Veterinary
Anaesthesia and Analgesia
Formerly the Journal of Veterinary Anaesthesia

Veterinary Anaesthesia and Analgesia, 2014, **41**, 372–377 doi:10.1111/vaa.12150

RESEARCH PAPER

Sublingual administration of detomidine to calves prior to disbudding: a comparison with the intravenous route

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Abstract

Objective To study the effects of oromucosal detomidine gel administered sublingually to calves prior to disbudding, and to compare its efficacy with intravenously (IV) administered detomidine.

Study design Randomised, prospective clinical study.

Animals Twenty dairy calves aged 12.4 ± 4.4 days (mean ± SD), weight 50.5 ± 9.0 kg.

Methods Detomidine at 80 μg kg^{-1} was administered to ten calves sublingually (GEL) and at 30 μg kg^{-1} to ten control calves IV (*V. jugularis*). Meloxicam (0.5 mg kg^{-1}) and local anaesthetic (lidocaine 3 mg kg^{-1}) were administered before heat cauterization of horn buds. Heart rate (HR), body temperature and clinical sedation were monitored over 240 minutes. Blood was collected from the *V. cephalica* during the same period for drug concentration analysis. Pharmacokinetic variables were calculated from the plasma detomidine concentration-time data using non-compartmental methods. Statistical analyses compared routes of administration by Student's *t*-test and linear mixed models as relevant.

Results The maximum plasma detomidine concentration after GEL was 2.1 ± 1.2 ng mL^{-1} (mean ± SD) and the time of maximum concentration was 66.0 ± 36.9 minutes. The bioavailability of detomidine was approximately 34% with GEL. Similar sedation scores were reached in both groups after administration of detomidine, but maximal sedation was reached earlier in the IV group (10 minutes) than in the GEL group (40 minutes). HR was lower after IV than GEL from 5 to 10 minutes after administration. All animals were adequately sedated, and we were able to administer local anaesthetic without resistance to all of the calves before disbudding.

Conclusions and clinical relevance Oromucosally administered detomidine is an effective sedative agent for calves prior to disbudding.

Keywords calves, detomidine, disbudding, oromucosal, sedatives, welfare.

Introduction

Disbudding, the removal of calves' horn buds, is a common procedure in dairy animal husbandry, but the procedure causes severe acute pain, and is associated with behavioural and physiological responses (Morisse et al. 1995; McMeekan et al. 1998; Stafford & Mellor 2011). There is no EU legislation for pain management associated with disbudding. The European Council Directive 98/58/

EC (1976) allows any skilled person to destroy or remove the horn-producing area of calves aged <4 weeks by chemical or heat cauterization.

Application of appropriate anaesthetics and analgesics is not compulsory in most countries but it is strongly recommended (AVA 2004; New Zealand Government 2005; AVMA 2012). Cornual nerve block and ring block around the horn buds with local anaesthetics effectively alleviates disbudding pain or delays its onset (Graf & Senn 1999; Fierheller et al. 2012). However infiltration of local anaesthetics to non-sedated calves is often difficult. Disbudding-related postoperative pain has been successfully alleviated by non-steroidal anti-inflammatory drugs, such as meloxicam (Stewart et al. 2009; Heinrich et al. 2010), ketoprofen (McMeekan et al. 1998; Faulkner & Weary 2000) and carprofen (Stilwell et al. 2012).

Despite recommendations, pain and distress related to disbudding of calves often remains untreated (Hoe & Ruegg 2006; Vasseur et al. 2010; Gottardo et al. 2011). According to the ALCASDE (2009), it is assumed that some kind of medical treatment is administered prior to or after calf disbudding only on 20% of European farms. In Italy, producers reported that 10% of their disbudded calves received local anaesthetics, 4% received a sedative and 5% received analgesics prior to disbudding (Gottardo et al. 2011). In Canada, use of sedatives or local anaesthetics was reported for 45% of herds, but no analgesics (NSAIDs) were mentioned (Vasseur et al. 2010). In the United States, sedatives or local anaesthetics were utilized by 12% and analgesics by 2% of dairy farmers (Fulwider et al. 2008).

Detomidine is a potent α_2-adrenoceptor agonist that is used commonly for sedation or premedication in horses and cattle, including calves (Peshin et al. 1991). Sublingual administration of an oromucosal gel formulation of detomidine produced safe sedation in horses (DiMaio Knych & Stanley 2011; Kaukinen et al. 2011), and the bioavailability was approximately 22% (Kaukinen et al. 2011).

The primary objective of this study was to explore the use of oromucosal detomidine gel for sedation of calves prior to disbudding. Our hypothesis was that oromucosal detomidine would produce sufficient sedation to allow administration of local anaesthetics with minimum resistance. The secondary objective was to determine the plasma detomidine concentrations after sublingual administration and to compare level of sedation to intravenous (IV) administration of detomidine in calves undergoing disbudding.

Materials and methods

This study was conducted with permissions of the Animal Experiment Board of Finland and the Finnish Medicines Agency. Twenty clinically healthy dairy calves of both sexes were included. Their age was 12.4 ± 4.4 days (mean ± SD) and they weighed 50.5 ± 9.0 kg. The animals were disbudded as a routine measure of the farm. The calves were housed as other calves on the farm, and they were used to human handling. The calves were allocated randomly to one of two groups of 10 animals in each. One group was given sublingually (GEL) detomidine gel (Domosedan Gel 7.6 mg mL^{-1} oromucosal gel; Orion Pharma Ltd., Finland) 80 μg kg^{-1}, the other group was given IV detomidine (Domosedan 10 mg mL^{-1} solution for injection; Orion Pharma Ltd.) 30 μg kg^{-1}.

Prior to drug administration, the calves were examined clinically and the *V. cephalica* was cannulated (16 G Intraflon, 1.6 × 60 mm; Vygon, France) for blood sampling. In the IV group, the *V. jugularis* was also cannulated with a similar catheter for drug administration. Before placement of the catheters, local anaesthesia was provided by the subcutaneous infiltration of lidocaine (Lidocain 20 mg mL^{-1}; Orion Pharma Ltd.).

The detomidine gel for sublingual administration was drawn into a 1 mL syringe to achieve an accurate dose, and was administered under the tongue of the calf. The IV detomidine was given as a bolus *via* the jugular catheter, which thereafter was flushed with 10 mL of isotonic saline. To alleviate postoperative pain, meloxicam (0.5 mg kg^{-1}; Melovem 5 mg mL^{-1}; Orion Pharma Ltd.) was administered subcutaneously. When clinical sedation was evident, the local anaesthetic, Lidocaine 20 mg mL^{-1}, was injected subcutaneously around the cornual nerve and a ring block was inserted around both horn buds as previously described by Faulkner & Weary (2000). The total dose of lidocaine was 3 mg kg^{-1} *per* calf. The animal's response to administration of the local anaesthetic was recorded. The adequacies of the local blocks were tested with needle pricks, and once adequate, hot cauterization was used to destroy the horn buds.

Heart rate (HR) was measured by auscultation and the depth of sedation was recorded using a 17-point (0–16 where 0 is no sedation) behaviour-based