Dynamics of local anaesthetics for velvet antler analgesia

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Abstract

Velvet antler removal on commercial deer farms is the elective surgical amputation of a live, vascular and innervated tissue. This is ethically defensible only if the wellbeing of the stag is not unacceptably compromised, particularly in relation to surgical and post-surgical pain. Those removing velvet antlers are ethically bound to employ "best practice" analgesic techniques.

Investigation of routes and doses of lignocaine hydrochloride (2%) showed that the most effective procedure is a high dose ring block (1 ml/cm pedicle circumference) around the antler pedicle. Mean times to onset of analgesia were 30 and 36 seconds in two studies Mean time to onset of analgesia was 30 seconds for mepivacaine (2%) and 48 and 87 seconds for two formulations of bupivacaine (0.5%)

Long-acting local analgesia has the theoretical advantage of prolonged postoperative pain relief. Studies showed the mean duration of analgesia to be 88 minutes after lignocaine, 270 minutes after mepivacaine, and 270-460 minutes, depending on formulation, after bupivacaine Combinations of local anaesthetics provided no synergy for duration, but mixtures with lignocaine tended to provide more rapid onset of analgesia and longer duration These studies confirm that rapid onset, reliable and repeatable analgesia is achievable using injectable local anaesthetics Best practice, defined by this research, should be prescribed as the compliance standard in quality assurance programmes for velvet removal that exist in many deer farming countries Further research is required to evaluate justification and methods for postoperative pain control

Introduction

Velvet antler removal is ethically defensible only if the wellbeing of the stag is not unacceptably compromised, particularly in relation to surgical and post-surgical pain (Wilson, 1989, Wilson *et al*, 2001). Research into the use of lignocaine hydrochloride via different routes and dosages in yearling and adult stags has been undertaken recently (Wilson *et al*, 1999, 2000). A high dose ring block produces the most rapid onset and effective analgesia Local anaesthetics and other means or potential means of local analgesia for velvet antler removal, including electroimmobilisation, electroanalgesia and compression, have been described elsewhere (Haigh *et al*, 2001, Matthews and Suttie , 2001; Matthews *et al*, 1999a,b)

Long-acting analgesia has the theoretical advantage of prolonged postoperative pain relief A limited amount of research has been undertaken to evaluate the presence and/or impact of postoperative pain in velveted stags (Pollard *et al*, 1993)

Audit of the New Zealand deer industry's velvet removal programme indicated that analgesia was not achieved in all cases (National Velveting Standards Body data). A subsequent observational study of procedures used by deer farmers removing velvet antler under veterinary supervision (Morrow and Matthews, 1998, unpublished) showed eight of 11 farmers used a regional nerve block with or without a cervical or auriculopalpebral block Quantities of local anaesthetic (lignocaine hydrochloride 2%) varied from 10 to 35 mls per animal (range 2 5-7 5 mls per injection site) Three operators using a ring block all used 10 mls per antler The wait time was 2 5 - 9 0 minutes although there was no significant difference in stag behavioural response to cutting based on duration of the wait period Effective local analgesia was achieved on 65% of antlers after a ring block was used and 73% following a regional nerve block, but this difference was not significant Data showed the ring block to be more reproducible than regional blocks. There was significant variation between operators dependent on their supervising veterinarian

These data suggest that current methods for injectable local anaesthetic by ring block were more reproducible than the nerve block, despite being less effective Between-operator differences

suggested that technique was a significant factor. This prompted a series of studies to evaluate a range of techniques and dose rates (Wilson *et al*, 1999, 2000)

This paper presents preliminary results of recent studies involving a more detailed investigation of the dynamics of lignocaine 2%, its mixture with bicarbonate, and comparison in onset and duration of analgesia with longer acting local anaesthetics mepivacaine and bupivicaine, either individually or in combination It also presents data on the time sequence of events during velvet antler removal, to investigate the prospect of an uninterrupted process (ie no unoccupied wait time) for velvet antler removal, given that results to date suggest a 4 minute wait time appears unnecessary

Materials and Methods

A series of experiments were undertaken to determine both the time to onset, and duration of analgesia

General methodology

Deer and restraint

This research was conducted either at the Massey University Deer Research Unit using rising 1-year-old red and 25 Wapiti x red hybrid deer, or both mixed-age adult and rising 1-year-old stags on a commercial deer farm in the Manawatu

Deer on either property were restrained in a padded deer-handling device with free access to the head for application of analgesia and observations

Analgesia onset

A clip containing two electrodes attached to a grass stimulator (Grass Instruments, Quincey, MA, USA) was applied to the antler before analgesic was injected. Voltage was applied (range 0 - 75 V) and increased until the animal responded confirming that the deer was responsive to the stimulus After administration of the analgesic further voltage stimuli were applied at 15-second intervals and the voltage and animal response recorded If no response occurred to the maximum voltage the antler was deemed analgesic. This technique has been used previously (Wilson *et al.* 1999, 2000a), and provides a good predictor of surgical analgesia The antler was considered analgesic when there was no movement observed in response to the highest voltage

Duration of analgesia

A 3-channel remote stimulator (The Beagler, Tritronics, Tuscon, AZ, USA) was used to monitor the return of sensation in the antlers. Prior to administration of analgesia the electrode was attached to the antler with a colour-coded surgical tape to match one of the three transmission signals applied remotely Head movement by the stag after remote triggering was indicative of electrical contact and confirmed the antler was algesic.

After administration of the local anaesthetic the stag was released from physical restraint and placed either in a pen or paddock. At intervals the remote stimulator was triggered and the stag was observed for head movement simultaneous with the trigger. Once a head movement characteristic of that seen prior to anaesthetic administration was observed, it was considered the analgesia had ceased.

As the need arose for increasing numbers of observations, a second method was adopted. This involved a handler holding the electrodes against the antler A second observer triggered the voltage and observed for animal movement For this procedure, after local anaesthetic had been applied, deer were held in groups of five per pen and up to 15 animals were investigated at one time

Drugs used

The local anaesthetics used were

- Lignocaine hydrochloride 2% (L) ("Bomacaine", Bomac Laboratories Ltd, Batch 01728.DOM8/2000 Expiry 8/2003)
- 0.5% bupivacaine (B) ("Marcaine", Astra Pharmaceuticals Pty Ltd., NSW, Australia Batch 208854 Expiry 4/2002)

- Lignocaine hydrochloride 2% as above with 8.4% sodium bicarbonate (LBC) (David Bull Laboratories, Victoria, Australia. Batch JO28627.DOM 7/99. Expiry 10/2001).
- Low concentration LB combination (LLB)1% lignocaine hydrochloride, 0 25% bupivicaine (LB). Note. this combination used a different bupivicaine formulation to "marcaine"
- High concentration LB combination (HLB). 1 5% lignocaine hydrochloride, 0 5% bupivicaine. Note this combination used a different bupivicaine formulation to "marcaine"
- Mepivacaine 2% (Vet Pharm NZ Ltd)
- Lignocaine 1.5%/Mepicacaine 1.5%
- Mepivicaine 1 5%/bupivicaine combination 0 5% (MB) Bupivicaine: non-commercial formulation.

Time sequence of velvet removal procedures

A series of observations were taken by an experienced operator (PRW) to test the time interval between initiation and completion of the series of procedures conducted for velvet antler removal from adult stags. The operator called at the commencement and completion of each procedure Time was recorded by a timekeeper The procedures were start and finish of the first antler ring block, start and finish of the second antler ring block; tourniquet application, nick test for each antler; removal times for each antler These procedures were undertaken as a continuous uninterrupted sequence However, if the nick tests showed analgesia was incomplete, a 30-second wait time was applied

Analgesia dose and administration

Each analgesic was injected from a flexipack using a 2 ml vaccinator gun with a 1 inch x 20 gauge needle. The dose rate was 1 ml/cm pedicle circumference for each LA or combination. The infusion was by continuous ring block around the pedicle over the frontal bone at the junction between the frontal bone and the pedicle.

Interpretation of time intervals recorded

Measurements for onset of analgesia were at 15-second intervals The time recorded for data collection was that at which there was analgesia Thus, the precise onset of analgesia is somewhere between that time and 15 seconds earlier (average likely 7 5 seconds earlier)

Measurements for duration were taken at 30-minute intervals, thus data needs to be interpreted that algesia had returned by the times stated (average 15 minutes earlier than times observed)

Research and results

Onset of lignocaine (L), lignocaine bicarbonate (LBC) and bupivacaine (B) analgesia

Twenty-one 1-year-old deer were used Antlers were allocated to two of three treatments, ie: each antler received two treatments (28 antlers per treatment) The treatment order was randomised. Treatments were L, LBC and B

The electrical stimulation test was applied at 15-second intervals immediately after the completion of the ring block Results are presented in Table 1

Table 1. Time to analgesia (seconds) after injection of lignocaine (L), lignocaine bicarbonate (LBC) and bupivacaine (B)

	L	LBC	B
n	28	28	28
Min	15	15	15
Max	195	60	255
Mean	**31**	**21**	**48**
SE	7 0	2 5	12 7

Survival analysis (log rank test) showed the difference between LBC and B to be significant (p = 0 0225). The differences between L and B (p = 0.20) and L and LBC (p = 0.22) were not significant Data would suggest that addition of bicarbonate reduced variation in the rate of absorption, since all were analgesic within 60 seconds However, further studies of this combination in adult stags for velvet antler removal did not demonstrate such consistency

Duration of lignocaine and bupivacaine in 1-year-old stags

Eight antlers were randomly allocated to one of two treatments, lignocaine and bupivacaine (commercially available "Marcaine") Administration of local anaesthetic and remote electrical stimulation was undertaken as described above Results are presented in Table 2

Table 2. Duration of analgesia (minutes) after lignocaine (L) and bupivacaine (B)

	L	B
n	8	9
Min	60	195
Max	120	360
Mean	**88**	**273**
SE	7 7	19

A paired T-test showed a significant difference in mean duration (p < 0 001) These data are similar to duration reported in other species

Combination of lignocaine and bupivacaine at two concentrations

Onset of analgesia was investigated on adult stags using the methodology described above Twenty-five antlers were used per treatment combination

Analgesia onset times are presented in Table 3

Table 3. Time to analgesia (seconds) after high concentration (HLB) and low concentration (LLB) lignocaine/bupivacaine mixtures

	HLB	LLB
n	25	25
Min	15	15
Max	90	210
Mean	**37**	**55**
SE	4 4	8.8

The survival log rank test showed the difference in onset to be significant (p = 0 049)

Duration of analgesia was measured by methods described above on 1-year-old stags Results are presented in Table 4

Table 4. Duration of analgesia (minutes) following low (LLB) and high concentration (HLB) lignocaine/bupivacaine mixtures

	High	Low
n	10	10
Min	290	240
Max	535	475
Mean	**406**	**332**
SE	29	25

A paired T-test indicated a significant difference in mean duration ($p = 0.041$).

The prolonged duration after the high concentration combination suggested a synergistic effect when compared with bupivacaine alone, above This difference was later to be attributed to differences in formulation (see below)

Onset and duration of mepivacaine, bupivacaine, mepivacaine/lignocaine and mepivacaine/bupivacaine

This study was conducted on 1-year-old stags on a commercial deer farm. Results for onset and duration are presented in Tables 5 and 6, respectively.

Table 5. Onset of analgesia (seconds) following mepivacaine (M), bupivacaine (B) and mixtures of lignocaine/ mepivacaine (LM) and mepivacaine/bupivacaine (MB)

	M	LM	B	MB
n	6	7	7	7
Min	15	15	15	15
Max	75	75	300	60
Mean	30	34	86	30
SE	12 3	7 8	37 3	6 6

Survival analysis indicated no difference in mean onset times This probably was due to the small numbers of animals available for this trial, since similar differences in mean onset times for other observations above, using 25-28 antlers/treatment were significantly different. This observation does, however, highlight the variation between animals in onset times Precise anatomical placement of LA may differ in relation to tissue planes, influencing diffusion rates into nerves.

The mean onset time for bupivacaine using this formulation, which was a pharmaceutical company non-commercial formulation, was 86 seconds whereas the commercially available "Marcaine" had a mean onset time of 48 seconds (see above). Mepivacaine had a rapid onset equivalent to earlier observations of lignocaine

It would appear from this experiment and those above, that the combination of local analgesics had an onset time equivalent to the fastest acting component

Table 6. Duration of analgesia (minutes) following mepivacaine, bupivacaine and combinations of lignocaine/ mepivacaine and mepivacaine/bupivacaine

	M	LM	B	MB
n	7	7	7	7
Min	180	120	335	310
Max	375	270	570	570
Mean	**271**	**221**	**461**	**421**
SE	26	19	37	41

A one-way analysis of variance showed that there were statistically significant differences in duration between LM and MB ($p<0.001$), M and MB ($p<0.05$), B and ML ($p<0.001$), and B and M ($p<0.001$).

Note, the mean duration of analgesia following pharmaceutical company non-commercial formulation bupivacaine was significantly longer than that for "Marcaine", consistent with the observation from the onset study that a difference exists between those two product formulations

Summary - onset and duration data

Figures 1 and 2 describe graphically the mean (± SE) of onset and duration times for each of the combinations studied and described in the previous tables to highlight differences

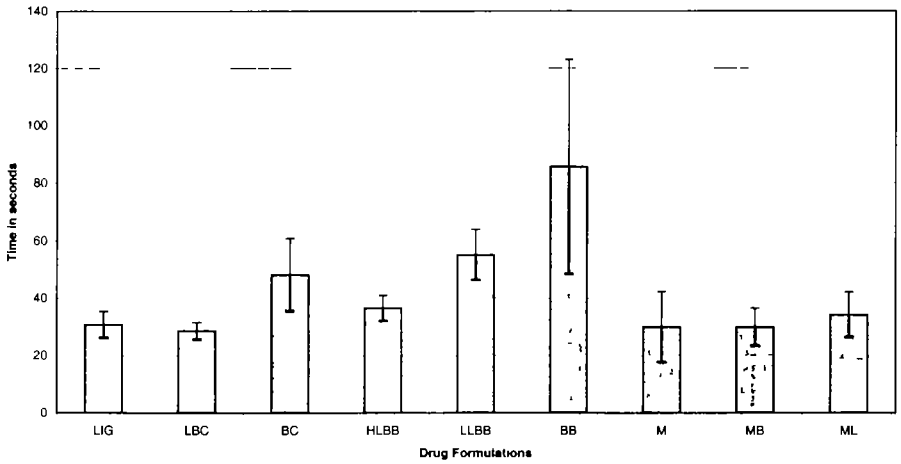

Figure 1. Summary of mean (and SE) onset times for analgesia (LIG = lignocaine, LBC = lignocaine + bicarbonate, BC = bupivacaine ("Marcaine"), HLBB and LLBB = high and low concentration, respectively, lignocaine + bupivacaine alternative formulation, BB = bupivacaine alternative formulation, M = mepivacaine, MB = mepivacaine + BB, ML = mepivacaine + lignocaine)

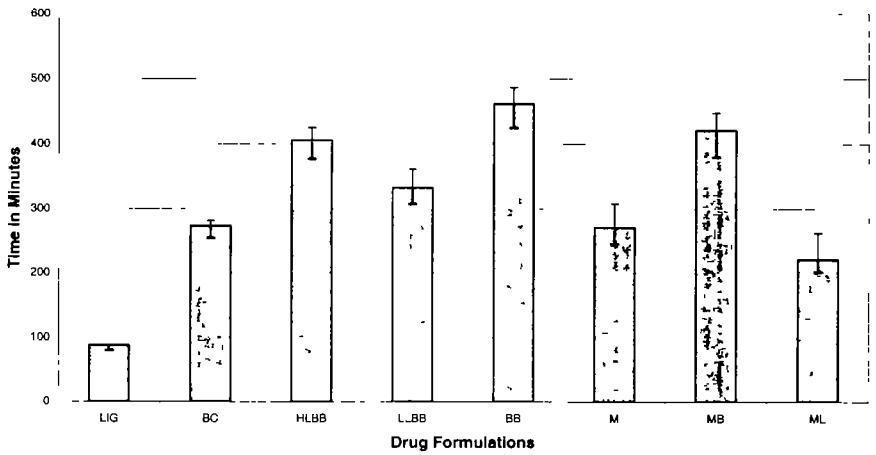

Figure 2 Summary of mean (and SE) duration times for analgesia (LIG = lignocaine, BC = bupivacaine ("Marcaine"), HLBB and LLBB = high and low concentration respectively, lignocaine + bupivacaine alternative formulation, BB = bupivacaine alternative formulation, M = mepivacaine, MB = mepivacaine + BB, ML = mepivacaine + lignocaine)

Time sequence for velvet antler removal procedures

Data are presented in Table 7. The time taken to infuse a ring block varied considerably between stags, and was influenced by the size of the pedicle, head position and subcutaneous tissue characteristics It is notable that, particularly in older stags, there appears to be a limited amount of elastic subcutaneous connective tissue, and apparently very thick dermis In those stags it can be extremely difficult to locate and infuse into the subcutaneous tissue. Further, if a stag moved or struggled during the local anaesthetic administration the time was extended. In optimum situations a ring block can be performed in 15 seconds or less The second ring block was commenced without delay, followed by dispensing with the injection equipment, uplifting and applying the tourniquet. This was then followed by retrieving the saw ready to apply a nick test. The primary purpose for the study was to determine the time interval between the completion of the ring block for each antler and the application of a nick test, when a continuous sequence is applied

Table 7. Mean, minimum and maximum time (secs) from completion of ring block on each antler to both the nick test and final antler removal.

	End of LA to nick test		End of LA to antler removal	
	Antler 1	Antler 2	Antler 1	Antler 2
N	16	16	16	16
Min	62	82	73	87
Max	206	351	337	390
Mean	**94**	**122**	**112**	**135**

It can be seen that in most cases, velvet antler can be removed without a wait time In some deer, a further 30-second wait was necessary These observations confirm observations on wait times from earlier studies.

Discussion

Studies of injectable local anaesthetic indicate that a high dose ring block is the preferred method for achieving analgesia of velvet antler Onset of analgesia following lignocaine 2% can be as rapid as 15 seconds in a high proportion of animals, yet in other animals analgesia may take 195 seconds This raises questions about the precise tissue sites of deposition of local anaesthetic in relation to sensory innervation, and shows that the reproducibility and repeatability of ring blocks are time dependent

Bicarbonate mixed with lignocaine did not produce significantly more rapid mean onset of analgesia than lignocaine alone, but the variation in onset time was less There is evidence from human medicine that onset is more rapid with bicarbonate. The onset time for bupivacaine alone was delayed compared with lignocaine, but the duration of analgesia persisted for 4.5 - 7 5 hours, depending on formulation Duration of more than 6 hours with a lignocaine/bupivacaine combination, coupled with the rapid onset achieved when this combination is used compared with bupivicaine alone, suggests that a mixture of lignocaine and bupivacaine can provide a local anaesthetic of rapid onset and prolonged duration.

Mepivacaine also had a rapid onset Its duration was equivalent to "Marcaine" (4.5 hours), but was not of such long duration as the combination with the non-commercial formulation of bupivacaine (7 hours). These results suggest that the combination of local anaesthetics given at the appropriate concentrations and dose rates give an onset time equivalent to the most rapid component, and a duration equivalent to the longest acting component

These studies have provided a range of options for adoption by veterinarians and for incorporation into compliance standards for velvet removal schemes, which should significantly improve the wellbeing of stags during and shortly after the removal of velvet antlers We have shown by tracing the sequence of events during velvet antler removal that it is unlikely that the time interval between injection and antler removal can be much less than 60 seconds with no wait time The wellbeing of the stag would not be jeopardised by following a continuous sequence of local anaesthetic injection,

tourniquet application and cutting of the antler, provided the contingency response of a further wait is applied if the stag responds to the nick test for analgesia This finding would encourage farmers to use physical restraint, since the current prescribed wait time is a disincentive

Currently, control of postoperative pain after velvet removal is not practised. Indeed, there is a question about the presence or relevance of post-operative pain Early studies with salicylate were inconclusive (Pollard *et al*, 1993) However, demand for the management of pain after velvet antler removal is likely, given industry moves to market product in more animal welfare-sensitive markets Those markets will insist upon animal-friendly, whole farming systems (Wilson *et al*, 2001) It is now well established that significant pain and distress persist once the effects of lignocaine or bupivacaine, or combinations of them, wear off 2 – 8 hours after amputation dehorning of calves (Petrie *et al*, 1996; McMeekan *et al*, 1998) It is therefore appropriate that the significance of pain after velvet antler removal is investigated further, using newer methodology Analgesia duration data as reported here is an essential prerequisite to such studies Observations of longer-acting local anaesthetics presented here now need to be evaluated in the context of their influence on behavioural and/or physiological parameters exhibited by the stag in the post-operative recovery period. These data are also prerequisite to potential studies of the new generation of more potent systemic analgesics now available.

Conclusions

- Onset of analgesia following lignocaine is generally more rapid than following bupivacaine or mepivacaine
- Mepivacaine and bupivacaine have significantly longer duration than lignocaine
- Combinations of local analgesics have an onset generally equivalent to that of the most rapid acting components, and duration generally equivalent to that of the longer acting component, but this is dependent on concentration of active ingredient
- There appears to be a difference in onset and duration of different formulations of bupivacaine.
- Time sequences of events during velvet antler removal suggest that it is unlikely that velvet antler would be cut within 60 seconds of completion of a ring block Thus, provided the contingency response is applied continuous velvet antler removal may be possible without compromising stag wellbeing
- Further research is required to elucidate why onset of analgesia is so variable between individuals, so that methods can be devised to improve repeatability and reproducibility within short time intervals
- Further research is required into the physiological and behavioural responses of stags after velvet antler removal, and the relevance of postoperative pain control, either by long acting local analgesia or systemic analgesia
- In practice, the compliance for achievement of analgesia could be considerably improved if standards under the Velvet Removal Programme were more prescriptive, allowing only those procedures shown by this research to be most effective

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