Antimicrobial resistance after fluoroquinolone treatment

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Presented at The Society for Veterinary Epidemiology and Preventive Medicine, Annual Conference 2017, 29. – 31. March 2016, Inverness, GB Scotland

Introduction

Penicillins, tetracyclines and quinolones are considered critically important antimicrobials for veterinary and human medicine. Hence, preservation of their effectiveness is a political target.

Since treatment with an antimicrobial can induce co-selection of resistance towards an antimicrobial belonging to another class (e.g. tetracycline and aminoglycoside), it is important to understand these effects. Little is known about possible co-selection through use of fluoroquinolones.

Hypothesis

Resistance to antimicrobials of different classes temporary increase in fecal *Escherichia coli* in pigs after fluoroquinolone treatment.

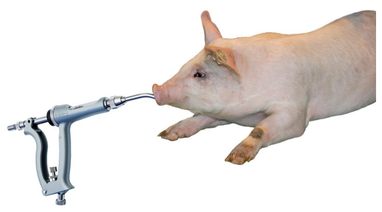
Materials & Methods

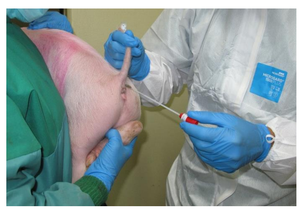
Pigs

- Five-weak-old weaners
- Not treated with antimicrobials before, nor their dams

Treatment

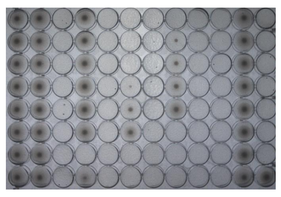
- Groups of 14 weaners each:
  - Orally treated with the fluoroquinolone enrofloxacin using a drencher on study days 1-5 (“Treated”)
  - Untreated weaners in contact with treated weaners (“Contact to Treated”)
  - Separated control (“Control”)





Sampling

- Rectal swabs
- From study day 1 (before treatment) To study day 42



Lab

- MacConkey-agar
- One *E. coli* isolate per swab sample
- Test plates (broth microdilution) with 14 antimicrobial agents (panel according to Decision 2013/652/EU)
- Minimum inhibitory concentration, cut-off values (resistant strain yes/no) according to EUCAST (2015)

Analysis

- Prevalence of resistance in *E. coli*
- Logistic analysis (SAS 9.4, GENMOD Procedure)
- Probability of resistance to antimicrobial agents in *E. coli* on single study days compared to the initial value on 1. study day

Results

During and shortly after enrofloxacin treatment, not the prevalence of resistance to enrofloxacin but resistance to ampicillin, sulfamethoxazole and trimethoprim increased in *E. coli* of orally treated pigs and their untreated roommates compared to pre-treatment. The development of the prevalence was similar for the antimicrobials (the example of ampicillin is presented in the Figure).

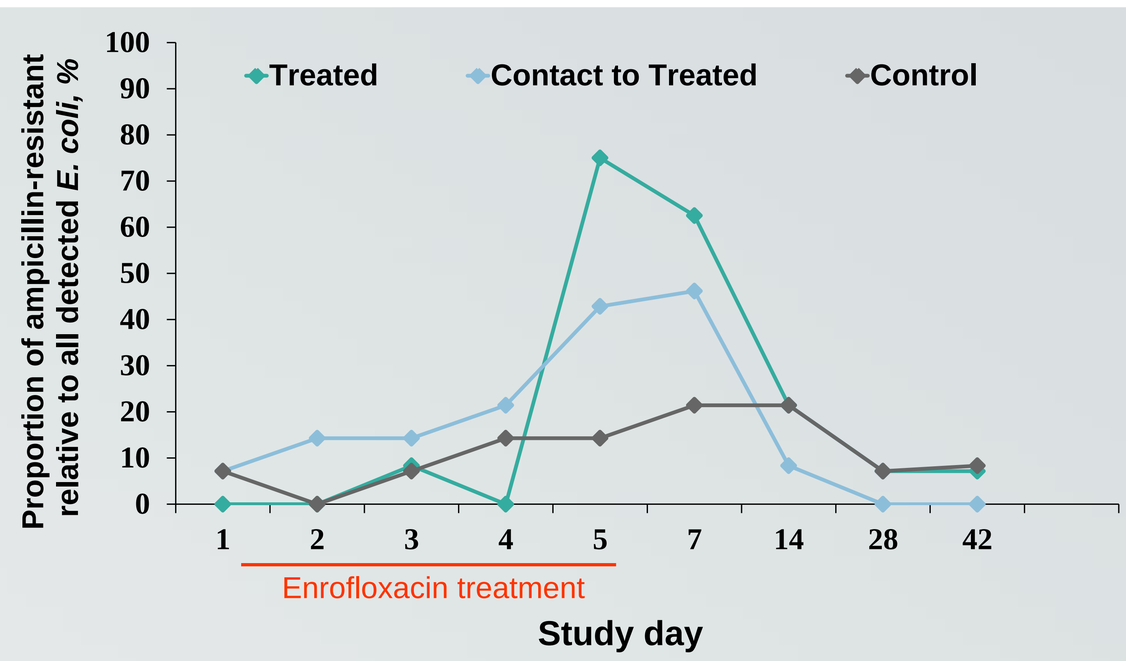


Figure: Proportion of ampicillin-resistant (minimum inhibitory concentration > 8 µg/ ml) ***Escherichia coli*** isolates from non-selective media per study day and treatment group (number of all detected *E. coli* = 345)

In the logistic analysis, the risk to carry resistant *E. coli* was higher on days 5 and 7 compared to day 1 ($p < 0.05$; example of ampicillin in Table 1). Thereafter the odds decreased and there were no significant differences within the groups anymore on study day 42 vs. day 1.

Table 1: Odds ratios (95th confidence intervals) on study days 5 and 7 compared to day 1 (number of 113 *E. coli*)

	Study day	
	5	7
Treated	2.1 (1.6; 2.9)	1.9 (1.3; 2.6)
Contact to treated	1.4 (1.1; 1.8)	1.5 (1.1; 1.9)

On study days 5 and 7, the minimum inhibitory concentration differed by at least 4 dilution steps between susceptible and resistant isolates within treatment groups (e.g. for ampicillin in Treated; Table 2) and compared to day 1 within isolates from the same animal that were resistant after treatment.

Table 2: Median minimum inhibitory concentration of susceptible and resistant isolates on study day 5 and 7 in Treated

	Ampicillin		Sulfamethoxazole		Trimethoprim	
Study day	**5**	**7**	**5**	**7**	**5**	**7**
Susceptible	4	3	8	16	1	1
Resistant	>64	>64	>1024	>1024	>32	>32

Conclusion

After enrofloxacin treatment, a transient increase in resistance prevalence to other antimicrobials than fluoroquinolones implies co-selection in treated and their contact animals.

Acknowledgements

The authors wish to thank C. Schwarck and R. Porstendorfer for conscientious caretaking of the pigs; A. Schabanowski, B. Lesniewsky and T. Skladnikiewicz-Ziemer for excellent lab work; D. Schlichting for statistical advice. The study was funded by BfR.

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