AMR

05

Reduction of antimicrobial use in the pork food chain – did it reduce antimicrobial resistance?

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Introduction

Antimicrobial use (AMU) selects for antimicrobial resistance (AMR) in bacterial populations. However, what happens to AMR when selection pressure declines due to a reduction of AMU in animal husbandry? The purpose of this study was to evaluate whether the reduction of antimicrobial use in pig husbandry in Germany was followed by a reduction in antimicrobial resistance. In 2014, Germany changed its drug legislation (Arzneimittelgesetz, AMG). The purpose of this legal change was the reduction of antimicrobial use in meat producing animals. Among other animal populations, the regulation addressed piglets ≤30 kg body weight and fattening pigs >30 kg body weight. The general principle of the regulation was a benchmarking approach. Data on antimicrobial use were collected in a systematic manner using treatment frequency as a measure. This measure was compared between farms housing the same type of animal populations, i.e. therapy frequency in pigs ≤30 kg in a farm was compared to therapy frequency in pigs ≤30 kg on the other farms. From all farm level therapy frequencies of the same type of population, the median and the 3rd quartile were determined twice a year. Farms with a therapy frequency above the 3rd quartile need to present a catalogue of measures aimed at reducing antimicrobial use to the respective local competent veterinary authority. Those above the median had to identify the reasons for the AMU above average.

The median and the 3rd quartile were published twice a year by the Federal Office for Consumer Protection and Food Safety (BVL). Figures for pigs up to and above 30 kg of body weight showed a substantial decline of both values indicating an overall substantial reduction of AMU in fattening pigs in Germany over the years.

Material and Methods

Based on the substantial reduction of antimicrobial use in pigs we compared AMR in commensal *Escherichia coli* from pigs from several years to determine whether the reduction in antimicrobial use also caused a decline in antimicrobial resistance. Antimicrobial resistance was observed in isolates of commensal *E. coli* from pigs over the years using harmonized methods based on technical specifications provided by EFSA (1). Minimum inhibitory concentrations of the antimicrobials for *E. coli* were evaluated according to epidemiological cut off values fixed in Commission Implementing Decision (CID) 2013/652/EU. Statistical analysis was based on logistic regression analyses on overall AMR (i.e. proportion of isolates that were susceptible to all tested antimicrobials and proportion of isolates resistant to more than three of the substances) and on AMR to specific antimicrobials. Isolates of *E. coli* were collected from randomized samples on farm and at slaughter, both reflecting domestic production only. AMR was determined using broth microdilution in line with the above mentioned CID.

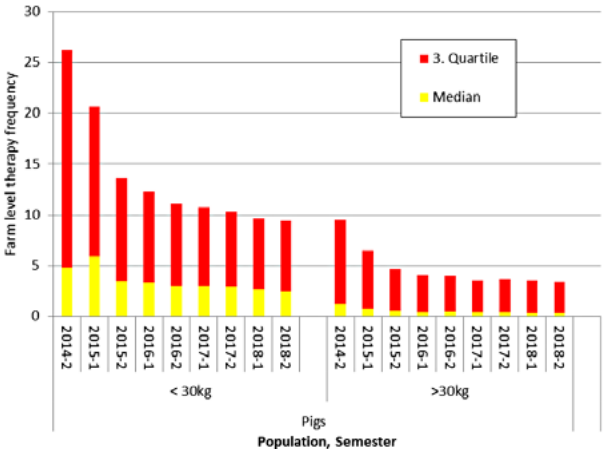

Figure 1: Development of median and 3rd quartile of farm level therapy frequency per half year as calculated according to § 58c of the German Medicine Act and published by the Federal Office of Consumer Protection and Food Safety

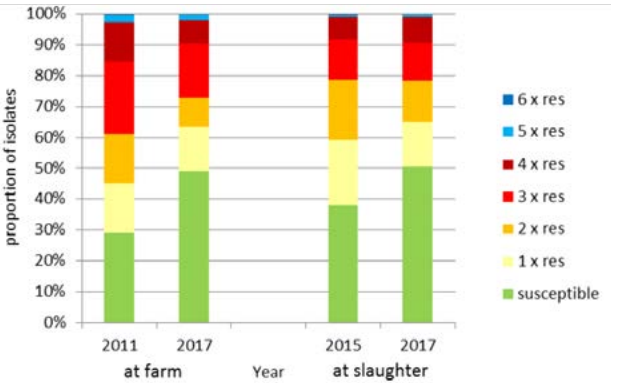

Figure 2: Antimicrobial resistance of E. coli from fattening pigs at farm (left two columns), caecal samples of pigs at slaughter (right two columns)

Results

Reduction of antimicrobial use in pigs can be seen in a decrease of the median and 3rd quartile of the therapy frequency as defined by the AMG (Fig. 1). Values for the 3rd quartile decreased from 26 treatment days per semester to less than 10 days in piglets ≤30 kg. They decreased from 9.5 to 3.7 days in pigs >30 kg. Overall, antimicrobial resistance decreased in isolates of *E. coli* from pigs that had been collected on farm and at slaughter between 2011 and 2017 (Fig 2). The proportion of fully susceptible isolates increased from around 30 % in 2011 to around 50 % in 2017 in fattening pigs at farm. In pigs at slaughter, samples had only been collected in 2015 and 2017. However, again, the proportion of fully susceptible isolates was higher in 2017 than in 2015.

With respect to individual antimicrobials a reduction in AMR of *E. coli* was observed for tetracycline, ampicillin, sulfamethoxazole and trimethoprim (Fig. 3). Resistance to ciprofloxacin, cefotaxime, gentamicin and colistin did not decrease. However, resistance to these substances had been on a low level from the start.

Discussion

Our results confirm a reduction of AMR in fattening pigs that goes along with the reduction of antimicrobial use in the German pig population based on data collected in the framework of a national monitoring program. The reduction was most obvious for the five substances that had the highest resistance level in 2011, i.e. tetracycline, sulfamethoxazole, ampicillin, trimethoprim and chloramphenicol. As use data were only available on an overall therapy frequency level, the share of the reduction that is taken by these substances is not known. However, tetracyclines, penicillins and sulfonamides are the substances with the largest quantity sold to veterinarians in Germany (2) and they are also known to be frequently used in pigs in Germany (3).

Selection pressure can on the one hand be exerted by the individual substance. On the other hand, co-selection is frequent as resistance determinants are often genetically linked. That means that use of one substance may indirectly select for resistance to another substance. This may for example have contributed to resistance to chloramphenicol despite the ban of chloramphenicol for food producing animals in the early 1990s.

Conclusion

Results indicate that a reduction in AMU in the population has beneficial effects on the AMR situation in the population especially to those antimicrobials that had high resistance rates in the first place. Further in-depth studies are needed to investigate the differences between the substances and to try to establish a dose-response relationship between AMU and AMR reduction.

References

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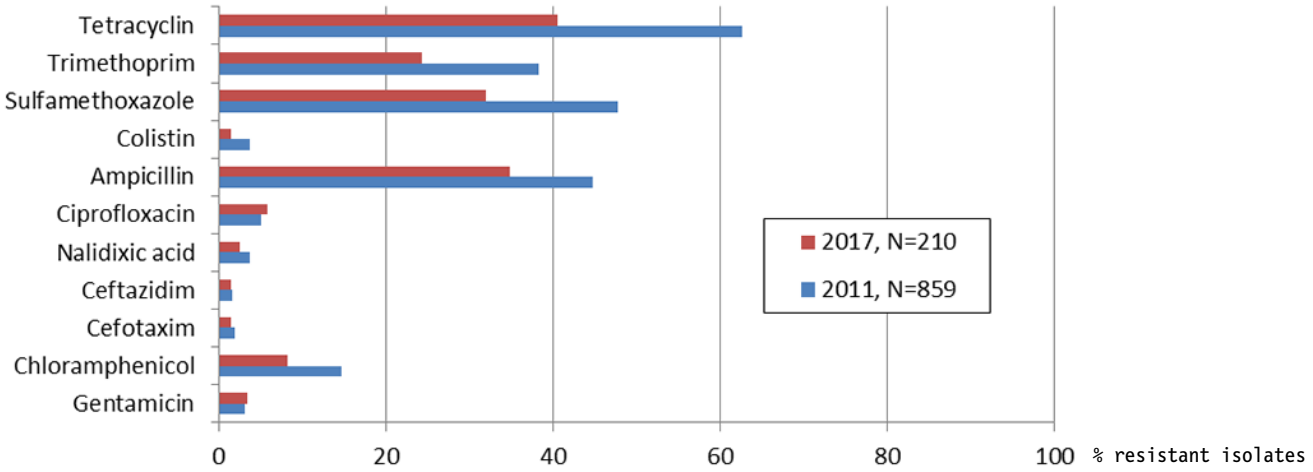

Figure 3: Resistance of E. coli from fattening pigs at farm to antimicrobials in 2011 and 2017