Impact of bovine respiratory disease on lung lesions, slaughter performance and antimicrobial usage in French beef cattle finished in North-Eastern Italy

Claudia Caucci, Guido Di Martino, Eliana Schiavon, Angelica Garbo, Elena Soranzo, Luca Tripepi, Anna Lisa Stefani, Laura Gagliazzo and Lebana Bonfanti

Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Italy

ABSTRACT

Bovine respiratory disease (BRD) is a major health concern in beef cattle, with several pathogens and environmental risk factors being involved. Clinical signs of BRD may remain undetected, preventing proper diagnosis. Yet, BRD-associated lung lesions can be detected at slaughter, providing a more sensitive way to estimate BRD prevalence, as these lesions are present also in subclinically affected animals. In April–August 2016, the lungs of 518 Charolaise males from 8 farms in North-Eastern Italy were scored at slaughter based on the presence of pleural adhesions and the percentage of affected parenchyma. Moreover, individual antimicrobial dosages were acquired from the farm registries. 64% of animals had at least one lung lesion; a negative association between lung lesions and carcass weight was found. No association between lung lesions and antimicrobial use was identified. The appropriateness of each antimicrobial treatment was evaluated based on the ratio between each actual daily dose used and the correspondent defined daily dose available in the Summary of Product Characteristics (SPC). Three methods based on different estimation of live-weight-at-treatment were applied and provided significantly different results for some antimicrobial classes. Aminoglycosides and high-priority critical antimicrobials like macrolides were those most frequently administered (20% and 42% of treatments, respectively). Evaluation of dosage appropriateness showed that aminoglycosides were administered properly in 60–75% of treatments, while macrolides were underdosed in 30–60% of treatments. In conclusion, this study shows a high prevalence of BRD-associated lung lesions at slaughter associated with carcass weight, and that antimicrobial use is frequently inconsistent with recommended doses.

ARTICLE HISTORY

Received 21 August 2017
Revised 7 December 2017
Accepted 7 December 2017

KEYWORDS

Beef cattle; BRD; antimicrobial therapy; lung score; critically important antimicrobials

Introduction

In beef cattle, bovine respiratory disease (BRD) is a highly problematic syndrome, which several aetiological agents, management- and environment-related risk factors can contribute to (Edwards 2010). Clinical signs of BRD include depression, decreased feed intake leading to reduced growth, breathing difficulty, fever, nasal and lachrymal discharges. BRD is the main cause of economic and productivity losses in beef cattle farming (Buchanan et al. 2016). The economic burden of BRD in beef cattle is mainly due to the costs for vaccination, veterinary care and monitoring of affected animals in addition to decreased weight gain (Wittum et al. 1996; Buchanan et al. 2016). For instance, Holland et al. (2010) reported that 20 additional days on feed were required for heifers treated 3 times for BRD to reach similar body weight as untreated animals. While clinical signs of BRD can remain partly undetected, the consequences of BRD in the feedlot can be appreciated by evaluating lung lesions and pleural adhesions at slaughter (Wittum et al. 1996; Schneider et al. 2009). Indeed, Schneider et al. (2009) reported a prevalence of BRD clinical signs of 8.17% in an American feedlot, whereas lung lesions at the time of slaughtering of these same animals revealed a prevalence of over 60%. Furthermore, Wittum et al. (1996) reported that 72% of 469 steers had at least one lung lesion, although only 35% had been treated for BRD in life. However, lung lesion scoring does not enable to attribute BRD specifically to the finishing period, as animals could have entered the feedlot with pre-existing pulmonary lesions.

Intensive beef cattle farming requires the development of interventions for BRD control, including vaccination and proper antimicrobial usage after prompt
BRD diagnosis, as well as antimicrobial susceptibility testing to minimise the metaphylactic use of antimicrobials and therefore reduce the development of antimicrobial resistance (European Community 2015). To this end, the ratio between the used daily dose (UDD) and the defined animal daily dose (ADD) is a reliable indicator for antimicrobial usage, providing a dimensionless value that quantifies the correctness of antimicrobial dosage and can be adopted to compare usage patterns for different antimicrobial classes. UDD/ADD ratios less than 0.8 and greater than 1.2 are often considered as indicative of underdosing and overdosing, respectively (Timmermann et al. 2006; Persoons et al. 2012).

**Material and methods**

In this study, we estimated BRD prevalence in French beef cattle by scoring lung lesions at slaughter to examine their potential associations with production parameters and antimicrobial usage. Additionally, antimicrobial treatments on farm were evaluated using the UDD/ADD ratio.

The sample consisted of 518 Charolaise males fattened in eight farms in North-Eastern Italy that were slaughtered in April–August 2016. Animals had been imported from France at 11 months of age and finished up to 16 months. Farms were within the same integrated production chain, which provided the same feeding, vaccination protocols, management and veterinary care. All individual dosages of antimicrobial treatments for major health conditions (respiratory, articular or enteric) were obtained from the farm registries. Data regarding carcass weight and SEUROP classification (Superior, Excellent, Very good, Good, Fair, Poor) (European Community 2006) were obtained from the slaughterhouse registry.

Evaluation of lung lesions was based on the scoring of three lung areas: the cranial part of the cranial right lobe, the caudal part of the cranial right lobe, and the cranial lobe of the left lung (Thompson et al. 2006). The evaluation criteria were: (1) the percentage area of affected parenchyma and (2) the presence of pleural adhesions. Specifically, scores were assigned for each above-mentioned area, based on the extension of lesions in the parenchyma on a scale from 0 to 2: 0 = no visible lesion and mild hyperaemia without any consolidation, 1 = consolidation of up to 50% of the lobe, and 2 = consolidation of 51% to 100% of the part. The maximum score per animal for this criterion was 6 (in case of score 2 for all of the three areas). Pleural adhesions for each above-mentioned area were scored on a scale from 0 to 2: 0 = no adhesions or pleuritic, 1 = adhesion or pleuritic present, involving less than 50% of the lung/pleural surface, and 2 = adhesions or pleuritic present, involving more than 50% of the lung/pleural surface. The maximum score per animal for this criterion was 6 (in case of score 2 for all of the three areas). In total, the maximum total score per animal was 12 (in case of score 2 for each part for both the examined criteria). According to data distribution, three classes were defined: class A, animals unaffected by BRD (score 0); class B, animals affected by mild BRD (score 1–2); class C, animals affected by severe BRD (score 3–12).

Antimicrobial usages were analysed as the number of used daily doses (nUDDs) for each antimicrobial class, according to Merle et al. (2014). Therefore, antimicrobial usage was evaluated by UDD/ADD ratio for each treatment. This index is based on an estimate of live weight for each animal as to define the correctness of dosing (UDD/ADD ratio). To this end, three live-weight estimates and instructions from Summary of Product Characteristics (SPCs) were considered. Method 1: a standard live weight was defined as 600 kg, according to Merle et al. (2014); method 2: a standard live weight was defined as 500 kg, according to MARAN (2012); method 3: the actual live weight (AW) at the time of treatment was calculated per each animal, on the basis of the slaughtering weight (SW) and a 1.4 kg average daily gain (ADG, data provided by the producing company): \(AW = SW - (n. \text{ days from treatment to slaughter} \times ADG)\). All procedures and animal care were performed in compliance with Council Regulation (EC) n. 1099/2009 on the protection of animals at the time of killing and Council Regulation (EC) n. 1/2005 on the protection of animals during transport. The experimental procedures did not involve living animals and fell within the routine post-mortem inspection by official veterinarians at the abattoir.

To explore data distribution and to identify possible outliers, a descriptive analysis was performed. As the data were normally distributed, a general linear model (GLM) was used to assess differences in weight and age among the three groups defined by the lung lesion scores (main effect). Post-hoc pairwise comparisons were then performed using Bonferroni’s correction; the individual animal was the statistical unit. The Chi-square test was used to assess associations between the groups of lung lesions and those defined by SEUROP and nUDDs. Chi-square test (or Fisher’s exact test in the case of <5 expected frequencies) were also applied to assess differences among antimicrobial underdosage, proper dosage and overdosage according to the three methods used. Statistical
significance was set to $p < .05$. All statistical analyses were performed using STATA v.12 (Stata Corp. LP, TX).

Results

Results showed a 64% prevalence (95% CI: 60–68%) of BRD (score ≥1) (Table 1). Respiratory conditions were the main reason for antimicrobial treatment (~80% of nUDDs), followed by articular (~19%) and enteric (~1%) ones. Cattle treated more than once received 6.1 ± 3.3 (SD) nUDDs. Associations between lung lesions, carcass weight, age at slaughter, SEUROP class and number of antimicrobial treatments for respiratory conditions are showed in Table 1. Ninety-nine percent of carcasses were categorised as either E or U class, while <1% was categorised as either S or R. However, a significant association between lung lesions and a lower carcass weight was evidenced (Table 1). Table 2 shows that the three methods used led to similar results regarding the percentage of nUDD administered correctly (50–63%), although method 1 presented a significantly higher percentage of underdosed nUDDs.

Discussion

The 64% prevalence of BRD observed in this study is in line with the wide range (43–72%) of reported prevalences in previous studies (Wittum et al. 1996; Thompson et al. 2006).

Particularly, lesions were present in 65% of animals that were never treated for BRD, indicating a frequently occurring subclinical or at least hardly detectable condition. Conversely, 30% of animals treated more than once were affected by a moderate to severe bronchopneumonia (score 3–12), raising some concerns regarding the efficacy/readiness of therapeutic protocols.

Pre-existing lung lesions could not be excluded, as they may have occurred in the herd of

| Table 1. Associations between lung lesion scores (class A = score 0; class B = score between 1 and 2; class C = score higher than 2), carcass weight, age at slaughter, SEUROP class and nUDDs in 518 Charolaise males. |
|---------------------------------------------------------------|
| Lung score class (% and number of animals) | A (36%, n.=186) | B (37%, n.=190) | C (27%, n.=142) | Sig. |
| Carcass weight (kg), mean ± sd | 469.6 ± 33.0* | 459.6 ± 35.3b | 460.4 ± 33.6b | * |
| Slaughter age (weeks), mean ± sd | 73.0 ± 6.6 | 72.7 ± 7.6 | 71.9 ± 5.2 | ns |
| SEUROP class, % cattle (n.) | E | 70.1% (129) | 66.1% (125) | 63.1% (89) | ns |
| | U | 29.9% (55) | 33.9% (64) | 36.9% (52) | ns |
| Antimicrobial treatments, % cattle (n.) | 0 nUDD | 29.6% (55) | 29.5% (56) | 32.4% (46) | ns |
| | 1 nUDD | 34.9% (65) | 31.1% (59) | 37.3% (53) | ns |
| | >1 nUDD | 35.5% (66) | 39.5% (75) | 30.3% (43) | ns |

Different exponent letters indicate significant differences for $p < .05$. nUDDs: number of used daily doses.

*Significant at $p < .05$.

Different exponent letters indicate significant differences for $p < .05$.

Table 2. Percentages of nUDDs in 518 Charolaise males per each antimicrobial class. The correctness of dosage (under/over dosing) was esteemed on the basis of 3 methods.

| Antimicrobial class | Method 1* | Method 2b | Method 3c |
|---------------------|-----------|-----------|-----------|
|                     | % nUDD (n. nUDD) | % over (nUDD) | % under (nUDD) |
|                     | % over (nUDD) | % under (nUDD) |
|                     | % over (nUDD) | % under (nUDD) |
|                     | % over (nUDD) | % under (nUDD) |
| Aminoglycosides      | 20.2 (213) | 0 (0) | 42.7 (91) |
| Beta-Lactams         | 14.1 (149) | 25.5 (38) | 20.8 (31) |
| Cefalosporins 3rd–4th gen. | 0.2 (2) | 0 (0) | 0 (0) |
| Fenicols            | 11.4 (120) | 1.7 (2) | 62.5 (75) |
| Fluoroquinolones    | 6.7 (71) | 0 | 14.1 (10) |
| Lincosamides        | 0.6 (6) | 0 | 0 |
| Macrolides          | 42.1 (444) | 0 | 59.5 (264) |
| Sulfonamides        | 1.3 (14) | 21.4 (3) | 0 |
| Tetracyclines       | 3.4 (36) | 0 | 19.4 (7) |

*Significant at $p < .05$. **Significant at $p < .01$. ***Significant at $p < .001$. nUDDs: number of used daily doses.

*No not significant.

*No tests were calculated for cephalosporins and lincosamides, due, respectively, to insufficient variability and to accordance of results.

*Assumed live weight of 600 kg (Merle et al. 2014).

*The live weight was calculated for each animal.

Highest Priority Critically Important Antimicrobials (WHO 2017).

Chi-square test for the difference between overdosage and proper dosage. No tests were calculated for overdosage because the number of results was <5%.

Chi-square test for the difference between underdosage and proper dosage. No tests were calculated for underdosage because the number of results was <5%.
origin or during transportation, which are not unusual in newly received beef cattle (Sgoifo Rossi et al. 2013).

No significant association between nUDDs and lung lesions was found, similar to Holland et al. (2010). The significant association observed between lung lesions and lower carcass weight stresses the importance of managing BRD to reduce economic losses and improve growth rate, as also pointed out by others (Gardner et al. 1999).

As regard the three methods for the evaluation of the antimicrobial use, method 1 provided slightly different results regarding the evaluation of underdosed nUDDs, possibly due to an overestimation of the weight at treatment (600 kg). Considering a standard weight of 600 kg for beef cattle, also Merle et al. (2014) found antimicrobial treatments to be often below the recommended doses (~60% of all nUDDs). Similar to Merle et al. (2014), the three methods revealed an underdosage of macrolides (30–60% of nUDDs) and folic acids (48–63%). Aminoglycosides were administered properly in 57–75% of nUDDs and a correct dosage for tetracyclines was also determined (81–91%), whereas Merle et al. (2014) reported in Germany an underdosage and overdosage, respectively.

Highest Priority Critically Important Antimicrobials (CIA) (WHO 2017), such as macrolides, were more frequently administered (42% of nUDDs) than what previously reported (Merle et al. 2014, reported a usage of ~6% of nUDDs). Fluoroquinolones constituted 7% of the total treatments, whereas Merle et al. (2014) reported a usage of ~2.5%. These remarkable differences should move towards a more responsible use of CIA, in order to preserve for the future as much as possible the effectiveness of antibiotics that are crucial both for animal and human health.

Conclusions
This study shows a high prevalence of BRD-related lung lesions associated with lower slaughter performances, but not with the number of administered antimicrobial treatments. Yet, respiratory conditions in these animals were the main reported cause of antimicrobial usage, which was often inconsistent with the recommended dosages. Taken together, these results suggest the need for more rational and targeted BRD treatments (e.g. based on clinical diagnoses and antimicrobial susceptibility testing). Narrow-spectrum antimicrobials should be the first choice, while broad-spectrum ones, combinations and CIA should be avoided or reduced. Results also highlights that methods currently available for estimating the appropriateness of antimicrobial treatment need to be taken with caution, given that beef cattle are often treated at a different weight than the average standard defined.

Disclosure statement
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

Funding
This work was funded by Regione del Veneto “Farmacogenetica, salute e benessere animale: possibili effetti sulla qualita delle carni bovine venete e sulla sicurezza del consumatore” [DGR 2080/2015].

References
Buchanan JW, Mac Neil MD, Raymond RC, McClain AR, Van Eenennaam AL. 2016. Rapid Communication: Variance component estimates for Charolais-sired fed cattle and relative economic impact of bovine respiratory disease. J Anim Sci. 94:5456–5460.
European Community (EC). 2006. Council Regulation No 1183/2006 of 24 July 2006 concerning the Community scale for the classification of carcasses of adult bovine animals (codified version). Off Jour Eur Comm. 214.
European Community (EC). 2015. Commission Notice 2015/C 299/04 of 11 September 2015. Guidelines for the prudent use of antimicrobials in veterinary medicine. Off Jour Eur Un. C299:7–26.
Edwards TA. 2010. Control methods for bovine respiratory disease for feedlot cattle. Vet Clin North Am Food Anim Pract. 26:273–284.
Gardner BA, Dolezal HG, Bryant LK, Owens FN, Smith RA. 1999. Health of finishing steers: effects on performance, carcass traits, and meat tenderness. J Anim Sci. 77:3168–3175.
Holland BP, Burciaga-Robles LO, Van Overbeke DL, Shook JN, Step DL, Richards CJ, Krehbiel CR. 2010. Effect of bovine respiratory disease during preconditioning on subsequent feedlot performance, carcass characteristics, and beef attributes. J Anim Sci. 88:2486–2499.
MARAN. 2012. Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands. Wageningen, Central Veterinary Institute, Agricultural Economics Research Institute. http://www.maran.wur.nl.
Merle R, Robanus M, Heger-Graevenhorst C, Mollenhauer Y, Hajek P, Käsböhrer A, Honscha W, Kreienbrock L. 2014. Feasibility study of veterinary antibiotic consumption in Germany-comparison of ADDs and UDDs by animal production type, antimicrobial class and indication. BMC Vet Res. 10:7.
Persoons D, Dewulf J, Smet A, Herman L, Heyndrickx M, Martel A, Boudewijn C, Butaye P, Haesebrouck F. 2012. Antimicrobial use in Belgian broiler production. Prev Vet Med. 105:320–325.
Schneider MJ, Tait RG, Busby WD, Reecy JM. 2009. An evaluation of bovine respiratory disease complex in feedlot cattle: Impact on performance and carcass traits using...
treatment records and lung lesion scores. J Anim Sci. 87:1821–1827.
Sgoifo Rossi CA, Compiani R, Baldi G, Bonfanti M. 2013. Determination and assessment of BRD risk factors in newly received beef cattle. Lar Anim Rev. 19:65–72.
Thompson PN, Stone A, Schultheiss WA. 2006. Use of treatment records and lung lesion scoring to estimate the effect of respiratory disease on growth during early and late finishing periods in South African feedlot cattle. J Anim Sci. 84:488–498.
Timmermann T, Dewulf J, Catry B, Feyen B, Opsomer G, de Kruijff A, Maes D. 2006. Quantification and evaluation of antimicrobial drug use in group treatments for fattening pigs in Belgium. Prev Vet Med. 74:251–263.
World Health Organisation (WHO). 2017. Critically important antimicrobials for human medicine, 5th revision. Geneva, Switzerland. http://www.who.int/foodsafety/publications/antimicrobials-fifth/en/
Wittum TE, Woollen NE, Perino LJ, Littledike ET. 1996. Relationships among treatment for respiratory tract disease, pulmonary lesions evident at slaughter and rate of weight gain in feedlot cattle. J Am Vet Med Assoc. 209:814–818.