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Quantitative and qualitative analysis of antimicrobial usage in white veal calves in France

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ABSTRACT

The development of antimicrobial resistance has made it necessary to measure antimicrobial usage in animal production sectors. France is a major European producer of white veal calves, but few data were previously available for that sector, even though these young animals are particularly susceptible to infection and considered as a reservoir of antimicrobial resistance. A cross-sectional study was conducted on 186 batches of French calves to estimate the exposure of white veal calves to antimicrobials and identify the potential risk factors related to antimicrobial usage. An indicator of calf exposure was calculated as a count of the number of antimicrobial treatments per calf. The indicator was based on veterinary prescriptions (products, quantity dispensed and dosage prescribed) and the estimated weight of calves at treatment, using the dates of treatment collected from farm registers.

The study showed that calves were exposed to an average of 8.55 antimicrobial treatments (SD: 2.21, range: 2.75–15.86) over the five to six months of the fattening process. Group treatments were predominant (95.8%) and administered by the oral route. The "starting treatments", given during the first two weeks of the fattening period, were administered systematically (to all the calves in all the farms) and accounted for a third of all treatments. Tetracyclines, polypeptides and macrolides were the most widely used antimicrobials, with respectively 4.32, 1.59 and 1.01 treatments per calf. Only rare uses of 3rd and 4th generation cephalosporins and fluoroquinolones, considered as critically important in human medicine, were reported.

Despite low variability of exposure between farms, a linear mixed-effects model highlighted a higher variability between farmers (ICC = 0.14) or veterinarians (ICC = 0.12), than between integrators (ICC = 0.06). The number of calves per pen, introduced as a fixed effect in the model, was also significant: calves housed in pens of 6–10 and fed in buckets had on average 2.55 more antimicrobial treatments per calf than calves housed in pairs with the same feeding system. The model also highlighted an increase of 1.48 treatments per calf for farms with more than five percent of mortality, versus those with two percent or less.

The present study showed that antimicrobial treatments are numerous in veal calf fattening farms, particularly at the arrival of the animals. Taking into account the development of resistance to antimicrobials, the necessity and the effectiveness of some of these treatments should be re-evaluated.

1. Introduction

Antimicrobials are widely used in livestock productions and some food-producing animals, such as calves, are considered as reservoirs of antimicrobial resistance (Haenni et al., 2014). Some statistical links between uses of antimicrobials and resistance levels to these drugs were already demonstrated (Berge et al., 2006; Checkley et al., 2010; Catry et al., 2016). The need to monitor antimicrobial use in animals is recognized by a wide range of countries (EU, 2012; WHO, 2015). In Europe, for animals, several monitoring programs outline a macroscopic picture of antimicrobial consumption through annual antimicrobial sales (DANMAP, 2013; ANMV, 2014; MARAN, 2015). These programs are essential in observing trends at the national level and comparing results between years and countries (Grave et al., 2010; ECDC/EFSA/EMA, 2015; EMA, 2015), but are unable to provide more precise information (usage at the production type level, variability between farms, etc.).

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White veal calf production in Europe is achieved through "integrators", companies that often manage the entire production process: feed production, purchase and placement of calves during the fattening period, and slaughter (Sans and De Fontguyon, 2009). The young calves are collected from farms (mostly dairy farms) a few days old, batched and placed in fattening farms. They are fed with milk replacers throughout the fattening period which keeps their meat white and explains the term "white veal" usually used for these calves. Their diet is also supplemented by some solid feed. The calves are usually slaughtered at the age of around six months. Like all young animals, calves are particularly susceptible to infection (Hill et al., 2009), especially as the batches often bring together animals from different origins. They are therefore potentially treated by antimicrobials, mainly administered via the oral route in milk replacers. France is the leading producer (and also consumer) of veal calves in Europe, followed by the Netherlands, Italy and Belgium. France produces nearly 30% of all European tonnage, with 1.3 million finished calves slaughtered in 2014.

In France, a first approach for estimating antimicrobial exposure in veal calves was conducted in 2013 using annual sales of veterinary antimicrobials (ANMV, 2014). It estimated that a calf was exposed to 2.6–4.2 antimicrobial treatments during its fattening period. These results are rough estimations due to the difficulty of correctly assigning the antimicrobials used in this sector (versus those consumed by calves in conventional farms) and the lack of information on the biomass exposed (which is particularly important for calves whose weight may increase five-fold during production). Quantification of antimicrobial usage is a major methodological concern. The indicators are numerous and have evolved considerably over time. From simple counts of antimicrobial quantities (in kilograms or tons), they have become more complex, and attempts have been made to better estimate real animal exposure to antimicrobials by taking more parameters into account (dosage, number of animals and their weight at treatment, etc.). The indicators used most recently are largely based on the animal daily dose (ADD) taken from the recommendations of the Summary of Product Characteristics (SPC) and are expressed in milligrams of active ingredient per kilogram of animal. That dosage unit can also be expressed as the used daily dose (UDD) or the prescribed daily dose (PDD). On that basis, various more complex exposure indicators were developed, such as the number of treatment days per animal per year (Bondt et al., 2013), the number of veal calves out of 1000 treated with one ADD (Pardon et al., 2012a) and the number of ADD per year (Bos et al., 2013; MARAN, 2015).

The present study aimed to provide quantitative data on antimicrobial exposure of white veal calves in France and to identify the potential risk factors for antimicrobial usage. The major challenge was to define an accurate exposure indicator understandable and easily reusable by the different stakeholders in the sector: farmers, technicians, veterinarians and integrators.

2. Materials and methods

2.1. Study design

Data were collected via a cross-sectional field survey in French veal calf farms. The farms had to meet the following inclusion criteria: i) having a minimum herd size of 50 calves; ii) having reared two successive batches of calves in the previous two years; iii) being located in one of the four main production regions of France. A batch was defined in the study as a group of calves entering the farm at the same time and reared together until slaughter.

A random sample of 120 farms was targeted, to reach at least 5% of French production and to estimate a mean number of treatment per calf with a margin of error of 0.5 treatment associated with a 95% confidence level. To take into account potential seasonal bias in the study, two successive batches were studied in each farm.

In practice, the representatives of veal calf production in France (integration groups and cooperatives) were contacted to draw up a list of veal farms matching the first two study criteria. Twenty two representatives (out of 32), including the largest organizations, responded positively to the request and transmitted a list of 2011 veal farms. Among these, 120 farms were randomly selected (with stratified sampling by region), to form the study sample. All the elements for identifying and contacting the farmer, the veterinarian and the technician responsible for the farm were transmitted by the integrators.

2.2. Data collection

The quantification of antimicrobials used for each calf batch was based on veterinary prescriptions and dispensing records. The veterinarians related to the studied farms were asked to transmit all the antimicrobial prescriptions or dispensing records established for the batches concerned over the complete production cycle. The data collected were the antimicrobial trade name, the pharmaceutical form (oral solution, oral powder, parenteral solutions, tablets, bolus, etc.), the pack size (in L or mL for liquids, in g or kg for solids, in unit number for bolus or tablets, etc.), the total number of packages prescribed and dispensed to the farm and the prescribed therapy (dose, administration frequency, duration). Furthermore, a short questionnaire was completed by veterinarians to indicate whether or not calves were vaccinated for respiratory diseases.

In parallel to this, a survey was conducted in the farms by a surveyor trained for this purpose. A standardized questionnaire was completed with the farmers. It addressed the farm characteristics, the housing conditions, the feeding system, the sanitary processes and the specifications of the two batches of calves studied. The dates of implementation of group treatments were collected from the farm health register (antimicrobial name, date of beginning of treatment).

Data on the quantity of active ingredients by product and ADD (as recommended by the SPC) were provided by the French agency for veterinary medicinal products (ANMV).

2.3. Measuring antimicrobial usage

The aim was to estimate, for each batch, the number of antimicrobial treatments carried out per calf (NTPC) over the entire fattening period, considering a treatment as the use of a single antimicrobial active ingredient at the prescribed dose during the whole treatment course. For each active ingredient *i*, of each antimicrobial product *p,* prescribed and dispensed to the farm, the total quantity of active ingredient (*Qai*) was first calculated. That quantity represented a number of theoretical treatments taking into account the prescribed daily dose of active ingredient per kilogram of animal (PDD) and the duration of treatment advocated by the veterinarian, the calf weight estimated at treatment and the number of calves treated (Formula (1)). For products containing two active ingredients, two treatments were counted, except for clavulanic acid, which is always used in association with amoxicillin, and sulfonamides, always used with trimethoprim. Trimethoprim was nevertheless presented in results by antimicrobial family for information.

$$NTPC = \sum_{p=1}^{n}\sum_{i=1}^{m}\sum_{t=1}^{k} NTPC_{t,i,p} = \sum_{p=1}^{n}\sum_{i=1}^{m} \frac{Qai_{i,p}}{\sum_{t=1}^{k}\left(PDD_{i,t} * calf \quad weight_t * duration_t * batch \quad size\right)} \quad (1)$$