The rumen contractions and serum calcium after oxytetracycline administration (x ± s)

Collection time hours	Rumen contractions n/5 min	Serum calcium [$Mmol.l^{-1}$]
0	7.31 ± 1.55	2.42 ± 0.11
12	5.17 ± 1.32*	
24	4.09 ± 1.16*	2.26 ± 0.04*
36	5.00 ± 1.21*	
48	5.96 ± 1.19*	
60	7.17 ± 1.34	
72	7.65 ± 1.37	2.28 ± 0.09*
84	7.57 ± 1.34	
96		2.41 ± 0.05
ANOVA	P < 0.01	P < 0.01

* — values differ from 0 at P < 0.05 (Bonferroni test)

24 hours after the administration (Table 1). The serum calcium concentrations continued to decrease reaching the lowest values 48 hours after the drug injection (2.23 mmol.l^{-1}). The ANOVA showed a strong significant effect of the oxytetracycline administration on serum calcium ($P < 0.01$).

DISCUSSION

The rumen motility has a direct effect on the productivity levels of livestock, particularly on milk production. In sheep used for milking or ewes nursing lambs, a decreased rumen motility can cause a significant drop in milk quantity or decreased weight gains in lambs. The number of ruminal contractions is dependent upon: the type of feed (forage, concentrate), feed quality (herbage, rice straw), the form in which feed is ingested (hay, pellets), the amount of feed consumed and rumen wall stimulation [4]. The ruminal contraction frequency is highest during feeding (2.7 frequency.min^{-1}). The second highest frequency is recorded during rumination (2.3 frequency.min^{-1}), while the lowest frequency is recorded during rest periods (2.0 frequency.min^{-1}) [13]. In the present experiment in 23 sheep, the frequency of ruminal contractions decreased by 44 %, with the lowest number of contractions recorded 24 hours after application of long acting oxytetracycline. However, our study did not take into account other factors affecting rumen contractions, such as feeding regimen, composition of the dietary ration, underlying disease processes, and environmental temperature [2, 11].

Rumenal and abomasal motilities are reduced in hypocalcaemia due to the general effects of a depression of the levels of ionised calcium on smooth muscle contractility and on neuromuscular transmission [5]. In general, the tetracyclines can be divided into three groups based on their pharmacokinetic and antibacterial properties. The mostly used drugs are from the group 1. This group consists of the older agents which have reduced absorption and are less lipophilic than newer drugs and include tetracycline, oxytetracycline, chlortetracycline, demeclocycline (demethyl chlorotetracycline), lymecycline, methacycline, and rolitetracycline. All of these tetracyclines form insoluble complexes with calcium, magnesium, iron and aluminium, which can markedly reduce their absorption [1]. According to a pharmacodynamic study, intramuscular administration of oxytetracycline resulted in plateau-shaped concentration-time curves in serum and synovial fluid. Peak levels in serum (1.68 ± 0.47 μg.ml^{-1}) occurred at 3—8 hours post injection [3]. As oxytetracycline chelates Ca^{2+} ions [9], once the antibiotic reaches the bloodstream it will chelate with calcium in the serum, resulting in hypocalcaemia. One mole of oxytetracycline may form complexes with 1—2 moles of calcium, depending on the relative concentrations [8].

The calcium homeostatic mechanism operates very tightly to maintain extracellular calcium within physiological ranges. A change in physiological status, such as the initiation of lactation, creates a rapid disturbance in this mechanism. Plasma calcium exchanges with a large mass of calcium in soft tissues and bone surfaces, which may function to buffer the effect of such rapid changes in these pools. The sufficient calcium levels are necessary to decrease the incidence of periparturient hypocalcaemia (milk fever) in sheep [12]. The results presented in this study did reveal a significant serum calcium-lowering effect when each of the 23 animals were given oxytetracycline. The drop in blood calcium was not associated with any clinical sign, like neurological or locomotor disturbances. However, most of the experimental animals demonstrated a decrease in ruminal contractions.

In conclusion, the administration of tetracycline in sheep can be associated with a decline in ruminal motility, potentially causing the decline in ruminal motility which can cause production losses, particularly in lactating ewes. Despite the resulting transient production decreases, oxytetracycline remains the antibiotic drug of choice for the treatment of bacterial infections in small ruminants, especially foot rot.

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