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A field study to evaluate the effects of meloxicam NSAID therapy and calving assistance on newborn calf vigor, improvement of health and growth in pre-weaned Holstein calves

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Abstract

The objective of this research was to evaluate the usefulness of a novel calf VIGOR assessment tool to measure birth trauma and associations with future health and growth. In addition, pain management therapy using meloxicam injectable solution was evaluated for calves suffering from birth trauma and reduced vigor. A total of 842 heifer and bull calves from 10 commercial dairy herds were enrolled in a randomized, double-blind clinical field trial. At birth, newborn VIGOR was evaluated by the dairy producer to assess the **V**isual appearance, **I**nitiation of movement, **G**eneral responsiveness, **O**xygenation, as well as heart and respiration **R**ate of the calf. Subsequently, calves were administered either a 1.0 mL subcutaneous injection of meloxicam or placebo solution. Each calf was measured for growth and assessed using a standardized clinical score for health at 1, 2, 3, and 6 weeks of age. Compared to unassisted calvings, calves born with assistance had lower vigor. Assisted calves treated with meloxicam had improved weight gain in the first week compared to placebo-treated calves. In contrast, treatment with meloxicam resulted in lower gains in observed but unassisted calves. Calves with improved newborn vigor and better health had significantly greater weight gain up to 6 weeks of age. Meloxicam-treated calves had better health from birth to 6 weeks of age. Overall, the calf VIGOR score is a good indicator of trauma at calving. Meloxicam therapy shows promise for improving health and growth, particularly for calves born with assistance.

Key words: dystocia, calf, vigor, pain, meloxicam

Résumé

L'objectif de ces travaux était d'examiner l'utilité d'un nouvel outil d'évaluation chez les veaux basé sur des critères établis pour mesurer le traumatisme de la naissance et son association avec la santé et la croissance à venir. En plus, la thérapie de la gestion de la douleur avec une solution injectable de méloxicam a été évaluée chez des veaux ayant subi un traumatisme à la naissance et montrant peu de vigueur. L'essai clinique sur le terrain randomisé et à double aveugle a impliqué 842 veaux mâles et femelles provenant de 10 troupeaux laitiers. À la naissance, plusieurs critères ont été évalués chez les nouveau-nés par le producteur du troupeau incluant l'apparence visuelle, l'initiation du mouvement, la réactivité générale, l'oxygénation de même que la fréquence cardiaque et respiratoire du veau. Par la suite, les veaux ont reçu une injection sous-cutanée de 1.0 ml de méloxicam ou d'une solution placébo. La croissance et le score clinique de santé ont été évalués chez chaque veau après un délai de 1, 2, 3 et 6 semaines. Les veaux nés avec assistance avaient une vigueur moindre que les veaux nés sans assistance. Le gain de poids à la première semaine était plus élevé chez les veaux assistés traités avec le méloxicam que chez les veaux assistés du groupe placébo. Au contraire, l'injection de méloxicam a réduit le gain de poids chez les veaux observés mais nés sans assistance. Le gain de poids était significativement plus élevé chez les veaux avec une amélioration de la vigueur et une meilleure santé jusqu'à l'âge de 6 semaines. Les veaux traités au méloxicam avaient une meilleure santé de la naissance jusqu'à l'âge de 6 semaines. Dans son ensemble, le score de santé proposé ici est un bon indicateur du traumatisme au vêlage. La thérapie impliquant l'injection de méloxicam est prometteuse sur le plan de la santé et de la croissance particulièrement chez les veaux nés avec assistance.

Introduction

There is great need for improved calving intervention strategies, as well as newborn calf monitoring protocols for use on-farm.[4,21] Holstein calves with birth weights above an average of 88.7 lb (40.3 kg) have increased risk of post-natal problems and mortality.[17] A considerable proportion of post-natal problems and the majority of calf deaths within the first month of age are associated with fetal stress at birth.[5,19]

Trauma resulting from inappropriate timing of assistance or the use of excessive force during calving can result in a large number of calf deaths.[10] When excessive force is applied during the delivery process, trauma inflicted can cause fractures to the ribs and vertebrae.[29] Another consequence of forced extraction of the fetus is premature rupture of umbilical vessels. If the calf is unable to regulate its own respiration, respiratory and metabolic acidosis will develop. Acidosis, as well as trauma, stress, and injury from dystocia, can result in the calf's inability to maintain homeostasis, stand, and suck colostrum in a timely manner, leading to increased risk of failure of passive transfer (FPT).[23] It has been shown that colostrum consumption during the first 12 hours after birth is reduced by 74% in calves with fetal distress.[35] In addition, severe acidosis can cause immediate death of the calf, or reduce long-term health and survival.[5]

It is logical that pain and inflammation following an assisted calving may interfere with the physiological and behavioral status of newborn calves, including their motivation to consume colostrum. Little is known about the effect of this pain on calf vigor, health or growth. There is little published data on appropriate therapeutic interventions that can be used to control pain and inflammation in the calf following dystocia. Alleviation of this pain and distress may have benefits in improving behavior, total milk intake, success of passive transfer and, subsequently, reduce the risk of developing disease.

It has been reported that through the administration of non-steroidal anti-inflammatory drugs (NSAIDs), alterations to the activity of the enzyme cycloxygenase-2 can have analgesic, anti-inflammatory, antipyretic, and anti-endotoxic effects.[16,18] Meloxicam is an NSAID that preferentially inhibits cycloxygenase-2 activity in horses, rats, humans, dogs, and cats.[3,6] However, its affinity has not yet been determined in cattle, and it has a mean plasma half-life of approximately 26 hours in bovine plasma irrespective of the route of administration.[11] The objective of this research was to evaluate a novel calf VIGOR assessment tool to measure birth trauma and associations with future health and growth. It was hypothesized that an index of newborn calf vigor, using on-farm visual observations and measurements, would be correlated with the actual physiological status of the calf. Furthermore, it was hypothesized that this index would predict the efficiency of absorption of Ig from colostrum, as well as the future health status and growth of newborn dairy calves. In addition, the efficacy of meloxicam for treatment of pain and inflammation developed during calving, and for enhancement of calf health and performance, was evaluated.

Materials and Methods

Study Farms, Calf Enrollment and Vigor Assessment

Before the study commenced, it was approved by the University of Guelph Animal Care Committee (#10R084, Guelph, ON, Canada) and all work with animals was done according to Canadian Council on Animal Care guidelines.[8]

A convenience sample of 10 dairy farms was selected to participate in this study based on previous research participation and proximity to the University of Guelph main campus (within a 2-hour drive).

Holstein and cross-bred heifer and bull calves born between September 01, 2010 and March 31, 2011 were enrolled in the study. On each farm, at the time of discovery of a newborn calf and prior to colostrum feeding, the producer or farm worker in charge of calving management completed a VIGOR score sheet (Table 1). VIGOR, as used in this paper, is an acronym for the assessment of **V**isual appearance, **I**nitiation of movement, **G**eneral responsiveness, **O**xygenation, and heart and respiration **R**ates. This is a novel scoring system developed by the authors for the purpose of assessing newborn calf vigor in this study. Within the categories of the VIGOR score, different variables were chosen and tested based on previous experience and research (Table 1). Under the Oxygenation category, the variable 'tongue length' was based from work suggesting that the tongue in calves born from a difficult birth protrude further beyond the lips.[13] Also, tongue length was positively associated with CO_2 and negatively with pH.

Scores for each criterion were added together to get a composite VIGOR score. The higher the score, the less vigorous the calf was deemed to be. The producer or farm worker also recorded the approximate time interval between birth and VIGOR score assessment. This variable was later categorized into 0-to-30 minutes, 30 minutes-to-1.5 hours, 1.5-to-3 hours, and >3 hours to assist with linearity.

Treatments, Randomization, and Blinding

Following VIGOR assessment, calves were randomly assigned to receive a subcutaneous injection from a numbered treatment vial containing 1 of 2 treatments: 1.0 mL of either meloxicam[a], with a target dosage of 0.227 mg/lb (0.5 mg/kg), or a placebo solution. Each mL of injectable meloxicam contained 20.0 mg meloxicam and 150 mg ethanol (as preservative). The placebo used in this study was an identical base formulation of the product without the active ingredient, meloxicam. The placebo product was a visually identical product to the meloxicam injectable.

This study was conducted as a randomized double-blinded clinical trial, and treatment allocation was randomized using a random number generator. Treatments were randomized so that every 10 vials included 5 meloxicam and 5 placebo treatments. Treatment vials were distributed to farms in multiples of 10 to ensure that an approximately equal number of treated and control calves were enrolled on each farm.

Calf Birth Record

Following injection, producers completed a birth record documenting information about the calving event, including date and time of calving; calving difficulty; quantity; timing; and source of colostrum fed to each calf; and the experimental treatment vial number assigned to the calf. Calving difficulty was recorded by producers as 1) unobserved; 2) observed but unassisted; or 3) requiring assistance at calving (either an easy or hard pull). Time of birth and colostrum feeding was recorded by producers as a time interval rather than an exact time. Date of calving was later categorized into seasons based on the calendar date. Summer was from June 20 to September 21, fall from September 22 to December 20, winter from December 21 to March 20, and spring from March 21 to June 19.

Farm Visits and Calf Sampling

During a routine weekly farm visit, trained research technicians collected measurements and samples from previously enrolled animals during their first, second, third, and sixth week of life. Bull calves were enrolled and followed until they left the farm. A blood sample was taken for each calf between 24 hours and 8 days of age. Blood was collected into 10 mL sterile Vacutainer® collection tubes via jugular venipuncture. Blood was transported on ice to the laboratory where it was allowed to clot, and then centrifuged at 970 × *g* for 12 minutes at ~ 68°F (~20°C). Serum was analyzed for total protein (STP) using a digital refractometer[b]. Successful passive transfer was defined as a STP concentration of ≥5.2 g/dL from calves sampled during the first 8 days of life. Calves having a STP concentration <5.2 g/dL were considered to have FPT.

At weekly farm visits, research technicians assessed calf health and measured and recorded weight and height on enrolled calves that were in their first, second, third, and sixth week of life. Based on weight measurements obtained at the first and sixth week, average daily gain (ADG) and total weight gain were calculated for the 6-week study period. Calf weight was recorded using a heart girth weight tape for Holstein calves[c]. Height was measured with a height-measuring device[d]. Health was assessed by recording rectal temperatures taken at each visit using a digital thermometer. In addition, calves were assessed for attitude, eye discharge, ear droop, nasal discharge, and fecal consistency using a graded scoring system with scores ranging from 0 to 4[20] (Table 2).

Statistical Analysis

Data were entered in Microsoft Excel[e] and exported into Stata-IC 10.1[f] for variable screening and statistical modeling. A causal diagram was constructed to examine the possible relationships to be tested among variables in the model. All variables were examined with descriptive statistics to determine the distribution of the data, and to look for missing values. If outliers were detected, data were checked against the original hard copy of data to ensure accuracy. Univari-

Table 1. VIGOR score sheet.

Visual Appearance				
Score	**0**	**1**	**2**	**3**
1. Meconium staining	Normal: no staining	Slight: around anal/tail head area	Moderate: extending over body	Severe: completely covered
2. Tongue/head	Normal (no swelling, tongue not protruding)	Tongue protruding but not swollen	Tongue protruding and swollen	Head and tongue swollen, tongue protruding
Initiation of Movement				
3. Calf movement	Standing/walking	Attempts to stand	Sternal	On side, no efforts to rise
Taken within	0 - 30 min	30 min - 1.5 h	1.5 h - 3 h	> 3 h
General Responsiveness				
4. Head shake in response to straw in nasal cavity	Shakes head vigorously	Moves head away	Twitches or flinches	Does not respond
5. Tongue pinch	Actively withdraws tongue	Attempts to withdraw	Twitches tongue	Does not respond
6. Eye reflex (in response to touching eyeball)	Actively blinks and closes eye	Slow to blink	Does not respond	-
Oxygenation				
7. Mucous membrane colour	Bright pink	Light pink	Brick red	White/blue
8. Length of tongue*	< 50 mm	50 - 61 mm	> 62 mm	-
Rates				
9. Heart rate†	80 - 100 bpm	> 100 bpm	< 80 bpm	-
10. Respiration rate‡	~ 24- 36 bpm	~ 24 bpm	~ > 36 bpm	-

*Measure from lips. Record this measurement only if within 5 minutes of calving.
†Place hand on the calf's chest. Take pulse for 15 seconds then multiply by 4 to get beats per minute (bpm).
‡View and/or place hand on the calf's abdomen to count the approximate number of breaths for 15 seconds and multiply by 4 to get breaths per minute (bpm).

able mixed linear regression models were created to assess associations of interest.

Four separate multivariable linear regression models were constructed using the xtmixed command in Stata, with farm included as a random intercept in all models. Models were built to assess whether there were statistically significant associations between independent variables and the following outcomes: VIGOR score, weight gain from the first to second week, 6-week weight gain, and total health score. Under the Oxygenation section of the VIGOR score, the variable tongue length was excluded from the total VIGOR score tabulation as observations were limited in which this variable could be recorded. Only heifers were used as observations in all models, except in models describing the VIGOR score and weight gain from the first to second week of life; only 1 farm involved in the study kept their bull calves past 1 week of age, which they raised for veal production. As such, it was not possible to assess outcomes for bull calves beyond 1 week of age with this small sample size.

All variables hypothesized to be related to the outcome of interest were screened for unconditional associations with the outcome variable in univariable analyses, including farm as a random intercept. Any predictor variables that were associated with the outcome using a liberal *P*-value ($P < 0.15$) were considered for inclusion in the final model.

Spearman correlation coefficients were calculated for all main effects variables considered for inclusion in the final model to avoid issues associated with collinearity. Consequently, if the correlation coefficient between 2 variables had an absolute value greater than 0.8, the variable that made the most biological sense, or had the fewest missing observations, was included in the multivariable model building process.

Linearity was assessed graphically for continuous variables with the outcome variable using lowess smoothers. If a variable was non-linear, a quadratic term was constructed and tested in the model. If the quadratic term was significant ($P < 0.05$) in the model, and the relationship was adequately modeled using a curve, the quadratic term was retained in the model. If not, the quadratic term was removed and log and square root transformations of the variable were assessed for linearity and significance. If none of the transformations allowed the variable to meet the linearity assumption, the variable was categorized.

Confounding was assessed by backward elimination. Confounding was defined as a >25% change in the coefficients of significant variables with the removal of the potential confounder. Regardless of the *P*-value, a confounding variable was retained in the model.

Interaction terms between experimental treatment and main effects variables were tested in each multivariable model. In addition, interaction terms between VIGOR score and main effects were investigated. Statistically significant interaction terms ($P < 0.05$) were considered to be evidence of interaction, and were retained in the final model. Interaction effects were interpreted graphically or through assessing contrasts among different combinations of the interacting variables. In the final multivariable model, variables were retained if their significance level was $P < 0.05$.

Model fit was assessed by plotting residuals and best linear unbiased predictors (BLUPs), and visually assessing whether the assumptions of heteroscedasticity and normality were met. Standardized residuals were examined graphically to look for outliers.

Results

Animal Enrollment, Calving and Experimental Treatment

A total of 842 Holstein and cross-bred calves were enrolled in the study between September 01, 2010 and March 31, 2011. Animals were enrolled from 10 farms (range in

Table 2. Health scoring criteria.*

Attitude Score				
Bright/alert	Quiet/dull	Depressed	Non-responsive	Dead
0	1	2	3	4
Ear Score				
Normal	One droopy	Both slightly droopy	Both straight downwards	Head tilt
0	1	2	3	4
Nasal Score				
Normal, no discharge	One nostril, small amount of cloudy discharge	Both nostrils, cloudy/excessive clear discharge	Both nostrils, excessive thick cloudy discharge	
0	1	2	3	
Fecal Score				
Normal	Semi-formed, pasty	Loose	Watery	
0	1	2	3	
Eye Score				
Normal	Small amount of ocular discharge	Moderate amount of bilateral discharge	Heavy ocular discharge	
0	1	2	3	

*Based on McGuirk SM. Disease management of dairy calves and heifers. *Vet Clin North Am Food Anim Pract* 2008; 24:139-153.

herd size 70 to 600 milking cows) located in southwestern Ontario, near the University of Guelph. A mean of 84 calves/farm were enrolled (range 31 to 218 calves/farm). Across all farms, the level of calving assistance by sex is presented in Table 3. Ten calves (1.2%) did not have a level of calving assistance recorded.

Calf Vigor

Accounting for the random effect of farm, and controlling for time from birth to VIGOR assessment, almost all variables included in the VIGOR score were significantly associated with being born from an assisted calving (Table 4). To be specific, assistance at calving was significantly associated with having reduced vigor (higher VIGOR scores) for visual appearance of the tongue and head, initiation of movement after birth, general responsiveness to straw in the nasal cavity, tongue pinch and mucous membrane color, as well as heart and respiration rate. Variables in the VIGOR score not associated with assistance at calving included speed of eye reflex and level of meconium staining. Mean VIGOR score by sex, calving assistance, and treatment can be seen in Tables 3, 5, and 6, respectively.

The VIGOR score was used as an outcome variable in a mixed linear regression model, with farm included as a random intercept (Table 7). Time after birth that the score was measured by farm staff was associated with VIGOR score. Compared to being scored within 30 minutes of birth, calves had significantly improved vigor (lower VIGOR score) if

Table 3. Number of calves in each category of calving assistance and relationship between serum total protein (STP) and VIGOR score with sex, accounting for the random effect of farm.

	Heifers	Bulls	Total
N	635 (75.4%)	207 (24.6%)	842 (100%)
Calving assistance			
Unobserved	313 (49.9%)	97 (47.3%)	410 (48.7%)
Observed but unassisted	115 (18.3%)	38 (18.5%)	153 (18.2%)
Assisted	199 (31.7%)	70 (34.1%)	269 (31.9%)
Total	627	205	832
STP (g/dL)			
Mean±SD	5.47±0.75	5.69±0.77	5.52±0.76
Coefficient	-0.077	Ref*	
95% CI	-0.21 to 0.052	-	
P-value	0.24	-	
VIGOR score			
Mean±SD	2.04±2.67	3.00±3.00	2.28±2.78
Coefficient	-0.51	Ref*	
95% CI	-0.96 to -0.06	-	
P-value	0.026	-	

*Ref - referent category

Table 4. The impact of calving assistance (independent variable) on each individual variable included in the VIGOR score (dependent variables), controlling for the random effect of farm and time taken to conduct the VIGOR assessment after birth.

VIGOR score component	Coefficient*	95% Confidence interval		*P*-Value
		lower limit	upper limit	
Visual appearance				
Meconium staining	0.042	-0.047	0.13	0.35
Tongue/head	0.21	0.11	0.30	<0.001
Initiation of movement				
Calf movement	0.17	0.025	0.32	0.02
General responsiveness				
Straw in nasal cavity	0.21	0.10	0.31	<0.001
Tongue pinch	0.16	0.062	0.27	0.002
Eye reflex	0.043	0.0068	0.093	0.09
Oxygenation				
Mucous membrane color	0.16	0.055	0.25	0.002
Rates				
Heart rate	0.18	0.061	0.31	0.003
Respiration rate	0.19	0.084	0.29	<0.001

Assistance at calving – independent variable scored between 30 minutes and 1.5 hours, 1.5 and 3 hours or >3 hours. Being born from an assisted calving, compared to an observed but unassisted calving, was significantly associated with reduced vigor (higher VIGOR score). In addition, heifer calves were significantly associated with having better overall vigor (lower VIGOR score) following birth than bull calves.

Colostrum Feeding Practices and Passive Transfer

The majority of calves enrolled in this study received colostrum management compliant with industry standards. A total of 548 (65.1%) calves were fed colostrum within 2 hours of birth, whereas 171 (20.3%) were fed between 3 and 4 hours, 38 (4.5%) between 5 and 6 hours, and 20 (2.4%) between 7 and 12 hours. This information was not recorded for 65 calves (7.7%). Study calves were fed colostrum by esophageal tube feeder (40.3%), by bottle (39.2%), or by a combination of these 2 methods (18.9%). A small number of calves were allowed to suckle the dam (0.87%) or fed by bucket (0.25%). The remaining calves (0.5%) were fed by various combinations of the 4 methods. Only 22 (2.6%) calves were given <2 L of colostrum, whereas 797 (94.7%) were given ≥2 L. Volume fed was not recorded for 23 (2.7%) calves. The volume of colostrum fed was positively associated with STP, accounting for the random effect of farm (β=0.09; 95% CI=0.003 to 0.176; $P = 0.04$).

The descriptive results for STP by sex, calving assistance, and treatment can be seen in Tables 3, 5, and 6, respectively. Mean STP across all calves was 5.5±0.75 g/dL. Prevalence of FPT among all study calves was 30.3% (239/788 calves). However, passive transfer rates were highly variable by farm. Two of the 10 farms had mean STP <5.2 g/dL. When FPT was considered at the individual herd level, it ranged from 13.7% to 51.4% of calves/farm. Vigor score was not significantly associated with passive transfer when controlling for volume of colostrum fed (β=0.15; 95% CI=-0.10 to 0.40; $P = 0.24$). Passive transfer was also not significantly affected by treatment with meloxicam (β=0.0096; 95% CI=-0.108 to 0.088; $P = 0.85$). Mean STP was 5.53±0.76 g/dL for calves treated with meloxicam, and 5.52±0.76 g/dL for placebo calves. When looking at management and environmental factors that affected passive transfer, it was found that season of birth had a significant effect. Calves born in winter had significantly lower STP than calves born in fall, accounting for the time after birth that blood was taken to measure STP and the random effect of farm (β=-0.30; 95% CI=-0.42 to -0.18; $P < 0.001$). Other seasons were not found to be significantly associated with reduced or improved STP.

Calf Growth

Weights from the first and sixth week were used to obtain ADG over the study period for each calf that remained in the herd for that duration. Mean ADG for calves from all farms was 1.65 ± 0.55 lb (0.75 ± 0.25 kg)/day. Mean weight gain for these calves over the 6-week period was 64.92 ± 22.26 lb (29.51 ± 10.12 kg).

Factors affecting weight gain were analyzed in 2 separate models: 1) from the first to the second week of life; and 2) during the entire 6-week follow-up period. Both outcomes were modeled with a mixed linear regression, with farm included as a random intercept.

A model for weight gain from week 1 to 2 is presented in Table 8. Weight gain from the first to the second week of life was significantly lower for heifer calves compared to bulls. Calves born in summer compared to spring had lower weight gain. Calves with lower STP and a more depressed attitude (higher attitude score) were also associated with reduced weight gain. An interaction was found between treatment with meloxicam and level of calving assistance (Figure 1). Calves given meloxicam that were assisted at birth gained 2.42 lb (1.1 kg) more in their first week than assisted calves given placebo. However, the opposite effect was seen in calves that were observed but unassisted at calving. Those treated with meloxicam gained 3.08 lb (1.4 kg) less in their first week than observed but unassisted calves given placebo. There was no difference in weight gain between treatments for calves unobserved at calving (Table 9).

Total weight gain during the 6-week follow-up period was not associated with meloxicam treatment (Table 6 and Table 10). Variables significantly associated with decreased 6-week weight gain in the final model included being born in winter compared to fall, receiving <2 L of colostrum after birth compared to ≥2 L, having reduced vigor at birth (higher VIGOR score), as well as having worse health (higher total health score) over the 6-week study period (Table 10).

Table 5. VIGOR score (mean±SD) and serum total protein (STP) (mean±SD) by level of calving assistance for heifer and bull calves.

Calving difficulty	Unobserved	Observed but unassisted	Assisted
N	410	153	269
VIGOR score			
Heifers	1.30±1.60	1.88±1.92	3.30±3.72
Bulls	1.82±1.95	2.45±1.86	4.84±3.66
Heifers & bulls	1.42±1.71	2.02±1.91	3.70±3.76
STP (g/dL)			
Heifers	5.48±0.76	5.35±0.69	5.53±0.76
Bulls	5.74±0.78	5.54±0.71	5.67±0.79
Heifers & bulls	5.54±0.77	5.39±0.70	5.57±0.77

Calf Health

Higher calf health scores for attitude, eye discharge, ear droop, nasal discharge, and fecal consistency were indicative of a less-healthy calf. Using cumulative health scores over the 6-week follow-up period as an outcome variable, a multivariable linear mixed model was constructed to assess predictors of health (Table 11). Only heifers were included as observations in this model. Calves treated with meloxicam had better health (lower total health score) than placebo-treated calves from birth to 6-weeks old. Other factors associated with better health were colostrum feeding <2 hours compared to >7 hours after birth, and being born in fall compared to winter or spring.

Table 6. Effects of treatment with meloxicam and placebo on serum total protein (STP), VIGOR score, health scores, weight gain, and height growth for all calves in the study (mean±SD).

Variable	Meloxicam	Placebo
N	418	413
STP (g/dL)	5.53±0.76	5.52±0.76
VIGOR	2.24±2.79	2.28±2.74
Health scores		
Week 1	0.98±0.61	1.06±0.70
Week 2	1.25±0.82	1.30±0.92
Week 3	0.99±0.83	1.05±0.90
Week 6	0.39±0.76	0.38±0.75
Total	3.60±1.83	3.76±2.02
Weight gain (kg)		
Week 1 gain	3.23±4.00	3.11±4.02
6 week gain	29.52±9.88	29.46±10.39
ADG	0.75±0.24	0.75±0.25
Height growth (cm)		
Week 1 growth	1.98±2.06	1.83±1.91
6 week growth	9.58±3.02	9.27±3.38

Discussion

The effects of dystocia on the calf can be numerous, leading to reduced calf vigor followed by compromised health and survival. There is a greater need for improved on-farm calving intervention strategies, as well as newborn calf monitoring protocols, to reduce the impacts of calving difficulty.[4,21] Recently, interest has increased in the knowledge and practicality of administering NSAIDs to cows and calves at calving for the alleviation of pain and inflammation associated with dystocia. Appreciably more studies have evaluated the use of NSAIDs in cows,[18] but these studies have been mostly limited to the impact of NSAID treatment on placental retention or future fertility, or have investigated the benefits of treating all cows after calving rather than focusing on benefits of treating dystocia specifically.[18]

In a survey of Canadian veterinarians, use of analgesics in dairy cattle is relatively low.[14] It was found that only 26.5% of cows with dystocia received any sort of analgesia, with the most common being lidocaine or ketoprofen.[14] In this survey, veterinarians subjectively rated the pain level of dystocia for the cow on a scale from 1 to 10 if no analgesia was given. It is noteworthy that dystocia was rated at 5.3, which was the same pain level given to acute lameness.[14] Information on calves receiving analgesics after dystocia was not included in the survey, likely because NSAIDs are not approved for use in newborn calves in Canada. In Europe, NSAIDs are approved for use in calves for neonatal diarrhea and for alleviation of pain following dehorning, but there is currently no label claim for the use of NSAIDs in newborn calves following dystocia. Thus, current use of analgesics in newborn calves is likely very rare.

This is the first study performed to determine the benefits of NSAIDs in calves following calving. Lack of scientific evidence may be the major contributing factor as to why there is no approval and very limited NSAID usage in new-

Table 7. Mixed multivariable linear regression model of the predictor variables for VIGOR score accounting for the random effect of farm (n=799).

VIGOR score	Coefficient	95% Confidence interval		*P*-value
		lower limit	upper limit	
Calving assistance				
Assisted	1.30	0.79	1.81	<0.001
Unobserved	-0.29	-0.78	0.20	0.25
Observed but unassisted	Ref	-	-	-
Sex				
Heifer	-0.45	-0.86	-0.034	0.034
Bull	Ref	-	-	-
Time VIGOR score assessed after birth				
0-30 min	Ref	-	-	-
30 min-1.5 h	-0.91	-1.35	-0.47	<0.001
1.5-3 h	-1.01	-1.52	-0.50	<0.001
>3 h	-1.91	-1.35	-1.47	<0.001

Ref - referent category

The intra-class correlation coefficient reveals that 8.2% of the total variance in the population can be attributed to variation between farms.

born calves. Yet, studies have been performed to investigate the effects of calving assistance on calf vigor, which indirectly indicate that calves may benefit from pain management therapy to assist with inflammation, pain, trauma, stress, and other physiological and behavioral factors associated with dystocia.[1,9,27,30] In the current study, all calves were assessed only once with the VIGOR score, following birth just prior to treatment administration. Thus, it could not be determined whether administration of meloxicam following calving improved calf vigor.

Studies have suggested that a calf's motivation to stand is a useful assessment of calf vigor at birth. Calves born with assistance take longer to attain sternal recumbency and stand than those born unassisted due to a slower recovery from trauma and such physiological factors as acidosis.[9,30] Barrier et al[1] found that a longer time taken to stand after birth may have meaningful consequences, such as increasing the time taken to reach the udder and receive colostrum. In the current study, calves born from an assisted calving had poor overall vigor at birth, although time to standing was not specifically measured. While the VIGOR score is a combination of several different measures, 'initiation of movement after birth' was significantly associated with being born from an assisted calving, along with most of the other variables included in the VIGOR score. Thus, the current study is in agreement that calves born from an assisted calving are less vigorous and take longer to stand after birth.

Other studies have suggested that calves with poor vigor that are weaker and slower to stand at birth are at an increased risk of FPT.[12,34] Vigor at birth is a key survival characteristic for newborns, helping them reach a teat and ingest colostrum earlier, assisting in passive transfer.[2,24] Failure of passive transfer due to reduced vigor at birth may consequently impact health and productivity. Furman-Fratczak et al[12] found that Holstein calves with poor vigor associated with dystocia were at increased risk of FPT, and those calves with FPT had a reduced rate of gain and a higher incidence of disease. In that study, calves were fed by bottle when they made an effort to stand. Thus, vigor had an impact on the timing of colostrum intake. In the current study, calves with poor vigor, and calves that received <2 L of colostrum compared to >2 L, had lower weight gain throughout the 6-week study period. This suggests that colostrum feeding and calf vigor play a vital role in future health and growth. However, no relationship was found between VIGOR score and STP. This finding is likely because almost all calves on the current study were fed colostrum manually by bottle or esophageal tube feeder, regardless of their state of vigor. Thus, a calf's motivation to consume colostrum, measured through time taken to feed or voluntary intake, could not be measured. Also, STP results may be affected by the timing of blood collection, as it has been shown that serum total protein concentrations decrease with age.[22] This has been attributed to the degradation of absorbed immunoglobulin in colostrum.[22] If blood was collected on all calves at a standard-

Table 8. Mixed multivariable linear regression model of predictor variables for weight gain (kg) in the first week of life, accounting for the random effect of farm (n=626).

Weight gain from week 1 to 2 (kg)	Coefficient	95% Confidence interval		*P*-value
		lower limit	upper limit	
Sex				
Heifer	-1.41	-2.61	-0.21	0.021
Bull	Ref*	-	-	-
Season of birth				
Spring	Ref	-	-	-
Summer	-2.73	-5.08	-0.37	0.023
Winter	-1.56	-3.85	0.73	0.18
Fall	-1.91	-4.18	0.36	0.099
****STP (g/dL)**	0.69	0.28	1.10	0.001
Week 1 attitude score	-1.30	-2.40	-0.21	0.020
Treatment				
Meloxicam	-1.38	-2.67	-0.086	0.037
Placebo	Ref	-	-	-
Calving assistance				
Observed but unassisted	Ref	-	-	-
Unobserved	-0.81	-1.89	0.27	0.14
Assisted	-1.80	-2.96	-0.65	0.002
Treatment/calving assistance interaction				
Meloxicam/assisted at calving	2.49	0.85	4.12	0.003
Meloxicam/unobserved at calving	1.52	0.013	3.04	0.048
Placebo/observed but unassisted at calving	Ref	-	-	-

*Ref - referent category

**Serum total protein

The intra-class correlation coefficient reveals that 4.9% of the total variance in population can be attributed to variation between farms.

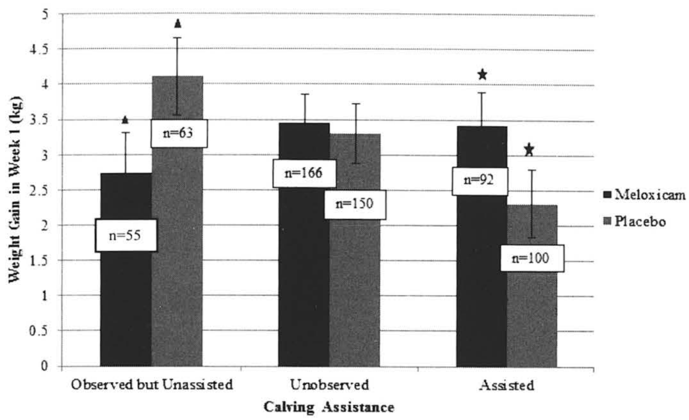

Figure 1. Predicted values for weight gain (kg) in the first week of life as treatment interacts with the level of calving assistance. All fixed effects are set to median values.
▲Statistically significant difference between calves given meloxicam that were observed but unassisted at calving compared to observed but unassisted calves given placebo (*P*=0.037)
★Statistically significant difference between calves given meloxicam that were assisted at calving compared to assisted calves given placebo (*P*=0.032)

ized time following birth, rather than between 1 and 7 days, results might be more meaningful.

In the current study, treatment with meloxicam was associated with improved health scores compared to placebo-treated calves. Also, the administration of meloxicam to calves from assisted births may improve weight gain, as shown through the interaction between treatment and calving assistance with weight gain in the first week of life. Treatment with meloxicam following birth may decrease the effects of pain, inflammation, and other physiological factors associated with difficult calving in newborn calves. Decreasing these effects may improve the calf's ability and efficiency to perform tasks for survival, such as building immunity to fight disease and putting energy towards growth. As mentioned previously, this is the first study to show the effects of administration of NSAIDs to newborn calves. Further research is required to confirm these findings, and to determine whether NSAID therapy to calves experiencing dystocia can improve calf vigor, leading to improved health, growth, and perhaps subsequent performance. If additional research agrees, treatment with NSAIDs at birth to calves that have experienced dystocia may be advisable.

Table 9. Contrast based on week 1 weight gain model examining the interaction effects between experimental treatment and calving assistance (n=626)*.

Calving assistance & treatment	Coefficient (kg)	95% Confidence interval		*P*-value
		lower limit	upper limit	
Observed but unassisted meloxicam vs observed but unassisted placebo	-1.38	-2.67	-0.086	0.037
Unobserved meloxicam vs unobserved placebo	0.15	-0.64	0.93	0.72
Assisted meloxicam vs assisted placebo	1.11	0.098	2.12	0.032

Table 10. Mixed multivariable linear regression model of the predictor variables for 6-week weight gain (kg), accounting for the random effect of farm (n=534).

6-week weight gain (kg)	Coefficient	95% Confidence interval		*P*-value
		lower limit	upper limit	
Season of birth				
Spring	-4.86	-10.87	1.15	0.11
Summer	-1.10	-3.18	0.98	0.30
Winter	-3.85	-5.63	-2.07	<0.001
Fall	Ref*	-	-	-
Colostrum volume				
<2L	-5.12	-9.65	-0.60	0.026
>2L	Ref	-	-	-
VIGOR score	-0.38	-0.71	-0.053	0.023
Time VIGOR score taken after birth				
0-30 min	Ref	-	-	-
30 min-1.5 h	0.14	-1.83	2.13	0.88
1.5-3 h	-0.59	-2.86	1.68	0.61
>3h	2.35	0.12	4.58	0.039
Total 6-week health score	-0.45	-0.88	-0.015	0.043
Treatment				
Meloxicam	-0.59	-2.03	0.85	0.42
Placebo	Ref	-	-	-

*Ref - referent category
The intra-class correlation coefficient reveals that 33.5% of the total variance in population can be attributed to variation between farms.

Treatment of newborn calves born observed but unassisted with NSAIDs should be further investigated. It is noteworthy that in the current study, meloxicam-treated calves born from an observed but unassisted calving had lower weight gain than calves given placebo. The administration of NSAIDs can have side effects associated with prolonged usage, including gastric ulceration and renal disease.[16] Yet, these conditions have not been well documented in farm animals.[16] It may be possible that meloxicam has a negative effect on calves that do not have any substantial inflammatory response following birth, as calves born from an observed but unassisted calving would be less likely to experience trauma at calving. It may have also been a spurious finding resulting from the small sample size, as the 'observed but unassisted' category had the fewest enrolled calves. Alternatively, weight gain could be a relatively poor indicator of NSAID efficacy in calves. Nevertheless, calves born observed but unassisted would not be prescribed treatment with meloxicam following birth. Furthermore, treatment with meloxicam for all calves as a standard procedure should not be recommended at this time.

In general, it is known that bull calves are heavier at birth than heifers, which may be due to longer gestation lengths and higher androgenic hormone production.[15] Because bull calves are heavier, they are more likely to require assistance at birth.[19] In the current study, it was hypothesized that calves born with assistance would have lower vigor due to the stress and trauma associated with dystocia. Compared to unassisted calves, those born with assistance had significantly lower vigor. In addition, the effect of calf sex was significantly associated with vigor score. Bull calves had significantly lower vigor compared to heifers following birth. This is expected, as heifer calves are smaller both in weight and frame. Thus, the need for assistance is less for heifers, having a lower impact on newborn vigor. However, it is interesting that in the current study, the percentage of bull calves born from an assisted calving was almost the same as that of heifers. Since calving assistance was not differentiated between easy and hard pulls in this study, it is possible that more bulls were born following a hard pull, resulting in lower vigor compared to heifers. Also, scoring calving difficulty and determining the need for assistance is very subjective. The differences in determining the need for assistance between farms could also have affected this relationship.

It was found that VIGOR score was significantly associated with the time the score was measured after birth. As the time after calving to the assessment of VIGOR score increased, calves were significantly more vital. As recovery time increases, it is logical that calves will become more vigorous.

Newborn calves are particularly susceptible to environmental stressors at birth, which may also affect calf vigor and subsequent health and productivity. At parturition, the calf moves from a controlled, sterile environment to a hostile external environment in which the calf must make physiological changes to maintain homeostasis.[7] This situation can pose a number of challenges, depending on the calving environment and the season of birth. Exposure to extreme environmental temperatures, hot or cold, may cause stress in the newborn, resulting in the mobilization of energy reserves from brown adipose tissue to achieve homeostasis.[25] Diesch et al[9] found that calving environmental conditions affected calf vigor. Calves born in temperatures below 50°F (10°C) or in windy/wet conditions were slower to stand after birth than calves born in temperatures greater than 50°F (10°C) or in still/dry or windy/dry conditions.[9] The current study did not find an association between calves born in the winter and calf VIGOR score. However, environmental temperature was not recorded.

Table 11. Mixed multivariable linear regression model of predictor variables for total health score over the 6-week study period, accounting for the random effect of farm (n=532).

Total 6-week health score	Coefficient	95% Confidence interval		*P*-value
		lower limit	upper limit	
Treatment				
Meloxicam	-0.36	-0.64	-0.073	0.014
Placebo	Ref*	-	-	-
Season of birth				
Spring	1.21	0.082	2.34	0.036
Summer	-0.16	-0.57	0.25	0.44
Winter	1.40	1.06	1.74	<0.001
Fall	Ref	-	-	-
Time colostrum fed after birth				
<2 h	Ref	-	-	-
3-4 h	-0.15	-0.54	0.25	0.43
5-6 h	-0.27	-0.98	0.45	0.46
7-12 h	1.20	0.21	2.10	0.018

*Ref - referent category
The intra-class correlation coefficient reveals that 14.4% of the total variance in population can be attributed to variation between farms.

Various studies have found that calves exposed to heat stress have a higher risk of mortality, higher serum corticosteroid concentrations, and lower serum IgG concentrations.[32,33] Others have suggested that cold stress can impact the absorption of colostral Ig by delaying the onset and decreasing the rate of absorption.[26] In the current study, calves born in winter had significantly lower STP than calves born in the fall. Winter-born calves may have experienced cold stress, which had an impact on Ig absorption. This finding is in agreement with another study that found an association between being born in the winter months and having a lower mean serum IgG concentration, compared to calves born in the warmer months of the year.[28]

In the current study, season of birth was associated with heifer calf health and weight gain, which may be an indirect effect of IgG absorption and the resulting STP concentration. Heifer calves born in the winter and spring had reduced health compared to those born in the fall. This is in agreement with Lombard et al,[19] who found that heifer calves born in the winter and spring were more likely to experience a health event, either respiratory or digestive, compared to those born in the fall. Calves were also more likely to die between birth and 120 days of age.[19] Temperature fluctuations and increased susceptibility to heat or cold stress may compromise a calf's immune system. Compromised health, leading to increased morbidity events, may have an effect on weight gain. In the current study, calves born in the summer had reduced weight gain from the first to the second week of life, whereas calves born in the winter had reduced weight gain throughout the pre-weaning period. In other studies, it has been shown that young calves housed in cold winter temperatures have reduced daily weight gain compared to those housed in the range of their thermoneutral zone, between 50 and 68°F (10 and 20°C).[31] At temperatures below their thermoneutral zone, calves have higher maintenance energy requirements, which are often not met by nutrient intake. This situation results in reduced gain or even a loss in body weight.[31]

Injectable meloxicam is approved in Canada for use in cattle; however, neither injectable nor oral meloxicam is approved for use in cattle in the United States. Under current laws and regulations in the US, meloxicam can be used extra label provided no suitable labeled product is available for the condition treated, and a valid veterinarian-client-patient relationship exists. Finally, calves in the current study were treated with injectable meloxicam; therefore, these data may not be applicable if meloxicam is administered orally.

Conclusions

Calves born from an assisted calving had lower vigor at birth than calves born unassisted. Calves with reduced vigor at birth had lower weight gain over the 6-week study period. The interaction between experimental treatment and calving assistance indicated a positive effect of meloxicam on weight gain from the first to the second week of life in calves born from an assisted calving, but a negative effect on calves born from observed but unassisted calving. Meloxicam treatment was not associated with passive transfer or 6-week weight gain, but improved total health score. In conclusion, the administration of meloxicam at birth offers considerable value in the improvement of overall health, as well as weight gain in the first week of life, in calves born following an assisted calving.

Endnotes

[a]Metacam®, Boehringer Ingelheim (Canada) Ltd, Burlington, Ontario, Canada
[b]KS – 0050, Kernco Instruments Co., Inc., El Paso, TX
[c]Nasco, Modesto, CA
[d]Ketchum Manufacturing Inc., Brockville, ON, Canada
[e]Microsoft, Redmond, WA
[f]StataCorp, College Station, TX

Acknowledgements

This study was funded by Boehringer Ingelheim (Canada) Ltd., along with the Agriculture Adaptation Council through the Ontario Veal Association.

The authors declare no conflict of interest.

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