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# A randomised field study evaluating the effectiveness of buccal meloxicam and topical local anaesthetic formulations administered singly or in combination at improving welfare of female Merino lambs undergoing surgical mulesing and hot knife tail docking

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ABSTRACT

This study was a field-based behavioural assessment of the pain responses to surgical mulesing modulated by a buccal formulation of meloxicam (Buccalgesic) and a topical local anaesthetic wound dressing (Tri-Solfen). 20 lambs were randomly allocated to each of: 1) Placebo and sham handled (Sham); 2) Placebo and mulesing (Mules); 3) Buccalgesic and mulesing (Mules + B); 4) Tri-Solfen and mulesing (Mules + T); 5) Placebo, Tri-Solfen and mulesing (Mules + T + P); 6) Buccalgesic, Tri-Solfen and mulesing (Mules + T + B). Lamb behaviour was observed by scan sampling every 15 min for 6 h post mulesing then for 1.5 h daily over the subsequent 10 days. Wound score, wound sensitivity and body weight were recorded on day 4, 7 and 10. On the day of mulesing, abnormal behaviours were reduced for all groups that received the analgesic drugs compared to the Mules group ($P < 0.05$). Tri-Solfen reduced expression of abnormal behaviours in the first 4 h; Buccalgesic reduced expression of abnormal behaviours between 2 and 6 h; and combination treatment reduced expression of abnormal behaviours over the entire observation period. On the subsequent two days, the drug combination resulted in fewer abnormal postures than Tri-Solfen alone. The drug combination tended to result in lower pain sensitivity (965.3 g tolerated) than either Mules + T + P (828.8 g), or Mules + B (791.2 g) on day 7 ($P < 0.05$). Use of Tri-Solfen and Buccalgesic singly or in combination improved the welfare of lambs undergoing surgical mulesing. The residual effect of pain and discomfort caused by mulesing, were evident despite provision of analgesic drugs.

## 1. Introduction

Surgical mulesing is a painful husbandry procedure that is carried out on Merino lambs in Australia's extensive wool industry. The procedure involves the surgical removal of skin adjacent to the perineum and on the sides of the tail, which leads to reduced wrinkle and a wool free area when healed. The purpose of the procedure, which is predominantly performed on female lambs is to reduce the life-time risk of cutaneous myiasis of the breech (breech strike) in these extensive farming systems (Rothwell et al., 2007). There are alternative management strategies that can be used to minimise the risk of breech strike such as the use of insecticide, crutching or selection of genotypes that are resistant to breech strike. However these methods can be difficult to implement in extensive production systems (James, 2006; Rothwell et al., 2007). Despite genetic selection being available to producers, it will take many generations of selective breeding to remove the need to mules across the Australian sheep industry. Therefore, there is an urgent need to make available a range of analgesic options to those producers who still need to carry out mulesing. Currently Australian farmers have access to a pain relief agent containing lignocaine, bupivacaine, adrenaline and cetrimide (Tri-Solfen®, Bayer Australia Ltd) for topical application at the time of mulesing. Tri-Solfen is effective at providing pain relief over the first 12–24 h following mulesing (Lomax et al., 2008; Paull et al., 2007), however pain following mulesing can last from several days to weeks (Chapman et al., 1994; Fell and Shutt, 1989; Fisher, 2011; Hemsworth et al., 2009). Repeated handling of lambs in the days following mulesing is both impractical and undesirable due to the additional stress it imposes on the animals. Due to this a combination drug approach that provides a longer duration of action (or greater short term efficacy) is desirable.

The effectiveness of combination therapy with local anaesthetics and a non-steroidal anti-inflammatory drug (NSAID) prior to painful husbandry procedures has been previously demonstrated (Paull et al., 2007; Webster et al., 2013). Recently, a buccal formulation of the

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NSAID meloxicam (Ilium® Buccalgesic® OTM, Troy Laboratories Pty Ltd., Australia) has been registered for use in sheep in Australia. The formulation is designed for retention in the buccal cavity and absorption of the active (meloxicam) across the adjacent mucosa. The buccal meloxicam formulation was recently demonstrated to be effective at providing analgesia to lambs following surgical castration and hot-iron tail docking (Small et al., 2014). Buccalgesic is administered to lambs using a proprietary oral dosing gun and could readily be administered at the time of mulesing as an adjunct to a topical anaesthetic agent such as Tri-Solfen.

In this study Buccalgesic was administered immediately prior to mulesing, while the lamb was restrained in the mulesing cradle. This timing of administration of a NSAID was selected on the basis that: a) delivery of the NSAID 30–45 min prior to mulesing would involve a second handling event, which would compromise welfare; and b) the active agent, meloxicam, is a selective COX-2 inhibitor that is rapidly absorbed through the buccal mucosa, reaching high plasma concentrations within 15–20 min and Cmax after 2.6 h (F. Cotter, Troy Laboratories, personal communication), i.e. during, and prior to significant, expression of COX-2 receptors at the site of injury (Masferrer et al., 1994; Seibert et al., 1994; Small et al., 2018).

The objectives of the study were to assess the impact of Buccalgesic, Tri-Solfen, or a combination of both agents on behavioural and inflammatory responses to mulesing plus tail docking (hereafter termed mulesing) in the field. The hypotheses being tested were that surgically mulesed lambs that received Buccalgesic or Tri-Solfen would show a reduction in the frequency of behaviours and postures as associated with pain and improved wound healing, compared to lambs that received no pain relief, while those lambs that received the combination of Buccalgesic and Tri-Solfen would show a reduction in the frequency of behaviours and postures as associated with pain and improved wound healing, compared to lambs that received administration of one of the agents alone.

The efficacy of Buccalgesic and Tri-Solfen, alone or in combination, in lambs undergoing mulesing and tail docking, evaluated in a pen study design incorporating physiological and behavioural evaluations, are reported in a companion paper (Small et al., 2018).

## 2. Materials and methods

### 2.1. Animals

The trial included 120 unweaned female Merino lambs, aged between 6 and 10 weeks and weighing between 11.2 and 26.4 kg at the time of mulesing. Ewe–lamb pairs were identified at birth, with only single-born lambs used in the study. The experiment was undertaken at CSIRO's FD McMaster Laboratory, Armidale, New South Wales (NSW), Australia. The protocol and conduct of the experiment was approved by the CSIRO Armidale Animal Ethics Committee under the NSW Animal Research Act, 1985 (Animal Research Authority 15/15).

### 2.2. Experimental procedures and treatments

Testing occurred in 4 cohorts of 30 lambs. Lambs were paint-marked with individual identification numbers and weighed 6 days prior to treatment. They were subsequently ranked by weight and within a block of six, randomly allocated to a treatment group (Table 1). A day prior to treatment, ewes and lambs were acclimated to the observation paddock (0.34 ha), which had an observation hide located in its centre.

On the day of treatment (day 0), ewes and lambs were separated, and the ewes returned to the observation paddock, while the lambs were held in a treatment pen adjacent to the paddock. Lambs were picked randomly from the pen and weighed for dose calculation, prior to treatment and surgery. Lambs were then restrained on their back in a marking cradle. Buccalgesic (meloxicam 10 mg/mL, batch 150395, Troy Laboratories Pty Ltd) and the volumetric equivalent of buccal placebo (the base of Buccalgesic, minus the active agent, meloxicam, provided by Troy Laboratories Pty Ltd) were administered by the buccal route using a proprietary dosing gun supplied by the manufacturer with 0.5 mL increments. The dose was applied into the sulcus between the molar teeth and the inside of the cheek. Buccalgesic and the buccal placebo were administered at a target dose rate of 1.0 mg/kg meloxicam. Individual dose volumes for Buccalgesic and the buccal placebo were calculated based on individual body weight and prepared to the dose volume based on weight groups, 10.1–15.0, 15.1–20.0, 20.1–25.0 kg and 25.1–30.0 kg, allowing the target dose rate to be delivered at the maximum weight range for that group. Lighter lambs within a weight bracket received a dose slightly above 1 mg/kg.

For tail-docking a Primus BJ5000 gas-fired hot knife (Leader Agriproducts, Australia). Surgical mulesing was carried out by an accredited commercial mulesing practitioner, and involved cutting off excess skin on the breech and tail, using mulesing shears as described by Lee and Fisher (2007). Removed tissue, including breech skin, tail skin, and the removed tail from each mulesed animal was collected and weighed. These data were compared across treatments to confirm that the outcomes of the mulesing procedure were similar across treatment groups. Tri-Solfen (Lignocaine 40.6 g/L, bupivacaine 4.5 g/L, adrenaline 24.8 mg/L, cetrimide 5 g/L, batch V12177/1 and V12369/1, Bayer Australia Ltd) was applied by spraying to cover the mulesed area and tail docking wound, using the commercial applicator, at dose rates of: lambs 5–10 kg 6 mL; 11–15 kg 8 mL; 16–20 kg 10 mL; > 20 kg 12 mL. Sham control lambs were placed on their backs in the lambing cradle and the breech skin and tail gently handled for a duration similar to that experienced by lambs that underwent the mulesing and tail docking procedure. Following its treatment, each lamb was released into the observation paddock.

### 2.3. Behavioural observation

All observers were blinded to treatment. Three observers recorded lamb behaviour at 15 min intervals from the time of treatment by scan sampling for 6 h. Scan sampling involved locating the individual of interest, based on side markings, at the time point relative to marking and recording the behaviour the lamb was displaying. In each cohort, each observer was responsible for recording the behaviours performed by 10 lambs. Behaviours were classified and combined into lying, standing and abnormal behaviours (Table 2). At 24 h, eight scan samples at 15 min intervals were undertaken by two observers. The lambs and ewes were then moved to a larger paddock (1.0 ha) which did not contain an observation hide. On days 2–10, two observers located in a vehicle to which the ewes and lambs were accustomed took five scan samples of lamb behaviours at 15 min intervals. Behavioural observations on days 1 to 10 were conducted between 8:00 am and 12:00 noon on each day.

### 2.4. Clinical observation

On days 4, 7 and 10, lambs were mustered, weighed, restrained in the marking cradle and wounds on the tail and breech were scored for the presence of swelling and exudates; sensitivity was also assessed by measuring applied pressure using a digital algometer (Bioseb SMALGO-GT, Vitrolles, France) applied to the wound edges at defined locations (Fig. 1). Wound appearance and swelling were scored on a 5-point scale from 0 (no visible wound or palpable swelling) to 4 (large area of wound or substantial pitting oedema). Wound sensitivity assessment consisted of an applied pressure reading at which a behavioural response of the hind quarters and the face (Guesgen et al., 2016; McLennan et al., 2016) was observed in the lamb and a nociceptive response characteristic scored. The response characteristics were scored by intensity on a 4-point scale from 0 (no response) to 3 (strong physical response, struggle or escape attempt) (Table 3). The applied