ORIGINAL ARTICLE

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Therapeutic efficacy of marbofloxacin and ceftiofur in feedlot steers with bovine respiratory disease complex

Eficácia terapêutica da marbofloxacina e ceftiofur em bovinos confinados com complexo doença respiratória de bovinos

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ABSTRACT: Treatment of the bovine respiratory disease complex (BRDC) can elicit high bacterial resistance and stress to steers in a feedlot. Therefore, the present study aimed to evaluate three therapeutic protocols with long-acting antibiotics against BRDC naturally acquired in steers finished in feedlot. In a total of 80 animals finished in a feedlot, 18 steers showed clinical signs compatible with BRDC (mucopurulent nasal secretion, lung auscultation alteration, leukocytosis, and decrease of dry matter intake). These animals were randomly treated: marbofloxacin in a single dose (M1), marbofloxacin in two doses (M2), or ceftiofur in a single dose (C1) on Day 0. The clinical score of pneumonia, hemogram, daily food intake, and body weight were analyzed during 7 days. On slaughter day (Day 100), the body weight and frequency of lungs with pneumonia was evaluated. On Day 7, M2 showed absence of pneumonia, and M1 and C1 still showed a clinical score of mild pneumonia (P = 0.01). On day 2 and day 3 M2 showed a higher dry matter intake than others treatments (P = 0.05). C1 showed a lower body weight than others group on day 1 and 2 (P = 0.05). The C1 and M1 showed a higher pneumonia frequency than M2 (P = 0.02). The M2 slaughter weight was numerically higher than the other treatments. We conclude the marbofloxacin in two doses eliminated the pneumonia´s clinical symptoms and allowed the animals to return the productivity earlier than other protocols.

KEYWORDS: Hemogram; dry matter intake; body weight; pneumonia score; beef cattle.

RESUMO: Tendo em vista a alta resistência bacteriana e o estresse que o tratamento do complexo doença respiratória dos bovinos (CDRB) pode trazer para novilhos terminados em confinamento, o presente trabalho teve por objetivo avaliar quais dos três protocolos terapêuticos com fármacos de longa ação apresentaria maior eficácia contra o CDRB naturalmente adquirida. Entre 80 animais terminados em confinamento, 18 garrotes apresentaram sinais clínicos compatíveis CDRB (secreção mucopurulenta nasal, alteração em ausculta pulmonar, leucocitose e diminuição de consumo alimentar). Estes animais foram aleatoriamente tratados com: marbofloxacina em dose única (M1), marbofloxacina em duas doses (M2) ou ceftiofur em dose única (C1) no dia 0. Escore clínico de pneumonia, hemograma, consumo alimentar e o peso corporal dos animais foi avaliado durante 7 dias. No dia do abate (dia 100), o peso e frequência de lesões histopatológicas de pneumonia foram avaliadas. No dia 7, os animais do M2 apresentaram ausência de pneumonia enquanto que os animais M1 e C1 ainda apresentavam escore clinico de pneumonia moderada (P = 0.01). Nos dias 2 e 3, o consumo alimentar diário foi maior em M2 que os outros tratamentos (P = 0.05), e o peso corporal de C1 foi menor que os outros grupos em D1 e 2 (P = 0.05). C1 e M1 apresentaram maior frequência de pneumonia no dia do abate que os demais grupos (P = 0.02). O peso ao abate do M2 foi numericamente maior que os demais grupos. Conclui-se que a marbofloxacina em duas doses foi mais precoce na eliminação dos sinais clínicos e no retorno a produtividade.

PALAVRAS CHAVE: Hemograma; consumo de matéria seca; peso corpóreo; escore de pneumonia; gado de corte

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INTRODUCTION

Investments in feedlot systems promote an increase in daily weight gain and meat quality, increasing productivity. However, this system favors the occurrence of diseases, as bovine respiratory disease complex (BRDC), which has a mortality rate until 33%, and causes considerable losses in cattle performance and quality. Treatment costs are estimated at around US $5 - 10 for every 100 kg of live weight (BAPTISTA et al, 2017, 2009; SMITH et al., 2020).

The BRDC is frequently found in feedlot animals, because conditions such as transport, grouping animals in pens, extremes temperatures, high environmental humidity, sudden changes in the diet, and stress compromise the efficiency of defense respiratory mechanisms (SMITH et al., 2020). This situation allows viral agents present in the environment, such as *infectious bovine rhinotracheitis virus (IBR), parainfluenza type 3 (PI-3), bovine respiratory syncytial virus (BRSV)*, *bovine viral diarrhea virus (BVD),* and commensal bacteria of anterior respiratory tract such as *Mannheimia haemolytica, Pasteurella multocida,* and *Histophilus somni* to colonize and multiply in the lungs (BOSCH et al.,2013).

Viral colonization in association with bacteria promotes pneumonia of variable severity, ranging from subclinical disease to irreversible conditions. In the advanced stages of the disease, there are areas of fibrosis, adhesions, and abscesses, and the large extensions of the respiratory tract limit the immune response and the penetration of antibiotics. Thus, prompt diagnosis and treatment of these diseases are crucial to obtaining a cure and consequent early return to animal productivity (SMITH et al., 2020).

Numerous treatments with antibiotics have been proposed. Drugs that reach the lung tissues quickly in sufficient doses and remain in the tissues for prolonged periods are preferred, reducing the need for reapplication of medications. This strategy avoids the stress caused by frequent management, which may prolong the disease in beef cattle (KROEMER et al., 2012).

However, erroneous antibiotic treatment protocols, mainly regarding dose and frequency of application, have increased bacterial resistance to antibiotics such as oxytetracycline and penicillin, and until recent antibiotics as tulathromycin. There is still no reported resistance to florfenicol, enrofloxacin, ceftiofur and marbofloxacin (PAULIN et al, 2017; TIMSIT et al., 2017).

Because marbofloxacin and ceftiofur are drugs with good penetration and prolonged permanence in lung tissue and there are no reports of resistance from pneumonic bacteria to them (FOSTER; MARTIN; PAPICH, 2016; PAULIN et al., 2017;). Besdides ceftiofur can be used in a low (1mg/hg during 3 to 5 days) or a high doses (3.3-5.5 mg/kg given in a single) (FOSTER; MARTIN; PAPICH et al., 2016), Hibberd et al, (2002) showed the high doses was an effective treatment for BRDC in feedlot cattle in control and field study, without promoted residues at the injection site for extended periods of time. Marbofloxacin can be used in a low (2 mg/kg during 3 to 5 days) or a high dose (10 mg/kg given in a single injection) and the both exerts a moderate selective pressure on commensal Enterobacteriaceae in young beef cattle (LHERMIER et al., 2017). This study aimed to evaluate the efficacy of ceftiofur in a single dose or marbofloxacin in a intermediary dose in a single or two injections for treatment of BRDC in naturally affected steers finished in feedlot.

MATERIAL AND METHODS

For this purpose, 18 steers naturally infected with BRDC were selected from a comercial feedlot. In the feedlot, there were 80 uncastrated angus x nelore steers (mean weight, 320 ± 10 kg; mean age, 11 ± 0.5 months). They were transported by a property 50 km away from the experimental site and housed in pens at UNICENTRO located in Guarapuava, Paraná, with two animal per pen during 100 days. Each pen was semi covered (15 m^2), with a concrete feeder (2.30 m X 0.60 m X 0.35 m) a metal drinking fountain controlled by automatic float. The animals received the same diet as provided at the farm they came from, consisting of 50% concentrate and 50% corn silage until the end of feedlot. The diet was provided twice a day, ad libitum (Table 1).

For identification of BRDC, the steers were daily monitored to identify clinical manifestations such apathy, nasal and ocular discharge, cough, tachypnea, dyspnea or reduced food intake. Sick animals were subjected to general and specific physical examination of the respiratory system. When

Table 1. Chemical composition of aliment used in animal feed and average values of the experimental diet, based on total dry matter.

Parameter	Corn silage	Concentrate	Experimental diet [1]
Dry matter %	33,38	90,40	62,12
Mineral matter %DM	2,51	6,36	4,44
Crude protein% DM	8,44	20,20	14,32
Ethereal extract % DM	2,65	2,05	2,35
Neutral detergent fiber % DM	46,14	31,47	38,80
Acid detergent fiber % DM	25,98	13,08	19,53
Lignin % DM	8,43	4,73	6,58
Total digestible nutrients % DM	68,66	78,68	74,18
Ca %	0,14	1,67	0,91
P %	0,22	0,58	0,40

1 Premix guarantee level per kg of concentrate: vitA 16000UI, vit D3: 2000 IU, Vit E25 IU; S 0.36 g; Mg 0.74 g; Na: 3.6 g; Co: 0.52 mg; CU: 22.01 mg; F: 18.00 mg; I: 1.07 mg; Mn 71.80 mg; Se: 0.64 mg and Zn 95.20 mg.

pneumonia was confirmed by abnormal lung auscultation (stertor, wheezes, or stridor) evaluated by two experients veterinarians, blood samples were collected from the animals by venipuncture of the jugular vein for hemogram analysis, before the treatment. Pneumonia severity was based on the scale proposed by Schaefer et al. (2012). The summa of each variable varied between 0 until 7. It was classify as Score 0 – 1: absence of pneumonia, 2 – 3: mild pneumonia, 4 – 5: moderate pneumonia, and 6 – 7: severe pneumonia (Table 2).

The experiment was randomized, the 18 steers naturally infected with BRDC were sub-divided into three groups of six steers each, in a blind study about the treatment , administrated on day zero (0) with one of the treatments described: M1- single dose of marbofloxacin (Resolutor®, Ourofino Saúde Animal, São Paulo, SP) 8.0 mg/kg subcutaneously, M2- two doses of 8 mg/kg of marbofloxacin (Resolutor®, Ourofino Saúde Animal, São Paulo, SP) with a 24h00 interval or C1- single dose of ceftiofur (Lactofur®, Ourofino Saúde Animal, São Paulo, SP) 3.3 mg/kg intramuscularly.

Each treatment had five animals with mild pneumonia (score 2 to 3) and one animal with a moderate score (score 4) on day 0. Response to treatment was assessed at 2 and 7 days after treatment by clinical score and hemogram. The animal's body weight was measured on 1, 2, 7 and 100 days by a digital scale, at the same time of day. Average dry matter intake was analyzed daily, measured by the difference between the daily amount of food provided and the amount of leftovers from the previous day. It was possible to verify consumption two days before the identification of the disease (d - 2) and after treatment until day 7, as this management was routine in feedlot.

Between 30 until 100 days of the feedlot, the animals were inspected for the pneumonia clinical signs as apathia, mucopurulent nasal secretion, or dry matter intake reduction. On 100 days of the feedlot, the animals were slaughtered in a commercial slaughtered. The animals were weighed after a 12h00 fast, and in the slaughter line, the lungs of these animals were examined macroscopically. The severity of pneumonia was based on the extent of pulmonary consolidation, according to Ceribasi, Ozkaraca and Ceribasi (2014). Absence of injury was considered score 1; score 2 for injuries up to 50%; score 3, injuries between 50% and 75%; and score 4, injuries greater than 75% of the lungs based on inspection and palpation. The lung fragments of approximately 2 cm^2 in the transition area between normal tissue and consolidation areas were then collected for histopathology analysis. The tissues were fixed in 10% formaldehyde for 48h00, embedded in paraffin, sectioned to make histopathological slides stained with hematoxylin and eosin (HE), and finally observed under optical microscopy. The fragments were classified as absence of pneumonia, pneumonia, or bronchopneumonia suppurative, fibrinous, or interstitial according to Zhang et al. (2019).

The data collected for each variable were analyzed using the statistical software Instat Graphpad. To evaluate the differences between the means of the results obtained for each treatment, the ANOVA one-way analysis of variance test (Unstacked) and the Tukey post test were performed. The clinical score was subjected to a non-parametric ANOVA and Dunn's post test. The pneumonia score and classifications were transformed into animal frequencies with each characteristic and submitted to the chi-square test. For all results, data were considered significant at $P \leq 0.05$.

RESULTS AND DISCUSSION

All the 18 steers showed clinical signs of pneumonia between the 10th to 30th of the feedlot, and after this time point, there was no evidence of pneumonia. The pneumonia clinical scores are showed in Figure 1. In each group, there were five animals with mild pneumonia and one animal with a moderate score on day 0. Two days after treatment, animals in all groups showed improvements, as observed by the reduction in clinical scores without statistical difference between groups; however, the C1 and M1 increase the pneumonia clinical score on day 7, while M2 showed absence of pneumonia ($P = 0.01$). On day 7, two animals from C1 had a rectal temperature above

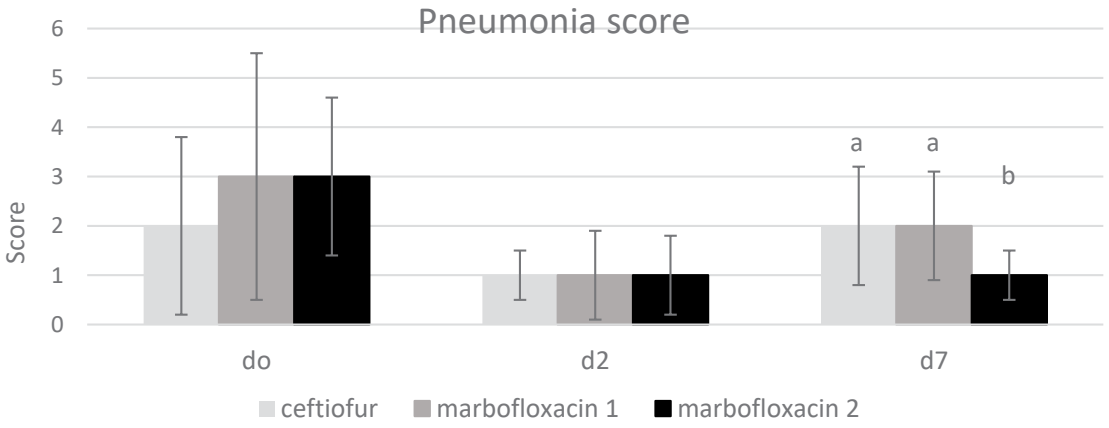
Table 2. Variables used to classify pneumonia score in confined cattle (SCHAEFER et al., 2012).

Variable	Criterion	Score
Rectal temperature	Above 40o.C	1
Total leukocytes	Below 7 X 10^3 / mm^3 or above 11 X 10^3 / mm^3	1
Neutrophil / lymphocyte ratio	Below 0,1 or above 0.8	1
Lung auscultation	Normal	0
	Thin stertor and spontaneous cough	1
	Moderate stertor, nasal discharge and spontaneous cough	2
	Moderate stertor, nasal discharge and spontaneous cough, RF above 15% (92 bpm)	3
	Moderate stertor, nasal discharge and spontaneous cough, RF above 15%, dyspnea/wheezing or stridor	4
Summation		0-7

40°C. These same animals and two from M1 had anormal pulmonary auscultation (score 2). In M1, they had leukocytosis due to lymphocytosis with N/L ratio below 0.1 and the animals from C1 had leukocytosis due to neutrophilia, with N/L ratio above to 0,8. Similar results were obtained in dairy cattle treated with a high single dose of marbofloxacin (10 mg/kg), because one dose of antibiotic may not remain in the lung tissues for the entire course of pneumonia, and relapse may occur (GRANDEMANGE et al., 2012).

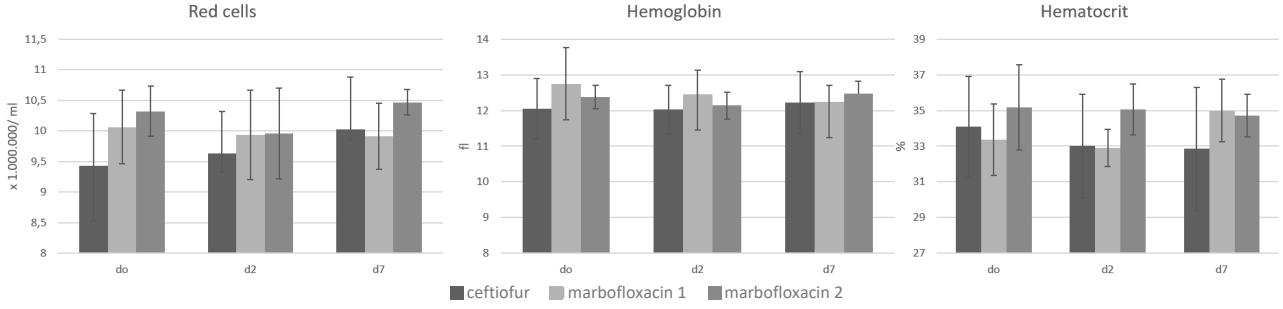
Data referring to the erythrogram are shown in Figure 2. All values remained within the reference parameters for the species during the experimental period, and the treatment or the disease did not influence this variable (WARDROP; WEISS, 2010). The leukogram of cattle with BRDC is shown in Figure 3. It was observed that most animals had leukocytosis due to neutrophilia and lymphocytosis about the reference parameters for the species (WARDROP; WEISS, 2010). In the C1 there was a leukocyte and a neutrophil count increase on day 7 compared with day 0 (P = 0.05 and P = 0.03). The M1 showed an increase of lymphocytes on day 7 in comparison to day 0 (P = 0.05) and there was no significant influence for this variable in M2 for time interaction. For the treatment interaction, there was a lower leukocyte and lymphocyte count in M1 than M2 on day 0 (P = 0.04 and P = 0.04, respectively).

The steers´s productive index are in Figure 4. The animal´s dry matter intake were higher two days before presenting clinical manifestations of the disease than the day of identification of the disease, on day 0 and return to returned to initial levels on day 6 for C1 (P=0,03), on day 4 for M1 (P=0.005) and on day 2 for M2 (P=0,05) On days 2 and 3, C1 and M1 showed a decrease of food intake in compare M2 (P = 0.04 and 0.05, respectively), and on Day 4 and 5, C1 showed a decrease of food intake in compare M2 (P = 0.05 and P=0.05). C1 showed a lower body weight than M1 and M2 on day 1 and 2 (P = 0.0, P=0,05) and a lower body weight than M1 on day 7 (P=0,05). Although the treatment influenced the productive index on the onset of the experiment, all the steers finished in the feedlot showed a similar body weight at slaughter day (mean and standard error of the mean of body weight: total feedlot cattle without treated - 479,17 ± 4,83 kg, M2 494,67 ± 14,11; M1- 21 455,62 ± 10,71 kg and C1 457,00 ± 19,18 kg; P = 0.20). As this variable presented a high standard error of the mean, especially for the treated groups, it is believed that the sample number (6 animal group) may not be representative for this analysis.



Medians and percentiles 5 and 95%. Pneumonia score according to Schaefer et al., (2012) , 0 - 1 absence of pneumonia, 2 - 3 mild pneumonia; 4 - 5 moderate pneumonia and 6 to 7 severe pneumonia. Different letters indicate statistical difference in the treatment interaction (P ≤ 0.05).

Figure 1. Pneumonia clinical score of cattle with BRDC treated with a single dose of ceftiofur, single dose of marbofloxacin or two doses of marbofloxacin.

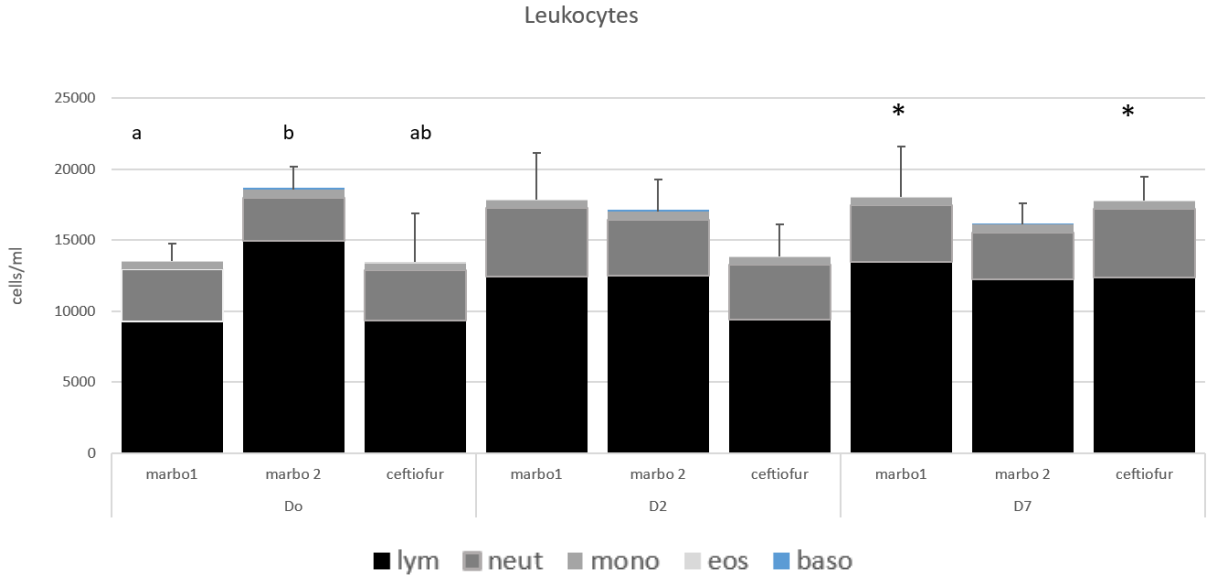


Means and standard error of the mean

Figure 2. Erythrogram of cattle with BRDC treated with a single dose of ceftiofur, a single dose of marbofloxacin or two doses of marbofloxacin.

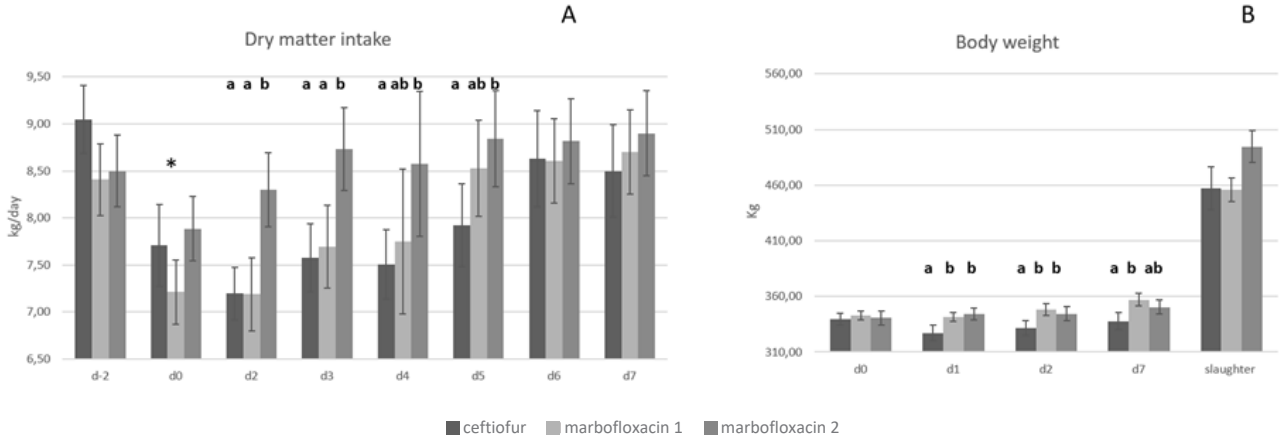
Leukocytosis caused by neutrophilia on day 7 and the lower dry matter intake and the body weight in C1 on day 1 and day 2 than M2 reinforces the hypothesis that these animals had not controlled the disease after 7 days. The severity of the clinical signs reduced on day 2 and then worsened again. According to Wardrop; Weisss (2010), neutrophilia and leukocytosis indicate local or systemic infections of bacterial origin, the main etiological agent of pneumonic infections in cattle.

As the most common etiological agent of BRDC is bacterial-associated viral pneumonia (BOSCH et al., 2013; ZHANG et al., 2019), it´s believed the increased of lymphocytes on day 7 for M1 indicate a slower recovery of bacterial pneumonia than the treatment with M2. It promotes a maximum bactericidal immune response and a minimum viral response, which favors the perpetuation of the virus in the respiratory tract in M1 (SMITH et al., 2020). This situation would explain because the M1 group did not show a reduction of weight body, but there was not a clinical cure because there was an increase in the clinical score of pneumonia on D7. Also, the M1 had lower leukocytes and lymphocytes count in comparison to the M2 on day 0. The severity of pneumonia in both groups was the same on day 0. It could indicate the increase of the leukocyte response was due to the perpetuation of infection in the animals of M1 (WARDROP; WEISS, 2010)).



Means for each leukocyte population. The sum is the absolute values of total leukocytes and their respective standard error of the mean. Lym- lymphocyte, neu- neutrophil, mono- monocyte, eos- eosinophil, baso- basophile * indicates statistical difference in time interaction (C1- leukocytes and neutrophils D7 > DO P = 0.05 and P = 0.03, M1- lymphocytes D7 > DO, P = 0.03) Different letters indicate statistical difference for treatment interaction (leukocytes and lymphocytes M1 < M2; P ≤ 0.05).

Figure 3. Leukogram of cattle with BRDC treated with a single dose of ceftiofur, a single dose of marbofloxacin or two doses of marbofloxacin.



Means and standard error of the mean. A: Dry matter intake; * indicates statistical diference in time interaction (C1: DO< D-2, D6, D7 P=0,03; M1: DO< D-2, D4, D5, D6 and D7 P=0,005, M2: DO< D-2, D2, D3, D4, D5 D6 and D7 P=0,05, different letters indicates statistical difference for treatment (P ≤ 0,05). B: Body weight, different letters indicates statistical difference for treatment (P ≤ 0,05).

Figure 4. Productive index of cattle with BRDC treated with a single dose of ceftiofur, a single dose of marbofloxacin or two doses of marbofloxacin.

On slaughter day, the lungs were macroscopic and microscopic evaluated (Table 3). Gross evaluation of the lungs of the cattle at the slaughter house revealed that pulmonary lesions indicative of BRDC were identified in 13.75% (11/80) of the lungs examined. From this number of affected lungs, 81,81% (9/11) of these were from steers diagnosed with BRDC (5/6 C1, 3/6 M1 e 1/6 M2) and treated while on feedlot, while 18,18% (2/11) represented cattle that were not diagnosed with BRDC and consequently not treated. Furthermore, the C1 and M1 had more animals with pneumonia than M2 (P = 0.02). The microscopic lesions showed an equal distribution between the groups, characterized mainly by interstitial bronchopneumonia, predominantly characterized by thickening of the interalveolar septum, degeneration, or desquamation of the bronchiolar epithelium, and intra-alveolar and peribronchiolar mononuclear infiltrates. Suppurative pneumonia was not observed.

Microbiological lung studies would be more accurate to determine which agent was involved, and if a microbiological cure was obtained (GONÇALVES et al., 2004). Although Ceribasi et al. (2014) did not find a correlation between histopathological findings and the agents causing BRDC. Zhang et al. (2019) observed that interstitial pneumonia and/or bronchopneumonia were more associated with bacterial pneumonia, especially *Pasteurella multocida*, reinforcing the hypothesis that pneumonia was bacterial or there was an association between viruses and bacteria.

We observed the M2 treatment was more efficient than others, because the animals maintained the hemogram response along the experimental period, returned faster the dry matter intake than others treatments, and showed a higher body weight than the C1 on day 1. Besides, there was a reduction of pneumonia clinical score on days 2 and 7, and a lower pneumonia frequency at slaughter. Unfortunately, there was not evaluated a treatment with two doses of ceftiofur, because Hibberd et al, (2002) affirmed more than one high doses of ceftiofur promote residues at the injection site for extended periods of time. Despite this, the cases of BRDC occurred about 70 days before slaughter, which would already coincide with the withdraw period (FOSTER; MARTIN; PAPICH et al., 2016)

The M1 treatment showed a moderate efficiency, because the animals presented a lymphocytosis and, an increase in the clinical score of pneumonia on day 7. Besides, this group reduced the dry matter intake during the first two days after treatment, although this reduction did not affect the animal's weight body. C1 was the treatment that demonstrated the lowest efficacy in the treatment of BRDC because the animals showed an increase in the pneumonia clinical score and, leukocytosis and neutrophilia on day 7. They showed a decrease of dry matter intake on days 1 and 2, and lower body weight on day 1 than M2. They showed the higher pneumonia frequency than other groups at slaughter day.

These differences in response to the treatments can be explained by the distribution, tissue penetration, and duration of the antibiotics used (FOSTER; MARTIN; PAPICH et al., 2016). The clinical course of pneumonia of the BRDC lasted between 7 and 15 days (SMITH et al, 2020), and the animals studied in the experiment remained in the feedlot for 100 days. They did not show pneumonia signs like apathy, decreases of dry matter or mucopurulent nasal secretion during this period.

In cattle, the plasma half-life of marbofloxacin 10 mg kg $^{-1}$ in a single dose is 5.2 days (VALLÉ et al., 2011; PAULIN et al., 2017) and the plasma half-life of ceftiofur 6.6 mg kg -1 slow-release is 4.2 days (FOSTER; MARTIN; PAPICH et al., 2016), which is less than the normal duration of pneumonia. However, the high bactericidal antibiotic load allows the restoration of natural defenses and commensal microbiota (GRANDEMANGE et al., 2012). Therefore, the repetition of the doses promoted a high antibiotic load for a longer time, thus promoting faster clinical recovery.

Another point to be highlighted refers to the penetration of antimicrobials into the interstitial fluid and pulmonary epithelial fluid. In the present study, most pneumonias were of the interstitial type, an inflammatory condition in which there is a rupture of the alveolar blood barrier. In this case,

Table 3. Lung lesions score in the slaughter of cattle with BRDC treated with a single dose of ceftiofur, a single dose of marbofloxacin or two doses of marbofloxacin.

Frequency (%)					
Pulmonary scores		**Ceftiofur**	**Marbofloxacin 1**	**Marbofloxacin 2**	**P**
Macroscopic evaluation	Score 1	16,67a	50,00a	83,33b	0.02
	Score 2	83,33	50,00	16,66	
	Scores 3	0	0	0	
	Score 4	0	0	0	
Microscopic evaluation	BP or P interstitial	83,33	83,33	83,33	0.99
	BP or P fibrinous	16,66	16,66	16,66	

Score 1: Absence of injury. Score 2: lesions between 25 to 50% of the cranioventral pulmonary lobe. Score 3: lesions between 50% to 75% of the pulmonary cranioventral lobe. Score 4: above 75% of the pulmonary cranioventral lobe. BP- bronchopneumonia, P-pneumonia; different lower case letters indicate statistical difference P ≤ 0.05.

there is a need for the antimicrobial to reach adequate minimum inhibitory concentrations in the interstitial fluid, which occurs with fluoroquinolones, but not with ceftiofur. This drug reaches adequate minimum inhibitory concentrations in the pulmonary epithelial fluid to protect the airways against bacterial colonization and is more effective in fibrinous pneumonia (FOSTER; MARTIN; PAPICH et al., 2016), which was not the case with the BRDC treated in this experiment.

Besides until the end of the feedlot, none of these animals presented clinical signs of the disease or requiring new treatment the C1 demonstrated the lowest efficacy in the treatment of BRDC because the animals showed an increase in the pneumonia clinical score and, leukocytosis and neutrophilia on day 7 and delay to return to productivity.

Although papers about the most effective treatment for BRDC studies a higher number of animals in their experiments (ABUTARBUSH et al., 2012, HIBBARD et al., 2002) they do not do an early identification of pneumonia neither about their severity, which raises the doubt whether a higher number of animals in our research would reflect in statistical differences between body weight, allowing us to conclude also which protocol would be the most interesting from the economic aspect.

CONCLUSION

The marbofloxacin in two doses was the most efficient protocol because it eliminated the pneumonia clinical sign earlier, and promote an earlier return to productivity. The second most efficient protocol was marbofloxacin single dose, because it promoted an earlier return to productivity than ceftiofur single dose but did not eliminate the pneumonia clinical score on day 7.

REFERENCES

ABUTARBUSH, S. M. et al. Comparison of enrofloxacin and ceftiofur sodium for the treatment of relapse of undifferentiated fever/bovine respiratory disease in feedlot cattle. **Can Vet J**. v. 53, n.1, p.57-62, 2012.

BOSCH, A. A. T. M. et al. Viral and Bacterial Interactions in the Upper Respiratory Tract**. Public Library of Science Pathogens**, v. 9, n. 1, p. e1003057, 2013.

CERIBASI, A. O.; OZKARACA M.; CERIBASI, S. Histopathologic, immunoperoxidase and immunofluorescent examinations on natural cattle pneumonia originated from Parainfluenza type 3, Respiratory Syncytial virus, Adenovirus type 3 and Herpesvirus type 1. **Revue de Médecine Vétérinaire**, v. 165, n. 7-8, p. 201-212, 2014

FOSTER, D. M.; MARTIN, L. G.; PAPICH, M. G. Comparison of Active Drug Concentrations in the Pulmonary Epithelial Lining Fluid and Interstitial Fluid of Calves Injected with Enrofloxacin, Florfenicol, Ceftiofur, or Tulathromycin. **Plos One**, v. 11, n. 2, p. e0159219, 2016.

GONÇALVES, R. C. et al. Lavagem traqueobrônquica por sondagem nasotraqueal em Bezerros. **Arquivo Brasileiro de Medicina Veterinária e Zootecnia,** v. 56, n. 3, p. 307-31, 2004.

GRANDEMANGE, E. et al. Efficacy of a single injection of marbofloxacinin the treatment of bovine respiratory disease**. Revue de Médecine Vétérinaire,** v. 163, n. 6, p. 287-294, 2012.

GRIFFIN, D. The monster we don't see: subclinical BRD in beef cattle. **Animal Health Research Reviews,** v. 15, n. 2, p. 138-141, 2014

HIBBARD, B. R. et al. Dose determination and confirmation of a long-acting formulation of ceftiofur (ceftiofur crystalline free acid) administered subcutaneously for the treatment of bovine respiratory disease. **Journal of Veterinary Pharmacology and Therapeutics**, v. 25, n. 3, p. 175-180, 2002

KROEMER, S. et al. Survey of marbofloxacin susceptibility of bacteria isolated from cattle with respiratory disease and mastitis in Europe. **Veterinary Record**, v. 170, n. 2, p. 53-58, 2012.

LHERMIE, G. et al. Impact of Low and High Doses of Marbofloxacin on the Selection of Resistant *Enterobacteriaceae* in the Commensal Gut Flora of Young Cattle: Discussion of Data from 2 Study Populations. **Foodborne Pathogens and Disease**, v. 1, n. 1, p. 152-159, 2016.

PAULIN, A. et al. Pharmacokinetic/pharmacodynamic evaluation of marbofloxacin as a single injection for Pasteurellaceaerespiratory infections in cattle using population pharmacokinetics and Monte Carlo simulations. **Veterinary Pharmacology and Therapeutics**, v. 41, n. 1, p. 39-50, 2017.

SCHAEFER, A. L. et al. The non-invasive and automated detection of bovine respiratory disease onset in receiver calves using infrared thermography. **Research in Veterinary Science**, v. 93, n. 2, p. 928-935, 2012

SMITH, R. A.; STEP, D. L.; WOOLUMS, A. R. Bovine Respiratory Disease. **Veterinary Clinics of North American: Food Animal Practice**, v. 36, n.2, p. 239–251, 2020 TIMSIT, E. et al. Prevalence and antimicrobial susceptibility of *Mannheimia haemolytica, Pasteurella multocida*, and *Histophilus somni* isolated from the lower respiratory tract of healthy feedlot cattle and those diagnosed with bovine respiratory disease. **Veterinary Microbiology,** v. 208, n. 1, p. 18-125, 2017.

VALLÉ, M. et al. Pharmacokinetic and pharmacodynamic testing of marbofloxacin administered as a single injection for the treatment of bovine respiratory disease. **Journal of Veterinary Pharmacology and Therapeutics**, v. 35, n. 6, p. 519-528, 2011.

WARDROP, J. N.; WEISS, D. J. **Schalm's Veterinary Hematology** 6. ed. Iowa: Blackwell Publishing Ltd, 2010. 1206 p.

ZHANG, M. et al. The pulmonary virome, bacteriological and histopathological findings in bovine respiratory disease from western Canada. **Transboundary and Emerging Diseases**, v. 67, n. 2, p. 924-934, 2019.