A global multilocation study to evaluate the effect of ceftiofur sodium on preweaning mortality and growth performance

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Summary

Objective: To evaluate the effectiveness of ceftiofur sodium administered to preweaned piglets in reducing mortality and improving growth performance.

Methods: This study was conducted at six sites in five countries. Eligible farms had a history of neonatal diseases with poor growth and/or abnormally high mortality in preweaned pigs. Pigs received either 3 mg ceftiofur free acid equivalent (CFAE) per kg bodyweight (n = 2693, "Ceftiofur"), or a placebo (n = 2734, "Controls"), administered by intramuscular (IM) injection on days 1 and 7 of age and at weaning (mean 20 days of age). Mortality and average daily gain (ADG) from birth to weaning and from birth to 7 days postweaning were statistically evaluated.

Results: Mortality tended (P =.06) to be reduced in the Ceftiofur group (7.5%) compared to Controls (11.0%). Average daily gain from birth to weaning was significantly (P=.04) improved in the Ceftiofur group (0.215 kg, 0.473 lb) compared to Controls (0.204 kg, 0.449 lb). Average daily gain in Ceftiofur-treated pigs through the end of the trial (7 days postweaning) was significantly (P =.02) improved over ADG in control pigs. The percentage of lightweight piglets (i.e., pigs that were <3.63 kg [<8 lb] at weaning) was reduced by 16.2% in the Ceftiofur group, significantly lower than Controls (P=.04). The effects of Ceftiofur treatment were consistent for all six locations with numerical superiority in at least one of the measured variables.

Implications: Ceftiofur sodium improved growth performance and tended to decrease mortality in pigs from birth to weaning and from birth to 7 days postweaning under a global variety of commercial production conditions.

Keywords: pig, swine respiratory disease, ceftiofur sodium, average daily gain, mortality, preweaned piglets

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Microorganisms, transmitted to piglets from their environment and their dams, pose a constant challenge to preweaned pigs. Early in life, maternal antibodies in milk may protect piglets from being colonized by these pathogens;[1] however, this protection diminishes over time as maternal antibodies decline. Pigs can then be overwhelmed by exposure to microbiological challenges, which is clinically manifest as high mortality and poor weight gain.

The objective of the present study was to determine, by comparing production data from six production systems in five countries, whether preweaning administration of ceftiofur sodium could improve weight gain and mortality rate from birth through weaning and into the nursery.

Materials and methods

This study included six sites in five countries (China, Japan, Mexico, Spain, and the United States) with a total of 5427 neonatal pigs. To be included in the study, herds had to have a history of neonatal diseases (respiratory disease, streptococcal infection, and/or diarrhea) accompanied by poor preweaning growth performance and/or mortality rates higher than the industry averages in that country. Before the trial began, a veterinarian and site coordinator conducted a diagnostic evaluation of 10- and 21-day-old piglets at each study location. This evaluation included any of several procedures, such as necropsy of selected pigs, serological profiling, clinical observations, and/or evaluation of growth performance and herd mortality based on the historical data from the farms.

Experimental design

The experimental units were litters made up of natural and cross-fostered pigs, resulting in an average of 10 pigs per litter from sows or gilts. Eligible gilts and sows were assigned to a farrowing room, each of which contained at least 24 farrowing crates. Separate randomization lists were provided for gilts and sows. Cross-fostering was allowed only before the first injection was given at 1 day of age.

Although weaning age varied from one location to another based on the local practice, it was recommended that weaning occur at 14–20 days in an all-in–all-out (AIAO) fashion. All pigs were identified by treatment group and litter of origin with colored ear tags at 1 day of age. In the nursery, littermates were kept together and penned only with those in the same treatment group. Piglet birthweight, sex, genetic origin, and other potential confounding variables were assumed to be randomly distributed within farrowing rooms.

All piglets in a room were allocated to the same treatment, either:

- a "Control" group that received a placebo (sterile water injection); or
- a "Ceftiofur" group that received ceftiofur (ceftiofur free acid equivalent) at the dose of 3 mg per kg bodyweight. To prepare ceftiofur for injection, a 1-g vial of the medication

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was reconstituted with 20 mL of sterile water for injection to achieve a concentration of 50 mg CFAE per mL (Table 1).

Herd staff administered the respective intramuscular (IM) injection to piglets on each of days 1 and 7 of age and at weaning (approximately 20 days of age).

In each location, the trial was either run once in four rooms (two Control, two Ceftiofur), or in two rooms and replicated once.

Piglets were individually weighed at birth, at weaning (days 14–20 of age), and 7 days postweaning. Weight and mortality data were recorded by herd staff at each location.

Statistical analysis

Trial site block, treatment, and random error were included in the model, using litter as unit of analysis. Overall mortality rate and ADG at weaning and 7 days postweaning were decision variables. Mortality rate (%), ADG from birth to weaning, and ADG from birth to 7 days postweaning were transformed by Freeman-Tukey arcsine. Each ADG variable analysis was based on location, treatment averages, and the number of pigs contributing to the weight gain. Secondary variables for descriptive purposes were litter weight at weaning, number of pigs per sow, age at weaning, and weights at birth, weaning, and 7 days postweaning. An analysis of lightweight piglets (i.e., piglets weighing <3.63 kg [<8 lb]) at weaning was also conducted. Piglets with weaning weights < standard were coded as 1, those ≥ were coded as 0.

An ANOVA was conducted using the PROC GLM and PROC MIXED procedures in the SAS system.[2] The models included location, treatment, and error, with location as a random effect and treatment as a fixed effect. The analyses were weighted by the number of pigs at each location and treatment average. The least-squares means for the decision variables reflect these weights. A coefficient of variation (CV) was calculated for each variable as the standard deviation divided by the overall mean to measure the relative amount of biological variation present for each variable.

A two-tailed test was used to analyze treatment effect for all decision variables. The percentage of lightweight pigs was calculated for each litter and a Freeman-Tukey transformation performed by litter to obtain *P* values. Calculations, using location and treatment in the model, were performed for mean squares, treatment means, least significant differences, and *P* value.

Results

An overall total of 551 newborn litters with 5427 piglets were included in the study, with a mean of 9.9 pigs per sow (Table 2). The overall mean weaning age was 20 days, ranging from approximately 16–28 days of age. Within a given location, the weaning age was relatively consistent. The mean weight of a pig at birth was 1.55 kg (SD = 0.36) with some variations in different locations.

Overall mortality tended (*P* =.06) to be improved in Ceftiofur-treated pigs (7.5%) compared to controls (11.0%).

Average daily gain (ADG) from birth to weaning was significantly improved in the Ceftiofur-treated litters compared to Controls (*P* =.04) (Figure 1). This difference persisted through 7 days postweaning (*P*=.02). The ADG advantage resulting from Ceftiofur treatment was observed in all locations. Among all locations, the ADG advantage of Ceftiofur treatment over Controls was the highest when the weaning age was 21 days, followed by pigs weaned at 18 and 24 days, respectively.

The percentage of lightweight pigs overall

Table 1: Ceftiofur dosage

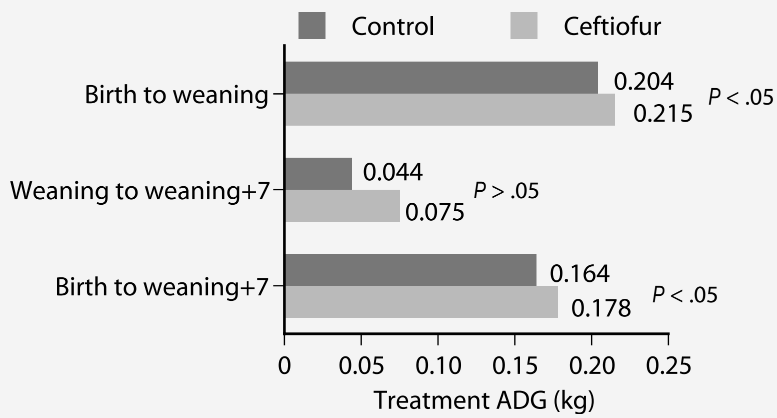
	Ceftiofur sodium (CFAE)			Placebo
Days of age	Dosage	Volume	Preparation	volume
≤ 1	4 mg	1.0 mL	1 g + 20 mL + 230 mL	1.0 mL
7	8 mg	1.0 mL	1 g + 20 mL + 105 mL	1.0 mL
At weaning*	12 mg	1.0 mL	1 g + 20 mL + 63 mL	1.0 mL

* For those pigs that were older than 14 days at weaning, the dose was adjusted to 3 mg CFAE/kg

Table 2: Ancillary variables of study herds

Location	Number of litters	Number of pigs born alive	Number of pigs/sow Mean	SD	Age at weaning (days) Mean	SD
Control						
China	50	451	9.0	1.9	28	0
Japan	47	503	10.7	0.9	21	1
Mexico	52	464	8.9	1.9	16	1
Spain	48	504	10.5	2.3	18	3
United States	26	254	9.8	1.0	24	3
United States	54	558	10.3	1.3	17	3
Overall	**277**	**2734**	**10.0**	–	**20**	–
Ceftiofur						
China	50	453	9.1	1.9	28	0
Japan	46	481	10.5	1.4	21	1
Mexico	54	472	8.7	1.4	16	0
Spain	46	502	10.9	2.4	18	3
United States	26	256	9.8	0.9	24	3
United States	52	529	10.2	1.9	15	3
Overall	**274**	**2693**	**9.8**	–	**20**	–
Study Overall	**551**	**5427**	**9.9**	–	**20**	–

Figure 1: Differences observed in ADG



was significantly reduced in the Ceftiofur-treated litters compared to Controls (P=.04) (Figure 2). Litter weight at weaning was (P =.12) improved for Ceftiofur-treated pigs compared to Control pigs (Figure 3).

Discussion

Our observation that mortality was numerically decreased and ADG significantly increased in the Ceftiofur-treated pigs is consistent with a number of field studies which indicate that using ceftiofur in weaned pigs with swine respiratory disease improved disease control and resulted in higher daily weight gains and lower mortality and cull rates.[4–7] A model study of colibacillosis also shows ceftiofur is effective in reducing mortality, bacterial shedding, and diarrhea, and in increasing weight gain.[8] In the present global multilocation study, greater reduction of mortality was achieved in those operations with the highest relative rates of mortality.

The cost-effectiveness of treatment with ceftiofur depends on several factors in addition to its biological impact. These factors include, minimally, the cost of the drug, the cost of feed, and the market price for hogs. Such variables will vary widely from country to country. A rigorous multinational economic analysis of ceftiofur treatment, however, is beyond the scope of this study. However, in a cursory cost:benefit analysis for the United States industry—using mean values for drug and feed costs and market hog prices—we found that ceftiofur treatment resulted in a positive return on investment in this study herd (D. Holtcamp, personal communication, 1999).

Decreasing the number of lightweight pigs at weaning is a constant challenge for the swine industry. A few production techniques (split weaning, split nursing) have been shown in a research setting to decrease the number of lightweights at weaning, but are too expensive or difficult to implement in commercial herds. In this study, treatment with ceftiofur not only increased mean weaning weight, but also reduced the number of lightweight pigs.

Weaning age plays an important role in controlling disease pathogens for improving herd health.[1] For practical reasons, the actual weaning ages used in herds included in this study varied from one location to another. Although we did not statistically evaluate the effect of weaning age on any of the performance parameters monitored in this study, we did observe that growth performance and mortality in Ceftiofur-treated pigs was numerically improved in those pigs that were weaned at older ages. Theoretically, the earlier pigs are weaned, the more pathogens can be eliminated.[1] However, early weaning may not reduce mortality in operations where early weaning requirements for nutrition, housing, and management technology cannot be adequately met.

Because this study ended at 7 days post-weaning, long-term outcomes could not be directly observed in later production stages. Additional trials could be conducted to follow the treatment effects all the way to market. However, based on previous reports, the advantages provided by this program are likely to continue on into the later phases of production.[7,10]

Antibiotic programs are health management tools recognized to enhance good husbandry practice to prevent, treat, and enhance production. Adding ceftiofur to a health program can easily be incorporated into the existing management practices. Such programs, however, cannot replace sound farm management and veterinary practices. Producers should be aware that key management strategies—including AIAO animal flow, strict biosecurity, herd vaccinations, herd health management, and segregated early weaning, if feasible—should not be neglected in a herd whether or not an antibiotic program is in place.

Implications

- A preweaning program using ceftiofur sodium increased ADG at weaning by 5.4% (P=.04). The effect continued

Figure 2: Distribution of weaning weight by treatment

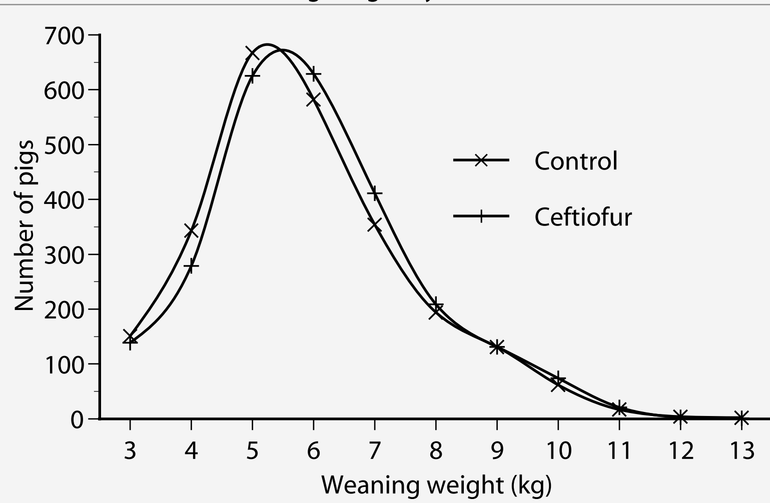


Figure 3: Litter weights by study and treatment group

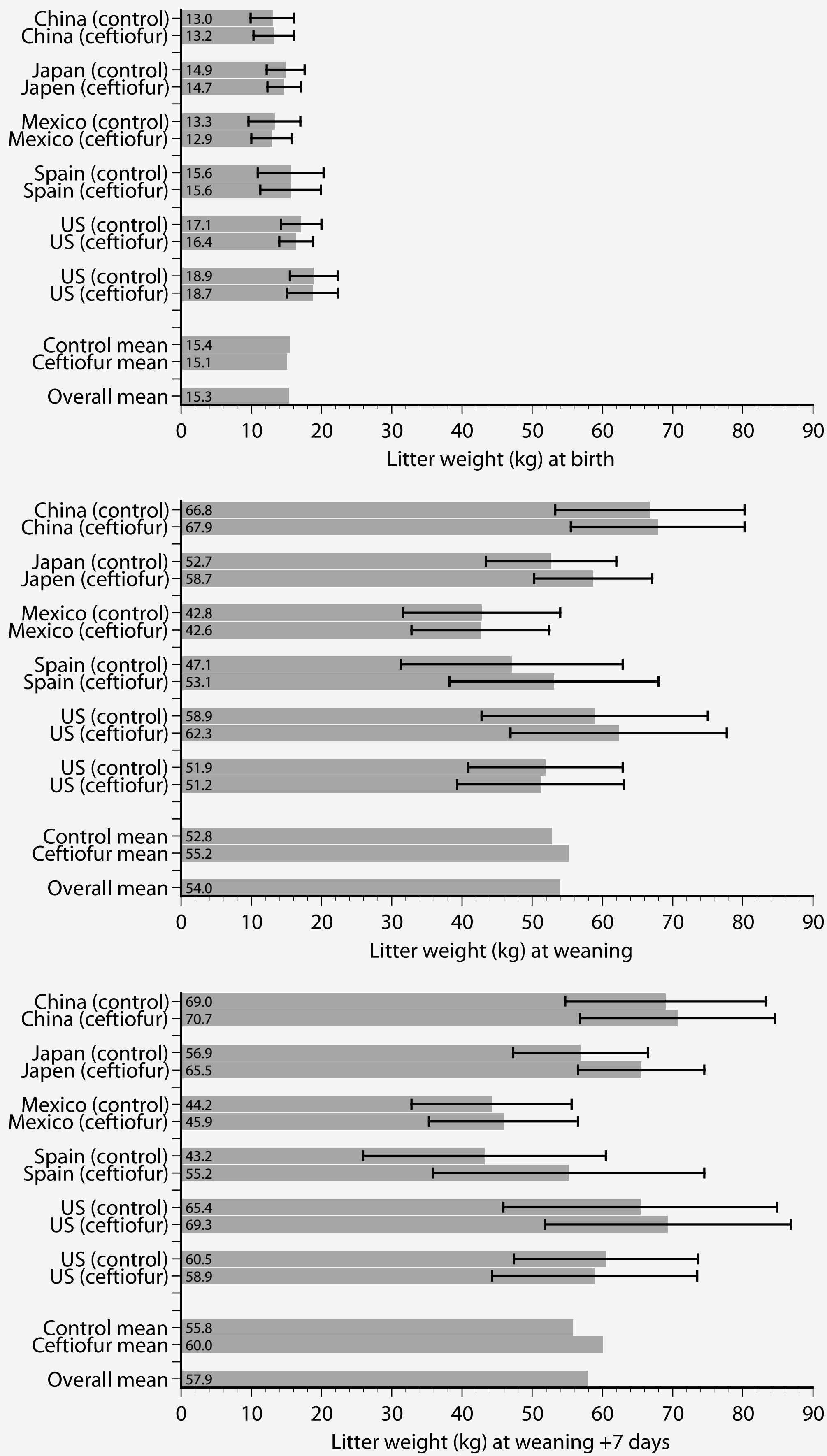


Table 3: Weight gain and mortality analysis

Source	Degrees of freedom	Average daily gain, lb (Birth to weaning)	Average daily gain, lb (Weaning to weaning +7)	Average daily gain, lb (Birth to weaning +7)	Percent Mortality*,‡	Percent Mortality†,‡
Location	5	.09 (.07)	1.81 (.05)	.26 (.01)	4050	2600
Treatment	1	.18 (.03)	1.32 (.11)	.28 (.01)	1720	1070
Error	5	.02	.36	.02	315	170
Coefficient of variation		68.6%	1052%	84.2%	210%	75.2%
Least significant difference (for two sided .05 test to assess relative precision among response variables)						
Least significant difference		.008	.033	.008	3.0	2.2

* ANOVA based on raw percentages

† ANOVA based on Freeman-Tukey transformation to satisfy the assumptions of ANOVA

‡ Ceftiofur versus control did not differ significantly, P = .06

through 7 days postweaning, for a significant total weight gain improvement of 8.5% in treated pigs (*P*=.02).

- Using ceftiofur also significantly reduced the percentage of lightweight piglets at weaning (*P*=.04).
- The treatment effects were consistent across scattered global locations.

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