The utility of ketoprofen for alleviating pain following dehorning in young dairy calves

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Abstract — To determine if ketoprofen, in addition to local anaesthesia, reduces pain following dehorning, we experimentally dehorned dairy calves, less than 2 weeks of age, with (20 calves) or without (20 calves) intramuscular injections of ketoprofen. All calves received a local anesthetic (lidocaine) prior to dehorning and were dehorned with heat cauterization. Cortisol concentration was measured via jugular blood samples taken immediately before dehorning and at 3 and 6 hours following dehorning. Calf behavior was recorded between 0 and 2, 3 and 5, and 6 and 8 hours following dehorning. There was no significant ($P > 0.10$) effect on creep feed consumption, cortisol concentration, or any of the behavioral measures during the time periods studied. However, the difference in cortisol concentrations from the time of dehorning until 3 hours later was significantly lower ($P < 0.05$) in the ketoprofen-treated group. These results suggest that ketoprofen, in addition to local anesthesia, may alleviate short-term pain following dehorning with a butane dehorning device in dairy calves less than 2 weeks of age.

Résumé — Utilité du kétoprofène pour soulager la douleur provoquée par l'écornage chez de jeunes veaux de races laitières. Afin de déterminer si le kétoprofène, ajouté à l'anesthésie locale, pouvait réduire la douleur qui suit l'écornage, nous avons expérimentalement écorné des veaux de races laitières, âgés de moins de 2 semaines : 20 veaux ont reçu une injection intramusculaire de kétoprofène et 20 veaux ont servi de témoins. Les veaux ont tous reçu un anesthésique local (lidocaïne) avant l'écornage et ont été écornés par cautérisation à la chaleur. Le taux de cortisol a été mesuré à partir d'échantillons de sang prélevés dans la jugulaire immédiatement avant l'écornage ainsi que 3 et 6 heures après. Le comportement des veaux a été consigné entre 0 et 2 heures après l'écornage puis entre 3 et 5 heures ainsi qu'entre 6 et 8 heures. Il n'y avait pas d'effet significatif ($P > 0,10$) sur l'alimentation à la dérobée, sur le taux de cortisol ou sur les comportements notés au cours des périodes d'observation. Cependant, la différence des taux de cortisol à partir du moment de l'écornage jusqu'à 3 heures après était significativement plus bas ($P < 0,05$) dans le groupe recevant du kétoprofène. Ces résultats laissent présager que le kétoprofène, ajouté à l'anesthésie locale, peut soulager la douleur à court terme qui suit l'écornage avec un écorneur à butane chez des veaux de races laitières âgés de moins de 2 semaines.

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Introduction

Horn buds of dairy and beef calves are normally removed to reduce the risk of injuries to other cattle or producers by using a number of techniques, including hot irons and caustic paste. Physiological (1,2) and behavioral studies (3–5) indicate that dehorning is painful for at least 2 h after dehorning, regardless of the dehorning method and response measures studied. Response measures have included behavioral responses to pain, such as ear flicks, head rubs, changes in posture, etc. In addition, some studies have attempted to gauge stress response through the measurement of serum cortisol concentrations. The use of local anesthetics has been found to reduce pain in the 2 to 4 h immediately following dehorning (1,3–9). The Canadian code of practice for dairy cattle recommends the use of local anesthetic for dehorning (10).

Local anesthetics may not significantly reduce cortisol response to dehorning overall, due to the sharp increase in cortisol levels that occurs once the local anesthetic wears off (6,9,11–13). The use of ketoprofen (a nonsteroidal antiinflammatory drug) has been shown to significantly reduce cortisol response to the scoop dehorning of 3- to 4-month-old calves when it is combined with the use of a local anesthetic (7,11). A behavioral study also found that ketoprofen given in addition to a sedative and local anesthetic and administered, PO, 2 h before, 2 h after, and 7 h after hot iron dehorning of 4- to 8-week-old calves reduced pain following dehorning (3). The responses identified in this latter study were a reduction in the frequency of ear flicking, head shaking, and head rubbing in animals receiving the ketoprofen treatment. Cortisol was not measured in this project.

The aim of our study was to evaluate the effects of using a local anaesthetic and a nonsteroidal antiinflammatory drug to reduce distress caused by dehorning in young dairy calves.

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Materials and methods

Forty Holstein dairy calves, aged between 2 d and 2 wk, from the Elora Dairy Research Herd (University of Guelph, Guelph, Ontario) were used in this study. This study was conducted in accordance with the university guidelines for animal research and with the approval of the University of Guelph Animal Care committee. Calves were housed indoors in rows of individual pens (1.3 m $\times$ 1.5 m). Each calf was randomly allocated to 1 of 2 treatments. "Control" calves were injected with 5 mL of 2% lidocaine hydrochloride with 0.05 mg/mL epinephrine (Bimeda-MTC, Cambridge, Ontario), SC, around each cornual nerve, and physiological saline (0.9% sodium chloride; Bimeda-MTC), IM, at a volume of 0.03 mL/kg body weight (BW), 10 min prior to dehorning. "Ketoprofen-treated" calves were injected, SC, around each cornual nerve with the same local anesthetic as above and with 10% ketoprofen (Anafen; Merial, Athens, Georgia, USA), 0.03 mL/kg BW, IM, 10 min prior to dehorning. The ketoprofen treatment was administered at this time because, if ketoprofen were to be efficacious, the time would be convenient for field application and reduce the need for additional handling. Calves were dehorned using a butane-powered dehorner (Portasol Dehorner II; Oglesby & Butler, Carlow, Ireland) (593°C). Dehorning took place at 1000 h (± 15 min) in each animal's own pen. Venous blood samples (5 mL) were taken from the external jugular vein immediately before dehorning and again at 3 and 6 h following dehorning. Cortisol concentration was analyzed by using serum that was frozen (−20°C) following centrifugation of blood samples.

Calf behavior was recorded by using a time-lapse video recorder (Panasonic, Model AG-6040, http://www.Panasonic.com) and wide angle camera lens (F 1.4/6 mm, Cosmicar, HS614GX; Pentax, Englewood, Colorado, USA) between 0 and 2, 3 and 5, and 6 and 8 h following dehorning. For each hour of video recorded per calf, 20 1-minute periods of time-lapse video were analyzed. The individual analyzing the video tape was blinded to which treatment the calves had received. The frequency of ear flicking (calf rapidly moved either one or both ears to the front and back), head shaking (calf rapidly shook its head from one side to the other), and head rubbing (with hind leg or against side of pen) were recorded as the number of times each activity occurred during each 1-minute period of observation. Lying (calf was lying on the ground), feeding or drinking (calf had head in bucket), and self grooming (calf was licking itself) were recorded as being present or absent for each calf at the start of each 1-minute observation period. The amount of creep feed (Rumax 20% calf starter; Floradale Feed Mill, Floradale, Ontario) supplement consumed on the day (24 h period) of dehorning was measured.

Data were tested for normality by using a Kolmogorov-Smirnov goodness of fit test. Distribution of calf weights, calf ages, and cortisol concentrations did not depart significantly ($P > 0.05$) from normal.

Weight and age were compared between control and ketoprofen-treated calves by using a one-way analysis of variance (ANOVA). Following log transformation, the amount of creep feed supplement consumed by control and ketoprofen-treated calves was compared by using a one-way analysis of covariance (ANCOVA) incorporating gender, weight, and age into the analysis as covariates. Cortisol concentrations immediately before and at 3 and 6 h after dehorning, and the change in cortisol concentrations between sequential time periods (immediately before and at 3 and 6 h after dehorning) were compared for control and ketoprofen-treated calves with a one-way ANCOVA incorporating gender and age into the analysis as covariates. Behavioral measures at 0 to 2, 3 to 5, and 6 to 8 h after dehorning, and the change in behavioral measures between sequential time periods (0 to 2 and 3 to 5 h after dehorning, 3 to 5 and 6 to 8 h after dehorning), between treatments were compared by using a nonparametric Mann-Whitney test. A statistical software program (SYSTAT) (14) was used for all statistical analyses.

Table 1. Number of males (M) and females (F), age (days), weight (kg), and creep feed consumption (kg) in control and in ketoprofen-treated calves

	Treatment	
Measure	Control	Ketoprofen
Gender	12 M, 8 F	9 M, 11 F
Age	6.6, $s_{\bar{x}} = 0.7$	5.8 , $s_{\bar{x}} = 0.7$
Weight	0.0 , $s_{\bar{x}} = 1.3$	49.6 , $s_{\bar{x}} = 1.4$
Creep feed consumption	0.12 , $s_{\bar{x}} = 0.02$	0.09 , $s_{\bar{x}} = 0.02$

$s_{\bar{x}}$ — standard error of mean

Results

Behavioral measures (number of ear flicks, head shakes, and head rubs, as well as percent time spent lying, feeding or drinking, and grooming) and creep feed consumption were not normally distributed. A log transformation of the creep feed consumption data provided a normal distribution and allowed for statistical analysis with ANCOVA. Gender, weight, age, and creep feed consumption were similar for control and ketoprofen-treated calves (Table 1).

The non-normal distribution of the behavioral response data, justified the use of nonparametric statistical analysis. Calves receiving the ketoprofen injection did not have significantly ($P > 0.1$) fewer ear flicks, head shakes, or head rubs than did control calves during the time periods studied (Table 2). Whether or not calves received a ketoprofen injection had no significant ($P > 0.1$) effect on the time that calves spent lying, feeding and drinking, or grooming during the time periods studied (Table 3). Change in number of ear flicks, head shakes, or head rubs, and change in percentage of time spent lying, feeding and drinking, or grooming between sequential time periods did not differ significantly ($P > 0.1$) between control and ketoprofen-treated calves.

Serum cortisol concentrations immediately before and at 3 and 6 h after dehorning were not significantly ($P > 0.1$; Table 4) different. The serum cortisol concentrations of ketoprofen-treated calves were lower at 3 h after than immediately before dehorning, while the serum cortisol concentrations of calves in the lidocaine-only treatment were higher (Table 4). The change in serum cortisol concentrations at 3 h after dehorning of ketoprofen-treated calves was significantly ($P < 0.05$) greater than that of

Table 2. Mean ± standard error ($s_{\bar{x}}$) number of ear flicks, head shakes, and head rubs per calf during 40 min of observation at 0 to 2, 3 to 5, and 6 to 8 h after dehorning in control and in ketoprofen-treated calves

		Treatment[a]	
Behavior	Time (h) after dehorning	Control	Ketoprofen
Ear flicks	0 to 2	3.0 , $s_{\bar{x}}$ = 0.9	2.4 , $s_{\bar{x}}$ = 0.7
	3 to 5	1.8 , $s_{\bar{x}}$ = 0.3	1.5 , $s_{\bar{x}}$ = 0.4
	6 to 8	1.1 , $s_{\bar{x}}$ = 0.4	1.7 , $s_{\bar{x}}$ = 0.4
Head shakes	0 to 2	1.5 , $s_{\bar{x}}$ = 0.4	1.2 , $s_{\bar{x}}$ = 0.4
	3 to 5	2.1 , $s_{\bar{x}}$ = 0.6	1.9 , $s_{\bar{x}}$ = 0.4
	6 to 8	2.1 , $s_{\bar{x}}$ = 0.6	2.0 , $s_{\bar{x}}$ = 0.5
Head rubs	0 to 2	0.8 , $s_{\bar{x}}$ = 0.3	0.3 , $s_{\bar{x}}$ = 0.2
	3 to 5	1.0 , $s_{\bar{x}}$ = 0.3	1.2 , $s_{\bar{x}}$ = 0.3
	6 to 8	1.8 , $s_{\bar{x}}$ = 0.4	1.1 , $s_{\bar{x}}$ = 0.4

[a]No significant differences ($P < 0.10$) noted between treatments

Table 3. Mean ± standard error ($s_{\bar{x}}$) percent of time calves spent lying, feeding or drinking, and grooming per calf during 40 min of observation at 0 to 2, 3 to 5, and 6 to 8 h after dehorning in control and in ketoprofen-treated calves

		Treatment[a]	
Behaviour	Time (h) after dehorning	Control	Ketoprofen
Lying	0 to 2	90.6 , $s_{\bar{x}}$ = 1.9	94.3 , $s_{\bar{x}}$ = 1.7
	3 to 5	86.5 , $s_{\bar{x}}$ = 2.2	89.3 , $s_{\bar{x}}$ = 1.8
	6 to 8	80.6 , $s_{\bar{x}}$ = 2.3	86.0 , $s_{\bar{x}}$ = 2.0
Feeding or drinking	0 to 2	1.0 , $s_{\bar{x}}$ = 0.8	1.1 , $s_{\bar{x}}$ = 0.6
	3 to 5	3.4 , $s_{\bar{x}}$ = 1.3	1.9 , $s_{\bar{x}}$ = 1.0
	6 to 8	3.5 , $s_{\bar{x}}$ = 1.1	2.3 , $s_{\bar{x}}$ = 0.8
Grooming	0 to 2	0.9 , $s_{\bar{x}}$ = 0.4	0.4 , $s_{\bar{x}}$ = 0.2
	3 to 5	3.0 , $s_{\bar{x}}$ = 0.9	1.9 , $s_{\bar{x}}$ = 0.6
	6 to 8	3.0 , $s_{\bar{x}}$ = 0.7	1.6 , $s_{\bar{x}}$ = 0.5

[a]No significant differences ($P < 0.10$) noted between treatments

lidocaine-only calves. The serum cortisol concentration of calves in both treatments was higher at 6 h after than at 3 h after dehorning (Table 4). The change in serum cortisol concentrations between 3 and 6 h after dehorning was not significantly ($P > 0.1$) different between ketoprofen-treated and lidocaine-only calves.

Older calves had lower serum cortisol concentrations immediately before ($P < 0.01$), 3 h after ($P < 0.05$), and 6 h after dehorning ($P < 0.01$). As a covariate, calf age uniquely ($P < 0.05$) adjusted serum cortisol concentrations at each time period. Age and gender were not significantly ($P > 0.1$) related to any of the behavioral variables during the time periods observed.

Discussion

The transient increase in plasma cortisol concentration that normally follows dehorning was reduced by the administration of ketoprofen in addition to lidocaine. Differences in cortisol levels between calves receiving both ketoprofen and lidocaine versus lidocaine only were similar to those in 2 previous studies (7,11). In contrast to those of the previous studies, our results suggest that the beneficial effect of ketoprofen was relatively short-lived. The pharmacokinetics of ketoprofen do not adequately explain this response, since ketoprofen and its primary metabolite are cleared quickly from the body (elimination half-life equal to 0.5 and 2 h, respectively), but the drug has a high affinity for inflamed tissue, resulting in a therapeutic response that lasts longer than predicted (15,16). Differences in methodology between the study by McMeekan et al (7) and ours could explain the difference in results. McMeekan et al used a different dehorner (scoop dehorner) and older calves (3 to 4 mo of age). As the amount of tissue damage and inflammatory pain increases with the size of horn bud removed, so too should the postoperative pain and the potentially beneficial effect of using a nonsteroidal antiinflammatory drug, such as ketoprofen. The duration of effect and relative benefit of using ketoprofen may be increased in older calves at dehorning. There is also some evidence that cauterization may help to decrease postoperative pain (1,9,12); therefore, the relative beneficial effect of ketoprofen could be reduced with butane dehorning compared with scoop dehorning, because cauterization itself could decrease pain response.

The administration of ketoprofen, in addition to lidocaine, had no significant effect on the behavior of calves following dehorning. A previous study (17) also found no significant behavioral differences between dehorned calves administered ketoprofen and lidocaine versus those administered lidocaine only. Our results differ from those in a study by Faulkner and Weary (3) where calves receiving ketoprofen and lidocaine spent less time head shaking and ear flicking than did calves receiving lidocaine only. In that study, the frequency of ear flicks, head rubs, and head shakes observed during similar time periods was 2 to 10 times greater than what

Table 4. Mean ± standard error ($s_{\bar{x}}$) serum cortisol concentrations (nmol/L) of calves immediately before dehorning (time 0), at 3 and 6 h after dehorning, and changes in serum cortisol concentrations between 3 and 0 h and 6 and 3 h after dehorning in control and ketoprofen-treated calves

	Treatment	
Time (h) after dehorning	Control	Ketoprofen
0	68.4 , $s_{\bar{x}}$ = 14.3	87.0 , $s_{\bar{x}}$ = 12.7
3	86.3 , $s_{\bar{x}}$ = 18.2	64.8 , $s_{\bar{x}}$ = 12.1
6	96.9 , $s_{\bar{x}}$ = 19.6	111.1 , $s_{\bar{x}}$ = 10.7
0 to 3	17.9 , $s_{\bar{x}}$ = 12.9	−22.2 , $s_{\bar{x}}$ = 14.0[a]
3 to 6	10.6 , $s_{\bar{x}}$ = 16.1	46.3 , $s_{\bar{x}}$ = 14.4

[a]Indicates significance at $P < 0.05$

we observed. Differences in methodology between the study by Faulkner and Weary and ours could also explain the difference in these results: we used a different dehorner (butane versus electric dehorner) and younger calves (less than 2 wk versus 1 to 2 mo of age). The electric dehorner is used in a similar fashion to the butane dehorner for the heat cauterization of larger horn buds and older calves. The use of the electric dehorner will result in more tissue damage and inflammation than does the butane dehorner and could explain both the increased frequency of behavioral indicators and the beneficial effect of using ketoprofen observed in that study.

Our finding that the cortisol response was still high 6 h after dehorning is consistent with that of numerous other studies (1,6,7,9). Those same studies also showed that the initial pain following dehorning is diminished by the administration of local anesthetic, but that some pain or distress occurs when the local anesthesia has worn off. In our study, a rise in serum cortisol levels when the local anesthesia had worn off (approximately 2 h (7)) was not discernable due to the sampling periods used. We chose to sample cortisol only 3 times to remove the need for catheter placement and minimize the stress on the animal due to repeated handling. Within the narrow range of calf ages used (2 to 14 d of age), we found that baseline serum cortisol concentrations were significantly negatively related to age. Calf age should be taken into consideration when designing and comparing studies involving cortisol levels as a measure of pain.

In conclusion, ketoprofen administration resulted in a slight, short-term reduction in serum cortisol concentration following butane dehorning of dairy calves less than 2 wk of age. Ketoprofen administration did not result in a reduction of behavioral indicators of pain. Based on these results, routine administration of both a local anesthetic and ketoprofen, rather than local anesthetic alone, to alleviate pain following dehorning in dairy calves less than 2 wk of age, when a butane dehorner is used, may not be justified if true pain is measured by behavioral response in the calf. However, the slight change in serum cortisol concentrations at about the same time as the anesthetic effect of lidocaine would be expected to wear off is consistent with other studies. Ketoprofen may be more beneficial in alleviating pain in older calves and in calves dehorned with devices other than the butane dehorner. The use of ketoprofen in older dairy calves dehorned with other methods needs further investigation.

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