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Summary

This experiment was conducted to determine the influence of the route of antibiotic administration (in-feed vs. in-water) on nursery pig growth performance. A total of 2,592 pigs (L337 × 1050, PIC Hendersonville, TN; initially 14.5 lb) were used in a 28-d trial. Pigs were weaned at 21 d of age and placed in a commercial research facility with 27 pigs per pen. After a 7-d pre-trial period, pens of pigs were assigned to weight blocks in a randomized complete block design. There were 12 replications per treatment with pen as experimental unit for in-feed medication treatments and a pair of pens as the experimental unit for water medication treatments. The six treatments included a control (no medication), chlortetracycline (CTC) provided via feed or water to achieve 9.98 mg/lb body weight (BW), tiamulin in feed (2.27 mg/lb BW) or water (10.43 mg/lb BW), or a combination of CTC and tiamulin in feed. Experimental treatments were provided for 14-d followed by a 14-d period without medication. For statistical analysis, the interaction of antibiotic type × route of administration was tested in a 2 × 2 factorial with main effect of antibiotic type (CTC or tiamulin) and route of administration (in-feed or in-water). Pairwise comparisons were also made between the control and all individual treatments. From d 0 to 14 ($P < 0.05$), d 14 to 28 ($P < 0.10$), and d 0 to 28 ($P < 0.05$) there was an antibiotic × route of administration interaction observed for average daily gain (ADG). The interactions were a result of pigs fed diets containing CTC having improved ($P < 0.05$) ADG compared to CTC in-water, whereas pigs provided tiamulin in-water exhibited improved ADG compared with tiamulin in feed. There was an antibiotic × route of administration interaction observed for feed-to-gain ratio (F/G) from d 0 to 14 and 0 to 28. Pigs provided tiamulin in the feed had the poorest F/G, whereas F/G was not different among the other treatments. Providing CTC in the feed or water or tiamulin in the water improved ($P < 0.05$) ADG compared to pigs fed the control diet. Providing either CTC or tiamulin in the

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feed increased ($P < 0.05$) average daily feed intake (ADFI) as compared with providing the antibiotics in water. Pigs fed antibiotics in the feed had increased ($P < 0.05$) ADFI compared to the control with those provided antibiotics in the water being marginally greater ($P < 0.10$) in ADFI than the control. For ADG (d 0 to 28), pigs provided CTC in feed, tiamulin in the water, or the combination of CTC and tiamulin in the feed during the treatment period had increased ADG ($P < 0.05$) compared to pigs fed the control diet. For ADFI, there was no evidence of an interaction or main effects; however, when compared to the control, pigs provided CTC in-feed, tiamulin in-water, or the combination in the feed all had increased ADFI. In summary, providing CTC in feed with or without tiamulin or tiamulin in the water improved nursery pig growth performance.

Introduction

Antibiotics have been widely used in swine diets to fend off or slow down the growth of bacteria and the diseases they produce in the gastrointestinal tract of the pig. Antibiotics have also proven to improve growth performance and feed efficiency.³ Feed-grade antibiotics have also been proven to have the most impact on pig growth and feed efficiency in younger pigs vs. older animals.⁴ Pigs at a young age can have improved nitrogen metabolism, increased nitrogen retention and reduced nitrogen excretion when fed an antibiotic. Due to improvements in nutrition, housing, production, and general herd health and management, antibiotic effectiveness may not be as great as in the past.⁵ The antibiotics that were used in this study were chlortetracycline (CTC) and tiamulin either added to the feed or provided via the drinking water. Chlortetracycline is used to control and for treatment of bacterial enteritis (scours) caused by *Escherichia coli* and *Salmonella* spp. Tiamulin is used for treatment of swine dysentery associated with *Brachyspira hyodysenteriae*. Thus, the objective of this study was to identify the effects of administering these antibiotics via feed or water on nursery pig growth performance.

Procedures

The Kansas State University Institutional Animal Care and Use Committee approved the protocol used in this experiment (IACUC #4033). The experiment was conducted at New Horizon Farms Nursery, a commercial nursery research facility located in southwest Minnesota (Pipestone, MN). Each pen (12 × 8 ft) had plastic slatted floors and was equipped with a six-hole stainless steel dry feeder and a pan waterer allowing *ad libitum* access to feed and water. Diets were manufactured at the New Horizon Farms feed mill in Pipestone, MN. Feed additions to each pen were delivered and recorded by a robotic feeding system (FeedPro; Feedlogic Corp., Wilmar, MN).

A total of 2,592 pigs (L337 × 1050 PIC, Hendersonville, TN) were placed in 96 pens with 27 pigs per pen. Pigs were weaned at approximately 21 d of age and placed in pens based on initial body weight (BW). After a 7-d pre-trial period, pens of pigs were

³ Helm, E. T, S. Curry, J. M. Trachsel, M. Schroyen, and N. K. Gabler. 2019. Evaluating nursery pig responses to in-feed sub-therapeutic antibiotics. Plos one. 14:4. doi: 10.1371/journal.pone.0216070.

⁴ Gaskins, H. R., C. T. Collier, and D. B. Anderson. 2002. Antibiotics as growth promotants: mode of action. Admin Biotenhnlol. 13:29-42. DOI: 10.1081/ABIO-120005768.

⁵ Jacela JY, DeRouchey JM, Tokach MD, et al. Feed additives for swine: Fact sheets – acidifiers and antibiotics. J Swine Health Prod. 2009;17(5):270–275.

assigned to weight blocks in a randomized complete block design and allotted to 1 of 6 dietary treatments for a 28-day experiment. The 6 treatments included a control (no medication), chlortetracycline (CTC) provided via feed or water to achieve 9.98 mg/lb BW, tiamulin in feed (2.27 mg/lb BW) or water (10.43 mg/lb BW), or a combination of CTC and tiamulin in feed. There were 12 replications per treatment with pen as experimental unit for in-feed medication treatments and pairs of pens as the experimental unit for water medication treatments. Experimental treatments were provided for 14-d followed by a 14-d period without medication. The diet fed prior to starting the experiment was a pelleted diet that did not contain an antibiotic. Experimental diets were fed in meal form (Table 1). Pens of pigs were weighed and feed disappearance was measured weekly to determine ADG, ADFI, and F/G. Diet samples were collected, homogenized, ground, and submitted for proximate analysis (Table 2; Ward Laboratories, Kearney, NE).

Data were analyzed using R Studio (Version 3.5.2, R Core Team, Vienna, Austria) with pen serving as the experimental unit. The study was a randomized complete block design with weight block included in the model as a random effect. Pre-planned contrast statements were used to evaluate the treatment effects on ADG, ADFI, BW, and F/G. The statistical analysis included testing for an interaction of antibiotic type $\times$ route of administration which was tested in a 2×2 factorial with the main effect of antibiotic type (CTC or tiamulin) and route of administration (in-feed or in-water). Pairwise comparisons were also made between the control and all individual treatments. Statistical models were fitted using the NLME package in R. Results were considered significant at $P \leq 0.05$ and marginally significant at $0.05 > P \leq 0.10$.

Results and Discussion

As expected, during the pre-test period immediately after weaning (d -7 to 0), there was no evidence for difference ($P > 0.386$) for ADG, ADFI, F/G, or BW. The ADG, ADFI, and F/G averaged 0.71, 1.00 lb/d, and 1.42, respectively.

From d 0 to 14, there was an antibiotic $\times$ route of administration interaction ($P < 0.05$) for ADG and F/G (Table 3). For ADG, pigs fed diets containing CTC had increased ($P < 0.05$) ADG compared with pigs provided CTC in the water with pigs provided tiamulin in the water having greater ADG than those fed tiamulin in the feed. Pigs provided CTC in the feed or water, tiamulin in the water, and the combination feed treatment had increased ADG ($P < 0.05$) when compared to the control, with pigs provided tiamulin in the feed showing no evidence of difference compared to the control. For F/G, pigs provided tiamulin in feed had poorer F/G compared to pigs provided CTC in feed or water, or tiamulin supplied in water ($P < 0.05$), which did not appear to be different. Pigs provided tiamulin in feed also had poorer F/G than pigs fed the control diet. Pigs fed CTC or tiamulin in feed had increased ADFI compared to the control with pigs provided antibiotics in the water having marginally greater ($P < 0.10$) ADFI than the control. Pigs provided the combination of CTC and tiamulin in feed were not different than those provided CTC in feed for ADFI. On d 14, there was an antibiotic $\times$ route of administration interaction for BW where pigs provided CTC in-feed had increased body weight compared to pigs provided CTC in-water, whereas pigs provided tiamulin in the water had greater BW than those pigs that were provided tiamulin in the feed ($P < 0.05$). Also for d 14 BW, pigs provided CTC in the feed had

increased BW compared to the control, with other treatments showing no evidence of difference ($P < 0.05$).

For the subsequent non-medicated period (d 14 to 28), there was a marginal antibiotic $\times$ route of administration interaction ($P < 0.07$) for ADG where pigs previously provided CTC in the feed had greater ADG than pigs provided CTC in the water, whereas pigs previously provided tiamulin in the water had greater ADG than pigs previously provided tiamulin in the feed. Pigs previously provided tiamulin in the water had increased ADG ($P < 0.05$) when compared to the control or other treatments. For ADFI from d 14 to 28, there were no main effects of antibiotic or route; however, pigs previously provided the combination of CTC and tiamulin in the feed had increased ADFI ($P < 0.05$) when compared to pigs provided the control treatment. For F/G, there was no evidence of difference between treatments ($P > 0.05$).

Overall (d 0 to 28), there was an antibiotic type $\times$ route of administration interaction ($P < 0.05$) for ADG. For ADG, pigs provided CTC in the feed during the treatment period had increased ADG compared to pigs provided CTC in the water, whereas pigs provided tiamulin in water had increased ADG compared to pigs provided tiamulin in the feed ($P < 0.05$). Compared with the control, pigs provided CTC in feed, tiamulin in the water, or CTC and tiamulin in feed during the treatment period had increased ADG ($P < 0.05$), with pigs provided CTC in the water having marginally greater ($P < 0.10$) ADG than the control. For F/G from d 0 to 28, there was an antibiotic type $\times$ route of administration interaction ($P < 0.05$) observed. Pigs provided tiamulin in the feed had poorer F/G compared to pigs provided other treatments. For ADFI from d 0 to 28, there were no interactions or main effects of antibiotic type or route of administration observed ($P > 0.05$). However, pigs provided CTC in the feed, tiamulin in the water, and the combination of CTC and tiamulin in feed had increased ($P < 0.05$) ADFI when compared to the control and other treatments. Finally, for BW on d 28, there was an antibiotic type $\times$ route of administration interaction ($P < 0.05$) where pigs provided CTC in-feed from d 0 to 14 had increased BW compared to pigs provided CTC in water, whereas pigs provided tiamulin in water had increased BW compared to pigs provided tiamulin in the feed.

In summary, providing CTC in feed with or without tiamulin, or tiamulin in the water improved nursery pig growth performance.

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Table 1. Composition of experimental diets (as-fed basis)¹

Ingredient, %	Control (d 0 to 14) ²	Common diet (d 14 to 28) ³
Corn	50.60	47.90
Soybean meal	20.95	28.85
Distillers dried grains with solubles	10.00	20.00
Fish meal	5.00	---
Dried whey	10.00	---
Monocalcium P	0.45	0.37
Limestone	1.00	1.4
Sodium chloride	0.50	0.50
L-Lysine-HCl	0.48	0.45
DL-Methionine	0.19	0.12
L-Threonine	0.20	0.14
L-Tryptophan	0.08	0.04
L-Valine	0.13	0.01
Phytase ⁴	0.05	0.05
Zinc oxide	0.25	---
Vitamin and mineral premix ⁵	0.15	0.15
Chlortetracycline	±	---
Tiamulin	±	---
Total	100	100

continued

Table 1. Composition of experimental diets (as-fed basis)¹

Ingredient, %	Control (d 0 to 14) ²	Common diet (d 14 to 28) ³
Calculated analysis		
Lysine	1.35	1.30
Isoleucine:lysine	57	63
Leucine:lysine	123	143
Methionine:lysine	39	35
Methionine and cysteine:lysine	60	60
Threonine:lysine	65	65
Tryptophan:lysine	21	21
Valine:lysine	72	72
Total lysine, %	1.52	1.50
ME, ⁶ kcal/lb	1,501	1,487
NE, kcal/lb	1,112	1,080
SID Lys:NE, ⁷ g/Mcal	5.51	5.46
CP, ⁸ %	22.2	24.0
Ca, %	0.81	0.70
P, %	0.67	0.56
Available P, %	0.55	0.40
Na, %	0.36	0.28
Cl, %	0.59	0.42

¹ Experimental diets were fed from d 0 to 14 after a 7-day pretrial period.

² Antibiotics replaced corn in the control diet to provide chlortetracycline (CTC) at 9.98 mg/lb body weight and tiamulin at 2.27 mg/lb BW or the combination of CTC and tiamulin. Pigs that received antibiotics in the water were fed the control diet.

³ Common diet fed from day 14 to 28 after treatment.

⁴ Optiphos 2000, (Huvepharma Inc., Peachtree City, GA) provided 227 phytase units (FTU)/lb of diet, for an estimated release of 0.14% available P.

⁵ Each kg of premix contained 66,700 mg Fe from ferrous sulfate, 73,300 mg Zn from zinc oxide, 26,700 mg Mn from manganese oxide, 10,000 mg Cu from copper sulfate, 500 mg I from calcium iodate, 200 mg Se, 5,344,484 IU vitamin A, 100,210 IU vitamin E, 21 mg vitamin B12, 4,007 mg riboflavin, 15,366 mg pantothenic acid, 29,061 mg niacin, 668 mg folic acid, 1,201 mg vitamin B6, 67 mg biotin, 1,336,122 IU vitamin D3, and 1,671 mg vitamin K.

⁶ ME = metabolizable energy. NE = net energy.

⁷ SID = standardized ileal digestible.

⁸ CP = crude protein.

Table 2. Chemical analysis of phase 2 and 3 diets (as-fed basis)¹

Item, %	Control	Chlortetracycline	Tiamulin	Chlortetracycline and tiamulin	Common diet ²
Dry matter	90.4	90.8	90.3	91.1	90.5
Crude protein	22.1	21.6	21.6	21.7	24.2
NDF ³	9.0	7.6	8.8	9.8	11.7
Ca	0.93	0.97	0.80	0.86	0.80
P	0.61	0.64	0.63	0.66	0.57

¹ A representative sample of each diet was collected from the feeders of each treatment, homogenized, and analyzed for proximate nutrients (Ward Laboratories, Kearney, NE).

² Common diet fed from day 14 to 28 after treatment period.

³ NDF = neutral detergent fiber.

Table 3. Evaluating the route of antibiotic administration and its effect on nursery pig growth performance¹

Item ^{2,3}	Control	Chlortetracycline ⁴		Tiamulin ⁵		Chlortetracycline and tiamulin	SEM	Antibiotic		
		In-feed	In-water	In-feed	In-water			× route	Antibiotic	Route
d 0 to 14 (treatment period)										
ADG, lb	1.01	1.10 ^x	1.05 ^x	1.02	1.06 ^x	1.09 ^x	0.020	0.002	0.010	0.529
ADFI, lb	1.37	1.49 ^x	1.42 ^y	1.43 ^x	1.41 ^y	1.46 ^x	0.028	0.162	0.117	0.014
F/G	1.36	1.35	1.35	1.40 ^x	1.34	1.34	0.012	0.001	0.028	0.001
d 14 to 28 (post treatment period)										
ADG, lb	1.28	1.33 ^y	1.31	1.30	1.34 ^x	1.33	0.024	0.071	0.980	0.669
ADFI, lb	2.00	2.09 ^y	2.06	2.05	2.08 ^y	2.12 ^x	0.051	0.375	0.706	0.986
F/G	1.56	1.57	1.57	1.58	1.55	1.59	0.032	0.220	0.628	0.478
Overall (d 0 to 28)										
ADG, lb	1.15	1.22 ^x	1.18 ^y	1.17	1.20 ^x	1.21 ^x	0.020	0.004	0.149	0.899
ADFI, lb	1.69	1.80 ^x	1.75 ^y	1.75 ^y	1.75 ^x	1.80 ^x	0.037	0.231	0.344	0.263
F/G	1.47	1.47	1.48	1.50 ^x	1.46	1.48	0.021	0.005	0.441	0.032
BW, lb										
d -7 (Pre-trial)	14.55	14.54	14.38	14.49	14.49	14.53	0.350	0.642	0.861	0.614
d 0	19.54	19.59	19.39	19.58	19.61	19.42	0.448	0.611	0.646	0.686
d 14	33.84	35.09 ^x	34.24	34.02	34.58	34.69	0.644	0.047	0.297	0.687
d 28	52.80	54.69 ^x	53.51	53.15	54.34 ^x	54.22 ^y	1.009	0.020	0.476	0.991

¹ A total of 2,592 pigs (initially 14.5 lb, BW) were used in a 28-d growth trial with 27 pigs/pen and 12 replicates/treatment. Treatment diets were fed from d 0 to 14. After the experimental period pigs were fed a common diet from d 14 to 28.

² BW = body weight. ADG = average daily gain. ADFI = average daily feed intake. F/G = feed-to-gain ratio.

³ Results were considered significant at $P \leq 0.05$ and marginally significant at $0.05 < P \leq 0.10$.

⁴ Chlortetracycline (CTC) provided via feed or water to achieve 9.98 mg/lb body weight.

⁵ Tiamulin in feed (2.27 mg/lb BW) or water (10.43 mg/lb BW).

^x Indicates this treatment had performance different from the control in a pairwise comparison ($P < 0.05$).

^y Indicates this treatment had performance different from the control in a pairwise comparison ($P < 0.10$).