

# The effect of oral meloxicam on piglet performance in the preweaning period

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## Summary

A total of 5045 piglets were castrated and received 1 of 2 treatments: control (C; surgically castrated); or meloxicam (M; surgically castrated and administered oral meloxicam). Oral meloxicam administration at castration required 5 additional seconds and had no effect on average daily gain, mortality, or survivability in the preweaning period.

**Keywords:** swine, castration, meloxicam, growth, mortality

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## Resumen - El efecto de meloxicam oral en el comportamiento de lechones durante el periodo de predestete

Un total de 5045 lechones fueron castrados y recibieron 1 de 2 tratamientos: control (C; quirúrgicamente castrados); o meloxicam (M; quirúrgicamente castrados y meloxicam oral). La administración oral de meloxicam al momento de la castración requirió de 5 segundos adicionales y no tuvo efecto en la ganancia diaria de peso, mortalidad o supervivencia en el periodo predestete.

## Résumé - Effet de meloxicam oral sur les performances des porcelets durant la période de présevrage

Un total de 5045 porcelets furent castrés et reçurent un des deux traitements suivants: témoin (C; castré chirurgicalement); ou meloxicam (M; castré chirurgicalement et administration orale de meloxicam). L'administration orale de meloxicam lors de la castration demandait 5 secondes additionnelles et n'avait aucun effet sur le gain moyen quotidien, la mortalité, ou la survie durant la période de présevrage.

In commercial swine production systems, surgical castration is a routine practice performed on male piglets within the first week of life.<sup>1</sup> This procedure results in a negative affective state of pain as demonstrated by physiological and behavioral deviations in the piglet.<sup>2</sup> Health and performance can also be compromised as castrated piglets are more likely to die during the preweaning stage<sup>3</sup> and lose weight post procedure.<sup>4</sup> Currently, both Canada and the European Union require analgesic administration prior to or at the time of castration.<sup>5,6</sup>

A class of analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), are ideal options for on-farm use based on low cost and administration ease.<sup>7</sup> Meloxicam is an NSAID that alleviates pain and inflammation by decreasing prostaglandin synthesis through inhibition of the cyclooxygenase 2 pathway.<sup>8</sup> In the United States, under the Animal Medicinal Drug Use Clarification Act, meloxicam can be prescribed extra-label to alleviate pain and suffering in pigs.<sup>9</sup> Meloxicam is a

potential candidate for castration pain management based on previous work demonstrating its efficacy when administered preemptively via intramuscular injection.<sup>10,11</sup>

While previous work has shown meloxicam to reduce pain sensitivity associated with castration, no studies to date have evaluated the effects of administering oral meloxicam at the time of castration on piglet performance in the preweaning period. Therefore, the objective of the present study was to evaluate the effects of oral meloxicam administered at the time of castration on piglet performance preweaning.

## Materials and methods

The protocol for this study was approved by The Ohio State University Animal Care and Use Committee.

## Animals

Male commercial crossbred piglets (n = 5045) across 783 multiparous sow

litters ( $\geq$  parity 2) were enrolled in 1 study during the preweaning period on 1 commercial sow farm in the Mideastern United States from May to August 2018 (11 weeks total). Formal sample size calculations were not conducted; rather, the sample size was determined utilizing previous literature evaluating the effect of meloxicam on production parameters in commercial preweaned piglets.<sup>7</sup> In addition, sample size was selected to ensure pigs were enrolled across all farrowing rooms and throughout the entire summer season to minimize seasonal or room effect and was limited based on farm productivity. Herd health was consistent throughout the study; the herd tested negative for porcine reproductive and respiratory syndrome virus, porcine epidemic diarrhea virus, and *Mycoplasma*, and showed no signs of swine influenza. For the entirety of the study, male piglets were housed with the sow and female littermates in a standard farrowing crate (1.5 m wide  $\times$  2.1 m long; Pig Saver Bowed Bar Farrowing Crate; Farmer Boy Ag). At 1 day of age, piglets were tail docked, ear tattooed, and processed according to farm standard operating procedures. Piglets had free access to the sow for nursing and to 1 water source throughout the study (Stainless Steel Farrowing Pan Waterer; Farmer Boy Ag).

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## Enrollment and treatments

Piglets were enrolled in the trial the day prior to castration. Enrollment was continuous over 11 weeks of production, with a daily target enrollment of 100 to 150 male piglets. Litters were selected across 8 farrowing rooms (72 stalls per room) based on litter age (2-4 days of age at enrollment), and all male piglets within the selected litters were enrolled. At the time of enrollment, piglets were weighed (start weight) and uniquely identified by ear tag (style 681 tag; National's Band and Tag Company). Piglets within a litter were blocked by weight and assigned to 1 of 2 treatments, ensuring both treatments were equally represented within a litter and the average start weight of both treatments were similar. Treatments were as follows: control (C; surgically castrated without treatment); or meloxicam (M; surgically castrated and administered 1.0 mL of 2.4 mg/mL oral meloxicam; target dose was 1.0 mg/kg; Aurora Pharmaceutical, LLC). No positive sham treatment group was included because this research was conducted on a commercial swine farm whose standard operating procedures required all male piglets be castrated. Given the individual castrating the piglets was also administering meloxicam, a saline control was not administered as the individual was already not blinded to the treatment groups.

Throughout the trial, enrolled piglets could be cross fostered by farm personnel to a recently weaned nurse sow if the piglets met the criteria outlined in the farm cross fostering protocol (eg, thin, small, overall poor doing, and < 10 days of age). Data on cross fostering, mortality, and end weights were recorded for each individual piglet.

## Castration procedure

Piglets were castrated the day following enrollment (average age [SD], 3.9 [0.4] days; range, 3-5 days of age). Piglets were individually removed from the farrowing stall and castrated by the same trained technician starting at 7:00 AM. One vertical incision was made through the scrotum over each testicle using a side cutter instrument (Multi-Use Side Cutter; Jorgensen Labs). Testicles were extracted through the fascia by applying pressure to the scrotal area and were removed by severing the spermatic cord using scissors (German Surgical Scissors; Jorgensen Labs). Piglets in the M treatment received a 1.0 mL oral drench of meloxicam immediately following castration, whereas

C treatment piglets did not receive drug administration. Once the castration procedure was complete, piglets were placed back into the farrowing stall. The castration procedure was timed for a subset of piglets ( $n = 9$  per treatment;  $N = 18$ ) during the final week of the trial to determine procedure length for both treatments. Castration time was defined as time from the first skin incision to placement of the piglet into the farrowing stall.

## Statistical analysis

Data were analyzed using SAS version 9.4 (SAS Institute Inc). Piglet was the experimental unit, treatment was the predictor of interest, piglet start weight, and sow parity were the relevant variables included. Outcomes included procedure time, average daily gain (ADG; kg/d), cross foster, mortality, and survival. Procedure time was analyzed using a linear mixed model (PROC MIXED) with time in seconds as the outcome and treatment as the only predictor. Average daily gain was calculated ( $[\text{end weight} - \text{start weight}] / \text{days on trial}$ ). Cross foster and mortality were recorded as binary outcomes (yes or no). Mortality data between castration to 18 days of age were analyzed to standardize the risk period for all piglets due to differences in time on trial. Start weight was grouped by quartiles into 3 categories: Small (S; < 1.6 kg), Intermediate (I; 1.6-2.2 kg), and Large (L; > 2.2 kg). Sow parity (range, 2-11) was collapsed into natural groupings based on similar piglet ADG and similar sow age. Average daily gain between parity was assessed using a mixed model with ADG as outcome and parity as the only predictor. Sequential parities with similar ADG ( $P > .05$ ) were collapsed together into 4 categories: Parity 2 (P2), Parity 3 and 4 (P34), Parity 5 and 6 (P56), and Parity 7 and older ( $\geq P7$ ). Univariable analysis was used to check for collinearity among sow parity category and start weight category.

Four separate multivariable models were constructed for each of the previously listed outcomes. All final multivariable models included litter as a random effect and treatment, sow parity category, and start weight category as fixed effects. Two-factor interactions were tested, found not to be significant ( $P > .05$ ), and removed from the model. Average daily gain was analyzed using a mixed linear model with the PROC MIXED procedure in SAS. Residuals of ADG were also plotted and checked for normality. Average daily gain data was also screened for outliers using visual inspection

of graphs and Cook's distance. The odds of a piglet on trial being cross fostered or dying prior to 18 days of age was analyzed using 2 separate generalized linear mixed models with the PROC GLIMMIX procedure in SAS. These generalized linear mixed models included a binary distribution and the logit link function to account for the binary nature of these variables. Survival analysis with Cox proportional odds (PROC PHREG) was used to determine the odds of a piglet surviving to 18 days of age, with death being the censored variable. Piglets with missing end weights due to unknown causes and unknown sow parity were not included in any of the final analyses ( $n = 215$ ). In addition, 881 piglets were removed from trial prior to 18 days of age due to early weaning. For all models, the significance level was set at  $P \leq .05$  and  $P \leq .1$  was considered a trend.

To determine which explanatory variables should be included in multivariable models, univariable analysis was performed between all potential explanatory variables and outcomes of interest using either a mixed or logistic model. Explanatory variables tested at the univariable level for all models included start weight, sow parity group, removal weight, days of age at removal, age at castration, and litter. Explanatory variables were used in multivariable analysis only if they were associated with the outcome and the predictor of interest ( $P < .20$ ).<sup>12</sup> Explanatory variables with  $P \leq .05$  were included in the final model by utilizing backwards stepwise elimination. A change in estimate criterion  $\geq 30\%$  for the predictor of interest detected confounding variables and these variables remained in the model.

## Results

For all piglets, the mean (SD) start weight was 1.9 (0.5) kg (C: 1.9 [0.5] kg; M: 1.9 [0.5] kg), the mean (SD) end weight was 5.6 (1.5) kg (C: 5.7 [1.5] kg; M: 5.6 [1.5] kg), and the mean (SD) days on trial was 16.6 (2.9) days (C: 16.6 [3.0] days; M: 16.6 [2.9] days). The mean (SD) castration time was 24.8 (2.5) seconds for M piglets and 19.9 (1.9) seconds for C piglets (Table 1).

A total of 4584 piglets were included in the final analysis for ADG ( $n = 246$  died before removal from trial). Start weight category influenced ADG (standard error of the mean; SEM) ( $P < .001$ ; S: 0.19 [0.01] kg/day; I: 0.23 [0.01] kg/day; L: 0.27 [0.01] kg/d). Treatment did not affect ADG SEM (Table 1).

A total of 4830 piglets were included in the final analysis for cross fostering. Start weight category influenced ( $P < .001$ ) cross fostering with S piglets being 11.6 and 4.4 times more likely to be cross fostered than L and I piglets, respectively. The odds of cross fostering tended to be 1.3 times higher in C piglets compared to M piglets (Table 2; C:  $n = 165$ , M:  $n = 138$ ).

A total of 3949 piglets were included in the final analysis for mortality from castration to 18 days of age ( $n = 881$  piglets did not die but were removed from trial prior to 18 days of age). Start weight category influenced mortality ( $P < .001$ ) with S piglets being 9.2 and 4.4 times more likely to die than L and I piglets, respectively. Treatment had no effect on mortality to 18 days of age (Table 2; C:  $n = 114$ , M:  $n = 124$ ). A total of 4830 piglets were included in the final analysis for survival. Based on Cox proportional odds, treatment did not affect survival to 18 days of age (Figure 1;  $P = .56$ ).

## Discussion

The objective of this study was to evaluate the effects of oral meloxicam administered at the time of castration on piglet performance.

Given the welfare consequences associated with castration and the pressure placed on producers to manage pain, establishing realistic protocols that can be utilized on-farm without negatively impacting performance is critical. Results from this study indicate oral meloxicam administration at the time of castration resulted in no differences in piglet performance as demonstrated by no changes in ADG, mortality, or survivability.

In this study, administering meloxicam added an additional 5 seconds to the procedure. This conclusion is based on a small subset of piglet castrations and not all the piglets on trial. However, mean procedure length was recorded the last week of the study from the one trained technician castrating all piglets on trial, therefore providing an estimate of additional time required to administer oral meloxicam. In perspective, administering meloxicam on a 5000-sow farm farrowing 240 litters each week with 6 male piglets per litter would result in 2 additional hours of labor a week. This suggests that oral meloxicam can be effectively integrated into a large production system without resulting in exorbitant labor cost.

In our study, M piglets demonstrated no difference in ADG, mortality, or survivability

compared to C piglets. Our results agree with previous work conducted by Kluijvers-Poodt et al<sup>10</sup> and others<sup>2,7</sup> who found meloxicam had no effect on growth or mortality when administered intramuscularly (IM) and preemptively. Although preemptive administration is likely to result in greater pain control,<sup>8</sup> it requires more handling and labor time and will not result in piglet performance benefits as demonstrated by our work.

In the present study, C piglets tended to have higher odds of being cross fostered compared to M piglets. Castration performed without analgesics has been shown to reduce nursing bouts and result in temporary weight loss in the days following the procedure.<sup>4,13</sup> Meloxicam administered IM prior to castration can eliminate this deviation in feeding behavior and prevent temporary piglet weight loss.<sup>10,14</sup> As per the cross fostering protocol on this farm, any piglet identified as small, thin, overall poor doing, and < 10 days of age was a candidate for cross fostering. The potential short-term effects of meloxicam on nursing behavior around the time of castration may have influenced piglet body condition resulting in more C piglets being cross fostered.

**Table 1:** Least squares means (SEM) for ADG and castration time for piglets castrated or castrated and given oral meloxicam

Parameter	Control*	Meloxicam <sup>†</sup>	P value <sup>‡</sup>
ADG, kg/day	0.23 (0.01)	0.23 (0.01)	.92
Castration time, s/pig	19.9 (1.05)	24.8 (1.05)	.002

\* Control pigs were surgically castrated without treatment.

† Meloxicam pigs were surgically castrated and administered 1.0 mL of oral meloxicam with a target dose of 1.0 mg/kg.

‡ The P value for ADG was obtained using a multivariable linear mixed model with litter as the random effect and treatment, sow parity category, and start weight category as fixed effects. The P value for castration time was obtained using a linear mixed model with treatment as the only fixed effect.

SEM = standard error of the mean; ADG = average daily gain.

**Table 2:** Probability of being cross fostered or dying for piglets castrated or castrated and given oral meloxicam

Variable	Odds ratio	95% CI	P value*
Probability of being cross fostered <sup>†</sup>			
Control <sup>‡</sup> compared to Meloxicam <sup>§</sup>	1.3	0.99-1.61	.07
Probability of dying between castration and 18 days of age			
Control <sup>‡</sup> compared to Meloxicam <sup>§</sup>	0.9	0.69-1.20	.5

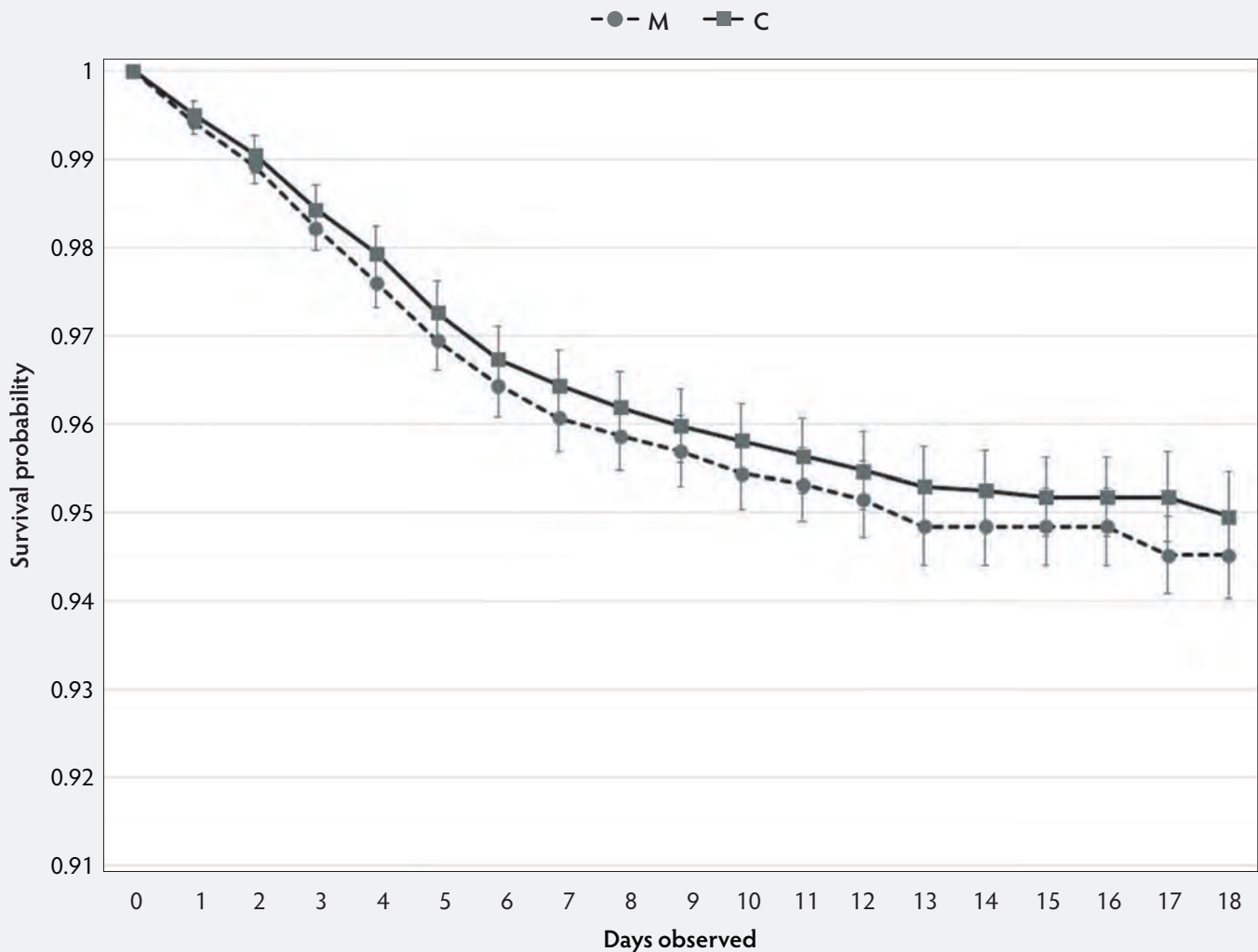
\* P values were obtained using multivariable linear mixed models with a binary distribution and a logit link function which included litter as the random effect, and treatment, sow parity category, and start weight category as the fixed effects.

† Cross fostered was defined as piglets being moved to a recently weaned nurse sow by farm personnel.

‡ Control pigs were surgically castrated without treatment.

§ Meloxicam pigs were surgically castrated and administered 1.0 mL of oral meloxicam with a target dose of 1.0 mg/kg.

**Figure 1:** Survival analysis using Cox proportional odds of surviving to 18 days of age for piglets castrated or castrated and given oral meloxicam. Data were analysed using PROC PHREG in SAS version 9.4 (SAS Institute Inc) and the model included treatment, sow parity, and piglet start weight as fixed effects. There was no treatment effect on piglet survival ( $P = .56$ ). Control (C; surgically castrated without treatment); or Meloxicam (M; surgically castrated and administered 1.0 mL of 2.4 mg/mL oral meloxicam; target dose 1.0 mg/kg).



However, this trend in cross fostering did not translate to a difference in ADG in our trial. This may be due to meloxicam's short-term effect on nursing bouts<sup>10,12</sup> and castration's short-term effect on weight gain.<sup>4</sup> Further research evaluating oral meloxicam's effect on nursing behavior and piglet body condition is needed.

Our study demonstrated that oral meloxicam administered at the time of castration had no effect on piglet preweaning performance. As consumers become increasingly concerned with animal welfare and pressure is placed on producers to manage pain, establishing realistic protocols that can be utilized on-farm without negatively impacting performance is critical. Based on our results, oral meloxicam administered at the

time of castration had no effect on ADG, mortality, or survivability in piglets during the preweaning stage and required only 5 additional seconds to administer.

### Implications

Under the conditions of this study, administration of oral meloxicam at the time of castration:

- Did not impact piglet ADG, mortality, or survivability.
- Decreased the odds of cross fostering, likely due to increased nursing bouts.
- Increased the castration procedure time by 5 seconds per piglet.

### Acknowledgments

#### Conflict of Interest

None reported.

#### Disclaimer

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\* Non-refereed references.



# CONVERSION TABLES

## Weights and measures conversions

Common (US)	Metric	To convert	Multiply by
1 oz	28.35 g	oz to g	28.4
1 lb (16 oz)	453.59 g	lb to kg	0.45
2.2 lb	1 kg	kg to lb	2.2
1 in	2.54 cm	in to cm	2.54
0.39 in	1 cm	cm to in	0.39
1 ft (12 in)	0.31 m	ft to m	0.3
3.28 ft	1 m	m to ft	3.28
1 mi	1.6 km	mi to km	1.6
0.62 mi	1 km	km to mi	0.62
1 in <sup>2</sup>	6.45 cm <sup>2</sup>	in <sup>2</sup> to cm <sup>2</sup>	6.45
0.16 in <sup>2</sup>	1 cm <sup>2</sup>	cm <sup>2</sup> to in <sup>2</sup>	0.16
1 ft <sup>2</sup>	0.09 m <sup>2</sup>	ft <sup>2</sup> to m <sup>2</sup>	0.09
10.76 ft <sup>2</sup>	1 m <sup>2</sup>	m <sup>2</sup> to ft <sup>2</sup>	10.8
1 ft <sup>3</sup>	0.03 m <sup>3</sup>	ft <sup>3</sup> to m <sup>3</sup>	0.03
35.3 ft <sup>3</sup>	1 m <sup>3</sup>	m <sup>3</sup> to ft <sup>3</sup>	35
1 gal (128 fl oz)	3.8 L	gal to L	3.8
0.264 gal	1 L	L to gal	0.26
1 qt (32 fl oz)	946.36 mL	qt to L	0.95
33.815 fl oz	1 L	L to qt	1.1

## Temperature equivalents (approx)

°F	°C
32	0
50	10
60	15.5
61	16
65	18.3
70	21.1
75	23.8
80	26.6
82	28
85	29.4
90	32.2
102	38.8
103	39.4
104	40.0
105	40.5
106	41.1
212	100

$$^{\circ}\text{F} = (^{\circ}\text{C} \times 9/5) + 32$$

$$^{\circ}\text{C} = (^{\circ}\text{F} - 32) \times 5/9$$

## Conversion chart, kg to lb (approx)

Pig size	Lb	Kg
Birth	3.3-4.4	1.5-2.0
Weaning	7.7	3.5
	11	5
	22	10
Nursery	33	15
	44	20
	55	25
	66	30
Grower	99	45
	110	50
	132	60
Finisher	198	90
	220	100
	231	105
	242	110
	253	115
Sow	300	135
	661	300
Boar	794	360
	800	363

1 tonne = 1000 kg

1 ppm = 0.0001% = 1 mg/kg = 1 g/tonne

1 ppm = 1 mg/L