Pilot testing an ethanol cornual nerve block as a long-term analgesic for calf disbudding

Alycia M. Drwencke,12 Sarah J. J. Adcock,13 Jenifer B. Walker,4 and Cassandra B. Tucker1* (Corresponding author: 530-754-5750, cbtucker@ucdavis.edu. © 2024, The Authors. Published by Elsevier Inc. on behalf of the American Dairy Science Association®. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). Received July 15, 2023. Accepted December 22, 2023)

Abstract: Disbudding prevents horn growth in calves through thermal or chemical cauterization and causes damage that is painful for weeks following the procedure. Current pain management strategies are only effective from 1 to 2 h (local anesthetic) to 1–3 d (non-steroidal anti-inflammatory drugs). A potential practical solution for addressing longer-term pain may be to administer ethanol as a cornual nerve block. When administered at a high concentration, ethanol damages the functionality of peripheral nerves, promoting localized long-lasting analgesia. It is also thought to be painful, thus ethanol may be combined with lidocaine, as a mixed solution or administered beforehand. We tested the use of an ethanol cornual nerve block for anesthesia around the horn bud in 2 pilot studies. We used different concentrations and amounts of ethanol (100 and 70%) in combination with different ratios of lidocaine in our attempt to identify an effective block. In pilot 1, 14 non-disbudded calves were administered 2–4 mL of 100% ethanol below the boney ridge on each side of the head to block the cornual nerve at 3–10 d of age (n = 28 horn buds) and observed for 5 wk. The duration of loss of sensation was evaluated using pinprick tests 10 min, 1, 3, and 7 d after the block, and then weekly thereafter until 35 d or full sensation had returned. Pinprick tests consisted of lightly pressing a needle in 10 evenly spaced locations around the base of the horn bud (0 responses = no sensation, 1–5 responses = partial sensation, 6–10 responses = full sensation). Pilot 2 looked at the 24 h after the injection and consisted of 9 non-disbudded calves (5 mL of 2:1, 70% ethanol and 2% lidocaine/horn bud) and 6 disbudded individuals (5 mL of 100% ethanol, 70% ethanol, or 2% lidocaine per horn bud). All treatments were administered at the calf level. Anesthesia was checked 10 min after the injection and 4 or 16 h later. In pilot 1, on the day of the ethanol injection (0-d), there was no sensation in 85% of horn buds. Sensation began to return as early as 1 d after blocking, with only 50, 21, and 3% of horn buds having no sensation at 1, 7, and 35 d, respectively. Partial sensation was present in 25, 17, and 10% of horn buds at these time points. In pilot 2, 27.8% of horn buds in the non-disbudded group had no sensation while 33.3% had partial sensation 10 min after the injection. In the disbudded calves 10 min after the injection, 100% of horn buds from the 100% ethanol group had partial sensation and 100% of horn buds administered 70% ethanol had full sensation. Four or 16 h later, 100% of horn buds had full sensation. Together, in these pilot studies, ethanol provided inconsistent anesthesia when used for a cornual nerve block.

Disbudding is a common husbandry procedure on dairy farms that prevents horn development with cauterization of free-floating immature horn tissue from a hot iron (heat) or caustic paste (chemical) (USDA, 2018). This procedure is painful in the acute period (Stafford and Mellor, 2011) and throughout the healing process (Adcock and Tucker, 2018; Casoni et al., 2019; Reedman et al., 2022a). Wounds take 7–9 wk to re-epithelialize on average following hot-iron disbudding (Adcock and Tucker, 2018; Adcock et al., 2019) and 16 wk following caustic paste application (Drwencke et al., 2023a). During this time, calves experience increased sensitivity to touch until wounds re-epithelialize (Adcock and Tucker, 2018; Drwencke et al., 2023a), pain-related behaviors at least 11 d later (Adcock et al., 2020), decreased rumination for 11 d (Adcock et al., 2023), conditioned place preference for pain mitigation 3 wk after the procedure (Adcock and Tucker, 2020), place aversion after 48 h (Ede et al., 2020), and more shelter use for at least 3 d (Gingerich et al., 2020). Together, these studies highlight the need for longer lasting pain relief following disbudding. However, current best practice to mitigate pain following disbudding is a combination of an NSAID and local block (Reedman et al., 2022b), which provides relief for up to 72 h at best (Mosher et al., 2012).

In humans, ethanol blocks are a well-established therapy for intractable, chronic pain (Jackson and Gaeta, 2008). When administered at a high concentration (typically > 98%), ethanol damages myelin, the fatty sheath surrounding nerves, disrupting electrical impulse conduction involved in pain perception, promoting long-lasting analgesia in that region (Guerrieri and Pascual, 2016). A single injection is effective at alleviating pain for at least 1 yr in peripheral nerve disorders such as trigeminal neuralgia (Han et al., 2017) and Morton’s neuroma (Pasquali et al., 2014). Administering lower concentrations of ethanol has been studied in pigs for pancreatic tissue ablation and was found to reduce bordering tissue damage (Matthes et al., 2007). Ethanol is reported to cause pain during the injection, but this effect can be mitigated by administering local anesthesia beforehand (Wiersema and Wiersema, 1996). Administering a lower concentration of ethanol simultaneously with a local anesthetic could reduce the number of injections while potentially reducing both acute and long-term pain.

Previous work in livestock shows ethanol blocks alleviate chronic rectal tenesmus in cattle for up to 5 wk with no adverse

1Center for Animal Welfare, Department of Animal Science, University of California, Davis, 95616, 2Animal Behavior Graduate Group, University of California, Davis, 95616, 3Department of Animal and Dairy Sciences, University of Wisconsin, Madison, 53706, 4Quality and Food Safety, Danone North America, 10605. *Corresponding author: 530-754-5750, cbtucker@ucdavis.edu. © 2024, The Authors. Published by Elsevier Inc. on behalf of the American Dairy Science Association®. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). Received July 15, 2023. Accepted December 22, 2023.
side effects (Noordsy, 1982). In horses, ethanol injections are considered a safe and economic treatment for clinical cases of osteoarthritis (70% or 100% ethanol: Lamas et al., 2012; Caston et al., 2013). Ethanol has also been used to achieve renal sympathetic denervation in sheep and pigs (Fischell et al., 2013; 99.6% ethanol: Firouznia et al., 2015). Administering an ethanol cornual nerve block was first demonstrated to numb the horn bud to mechanical stimulation for 3 d and to pinpricks for up to 178 d post disbudding (100% ethanol: Tapper, 2011). Similarly, local infiltration of ethanol was recently examined for dehorning in 20-wk old cattle (100% ethanol and lidocaine cornual nerve block: Martin et al., 2022).

Administering ethanol as a cornual nerve block before disbudding has some advantages over other analgesics: (1) it is administered using the same technique as a lidocaine block, (2) there are no residue concerns (personal communication, FARAD), and (3) a single dose could relieve both acute and long-term pain. Adverse symptoms described in humans include inflammation at the injection site and excessive or abnormal sensation such as tingling, pricking, numbness or burning. In cattle, untargeted structures around the cornual nerve could be harmed, causing permanent drooping of the eyelid. Our objective was to conduct a preliminary investigation into the use of an ethanol cornual nerve block for potential acute and long-term pain relief in young dairy calves. We aimed to better understand the duration of anesthesia from ethanol from administration through return of sensation for calves and gain experience with this tool in multiple contexts such as different facilities and age groups, across concentrations (70, 100%), and when combined with lidocaine.

Data were collected in a series of 2 pilot studies. Pilot 1 took place at the University of California, Davis Dairy Teaching and Research Facility between June 2019 and April 2020. The University of California Davis Institutional Animal Care and Use Committee approved procedures during this phase (protocol # 21170). Pilot 2 was run on a commercial farm in central California in July 2021 under the supervision of a licensed veterinarian. Treatments and sample size for each pilot study are outlined in Table 1. Total sample size was opportunistic and not determined by a power analysis. Researchers were not blind to treatment. All data and supplemental figures are available the Dryad repository (Drwencke et al., 2023b,c).

**Pilot 1**

Fourteen non-disbudded heifer calves (n = 6 Jersey and 8 Holstein) were housed individually in wire panel pens (2.5 × 1.2 × 0.9 m; length x width x height) bedded with rice hulls (~15–20 cm depth). Ad libitum access to water and grain (Starter Calf Feed 901033, Associated Feed and Supply Co) was provided. Milk was fed twice daily as described by Drwencke et al., (2023a) and calves were stepped up to 6 L/d by 32 d of age.

In pilot 1, 100% ethanol was injected subcutaneously as a cornual nerve block (Table 1). Groups 1–3 were administered 2 or 3 mL per side of 100% ethanol only. Group 4 was injected with 3 mL of buffered lidocaine, followed 10 min later by 4 mL of 100% ethanol in an effort to mitigate potential injection pain. During all injections, calves were placed in a head restraint in the home pen (see Jimenez et al., 2019). A 12 mL syringe with a 20-gauge × 25-mm needle was injected at a 45-degree angle toward the horn bud in the divot below the boney ridge that runs between the eye and temple. The needle was inserted to the hub, aspirated to confirm it was not in a blood vessel, and approximately half of the ethanol was injected with a side-to-side motion of the syringe. The needle was withdrawn approximately halfway, and the remainder of the ethanol was injected. Calves were checked for anesthesia 10 min after the injection and an additional 1 mL was provided if a behavioral response occurred (4 horn buds from 4 calves). Local swelling was observed after the first calf received ethanol injections. This calf was given 1 mg/kg meloxicam and thereafter the remaining 13 calves in pilot 1 received 1 mg/kg of meloxicam approximately 1 h before ethanol injections.

To evaluate anesthesia following injections, a clean needle was used to gently prick around the base of the horn buds while we monitored for a behavioral reaction (ear flick or pulling the head away). Pinpricks occurred in 10 evenly spaced locations (0 responses = no sensation, 1–5 responses = partial sensation, 6–10 responses = full sensation/bud). If a response occurred in any location, that spot was re-tested to confirm sensation. In pilot 1, calves had a pin prick test performed 10 min, 1, 3, 7, 14, 21, 28, and 35 d after the injection. At these same time points, calves were visually monitored for adverse side effects of the ethanol injections including swelling at the injection site and drooping eyelids. All pinpricks and assessments were conducted by a single person. Once a horn bud had 10 responses to a pinprick, it was not tested at future time points and assumed to have full sensation.

R (version 4.0.3 on macOS Big Sur 10.16) was used to create descriptive summaries and Figure 1 (R Core Team, 2022). One calf was missing a d3 pinprick; calves that received lidocaine were excluded from 0 d results to attribute loss of sensation solely to ethanol. Ethanol initially resulted in no sensation for 85% of horn buds.

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Sample</th>
<th>Age when injected</th>
<th>Disbudded at the time of injection?</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pilot 1</strong></td>
<td></td>
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</tr>
<tr>
<td>1</td>
<td>2 mL 100% ethanol, additional 1 mL if not numb after 10 min</td>
<td>3 Jerseys</td>
<td>3–4 d</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>3 mL 100% ethanol, additional 1 mL if not numb after 10 min</td>
<td>2 Jerseys, 1 Holstein</td>
<td>3–4 d</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>3 mL 100% ethanol, additional 1 mL if not numb after 10 min</td>
<td>1 Jersey, 3 Holsteins</td>
<td>9–10 d</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>3 mL buffered lidocaine, followed 10 min later with 4 mL 100% ethanol</td>
<td>4 Holsteins</td>
<td>9–10 d</td>
<td>N</td>
</tr>
<tr>
<td><strong>Pilot 2</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5 mL of mixed 2% lidocaine and 70% ethanol (2:1 ratio)</td>
<td>9 Holsteins</td>
<td>1–4 d</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>5 mL of 2% lidocaine only</td>
<td>2 Holsteins</td>
<td>9–8 d</td>
<td>Y</td>
</tr>
<tr>
<td>3</td>
<td>5 mL of 100% ethanol</td>
<td>2 Holsteins</td>
<td>12–13 d</td>
<td>Y</td>
</tr>
<tr>
<td>4</td>
<td>5 mL of 70% ethanol</td>
<td>2 Holsteins</td>
<td>10–11 d</td>
<td>Y</td>
</tr>
</tbody>
</table>
Sensation began to return as early as 1 d after the injection. No sensation was present in only 3.5% of horn buds 35 d later. At 35-d after injection, 10.7% of horn buds had partial sensation (Figure 1). No drooping eyelids were observed at any point. Swelling at the site of the injection (presence or absence; Supplemental Figures S1 and S2, Drwencke et al., 2023c) was observed and potential tissue hardening (“crunchy” texture; presence or absence) was detected multiple weeks after ethanol administration when a new lidocaine block was given before disbudding these calves.

**Pilot 2**

Fifteen Holstein heifer calves were housed in individual plastic sided pens (0.75 × 1.5 × 1 m; length x width x height) located within a curtain-sided barn. Straw bedding ~0.5 m in depth was provided for approximately 1 wk then plastic slatted flooring remained. Access to water and starter were available ad libitum. Calves were fed 3.8 L of colostrum at birth followed by 2 L of transition milk 2x/d through 2 d of age. Starting at 3 d, calves were fed 2.8 L pasteurized whole milk 2x/d via a bottle. Ad libitum access to water and grain (Ultimate Calf Starter 205111, Associated Feed and Supply Co) was provided from birth.

In pilot 2, 4 approaches were tested (Table 1), including a lower concentration of ethanol in an effort to mitigate the swelling and tissue hardening observed in pilot 1. Treatments were administered consistently within a calf and allocated first based on available non-disbudded calves (group 1), then with similarly aged calves (groups 2–4). All calves in pilot 2 were restrained so the shoulder blades were between a human’s legs, and the head was braced but the calf could drink from the provided milk bottle. Group 1 consisted of non-disbudded calves (n = 9) that received a 2:1 ratio of 2% lidocaine and 70% ethanol mixed in a 25 mL automatic injection syringe (Agri-Pro Enterprises). Lidocaine was drawn into the syringe first, followed by ethanol. Five mL per horn bud were administered (1.7 mL ethanol, 3.4 mL lidocaine) using a 20-gauge × 12.5-mm needle. The mixture was injected subcutaneously with the needle inserted to the hub and angled 45 degrees toward the horn bud in the divot below the boney ridge. The other 3 groups were calves (n = 2/group) that had previously been disbudded using Dr. Naylor’s caustic paste (H. W. Naylor Company Inc.) by the farm employees at 3–5 d of age. Disbudded calves were used to test unmixed injections within this pilot opportunistically since there were no additional non-disbudded calves available. The disbudded groups were injected using a 20-gauge × 12.5-mm needle attached to a 12 mL syringe. For each of these groups, 2 calves were injected with 5 mL of 100% ethanol, 70% ethanol, or 2% lidocaine per horn bud. Pilot 2 calves were provided ~1 mg/kg of meloxicam before injections. A pinprick test was used to assess anesthesia as described in pilot 1 for all groups. Restraint was performed in a similar fashion to the injections, with no bottle, and the head was not fully restricted. All calves had a pin prick test performed 10 min after their injection, group 1 had another 4 h later. Pin pricks were conducted the same day for group 1 (mixed lidocaine and ethanol). When 100% of calves had full sensation at 4 h, groups 2–4 were injected with lidocaine, or ethanol (70 or 100%) and checked for anesthesia. Groups 3 and 4 were tested a 2nd time 16 h later. All pinpricks were performed by a single person trained by the researcher from pilot 1. For ethical reasons, during 6 tests (10% of total tests) fewer than 10 pinpricks were used to assess anesthesia when calves had full sensation and showed escape attempts. Injection site swelling was observed at 15 sites across 9 pilot 2 calves, but no drooping eyelids occurred. After data collection, non-disbudded calves were provided lidocaine and meloxicam before hot-iron (pilot 1) or paste (pilot 2) disbudding.

Results are shown in Table 2; all animals were included. Desensitization was poor across groups with the exception of short-term loss of sensation for the lidocaine only group. Notably, the lidocaine is likely contributing to the sensation level in the mixed injection group at the 10-min observation. It is unclear if mixing the lidocaine and ethanol or total volume injected (5 mL total; 1.7 mL ethanol, 3.4 mL lidocaine) led to high levels of sensation.

In our 2 pilot studies, ethanol provided inconsistent anesthesia when used for a cornual nerve block. These results contrast with Tapper (2011) who found that ethanol provided consistent anesthesia in dairy calves for up to 178 d following the injection. However, Martin et al. (2022) found local infiltration of ethanol did not extend pain mitigation beyond that of lidocaine and meloxicam. While it is unclear what causes the inconsistency, it is possible ethanol concentration, age, nerve regeneration, tissue quantity, or injection location could play a role. Taken together, our results along with the work of others (Tapper, 2011; Martin et al., 2022) suggests that using ethanol as a cornual nerve block creates variable results and does not provide long-term pain relief for calves.

In pilot 2, we gave 4 calves pure ethanol injections while 9 calves received a mix of 70% ethanol and lidocaine 2% and achieved only 33% loss of sensation. In contrast, we had 85% loss of sensation in pilot 1, where all calves received 100% ethanol. Concentrations of ethanol as low as 20–40% have been reported to create local anesthetic effects in humans (Ritchie, 1996; Zafonte and Munin, 2001). Notably, human studies used lower concentrations in more tissue dense regions such as the spine and thigh (May, 1912; Zafonte and Munin, 2001). The same is true when lower concentrations of ethanol were injected into the pancreas of pigs (Matthes et al., 2007).

To prevent sensation, the cornual nerve must be sufficiently damaged by ethanol. The low quantity of tissue surrounding the tissue hardening observed in pilot 1. The work of others (Tapper, 2011; Martin et al., 2022) suggests that mixing the lidocaine and ethanol or total volume injected (5 mL total; 1.7 mL ethanol, 3.4 mL lidocaine) led to high levels of sensation.

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To prevent sensation, the cornual nerve must be sufficiently damaged by ethanol. The low quantity of tissue surrounding the
cornual nerve may have prevented the ethanol from being held in place to create long-lasting damage. Fierheller et al. (2012) suggested their ineffective use of local anesthetic with a percutaneous jet delivery administration could have been due to a lack of underlying soft tissue, or inadequate drug concentrations around the cornual nerve. In other animals where ethanol was effective, more soft tissue was present near the injection than what surrounds the cornual nerve. For example, ethanol was injected into the spine in cattle (Noordsy, 1982; Valverde and Sinclair, 2015), intra-articularly in horses (Lamas et al., 2012; Caston et al., 2013), and into the renal arteries in sheep and pigs (Fischell et al., 2013; Firouznia et al., 2015). Indeed, onset of the cornual nerve block relies on the placement and proximity of the anesthetic to the nerve, with delay or failure associated with deeper administration in the muscle rather than surrounding the branches (Skarda, 1996; Anderson and Edmondson, 2013; Bates et al., 2019).

Bates et al. (2019) attribute some possible differences in anesthesia to administrator skill with the technique, but even with ethanol injections that achieved no sensation at the 10-min check, the length of anesthesia was inconsistent. Studies that have used a lidocaine cornual nerve block have reported a wide range of success (reviewed by Sheedy et al., personal communication). These vary from 55% (Bates et al., 2019) to 75–91% with newly trained individuals (Winder et al., 2018) and 87.5% (Fierheller et al., 2012) achieving full anesthesia. The individuals performing ethanol injections (SJJA and AMD) have administered ~1800 lidocaine and 2012 achieving full anesthesia. The individuals performing ethanol injections that achieved no sensation at the 10-min check, anesthesia to administrator skill with the technique, but even with surgical pain in cattle. Vet. Clin. North Am. Food Anim. Pract. 29:157–184. https://doi.org/10.1016/j.cvfa.2012.11.006.

References


NOTES

Alycia M. Drwencke https://orcid.org/0000-0001-8201-5764
Sarah J. J. Adcock https://orcid.org/0000-0003-0227-5369
Jennifer W. Walker https://orcid.org/0000-0001-9821-6496
Cassandra B. Tucker https://orcid.org/0000-0002-6014-444X

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