Evaluation of meloxicam included in a modern health management of beef cattle adaptation phase

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SUMMARY

The effects on health and growth of meloxicam administration in comparison to preventive antibiotic mass treatment to newly received beef cattle was evaluated. 605 intact Charolaise and crossbreeds' males imported from France to an Italian beef fattening unit were enrolled in the trial. Those animals were considered to be at high risk of incurring in BRD (Bovine Respiratory Disease). At arrival, those animals were divided into two groups, Control (Ab) and Meloxicam (M). Ab group animals were treated with long acting oxytetracycline while those of M group were treated with meloxicam. Morbidity for BRD and other health problems was daily recorded. At day 0 and day 30, blood samples were collected to evaluate serum indicators of immune functionality (BHV-1 vaccination antibodies, serum bactericidal activity and γ-interferon) and inflammatory status (haptoglobin, lipopolysaccharide binding protein and Interleukin 6). Individual weight was recorded at study days 30, 100 and 180 to evaluate the growing performance. Cattle of M group showed a lower incidence of BRD. Considering the overall treatments for respiratory disease as the sum of first pull, relapse and chronic, the administration of meloxicam at arrival, led to a reduction of antimicrobial drugs use in the present experimental condition ($P<0,05$). Meloxicam administration in comparison to mass antibiotic treatment statistically improved cattle immune functionality. The production of BHV-1 antibodies due to vaccination resulted to be higher in M group (0,96 vs 0,44; $P<0,05$). Even the serum bactericidal activity resulted improved by meloxicam administration at study day 30 (83,8% vs 77,6%, $P<0,05$). Among inflammatory status indicators, only haptoglobin production tended to be positively affected by meloxicam administration. Regarding growth performance, animals of M group showed a better average daily gain and a higher weight at the end of the adaptation period (1,370 vs 1,280 kg/head/day and 444,61 vs 432,88 kg, $P<0,1$). In conclusion, the administration of meloxicam at arrival in the fattening unit to BRD high risky beef cattle, led to a good management of the respiratory disease. This strategy can be effective in a modern approach to manage the prevention of respiratory disease reducing the antibiotic administration.

KEY WORDS

Cattle; bovine respiratory disease; antibiotics; health; nonsteroidal anti-inflammatory drugs.

INTRODUCTION

The Italian intensive beef cattle production is mainly based on fattening weaned young cattle imported from abroad. The unavoidable long-distance transport represents an important stress factor for young animals, almost always combined with other stressors such as mixing (both in the markets or collection centres and in the arrival fattening units), creation of new hierarchy and adaptation to the new fattening facilities and nutritional management. Furthermore, some common medical procedures done after the arrival in not always suitable structures, such as vaccination and anti-parasites treatments, can represent another stressful situation due to the closed interactions with humans[1,2]. All these factors, along with many others, promote immunosuppression. In fact, stress has been demonstrated to affect the release of glucocorticoids that stimulate or inhibit, depending on the length of exposure, nearly all components of the innate immune response[3,4]. Stress related hormones, such as catecholamines and glucocorticoids, can generate an acute phase response (APR) similar to that which occurs when an animal reacts to an invading pathogen or tissue injury and trauma[5,6]. Activation of the innate immune system and APR results in several responses that include fever, metabolic adaptations and changes in behaviour. This reaction is also connected with a reduction in dry matter intake and growth to feed ratio, resulting in a lower production and efficiency[7,8]. Furthermore, during mixing and combining of animals from different origins, cattle are exposed to many different pathogens. This factor, combined with the lower immune function, due to stress action on the immune system, can lead to a massive pathogen colonization and proliferation, and cause various pathologies. Bovine respiratory disease (BRD) is currently the most common disease in beef cattle production world-wide. Besides being one the highest cause of morbidity and mortality in the beef cattle farming in the first weeks after arrival to fattening units, it is also associated in an overall reduction of productivity during the hole productive cycle[9,10]. In case of BRD, animals often show poor growth performance that can be reflected in a reduction in the average daily gain over the entire breeding period of nearly 150-200 g/day, with peaks of over 300 g in the event of multiple relapses[1]. Carcass quality can also be affect-

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ed: 5% lower hot weight, worse conformation and fattening score are reported[11]. BRD management is normally based on antimicrobials treatment of clinically affected animals and very often on preventive mass treatments considering the health status of the incoming batches of animals[12]. Due to the economic impact of the complex disease, the use of antibiotics for preventive purposes, has therefore found in the past a justification not only in animal welfare but also for the benefit of the farmer. Actually, the increase in the antimicrobial resistance infections in humans requires a different approach to the antimicrobial's use in farm animals, especially in terms of prophylaxis and mass treatments[13]. In this terms, alternative strategies to manage BRD lowering the antibiotic usage have to be explored and verified.
As a therapeutic support for the antibiotic treatment, nonsteroidal anti-inflammatory drugs (NSAIDs), are very frequently administered for their well-known positive effects[12]. In a modern approach to BRD management in beef cattle farms, NSAIDs can help animals to recover quickly from transportation stress and shipping fever[14,15]. Administration of flunixin meglumine to steers before a 24-h road transport and at feedlot arrival alleviated the resultant APR, reflecting a lower effect of stress on the immune function[16]. Another effective anti-inflammatory drug is meloxicam, a member of the oxicam class of NSAIDs. It inhibits the synthesis of prostaglandins and has anti-inflammatory, anti-exudative, analgesic and antipyretic properties[17,18].
The aim of the present field trial was to evaluate the effectiveness on health and growth of meloxicam administration to newly received BRD high risk beef cattle in comparison to preventive antibiotic mass treatment.

MATERIALS AND METHODS

A total of 605 intact male beef cattle of Charolaise and crossbreeds breed imported from France were enrolled in the trial. The study was conducted at a commercial fattening operation located in the north of Italy. Animals enrolled were considered to be at high risk of developing BRD based on the system proposed by Sgoifo Rossi et. al, 2013[1]. Animals were processed within 4 hours from the arrival to the fattening facility. Cattle were individually weighted and treated for internal and external parasites with ivermectin administered subcutaneously at 200 μg/kg of body weight. Animals were vaccinated against bovine herpesvirus-1, parainfluenza-3, bovine respiratory syncytial virus and bovine viral diarrhea. The cattle of the same batch (arrived on the same truck) were randomly divided into two experimental groups. Animal of control group (Ab) were treated with long acting oxytetracycline (Duphaciclina 300 LA, Boehringer Ingelheim; 30 mg oxytetracycline/kg LW) while those of treatment group (M) were treated with meloxicam (Metacam 40 mg/ml, Boehringer Ingelheim; 0,5 mg of meloxicam/kg LW). Animal BW obtained at processing was used for dose determination. At processing, individual rectal body temperature was recorded. Animals were then housed in straw litter pens, with ad libitum access to fresh water and feed formulated to meet or exceed the requirements of the National Research Council for maintenance and expected growth.
From day 0 to day 180 post-enrolment, general health evaluations were conducted in the pens through routine facility health procedures performed by the veterinary and qualified animal health care personnel who were not present during the treatment administration (blinded). Morbid animals were examined and diagnosed as having BRD or other health problems. BRD new events were recorded as first pull. Sick animals received concurrent medications according to the facility procedures and returned to their study pens or moved to infirmary while necessary. Blood samples were collected from 20 cattle for experimental group at processing and at study day 30 to evaluate some serum health indicators. As indicator of specific immunity modulation was evaluated the titration of BHV-1 vaccination antibodies with BHV-1 serum neutralization test[19]. Non-specific immunity was evaluated with the analysis of the serum bactericidal activity[20] and γ-interferon[21]. The evaluation of acute phase proteins as haptoglobin (HPT)[22], lipopolysaccharide binding protein (LBP)[23] and Interleukin 6[24] was performed to check the cattle inflammatory status.
Other than at processing, individual weight was collected at study days 30, 100 and 180 to evaluate the average daily gain. Statistical analyses were performed using SAS 9.4.

RESULTS AND DISCUSSIONS

Cattle at arrival experienced transport stress since their average body temperature was higher than physiological threshold of 39/39,5°C. In average 20,2% of the animals presented body temperature higher than 40,0°C accordingly to transport fever (Ab=19,6%; M=20.7%). Only 6 of those animals presented symptoms related to mild BRD at arrival (3 in the Ab group and 3 in M group). No statistical differences were found between groups.
Animal health conditions during the overall fattening cycle are reported in Table 1. BRD first pull incidence was tending lower in M group. Same trend has also been observed for incidence of those animals treated twice for respiratory disease relapse. The incidence of chronic cases, intended as animals that receive three or more treatments, was not different between groups. Considering the overall treatments for respiratory disease as the sum of first pull, relapse and chronic, the administration of meloxicam at arrival, led to a reduction of antimicrobial drugs use in the present experimental condition.

Table 1 - Health conditions.

	Bovine Respiratory Disease (BRD)					
	First pull, % (n)	Relapse, % (n)	Chronic, % (n)	Total treatments, % (n)	Hospitalized, % (n)	Premature loss, % (n)
Ab	27,9 (84)	6,0 (18)	2,3 (7)	36,2 (109)	1,0 (3)	2,0 (6)
M	26,0 (79)	3,9 (12)	1,0 (3)	30,9 (94)	1,0 (3)	1,3 (4)
P	<0.1	<0.1	ns	<0.05	ns	ns

Table 2 - Blood health indicators.

	Ab	M	*P*
BHV-1 serum neutralization, log (titration)			
d_0	0,00	0,00	ns
d_{30}	0,44	0,96	<0.05
Serum bactericidal activity, %			
d_0	69,4	67,2	ns
d_{30}	77,6	83,8	<0.05
γ-Interferon, pg/ml			
d_0	16,7	17,5	ns
d_{30}	14,2	13,7	ns
Haptoglobin, mg/mL			
d_0	0,56	0,62	ns
d_{30}	0,38	0,17	<0.1
LBP, ng/mL			
d_0	7.295,17	7.010,11	ns
d_{30}	6.342,15	6.404,14	ns
IL6, ng/mL			
d_0	0,082	0,076	ns
d_{30}	0,079	0,091	ns

No differences regarding hospitalized animals and premature loss for BRD problems were detected.
The chronological onset of BRD first pull and relapse events is graphically reported in Figure 1. As a probable consequence of effectiveness of preventive antibiotic mass treatment, the BRD cases were lower in the Ab during the first days after arrival. Conversely, in M group more cases appear immediately after arrival in the fattening unit. However, considering the overall adaptation period, the overall daily incidence was lower in M group respect to Ab as a consequence of a better immune status.
Indeed, as reported in Table 2, the meloxicam administration statistically improved the post vaccination antibody production against BHV-1 and the ability of serum immune components to counter mild infections. In fact, at day 30, the serum neutralization and the serum bactericidal activity resulted statistically higher in M group. In particular, regarding serum bactericidal activity, the animal of Ab group did not reach the "healthy" threshold of 80% after 30 days of adaptation respect to meloxicam treated animals that appeared to be even more stressed at arrival. Some tendency for pro-inflammatory status were also detected, as demonstrated by the tending lower levels of haptoglobin observed at day 30 in the M group. The lower levels reached showed a better recovery from transport stress in treated animals. This results are according with those of Guarnieri Filho et al., (2014)[17]. The researcher found out that the administration of meloxicam at loading, unloading and between day 2 and 7 after the arrival reduced the negative effects of stress and the entity of this stress, improving health status. Also, the ceruloplasmin response, chosen as pro-inflammatory status indicator, was found to be lowered by meloxicam administration, a sign of a lower production of proteins and metabolites implicated in APR[17]. Because of this efficacy, NSAIDs administration can booster the effect of the vaccination against respiratory disease. In fact, vaccination is a stressful situation, where the production of APR is high[18].
As reported in Table 3, animals treated at arrival with meloxicam showed a tending better weight at the end of the adaptation period and, consequently a better average daily gain during that period. This result is likely a consequence of a better health status of treated animals respect to controls. Conversely, no difference in the overall ADG were detected. This result disagrees with those of Guarnieri Filho et al. (2014)[17] where animals treated with meloxicam shown a better average daily gain respect to controls. The experimental condition was however different since the controls did not receive the antibiotic mass treatment, and meloxicam was administered to the animal not only at the arrival to the fattening unit but even before the transport. Comparing to similar study designs in very similar farming condition, the growth results are consistent since in the event of higher BRD incidence, the growth deficit accused in the first weeks can sometimes be recovered in the following months[25,26].

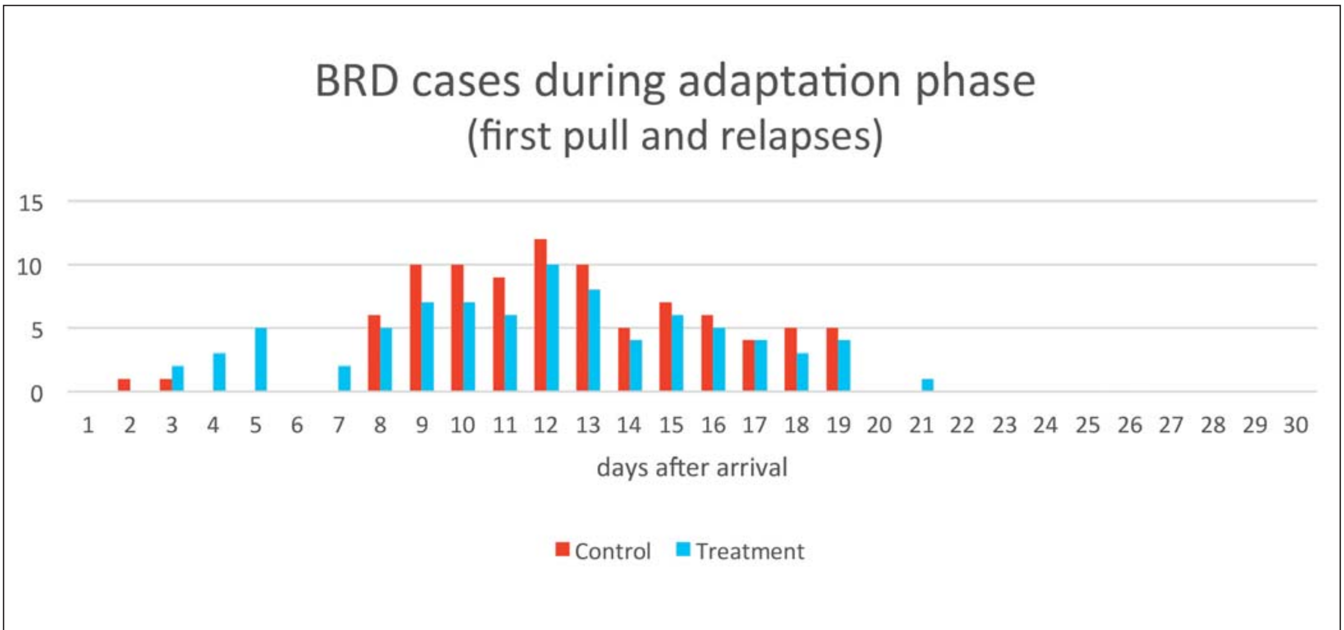

Figure 1 - BRD cases.

Table 3 - Growth performance.

	n°	Weight, kg				ADG, kg/d			
		d_0	d_{30}	d_{100}	d_{180}	0-30	30-100	100-180	0-180
Ab	301	394,48	432,88	538,58	652,18	1,280	1,510	1,420	1,432
M	304	403,51	444,61	550,17	664,41	1,370	1,508	1,428	1,449
P		ns	<0.1	ns	ns	<0.1	ns	ns	ns

CONCLUSIONS

In the present study conditions, the administration of meloxicam at arrival in the fattening unit to BRD high risky beef cattle, led to a good management of the respiratory disease. Incidence of first pull resulted similar to that among animals that received an antibiotic mass treatment. The overall treatments result even lower during the adaptation phase as a consequence of a better recover from transport stress related reduction of immune response and enhancement of acute phase response. This strategy can be effective in a modern approach to manage the prevention of respiratory disease reducing the antibiotic administration as requested by the world health organizations and accordingly with animal welfare and consumers demand.

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