Antimicrobial use in Belgian broiler production

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A B S T R A C T

The use of antimicrobials in production animals has become a worldwide concern in the face of rising resistance levels in commensal, pathogenic and zoonotic bacteria. In the years 2007 and 2008 antimicrobial consumption records were collected during two non-consecutive production cycles in 32 randomly selected Belgian broiler farms. Antimicrobials were used in 48 of the 64 monitored production cycles, 7 farms did not use any antimicrobials in both production cycles, 2 farms only administered antimicrobials in one of the two production cycles, the other 23 farms applied antimicrobial treatment in both production cycles. For the quantification of antimicrobial drug use, the treatment incidences (TI) based on the defined daily doses (the dose as it should be applied: DDD) and used daily doses (the actual dose applied: UDD) were calculated. A mean antimicrobial treatment incidence per 1000 animals of 131.8 (standard deviation 126.8) animals treated daily with one DDD and 121.4 (SD 106.7) animals treated daily with one UDD was found. The most frequently used compounds were amoxicillin, tylosin and trimethoprim-sulphonamide with a mean TI/DDD of 37.9, 34.8, and 21.7, respectively. The ratio of the UDD/DDD gives an estimate on correctness of dosing. Tylosin was underdosed in most of the administrations whereas amoxicillin and trimethoprim-sulphonamide were slightly overdosed in the average flock.

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1. Introduction

Although antimicrobial therapy is of essential importance in maintaining animal health, the use of antimicrobials in production animals has become a worldwide concern in the face of rising resistance levels potentially threatening treatment options in both veterinary and human medicines (Bywater, 2004; Prescott, 2008). In 2007, the World Health Organization recommended stopping intensive routine use of antimicrobials in production animals (Collignon et al., 2009). A first step in limiting routine use of antimicrobials has already been taken in 1999, when Europe scheduled a total ban of antimicrobial growth promoters by January 2006. After the ban, the fear in many countries was that therapeutic use would increase and in the end no real progress would be made in reducing antimicrobial consumption. In Sweden a temporarily increase of therapeutic use after the ban was indeed observed, but consumption levels have dropped again to the prior therapeutic level (Grave et al., 2004, 2006; Bengtsson and Wierup, 2006; Phillips, 2007). In Denmark (DANMAP, 2008) and the Netherlands (MARAN,
2007) on the contrary, the ban has been followed by a steady increase in consumption of therapeutic veterinary antimicrobial agents.

Pig, veal, and poultry production are largely making use of antimicrobials for therapeutic, methaphylactic or prophylactic purposes as a result of their intensive production system that frequently requires the application of mass medication (Catry et al., 2006; Timmerman et al., 2006; Prescott, 2008). In addition, precise dosing, an important aspect of the prudent use of antimicrobials (Mevius et al., 1999), is often more difficult when applying mass medication. A crucial step in the control of emergence and dissemination of antimicrobial resistance is the registration of consumption of antimicrobials (Gyssens, 2001; Mevius et al., 1999). Recently European authorities have issued the obligation for member states to register and report their national veterinary antimicrobial consumption (Anonymous, 2010). Some countries, like Denmark, Sweden, Norway, the Netherlands, Germany and the UK already have an established antimicrobial consumption monitoring program. Others, like Belgium, are currently developing a veterinary antimicrobial consumption monitoring system (www.belvetsac.ugent.be).

The aim of this study was to quantify the level of antimicrobial consumption in Belgian broilers. For this the amounts, indications for use and accuracy of dosing were registered during two non consecutive production cycles in 32 Belgian broiler farms. This study was conducted in parallel with a large scale study on the occurrence of antimicrobial resistance (Persoons et al., 2010).

2. Materials and methods

2.1. Sample design and sampling

From fifty randomly selected Belgian broiler farms holding at least 10,000 birds, 32 (64%) participated in a study on the prevalence of antimicrobial resistance in indicator bacteria (Persoons et al., 2010). The farms were selected from the official list of 730 matching broiler farms (sani- tel) by allocating a random number to all of them and then selecting the fifty smallest numbers. Growers from four farms refused participating in the survey. Five could not be included because they had recently ceased activity or were planning to do so in the near future. The nine other growers could not be contacted after several attempts to do so. The farms were visited twice leaving one production cycle in between unsampled to exclude time or seasonal effects, and for the antimicrobial resistance survey to evaluate whether resistance tended to persist in time (Persoons et al., 2010). The downtime in between visits ranged from 44 to 58 days, with a median of 48 days. The visits all took place in the years 2007 and 2008 each time when the birds were in their fifth week of production, corresponding to the week prior to slaughter. At each visit, individual fecal swabs from 30 conveniently selected broiler chickens were collected from which Escherichia coli and Enterococcus faecium were isolated followed by antimicrobial susceptibility testing as described elsewhere (Persoons et al., 2010). Additionally, data on antimicrobial use in the two sampled production cycles were collected. No farmers declined to have these data recorded.

2.2. Data collection

The antimicrobial use was registered by means of a treatment registration card on which time and duration of administration, product administered, dosage, amount administered, administration route and the person applying the treatment were retrospectively recorded at the end of the two monitored production cycles. To check for the completeness of treatments entered on the card, the farm’s official medication register was consulted. This register consists of all the veterinarian’s prescriptions, needed for every antimicrobial treatment of the birds, and is regularly controlled by the Federal Agency for Safety of the Food Chain. No information on treatments applied in hatchery was available since this information is not routinely provided with the day old chicks. Therefore this could not be included.

Besides the amount of antimicrobial drugs administered, the indications for use were registered. These were categorized into the following 8 possible indications: E. coli sepsis, necrotic enteritis, dysbacteriosis (non-specific bacterial enteritis), respiratory problems, skin or feather diseases, feet problems or arthritis, coccidiosis and general prophylaxis.

2.3. Data analysis

All the data were entered in an Excel spreadsheet (Microsoft corporation, Redmond, Washington, USA). Volumes of antimicrobials administered were converted to mg of active substance per kg live weight. The frequency of use of the different compounds (active substances) used was calculated as the ratio of production cycles where the compound was used to the total number of cycles followed (64).

Quantification of drug use can be done in different ways, using financial or commercial units, or weight indicators (Chaunin et al., 2001). In this study, weight indicators were chosen. The defined daily dose (DDD) is defined as the nationally determined average maintenance dose per day and per kg chicken of a specific drug (Jensen et al., 2004). For poultry, the DDD (Grave et al., 2004) was estimated based on the dosages mentioned in the Belgian Compendium on Veterinary Medicines (Anonymous, 2008a,b) and on the drug’s instruction leaflet.

The used daily dose (UDD) describes the amount of active substance actually administered to the animals in mg/kg. The UDD was calculated by dividing the amount of antimicrobial compound administered (mg) by the number of broilers times the average weight at treatment to define a standard treated bird (Timmerman et al., 2006). The UDD/DDD ratios were calculated as a way to assess the correctness of dosage. Ratios between 0.8 and 1.2 were considered as correct dosing (Timmerman et al., 2006). Values less than 0.8 and greater than 1.2 were considered to be underdosing and overdosing, respectively.

The frequency of treatments can be quantified by calculating treatment incidences (Grave et al., 1999). This
treatment incidence (TI) can be based on the DDD to calculate the treatment incidence as it should be when the prescribed dosing is applied, or based on the UDD, being the treatment incidence as it is in reality. The following formula was used to calculate treatment incidences.

\[
\text{total amount of antimicrobials administered (mg)} = \frac{\text{UDD or DDD (mg/kg)} \times \text{number of days at risk} \times \text{kg chicken}}{1000}
\]

In this equation, the total amount of antimicrobials administered is calculated per compound. The number of days at risk is the time—from in days—a broiler is possibly exposed to one or more treatments: this was set at 42 days, the normal life expectancy of a broiler in Belgium minus one day of minimum withdrawal time. Day zero up until day 41 gives a period of 42 days. The kg chicken was calculated as the number of chickens times their mean weight. This weight at treatment was standardized over the different flocks by dividing the sum of the total weight of the birds at each treatment occasion by the number of birds times the number of treatments (Timmerman et al., 2006), and was estimated at 984 g which was rounded to 1 kg, corresponding to the average weight at treatment that is applied in the Dutch MARAN (Monitoring of Antimicrobial Resistance and Antibiotic usage in Animals in the Netherlands) report (2007). The treatment incidence for chickens is thus defined as the number of chickens per 1000 that is treated daily with one DDD or UDD. To determine whether significant differences exist between the TlUDD and TlDDD, a paired samples t-test was applied using SPSS software (SPSS Inc., Chicago IL, USA). A P value of <0.05 was considered statistically significant.

3. Results

In 48 of the 64 (75%) production cycles that were monitored over the 32 farms, antimicrobial drugs were used. In seven farms no antimicrobials were used in both production cycles. In two farms, antimicrobials were only administered in one of the two monitored production cycles. All treatments were applied via drinking water administration, and were always applied by the farmers themselves, after provision of the drugs by the veterinarian. No discrepancies between the use reported by the farmer and the official medication record were found.

Amoxicillin is the antimicrobial agent that was used most frequently (in 43% of the monitored production cycles), followed by tylosin (30%), trimethoprim-sulphonamide (18%), lincomycin—spectominycin (15%) and enrofloxacin (10%). Doxycycline (8%), lincomycin (7%), tilmicosin (3%), flumequene (2%) and penicillin (2%) were less frequently used compounds.

The average dosage applied on farm, described as the DDD and UDD, is presented in Table 1. From the UDD/DDD ratio it can be seen that only tylosin was usually underdosed, while amoxicillin and trimethoprim-sulphonamide were slightly overdosed. The other compounds were usually dosed within the range of correct dosing (UDD/DDD = 0.8–1.2).

The TlUDD for overall consumption was 121.4, meaning that on average per day 121 chickens out of 1000 were treated with one UDD. Per compound, the mean TlUDD ranged from 1.3 for flumequene up to 36.1 for amoxicillin, with large variations between farms and production cycles (Fig. 1). A comparison of the TlUDD with the TlDDD (Fig. 1) shows that in reality, based on the UDD, a little less chickens were being treated than theoretically expected based on the DDD, namely 131.8 per 1000 chickens at risk a day.

In Fig. 2, the comparisons of the TlUDD for the two monitored production cycles per farm is presented. The TlUDD was identical over the two cycles for 13 out of the 32 farms.

The indications of use for the different compounds registered were necrotic enteritis (84.6%) and dysbacteriosis (15.4%) for amoxicillin use, dysbacteriosis (89%) and feet disorders (11%) for tylosin use, coccidiosis in all cases of trimethoprim-sulphonamide use, respiratory problems for all linco-spectin treatments and E. coli sepsis for enrofloxacin. For applying doxycycline, the main indication was a respiratory problem (75%), next to arthritis (25%), whereas for lincomycin it was dysbacteriosis in all cases, for tilmicosin E. coli sepsis and for flumequene and penicillin necrotic enteritis.

4. Discussion

For the first time in Belgium, antimicrobial consumption was monitored in 32 randomly selected broiler farms, allowing a representative assessment of the Belgian situation. Although initially 50 farms were selected only 32 were included in the study (64%). The reasons for non-inclusion were not all unwillingness to participate. Only four growers refused participating. Five farms were no longer active or were planning to cease activity in the near future, and for the other nine, no further attempts were made contacting them because there was no need for additional farms in the prevalence study (the initial reason of selection). Based on the knowledge of the farms at moment of selection (farm size, region or farm veterinarian), the farms included in the study were similar to the ones not included. Therefore, it is likely that the non inclusion of the non-participating farms did not substantially bias the results. The average farms size of the non-participating farms corresponded to the one of the participating farms. Neither the non-participating farms, neither the participating ones could be allocated to a particular region nor farm veterinarian. For the description of the antimicrobial use, the nine other farms may have been of value, although the range of variation in antimicrobial use seen between farms (Fig. 2) allows believing that a representative image of antimicrobial use in Belgian broiler farms was obtained. To obtain reliable data on antimicrobial drug consumption for the Belgian broiler farms, we chose to use on-farm registration at the respective ends of the two monitored production cycles. Validation of the treatments disclosed by the farmer was done by comparing the data with the farmer’s official medication register. By doing so recall or intervention bias from the farmer could be avoided as much as possible. This way, however, no knowledge on prior use in the hatchery of origin could be gained since no treatment information is provided along with the chicks to the grower. At the time of the farm visits, there was also no reason to assume that the chicks might have already been systematically treated with antibiotics in some hatcheries. Only recently, after the finding of high levels of ceftiofur resistance among broilers (Persoons et al.,
Table 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>UDD (mean)</th>
<th>DDD</th>
<th>Ratio (UDD/DDD)</th>
<th>Total use in kg (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tylosin</td>
<td>88.8</td>
<td>120</td>
<td>0.7</td>
<td>163.3 (56)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>25.3</td>
<td>20</td>
<td>1.3</td>
<td>50.6 (18)</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>16.5</td>
<td>15</td>
<td>1.1</td>
<td>29.0 (10)</td>
</tr>
<tr>
<td>Trim-sulfa</td>
<td>25.3</td>
<td>20</td>
<td>1.3</td>
<td>24.9 (9)</td>
</tr>
<tr>
<td>Tilmicosin</td>
<td>19.2</td>
<td>17.5</td>
<td>1.1</td>
<td>6.3 (2)</td>
</tr>
<tr>
<td>Linco-spec</td>
<td>55.8</td>
<td>50</td>
<td>1.1</td>
<td>5.9 (2)</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>11.5</td>
<td>10</td>
<td>1.1</td>
<td>3.7 (1)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>22.9</td>
<td>20</td>
<td>1.1</td>
<td>2.4 (1)</td>
</tr>
<tr>
<td>Lincomycin</td>
<td>19.1</td>
<td>17</td>
<td>1.1</td>
<td>2.0 (1)</td>
</tr>
<tr>
<td>Flumequine</td>
<td>13.7</td>
<td>12</td>
<td>1.1</td>
<td>1.0 (0)</td>
</tr>
</tbody>
</table>

Fig. 1. Treatment incidence (number of animals per 1000 treated daily with one dose) based on defined daily dose versus treatment incidence based on used daily dose per registered antimicrobial compound, classified according to their importance in human medicine (WHO, 2007). Class I, critically important antimicrobials for human medicine; class II, highly important antimicrobials for human medicine; class III, important antimicrobials for human medicine. Error bars represent the standard deviation.

2010, 2011), it has been suggested that freshly hatched chicks might have received off-label ceftiofur treatment in the hatchery as preventative measure for E. coli septicemia (Mevius, 2010). In the spring of 2010, this was confirmed by findings of the inspection services of the Federal Agency for Safety of the Food Chain. In view of these findings, hatcheries in Belgium and The Netherlands have claimed to immediately stop ceftiofur use. This matter has lead to an ongoing discussion on antimicrobial use in animal husbandry and a belief that the current reporting system may lack transparency. The description of antimicrobial use in this paper thus is most likely a small underestimation of the total antimicrobial burden broilers might undergo. Nevertheless, it gives a good and complete assessment of antimicrobial use on the broiler growing farm from setting in the barn to slaughter.

The use of standard measurement units for time at risk and average weight of the chickens at time of treatment is important for comparison of data between farms and between regions or countries. That is the main aim of using the treatment incidence to quantify antimicrobial use. It may not be 100% exactly what is used in that specific treatment, but quantifying the use systematically converted to the same denominator allows making valid

Fig. 2. Comparison of the treatment incidence (number of animals per 1000 treated daily with one dose) based on used daily dose for the two monitored production cycles per farm.
comparisons or to follow up the amount of antimicrobials used over time (Timmerman et al., 2006). A “standard treated broiler” was also determined in this study to act as reference for future studies and for quantifying antimicrobial consumption in the recently started up collection of National Veterinary Antimicrobial Consumption Data in Belgium (www.belvetsac.ugent.be).

More than half of the treatments applied consisted of amoxicillin and tylosin, beta-lactam and macrolide antibiotics, respectively. According to the WHO classification (2007) both are classified as class I or critically important antimicrobials in human health. In fact, 6 out of the 10 compounds recorded are members of this class. Many of them, such as amoxicillin, enrofloxacin and flumequin are broad spectrum compounds. Also the three compounds belonging to class II in Fig. 1 (highly important antimicrobials in human health) are broad spectrum drugs. Compared to the Netherlands, that has a very comparable broiler production (VEPEK, 2008), macrolides were used more frequently in Belgium. Fluoroquinolones and penicillins on the other hand are used more often in the Netherlands where they represent about half of the administrations (in animal doses per year) (Anonymous, 2007). These differences indicate that the antimicrobials most frequently used might vary largely between countries whereas the encountered pathologies are very comparable based on data from both country’s National Animal Health Services (DGZ, 2010; GDeventer, 2010).

The fact that antimicrobials are not used in all monitored production cycles shows that some farms are able to grow broilers without needing any antimicrobials.

To quantify the exposure to antimicrobials, the weight indicators UDD and DDD were applied to quantify antimicrobial consumption. The DDD used in this study is a derivative of the animal daily dose or ADD, introduced by Jensen et al. (2004) and an adjustment for poultry of the standard measurement of dose in human medicine: defined daily dose (DDD). The UDD was introduced in veterinary drug consumption by Timmerman et al. (2006) as an adaptation of the prescribed daily dose or PDD (Arnold et al., 2004; Chauvin et al., 2001, 2002). The UDD in this case is a measure that is very helpful when describing herd or flock level consumption data. Farmers do not always follow correctly the dosage prescribed by the veterinarian or what is in the medicine’s leaflet, so compared to the PDD, the UDD is not sensitive to non-compliance of prescription dose, a possible risk factor for antimicrobial resistance (Catry et al., 2003).

A T1UDD of 121.4 per 1000 corresponds to treatment with one UDD during one eighth of the life expectancy of a broiler (six weeks), or a broiler approximately receiving one UDD for five days of the growing period on average, but as mentioned before with large between farm and between flock variations. The treatment incidences calculated in our study are difficult to compare with what is reported in other countries since to our knowledge no similar studies in broilers have been published. Only a study from Grave et al. (2004) gives treatment frequencies that are comparable to our treatment incidence, but they only reported treatment frequencies of necrotic enteritis, which is only part of the total treatment incidence. In the Dutch MARAN report (2007), usage is reported as average number of Animal Daily Doses per animal year. This was 32.9 for broilers. This means that per 1000 broiler (days) 32.91 × 1000/365 or 90.2 broilers are being treated with one animal daily dose. Thus, both the treatment incidence calculated based on the UDD (121.4) and the one based on the DDD (131.8), were higher than the treatment incidences in the Netherlands.

The UDD/DDD ratio estimates the correctness of dosing. In this study amoxicillin and trimethoprim-sulphonamide on average were being overdosed, while tylosin on average was underdosed. Reasons for inappropriate dosing can be misunderstanding of the instruction leaflet, poor veterinary advice, ignoring veterinary advice or wrong evaluation of the kg broilers present in the flock, or by dosing per 10001 of water instead of per kg chicken (Timmerman et al., 2006).

The main indications for using antimicrobials were dysbacteriosis (non-specific bacterial enteritis) and necrotic enteritis. It was not always clear what the farmer’s interpretation of dysbacteriosis was. It was defined separately from necrotic enteritis, and was usually defined quite indifferently as “watery excrements”. It can be questioned whether treatment was always necessary in these cases, as mild digestive disturbances following change of feed or after vaccination of the birds might further resolve without therapy. The preferred treatment for these mild symptoms was tylosin. The more prophylactic character of treatment with tylosin could explain why this is often being underdosed.

5. Conclusions

Belgian broilers are treated with antimicrobials for on average one eighth of their life expectancy. Still a lot of broad spectrum compounds are used, mainly belonging to risk class I for human medicine. On the other hand, some broiler producers succeeded in raising chickens without using any antimicrobial drugs. More research is needed to find out what drives these variations in antimicrobial use between farms.

Conflicts of interest

No conflicts of interest to declare.

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