The Impact of Translactational Delivered Meloxicam Analgesia on Biomarkers of Pain and Distress after Piglet Processing

A.S. Leaflet R2836

Jessica Bates, Post Doctoral Research Associate, Swine Medicine Education Center (SMEC), Veterinary Diagnostic and Production Animal Medicine (VDPAM), College of Veterinary Medicine; Locke Karriker, Associate Professor, SMEC, VDPAM, College of Veterinary Medicine; Matt Stock, Graduate Assistant-Teaching, Pharmacology Analytical Support Team (PhAST), VDPAM, College of Veterinary Medicine; Kelly Pertzborn, Veterinary Intern, PhAST, VDPAM, College of Veterinary Medicine; Luke Baldwin, SMEC Intern, VDPAM, College of Veterinary Medicine; Johann Coetzee, Associate Professor, (PhAST), VDPAM, College of Veterinary Medicine

Summary and Implications

Oral meloxicam was administered to sows post-farrowing to investigate a novel route of providing analgesia to processed piglets via translactational drug transfer. Physiologic indicators of piglet pain were analyzed to determine the effects on pain control. An effective meloxicam dosage was reached in 4/5 sow litters with no adverse clinical effects. Both piglet cortisol and cranial skin temperature measured by infrared thermography indicated significant differences in pain biomarkers between treatment groups. This study demonstrates the successful transfer of meloxicam in sow's milk and description of physiologic pain indicators after processing. It provides the foundation for future research into refining a novel, efficacious, and practical method of providing analgesia to piglets during processing.

Introduction

Consumers are increasingly concerned with the well-being and quality of life of animals raised for food. One particular area of growing concern is the management of pain associated with routine animal husbandry practices such as castration and tail docking in piglets.

Objective, repeatable methods of measuring pain are also needed. In previous studies, both cortisol and Substance P have been used to assess pain in livestock. Additionally, infrared thermography, which shows a decreased temperature in anatomical extremities during pain, has been used to describe these processes in livestock.

Presently, there are no validated and approved drug regimens to alleviate pain in swine. It is clear the US needs pain mitigation for routine use in swine production systems that will be safe for both handler and animal, efficacious, easily administered, and that maintains domestic and export markets.

Materials and Methods

Ten sows were selected, based on farrowing date, to receive either meloxicam (30 mg/kg) or equivalent volume of whey protein placebo in their daily feedings starting four days post-farrowing and continuing for three consecutive days. Blood and milk samples were collected from the sows at 12 hour intervals beginning directly prior to first feeding for four days through the end of the study. On Day 5 post farrowing, three boars and three gilts from each litter were castrated or sham castrated, tail docked and given an iron injection. Piglet blood samples were collected immediately before processing, and then at predetermined times over an 84 hour period until the end of the study. Additionally, infrared thermography (IRT) images of the surface of the piglet's cranium, left and right ears, and snout were captured at each piglet blood collection point. Eight days post-farrowing, tissue samples were collected at necropsy from sows and piglets to determine potential toxic effects of the prolonged high meloxicam dosage.

Results and Discussion

Piglet plasma from each litter was tested to confirm the presence of meloxicam using a validated HPLC- MS technique. Meloxicam was found in all of the litters in the treatment group (Mean ± SEM:285 ± 61 ng/mL). Levels reached concentrations known to be effective in equine (EC_{50}) in 4 of the 5 treatment litters (Figure 1).This value was extrapolated because the EC 50 in swine in currently unknown.

No adverse clinical effects were noted in meloxicam treated sows and piglets. However, on histopathology exam, subacute gastritis was noted in 2/5 meloxicam treated sows. Similar lesions and gross button ulcers were seen in 10/11 of piglets born to these sows.

IRT demonstrated a significantly lower cranial skin temperature in placebo vs. meloxicam treated piglets differences in cranial skin temperature ($p<0.0001$). Temperature decreases are seen due to pain and stress causing sympathetic nervous system activation. This leads to vasoconstriction, and thereby temperature decrease in the periphery of the body. However, there was no significant difference between snout and both ear temperatures. (Table 1.)

Meloxicam-treated piglets had a significantly lower percentage change from baseline levels of cortisol than placebo-treated piglets ($p<0.0001$) at one hour post-castration. However, differences became insignificant at subsequent time points.

Measurement of Substance P indicated no difference between placebo and meloxicam treated groups ($p=0.8685$).

This study demonstrates the successful transfer of meloxicam in sow's milk and description of physiologic pain indicators. It provides the foundation for future research into refining a novel, efficacious, and practically administered analgesia method.

Acknowledgements

This study was funded in part by the Iowa Livestock Health Advisory Council (Account #109-05-56) and the ISU College of Veterinary Medicine. The authors thank the following individuals who provided invaluable support to the project: the Swine Medicine Education Center (SMEC) Summer Interns, Larry Wulf, Erica Voris, and Jackie Peterson.

Figure 1. Piglet plasma meloxicam concentrations.

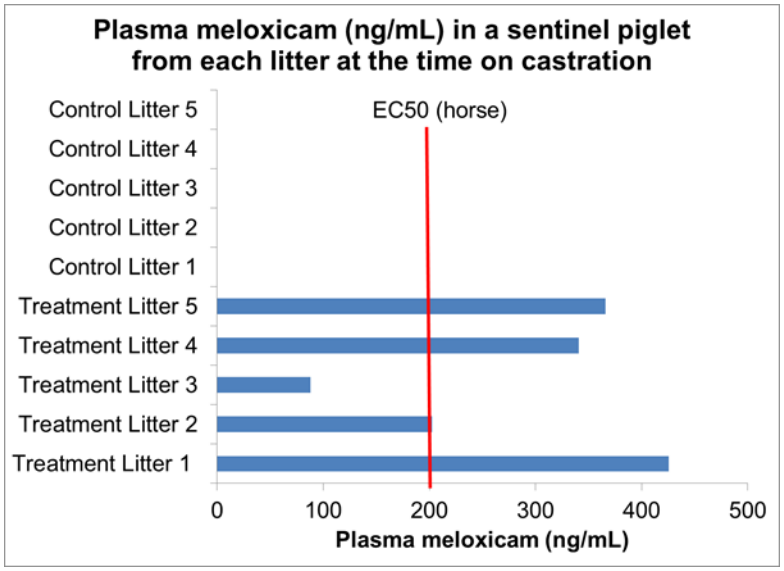

Table 1. Calculated pain biomarker parameters for piglets receiving via their dam's milk either lactose placebo (30 mg/kg to the sow) or meloxicam (30 mg/kg to the sow) mixed in feed and administered *per os*. Treatment was administered 24 h prior to processing and continued for three days.

	Experimental Group Calculated Means				P VALUES (model adjusted)		
Sex	CAST		SHAM				
Treatment	Placebo	Meloxicam	Placebo	Meloxicam			
Parameter					Time	Treatment1	Time*Treatment
Average Cortisol (ng/mL)	48.9	50.99	43.71	44.53	<0.0001	0.5947	0.0074
% change cortisol	36.37	11.6	50.72	-2.9	<0.0001	0.1196	<0.0001
Average Substance P (pg/mL)	89.24	95.53	81.13	96.63	0.2323	0.2367	0.8685
% change SubP	3.85	6.69	4.52	3.56	0.1196	0.8913	0.8879
Left Ear Temp (˚C)	32.06	32.44	32.56	32.35	<0.0001	0.0001	0.6108
Right Ear Temp (˚C)	34.37	33.83	34.07	33.85	<0.0001	0.9544	0.7653
Snout Temp (˚C)	31.56	32.43	32.1	31.93	<0.0001	0.5318	0.2337
Cranium Temp (˚C)	37.35	37.55	37.35	37.47	<0.0001	0.8615	0.1571

Treatment (Piglets received via milk from sow treated with meloxicam or placebo)