Monitoring of antimicrobial use and the association with cattle health parameters in the Netherlands

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Abstract

In 2008, an agreement was reached in the Netherlands to reduce antimicrobial use (AMU) in livestock. A reduction of AMU may require management adjustments from the farmer to maintain a good level of animal health. The aim of this study was to monitor AMU in time and to determine i) associations between AMU, herd characteristics and environmental factors and ii) associations between AMU and cattle health parameters in the Netherlands.

Data on cattle health parameters, herd characteristics, environmental factors and AMU were available for all Dutch cattle herds from January 2011 to July 2014. All data were combined and four different cattle herd types were distinguished: dairy, small-scale, young stock rearing and suckler herds. GEE population-averaged regression models accounting for repeated measurements in time on herd level were used for analysis.

This study showed that, although the average AMU in Dutch cattle herds is low, a large variation exists within and between cattle herd types. The median $DDDA_F$ decreased in time for dairy herds and remained stable over time for the other three cattle herd types. Relevant associations between AMU and herd characteristics, environmental factors and cattle health parameters were found. These included herd size, introduction of cattle on-farm, milk yield, meat price, mortality, BTM SCC, having >25% cows with postpartum high SCC, no. inseminations per cow and expected time between calvings.

By monitoring these data, both the developments in AMU in time and the impact of the (changing) level of AMU on cattle health can be assessed.

Keywords: *antimicrobial use, monitoring, routinely available data, cattle health*

Introduction

Worldwide, the emergence of antimicrobial resistance has become a major problem and has resulted in an increased awareness regarding the use of antimicrobials (1,2,3). Subsequently, it has become an important issue in many countries. To reduce and prevent antimicrobial resistance in both veterinary and human medicine, an agreement was reached in December 2008 to reduce antimicrobial use (AMU) in the Dutch cattle, veal, pig and poultry industry with 50% in 2012 and with 70% in 2017 relative to the use in 2009. In 2012, the reduction of AMU of 50% was achieved. A reduction of AMU may require management adjustments from the farmer to maintain a good level of animal health.

Many parameters providing information about cattle such as amongst others mortality, herd size, milk yield and meat prices are uniformly registered for all Dutch cattle herds in central databases. In addition, since 2012 all antimicrobials in cattle, which are supplied to Dutch cattle herds (proxy for AMU) are registered in a central database. The cattle health data that are routinely available in central databases are provided to GD Animal Health (GD) every quarter of the year for routinely cattle health surveillance (4). Combining data concerning antimicrobial supplies with cattle health data enables the possibility to determine i) associations between AMU, herd characteristics and environmental factors and ii) associations between AMU and cattle health parameters. In this study, the results of this assessment are presented.

Materials and methods

Data on cattle health parameters (such as mortality and BTM SCC), herd characteristics (such as herd size and milk yield), environmental factors (such as meat price) and antimicrobial supplies were compiled from different organisations within the Dutch cattle industry. For this study, the data were available for all Dutch cattle herds from January 2011 to July 2014 and were aggregated on herd and quarterly level (4).

Antimicrobial use was represented by calculation of the annually moving average of the Animal Daily Dose of AMU at herd level ($DDDA_F$) for each quarter of the year. This was according the Standard Operating Procedures (SOP) of the Dutch Veterinary Medicines Authority (SDa). It was assumed that all supplied antimicrobials were actually used to treat animals. In addition, the $DDDA_F$ for three different application methods, oral AMU ($DDDA_{F,oral}$), dry cow therapy AMU ($DDDA_{F,dry}$) and intramammary AMU ($DDDA_{F,mast}$), were assessed.

Four different herd types were distinguished based on milk delivery, herd size, introduction of cattle on farm and age of the animals present on-farm: i) Dairy, ii) Small-scale iii) Young stock rearing and iv) Suckler herds (4).

The associations between AMU and herd characteristics and environmental factors were analysed with a GEE population-averaged logistic regression model accounting for repeated measurements in time on herd level. Based on the $DDDA_F$, herds were categorised as herds with below or above median $DDDA_F$ using 2013 as reference. This categorisation of $DDDA_F$ was used as dependent variable in the models. Herd characteristics such as region, herd size, introduction of cattle on farm, milk yield and replacement rate and environmental factors such as meat and milk prices were included as independent variables.

Second, each of the available cattle health parameters (such as cattle mortality, (non-)eartagged mortality, trade to other herds, BTM SCC, SCM prevalence, SCM incidence, herds >25% cows with postpartum high SCC, no. inseminations per cow, age at first calving and expected time between calvings) was used as dependent variable in a GEE population- averaged linear, log-linear or logistic regression model. The $DDDA_F$ was included as independent variable and herd characteristics and environmental factors were included as possible confounders. Herds were grouped into four categories based on the $DDDA_F$ (10% with lowest level, 40% with lower level, 40% with higher level and 10% with highest level). Model fit was evaluated using the quasi-likelihood under the independent model criterion (QIC) (6) and the amount of variance explained by the model (pseudo R^2). The results are presented either by odds ratios (OR), incidence rate ratios (IRR) or estimates conditional to the distribution of the dependent variable. Statistical analyses were performed using STATA/SE version 14 software (5).

Because census data were modelled, only associations that were statistically significant (p-value ≤0.01) and biologically relevant are presented. Relevance was determined in accordance with cattle health experts and was set at an OR or IRR that is 1.5 times higher or lower compared to the reference category (usually the population mean). For normally distributed parameters such as BTM SCC, no. of inseminations per cow and expected time between calvings the cut-off value was set at ±10,000 cells/mL, ±0.05 inseminations and ±2 days, respectively (4).

Results

The results showed that the median $DDDA_F$ in the study period was 0 in small-scale and in young stock rearing herds (IQR: 0.0-0.59 and 0.0-0.51, respectively), 2.8 (IQR: 1.79-3.70) in dairy herds and 0.4 (IQR: 0.02-1.35) in suckler cow herds. The median $DDDA_F$ decreased with 0.05 per quarter in dairy herds and remained stable over time for the other three herd types.

Herd size, introduction of cattle on farm and meat price were positively associated with a higher than median $DDDA_F$ in dairy and suckler cow herds (Table 1). Milk yield was positively associated with a higher than median $DDDA_F$ in dairy herds. Regional differences in $DDDA_F$ were found for dairy, suckler and small-scale herds (results not shown).

Table 1. Associations between herd characteristics, environmental factors and $DDDA_F$ in dairy (N=17,747) and suckler herds (N=4,948) as result of GEE population-averaged logistic regression models.

Herd characteristic/ environmental factor	Dairy herds (cut-off: 2.8)	Suckler herds (cut-off: 0.3)
	OR	OR
	(95% CI)	(95% CI)
Herd size		
Population mean	**Reference**	**Reference**
10% smallest herds[1]	0.74[2] (0.72-0.77)	1.03 (0.97-1.09)
40% smaller herds	0.88 (0.87-0.90)	0.77 (0.74-0.80)
40% larger herds	1.03 (1.01-1.06)	0.82 (0.79-0.85)
10% largest herds	**1.47** (1.43-1.52)	**1.55** (1.46-1.65)
Purchase of cattle		
0 animals in last 12 months	**Reference**	**Reference**
1-2 animals in last 12 months	0.98 (0.94-1.01)	0.98 (0.92-1.04)
>2 animals in last 12 months	**1.46** (1.42-1.51)	**1.47** (1.39-1.55)
Milk yield		
Population mean	**Reference**	**Not applicable**
10% lowest[3]	**0.30** (0.29-0.31)	
40% lower	0.83 (0.81-0.85)	
40% higher	**1.60** (1.57-1.64)	
40% highest	**2.52** (2.43-2.61)	
Meat price (per euro/kg)	**1.49** (1.33-1.66)	**3.06** (2.30-4.06)

[1]Dairy herds: 10% smallest ≤40 cows >2 years; 40% smaller: 41-83 cows >2 years; 40% larger: 84-155 cows >2 years; 10% largest: ≥156 cows >2 years. Suckler herds: 10% smallest ≤ 9 cows >2 years; 40% smaller: 10-19 cows >2 years; 40% larger: 20-66 cows >2 years; 10% largest: ≥67 cows >2 years.
[2]Only herd characteristics and environmental factors for which relevant associations were found, i.e. statistically significant at p≤0.01 and OR≤0.67 or OR≥1.5, are shown (location not shown). Relevant associations are shown in bold.
[3]Dairy herds: 10% lowest: Net Profit (NP) ≤1,872 euro; 40% lowest: NP 1,873-2,325 euro; 40% higher: NP 2,326-2,673 euro; 10% highest: NP ≥2,674 euro.

The $DDDA_F$ was positively associated with cattle mortality in young stock rearing (OR 2.13 (95% CI: 1.76-2.58)) and small-scale herds (OR 1.76 (95% CI: 1.63-1.91)).

In dairy herds, a higher $DDDA_F$ was associated with a lower BTM SCC and lower odds of having >25% cows with postpartum high SCC (Table 2). A higher number of inseminations per cow was associated with a higher $DDDA_F$. A negative association was found between the expected time between calvings and the $DDDA_F$ in dairy herds (Table 3).

Table 2. Associations between the level of AMU on dairy herds (N=17,747) and udder health parameters as result of GEE population-averaged linear or logistic regression models. Associations are expressed as coefficient or Odds Ratio (OR) with 95% confidence interval (95% CI).

	Reproductive performance parameter	
Level of AMU	**BTM SCC** (*10^3c/mL)	**Herds >25% cows with postpartum high SCC** (OR)
Population mean	**Reference**	**Reference**
10% lowest[1]	**12.68** (11.90-13.46)	**1.47** (1.40-1.54)
40% lower	1.20 (0.67-1.74)	1.15 (1.11-1.19)
40% highest	-8.71 (-9.24- -8.17)	0.80 (0.77-0.83)
10% highest	-5.18 (-5.99- -4.37)	0.75 (0.70-0.79)

[1]10% lowest: $DDDA_{F,mast}$ ≤0.34; 40% lowest: $DDDA_{F,mast}$ 0.35-1.77; 40% higher: $DDDA_{F,mast}$ 1.78-2.99; 10% highest: $DDDA_{F,mast}$ ≥3.0.

Table 3. Associations between the level of AMU on dairy herds (N=17,747) and reproductive performance parameters as result of GEE population-averaged linear regression models. Associations are expressed as coefficient with 95% confidence interval (95% CI).

	Reproductive performance parameter	
Level of AMU	**Inseminations/cow** (no.)	**Expected time between calvings** (days)
Population mean	**Reference**	**Reference**
10% lowest	**-0.05** (-0.05- -0.04)	**4.18** (3.66-4.69)
40% lower	-0.02 (-0.02- -0.01)	1.26 (0.96-1.57)
40% highest	0.01 (0.01-0.02)	**-2.40** (-2.70- -2.10)
10% highest	**0.05** (0.04-0.05)	**-3.04** (-3.49- -2.60)

[1]10% lowest: DDDAF,>2 years ≤0.94; 40% lowest: DDDAF, >2 years 0.95-3.24; 40% higher: DDDAF, >2 years 3.25-5.44; 10% highest: DDDAF, >2 years ≥5.45.

Discussion

This study showed that AMU in Dutch cattle herds is low but with a large variation within and between cattle herd types. Several relevant associations between AMU, herd characteristics and cattle health parameters were found.

In dairy herds, a negative association was found between the level of AMU and BTM SCC, having >25% cows with postpartum high SCC and expected time between calvings. In addition, a positive association was found between the no. of inseminations per cow and the level of AMU. This may be due to different herd management practices between dairy herds with high and low AMU.

The level of AMU was positively associated with cattle mortality in young stock rearing and small-scale herds and may indicate that herds with a higher level of AMU have decreased cattle health with a higher mortality risk.

The level of AMU in a herd was determined on antimicrobial supplies to the individual herd. However, this might lead to an overestimation of AMU, because not the whole bottle might be used completely. Provided that this is true for all herds and herd types, this possible overestimation will not affect the associations that were found nor the conclusions.

When the $DDDA_F$ and associations with herd characteristics, environmental factors and cattle health parameters are regularly determined, AMU can be monitored in time and the impact of a changing level of AMU on cattle health can be assessed.

Because there is a relation between the AMU and development of antibiotic resistance (6), it is recommended to investigate herds with high AMU more closely and to develop measures to reduce antibiotic use in these herds.

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