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Reduction in pain response by combined use of local lidocaine anesthesia and systemic ketoprofen in dairy calves dehorned by heat cauterization

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Abstract — This study assessed the efficacy of ketoprofen for mitigating pain following dehorning with an electric cautery iron. Forty Holstein heifer calves, 4 to 8 wk of age, were randomized to receive a lidocaine cornual nerve block and either an injection of ketoprofen (3 mg/kg IM) or physiological saline, 10 min prior to dehorning. Cortisol was measured from serum obtained 10 min prior to dehorning and at 3 and 6 h post-dehorning. Calf behavior was video-recorded between 0 to 2, 3 to 5, and 6 to 8 h post-dehorning, and frequency of ear flicks, head shakes, head rubs, lying, standing, feeding, and grooming were recorded. Finally, 24-h intake of calf starter was recorded. There was no effect of treatment on cortisol ($P > 0.1$); however, ketoprofen-treated calves displayed less ear-flicks and total head behavior ($P < 0.05$), and tended to consume more starter ($P = 0.09$) than control calves. Ketoprofen is effective for mitigating behavioral effects of postsurgical pain following dehorning in 4- to 8-week-old calves.

Résumé — Réduction de la réponse à la douleur par l'usage combiné d'anesthésie locale à la lidocaïne et du kétoprofène systémique chez des vaches laitières écornées par cautérisation à la chaleur. Cette étude a évalué l'efficacité du kétoprofène pour l'atténuation de la douleur après l'écornage avec un fer à cautériser électrique. Quarante génisses Holstein, âgées de 4 à 8 semaines, ont été choisies au hasard pour recevoir un bloc nerveux cornual à la lidocaïne et soit une injection de kétoprofène (3 mg/kg IM) ou de solution saline physiologique, 10 minutes avant l'écornage. Le cortisol a été mesuré dans du sérum obtenu 10 minutes avant l'écornage et à 3 heures et à 6 heures après l'écornage. Le comportement des veaux a été enregistré par vidéo entre 0 et 2 heures, 3 et 5 heures et 6 et 8 heures après l'écornage et la fréquence des mouvements des oreilles, des secouements de la tête, des frottements de la tête, des positions couchée et debout, de l'alimentation et du toilettage a été consignée. Enfin, la consommation d'aliment de début des veaux pendant 24 heures a été consignée. Il n'y a pas eu d'effet du traitement sur le cortisol ($P > 0,1$); cependant, les veaux traités au kétoprofène ont réalisé un total inférieur de mouvements des oreilles et de la tête ($P < 0,05$) et avaient tendance à consommer plus d'aliment de début ($P = 0,09$) que les veaux témoins. Le kétoprofène est efficace pour atténuer les effets comportementaux de la douleur post-chirurgicale après l'écornage chez des veaux âgés de 4 à 8 semaines.

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Introduction

Horn buds of dairy and beef calves are normally removed to reduce risk of injuries to other cattle or producers. Dehorning refers to amputation of horns in mature cattle or removal of the horn buds of calves; the latter is also referred to as disbudding. Physiological and behavioral studies indicate that regardless of the dehorning method used, dehorning is painful for at least 2 h after dehorning (1) and potentially as long as 24 h or 44 h (2,3). There is evidence that dehorning by heat cauterization is less painful than dehorning by amputation methods (1). Pain associated with dehorning has been quantified through behavioral measures, such as ear flicks, head rubs, and changes in posture (2–5), and the magnitude and duration of physiological stress responses, such as serum cortisol

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ARTICLE

concentrations (1,3,4), heart and respiratory rates (3,5,6), and more recently, eye temperature (6) and electroencephalogram (7).

Local anesthetics reduce pain during the 2 to 4 h immediately following dehorning (4,5,8–11), depending on the type of anesthetic used. The Canadian Code of Practice for Dairy Cattle recommends the use of a local anesthetic for dehorning (12). However, there is evidence that local anesthetics delay, rather than alleviate pain associated with dehorning since sharp increases in cortisol levels have been observed after the local anesthetic wears off (8,9,13). When combined with a local anesthetic, ketoprofen (a non-steroidal anti-inflammatory drug) significantly reduced cortisol responses associated with scoop dehorning in 3- to 4-month-old calves (9,13). Similarly, frequencies of ear flicking, head shaking, and head rubbing following hot-iron dehorning were reduced in 4- to 8-week-old calves when ketoprofen was given in addition to a sedative and local anesthetic (2). However, it is unclear if these changes in behavior were due to pain reduction or due to sedation.

A survey of dehorning practices in Ontario revealed that most calves are dehorned using electric cautery with a larger (Rhinehart) iron at 4 to 8 weeks of age (14). The Canadian Veterinary Medical Association (CVMA) recommends that calves should be dehorned in the 1st week of life (15); however, there is a paucity of research on effects of dehorning on young calves. In 1 study, the impact of ketoprofen in addition to lidocaine cornual nerve block was evaluated in 2-day-old to 2-week-old calves that were dehorned using a small butane powered hot iron (16). Ketoprofen did not reduce the behavioral responses to dehorning relative to saline-treated calves, but there was a reduction in cortisol response.

The objective of this experiment was to assess a single injected dose of ketoprofen for addressing post-surgical pain, based on representative common practice in Ontario. Pain was assessed in terms of behavioral and physiologic responses.

Materials and methods

Forty Holstein heifer calves, ranging in age from 4 to 8 wk were housed in the calf nurseries of the Elora Dairy Research Centre (University of Guelph, Guelph, Ontario). Calves were individually housed in 1.3 m × 1.5 m pens, and had visual and tactile contact with the adjacent calves. Calves were fed 2 L of milk twice per day and had ad libitum access to calf starter (20% crude protein with lasalocid; Floradale Feed Mill, Elora, Ontario) and water from birth.

Calves were randomly assigned to 1 of 2 treatments. "Ketoprofen" calves were administered an intramuscular (IM) injection of ketoprofen (Anafen; Merial Canada, Baie d'Urfé, Quebec) at a dose of 3 mg/kg bodyweight (BW). "Control" calves were administered physiological saline at the same dose. All calves were administered 5 mL lidocaine (2% lidocaine HCl with 0.05 mg/mL epinephrine; Bimeda-MTC, Cambridge, Ontario) as a cornual nerve block for each horn bud. Treatments and nerve blocks were administered and the first jugular sample was obtained 10 min prior to dehorning. The order of procedures was cornual nerve block, jugular blood sample, and finally IM injection of ketoprofen or saline. This series of procedures typically took no longer than 30 s to complete. Calves were dehorned using an electric cautery iron (Rhinehart X30; Rhinehart Development Corporation, Spencerville, Indiana, USA) which was pre-heated for 10 min to approximately 600°C. Treatments and dehorning were always performed at 10.00 h (± 15 min) in the animal's home pen by the same trained veterinary technician.

Blood was collected by jugular venipuncture into glass tubes containing no anti-coagulant (Vacutainers; Becton Dickinson, Franklin Lakes, New Jersey, USA) immediately following the cornual nerve block 10 min prior to dehorning (0 h) and again at 3 h and 6 h. Samples were allowed to clot for 30 min at room temperature and then were placed on ice and transported to the University of Guelph where they were centrifuged at 1400 × *g*. Serum was harvested and frozen at −20°C until all samples were collected. Serum samples were then delivered to the Animal Health Laboratory of the University of Guelph for cortisol analysis using a solid-phase, competitive chemiluminescent enzyme immunoassay kit (Diagnostic Products, Los Angeles, California, USA).

Video cameras (Panasonic, Model WV BP100, http://www.Panasonic.com) and wide angle camera lenses (F 1.4/6 mm, Cosmicar, HS614GX; Pentax, Englewood, Colorado, USA) were installed on the wall facing the calf pens, providing a panoramic view of each pen. Calf behavior was recorded between 0 to 2, 3 to 5, and 6 to 8 h post-dehorning. Frequency of ear-flicks, head-shakes, and head rubs were recorded using continuous observation for 20-minute intervals immediately following dehorning (0 h) and at 1, 3, 4, 6, and 7 h post-dehorning. The observer was blind to treatment allocation. Scan sampling was conducted at the start of each 1-minute interval for the first 20 min of each observational hour and the posture of the calf (standing, lying, feeding, or grooming) at each of these time points was recorded. A complete ethogram of the behaviors observed is shown in Tables 1 and 2.

The amount of calf starter (Rumax 20% calf starter; Floradale Feed Mill, Elora, Ontario) consumed on the day of dehorning was measured by weighing the amount of starter offered at time 0 and the amount remaining 24 h later.

Normality was assessed using Proc Univariate in SAS (version 9.1.3; SAS Institute, Cary, North Carolina, USA). Cortisol data were log transformed and analyzed by analysis of covariance (ANCOVA) using Proc Mixed. The 0 h cortisol concentration was used as the covariate. Main effects of treatment, time, age, season, and calf weight were included in the model.

Frequencies of ear-flicks, head-shakes, head-rubs, and total head behavior (ear-flicks, head-shakes, and head-rubs combined) were analyzed by Poisson regression using Proc Genmod and a Poisson distribution, with treatment, time, age, season, and weight included in the model. Repeated measures on calf were also taken into account using an autoregressive correlation structure.

Postural behaviors (standing, lying, grooming) were analyzed by logistic regression using Proc Genmod and a binary distribution, with treatment, time, age, season, and weight being included in the model.

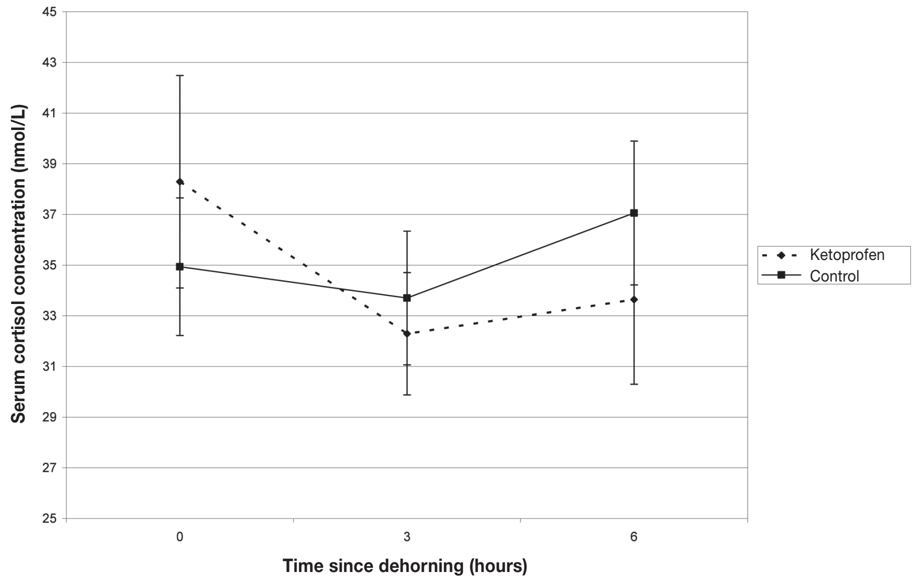

Figure 1. Mean (± standard error) serum cortisol concentrations (nmol/L) of calves 10 min prior to dehorning (time 0) and at 3 and 6 h after dehorning in control and ketoprofen-treated calves. There were no significant differences between treatments ($P = 0.28$).

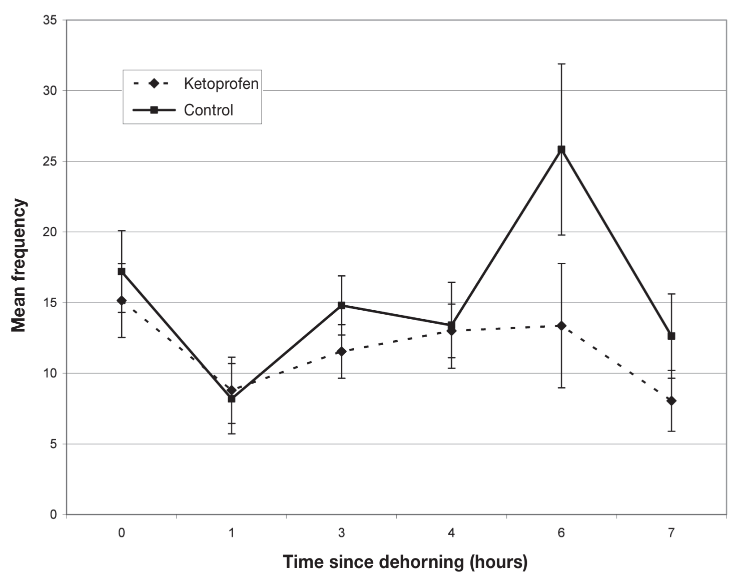

Figure 2. Mean (± standard error) of total head behaviors (ear-flicks, head-shakes, and head-rubs) following dehorning in control and ketoprofen-treated calves. Head behaviors occurred less frequently in ketoprofen-treated calves ($P = 0.046$).

Starter consumption was analyzed by a simple analysis of variance (ANOVA) using Proc Mixed (SAS Institute). Main effects of treatment, time, age, season, and weight were included in the model.

Results

There was no difference in serum cortisol concentrations between treatment groups at any of the time periods measured (Figure 1; $P = 0.28$).

Ketoprofen-treated calves displayed significantly less total head behaviors than control calves (Table 3; $P = 0.046$). There was significantly more total head behavior at 6 h post-dehorning (Figure 2; $P < 0.05$), but there were no treatment by time interactions. Similarly, ketoprofen-treated calves displayed significantly fewer ear-flicks than control calves (Table 3; $P = 0.01$) corresponding to a 50% reduction in the total number of ear-flicks over the 7 h of observation. Again, ear-flicking was significantly greater 6 h post-dehorning (Figure 3; $P < 0.05$),

Table 1. Description of behaviors recorded during 20-minute continuous observation periods

Behavior	Description
Ear flick	Calf rapidly moves 1 or both ears to the front and back, independent of a head shake
Head shake	Calf rapidly shakes head side-to-side
Head rub	Calf scrapes head against bars of the pen, feed buckets, or with the hind leg

Table 2. Description of behaviors recorded during 1-minute scan samples

Behavior	Description
Stand	Standing up in pen
Lie	Lateral or sternal recumbency
Feed	Head in feed or water bucket
Grooming	Licking any part of the body

Table 3. Mean (± standard error) frequency of head behaviors recorded over all 20-minute observational periods (120 min total)

	Treatment		
Behavior	Control	Ketoprofen	*P*-value
Total head behaviors	90.2 (13.35)	68.8 (8.92)	0.046
Ear flicks	53.7 (10.83)	31.7 (5.76)	0.01
Head shakes	19.9 (3.10)	18.4 (3.25)	NS
Head rubs	16.6 (2.81)	18.7 (2.57)	NS

Table 4. Mean (± standard error) number of occurrences of each of the postural behaviors recorded during the start of 1-minute scan samples for the first 20 min of each of 6 observation hours (total of 120 observations)

	Treatment	
Behavior	Control	Ketoprofen[a]
Standing	45.8 (3.62)	42.6 (4.05)
Lying	72.3 (3.85)	75.4 (4.23)
Feeding	10.6 (1.48)	10.2 (1.38)
Grooming	4.45 (0.56)	5.9 (0.81)

[a] There was no treatment difference for any of the behaviors.

but there were no treatment by time interactions. There were no treatment differences in the amount of head-shakes or head-rubs when these were analyzed individually (Table 3), and there were no detectable differences in the amount of standing, lying, feeding, or grooming (Table 4).

Consumption of calf starter during the 24 h following dehorning tended to be greater in the ketoprofen-treated calves ($P = 0.09$), amounting to approximately 0.25 kg more grain (Figure 4). There was also a significant effect of calf weight on starter consumption, with larger calves consuming more feed ($P < 0.001$).

Discussion

This was a follow-up study to work done by Milligan et al (16), in which 2-day-old to 2-week-old calves were dehorned using a small butane device. These authors concluded that there was little evidence to support the routine use of ketoprofen in very young calves dehorned with a small butane device, since only a small reduction in cortisol occurred between 0 and 3 h post-dehorning and behavior was not affected. It was our hypothesis that ketoprofen would mitigate postsurgical pain when calves are dehorned at older ages, which is typical in Ontario, and these effects would be particularly evident after the lidocaine nerve block wore off.

Calves in this study displayed more head behaviors, regardless of treatment, than calves in a previous study (16). This difference may be associated with calf age or the use of the larger Reinhart electric dehorner which would give a much larger area of burn as opposed to the smaller butane device used in the Milligan study.

We were surprised to find no apparent treatment differences in cortisol at any of the time periods measured. This was unexpected due to the wealth of evidence supporting the hypothesis that non-steroidal anti-inflammatory drugs reduce stress caused by dehorning (9,13,15,17). There are 3 possible explanations for the absence of treatment difference in cortisol response. First, there is evidence that cauterizing dehorning wounds can decrease the cortisol response to the procedure (1,18). Second, we used a chemiluminescent enzyme immunoassay (CLEIA) to determine cortisol concentrations whereas the more common techniques are radioimmunoassay (RIA) or enzyme-linked immuno-sorbent assay (ELISA). Although CLEIA results correlate well with RIA when analyzing certain molecules such as thyroxine and calcitonin (19,20), the method may be less sensitive for cortisol. Last, our experimental design conferred low statistical power for assessing cortisol response. There was a small numeric decrease in cortisol of 1.1 nmol/L in the ketoprofen group, but this difference would have required 158 calves per treatment group to be statistically significant at $P < 0.05$. Due to constraints of animals and the labor involved, blood samples were taken every 3 h, but variability in pharmacokinetics of lidocaine and pain responses between calves would have benefitted from more frequent sampling of more animals.

There was evidence that ketoprofen reduced the behavioral responses to dehorning pain. Ketoprofen-treated calves displayed fewer ear flicks following dehorning, which supports work done by Faulkner and Weary (2). These researchers also found no differences for head-shakes and head-rubs. Although Faulkner and Weary (2) and Heinrich (3) found transient increases in head-shakes after dehorning, these behaviors seem to occur less frequently, so may be more difficult to use as reliable indicators of pain. Also, it is possible that these behaviors may be more indicative of irritation, itching, or healing. In this study, head rubbing peaked numerically between 2 and 4 h (data not shown), and showed a similar pattern for both treatments, suggesting this behavior may represent generalized irritation to the local anesthetic wearing off. Ear-flicks peaked at 6 h in the control calves only, and this behavior appears to be most reliable for the indication of post-surgical dehorning pain (11,18,21). There was a similar numeric, but not statistically significant, increase in head-shakes during this phase.

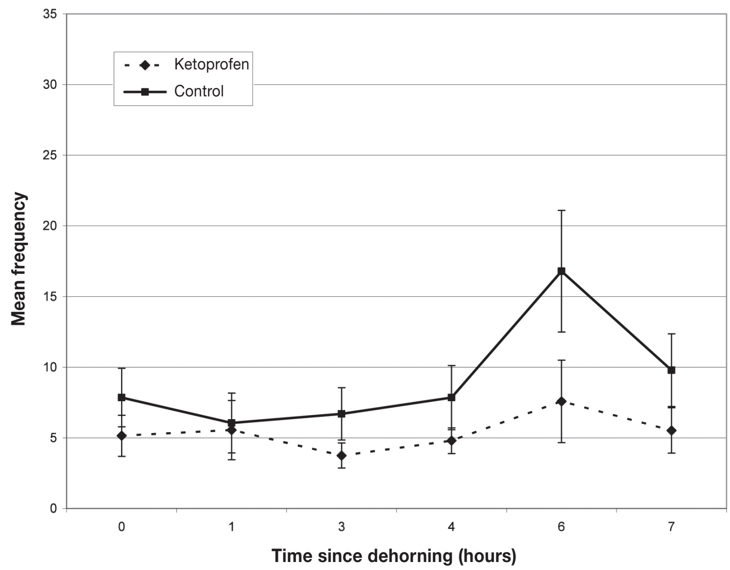

Figure 3. Mean (± standard error) frequency of ear-flicks that occurred following dehorning in control and ketoprofen-treated calves. Ear-flicking was significantly lower in ketoprofen-treated calves ($P = 0.01$).

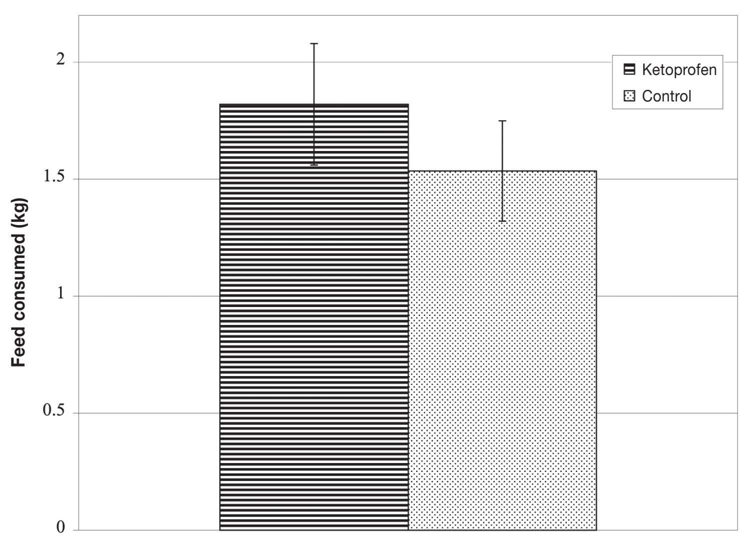

Figure 4. Mean (± standard error) feed consumption over the 24 h period following dehorning in control and ketoprofen-treated calves. Ketoprofen-treated calves tended to consume more feed than controls ($P = 0.09$).

Ketoprofen-treated calves tended to consume more calf starter following dehorning than the controls, amounting to an average increase of 0.25 kg of feed per day. Similar results regarding impact of NSAIDs on feed consumption in calves have been reported in other studies (2,3,22). Faulkner and Weary (2) saw an increase in BW of 1 kg in ketoprofen-treated calves over a 24-h period following dehorning. While these modest increases in feed intake may not be economically significant, they may be biologically important. Feed intake may suggest increased levels of comfort in the ketoprofen-treated calves, since appetite suppression is known to occur in the inflammatory response during sickness and pain (23,24).

The results of the current study support administration of ketoprofen in addition to local anesthetic for reduction of pain in response to cautery dehorning in 4–8 week old calves in comparison to local anesthetic alone.

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ARTICLE

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