

Zinc Oxide and Antimicrobial Resistance in Pigs

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SUMMARY

The objective of this research was to investigate whether therapeutic use of zinc oxide (ZnO) in swine production creates selective pressure for the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) due to co-location of the zinc-resistance gene (*czrC*) and methicillin-resistance gene (*mecA*) within the staphylococcal cassette chromosome *mec* (SCC*mec*). A randomized-controlled trial was completed using 110 pigs that were naturally colonized with *czrC*-positive MRSA. The prevalence of MRSA was significantly higher when pigs were fed a ration containing 3000 ppm of zinc oxide compared to the control group (100 ppm zinc). In an observational study of 26 farms, it was found that the use of therapeutic levels of zinc oxide (>2000 ppm) was associated with a higher likelihood of finding MRSA in nasal swabs of weanling pigs. The overall conclusion from these studies is that high levels of zinc oxide in starter rations are associated with a higher prevalence of pigs carrying MRSA.

INTRODUCTION

Zinc is an essential nutrient and needs to be provided in starter rations at around 100 ppm to meet the pig’s nutritional requirements. Levels of 2000 to 3000ppm of zinc oxide are often used in early starter rations as a therapeutic agent to control post-weaning *E. coli* diarrhea. Bacteria can carry resistance to heavy metals such as zinc and there is concern that the use of zinc oxide as a therapeutic agent might inadvertently co-select for antibiotic resistance. Of particular public health concern is methicillin resistant *Staphylococcus aureus* (MRSA), an organism commonly isolated from the nasal cavities of pigs and is often found on farms where antibiotics are not used. The objectives of this research was to determine whether the herd prevalence of MRSA among nursery pigs is affected by exposure to therapeutic levels of in-feed ZnO (3,000 mg/kg) when compared to the recommended dietary levels of in-feed ZnO (100 mg/kg), and to investigate risk factors for MRSA shedding in pigs in commercial nursery herds with a particular focus on antimicrobials, heavy metals, disinfectants, biosecurity, and management practices.

RESULTS AND DISCUSSION

Trial 1

Fifty weaner pigs received feed containing therapeutic levels of ZnO (3,000 ppm) and 49 pigs received a control feed containing 100 mg/kg of zinc. Pigs receiving therapeutic levels of ZnO were significantly more likely to carry MRSA on day 28 (OR=18.1, P=0.007) and day 35 (OR=3.01, P=0.015) when compared to the control pigs (see figure 1).

Trial 2

Nasal cultures for MRSA were completed for 390 pigs from 26 farms at the end of the suckling phase and again at 3-weeks post-weaning. Herd-level information was collected and a random subset of MRSA isolates was screened for resistance to zinc. Multivariate analysis revealed that the concentration of in-feed zinc (P<0.001) and frequent disinfection of nursery pens (P<0.001) were associated with pigs carrying MRSA (see Table 1). Furthermore, 62.5% (25/40) of MRSA isolates carried the zinc-resistance gene *czrC* and were phenotypically resistant to zinc. The use of therapeutic levels of zinc oxide in starter feeds appeared to be an important risk factor in the persistence of MRSA in commercial swine herds.

CONCLUSION

Overall, exposure to therapeutic levels of in-feed ZnO is associated with an increase in the prevalence and persistence of MRSA among pigs, particularly during the early phase of the nursery.

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Table 1. Factors associated with methicillin-resistant *Staphylococcus aureus* in nursery herds.

Parameters	MRSA positive cohorts (n=8)	MRSA negative cohorts (n=14)	P-value
Herd size (sows, SD)	698 (433)	425 (427)	0.076
Continuous nursery flow (%)	25	57.1	0.204
Average weaning age (days, SD)	22.4 (2.6)	24.5 (4.8)	0.351
Nursery stocking density (pigs/m ² , SD)	3.22 (1.23)	2.47 (1.17)	0.048
No outside breeding stock replacements (%)	62.5	71.4	0.999
Danish entry (%)	37.5	42.9	0.999
Shower-in/shower-out required (%)	62.5	28.6	0.187
Nursery pens disinfected for incoming pigs every time (%)	100	50	0.022
Corridors are disinfected on a weekly to monthly basis (%)	87.5	42.9	0.074
Cat(s) and/or Dog(s) on the property (%)	37.5	92.9	0.011
Live rodents observed in barn at sampling (%)	12.5	7.1	0.999
Wild birds observed in barn in past year (%)	12.5	42.9	0.193
Antibiotics administered by feed (%)	87.5	78.6	0.999
Antibiotics administered by water (%)	37.5	42.9	0.999
Antibiotics administered by injection (%)	87.5	71.4	0.613
Zinc therapy (≥2,000 ppm in-feed) (%)	100	50	0.022