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Evaluation of an intervention measure against MRSA spread in pig population using a MRSA bacteriophages cocktail

J. Honegger[1], HJ. Lehnherr[2], P. Torgerson[3], R. Stephan[4] and X. Sidler[1]

[1]Division of Swine Medicine, Department for Farm Animals, [2]Phage Technology Center GmbH (PTC), Boenen, Germany, [3]Section of Epidemiology, [4]Institute for Food Safety and Hygiene, University of Zurich, Switzerland

Key words
MRSA, Eradication/ Reduction, Bacteriophages, Pig production

Aim of the study
Even MRSA ST398 seems not to be very pathogenic to human until today, contact with pigs has been shown to be a risk factor for human colonization. This sequence type seems to be transmitted very easily from breeding to finishing farms trough purchase of MRSA-positive pigs. In Switzerland the MRSA colonization prevalence of fattening pigs increased form 3% in 2009 up to 26% in 2016. Due to this rapid MRSA spread, intervention measures have to be evaluated. The aim of this study was to test the use of bacteriophages to minimize or to eradicate MRSA in a farm with high MRSA colonization prevalence in weaned piglets in order to prevent a further MRSA spread to finishing farms.

Material and methods
Run 1
Prior to the start of the study, the bacteriophage cocktail was successfully tested *in vitro* against the MRSA strains isolated from pigs oft the study farm. Four MRSA positive and 6 MRSA negative sows received 5 ml of a bacteriophages cocktail with 10^8 phages / ml daily via top dressing 7 days before transfer to the farrowing pens. Before moving to the farrowing pens, the sows were washed with the high-pressure cleaner and sprayed with the phage cocktail. Additionally, nasal cavities, mouth and vagina were also flushed with the bacteriophages cocktail. Afterwards, the sows were housed in a cleaned and disinfected farrowing pen. During the suckling period, they received daily 5 ml of the phage cocktail by top dressing. The piglets were washed immediately after birth and twice a week with the bacteriophages cocktail. In the 4^{th} week of life the piglets were weaned and received a feed of which the bacteriophage cocktail was sprayed onto the feed after pelleting during the weaning period (5-6 weeks). Colonization status was checked twice a week during suckling period and weekly after weaning taking nasal and fecal swabs.

Run 2-4
In the following runs, 40-60 suckling piglets were tested for MRSA in the 4th week of lactation before weaning. Upon weaning, both MRSA-positive and negative piglets were mixed in a cleaned and disinfected weaning room. At the second run the bacteriophage cocktail was added via Dosatron to the drinking water in a 0.1% concentration and in the following two runs in a 3% solution. In addition, the room was nebulized twice a day with a nebulizer for 10 minutes. This nebulizer produced aerosols of a size that get stuck in the upper airways. In a preliminary experiment, the bacteriophage concentration was tested after nebulization. Nebulization did not cause any phage losses. The bacteriophage concentration in the feces also showed, that the largest part of the bacteriophages survived the gastrointestinal passage. Furthermore, bacteriophage concentration was tested before each use and proved to be very stable in the second batch.

Results and significance
In the first run, no reduction of the MRSA prevalence in the nose or feces of sows and piglets could be achieved at any time. When checking the phage cocktail, it was found that the phage solution was unstable and lost a log step reduction of bacteriophages weekly. Therefore, a new batch of phage cocktail using another buffer solution and with an increased bacteriophage concentration of 1010/ml was produced. However, even after various optimization steps, runs 2-4 led not to a significant reduction of the MRSA colonization in weaning pigs. Under the chosen conditions of the study design, bacteriophages were not able to combat MRSA effectively.

Publications, posters and presentations
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