

## EVALUATION OF LIGNOCAINE/ BUPIVACAINE MIXTURE FOR CENTRAL NEURAL BLOCKADE IN GOATS

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### ABSTRACT

The anaesthetic indices produced by the lumbosacral extradural injection of a mixture of 2 mg/kg lignocaine 2% and 0.95 mg/kg bupivacaine 0.5% (LBM) were compared with those produced by either 4mg/kg lignocaine 2% (LIG) or 1.9 mg/kg bupivacaine 0.5% (BUP) alone in goats. Changes in heart rate (HR), respiratory rate (RR) and rectal temperature (RT), including associated side effects, were also recorded.

The LBM had longer time to recumbency, similar onset of analgesia but longer durations of analgesia and recumbency than with LIG alone. LBM also had similar time to recumbency but shorter onset of analgesia and durations of analgesia and recumbency than with BUP alone. Changes in HR, RR and RT were not significant. A few side effects of some clinical concern were noted.

It was concluded that, despite its longer time to recumbency, LBM had some clinical advantages over the use of LIG or BUP alone for extradural blockade in goats.

### INTRODUCTION

The hazardous nature of general anaesthesia in the ruminant has led to the employment of regional anaesthesia achieved by peripheral or central neural blockade (1). The latter is produced within the spinal canal and includes intradural and extradural blocks that result in anaesthesia of the animal's hind quarters (2).

Extradural injection of lignocaine (LIG) is an established technique of producing central neural blockade in most species including goats because of its fast onset of action, production of excellent analgesia and muscle relaxation, and its associated fast recovery (1). However, the drawbacks with its use include short duration of action, the need for additional physical restraint of the animal and the drug's toxic potential (3, 2, 4). Bupivacaine has also been administered extradurally in goats in order to take advantage of its long duration of action and excellent analgesia (5, 4). This agent also has such drawbacks as slow onset of action, the need for additional restraint of the animal, prolonged recumbency from the blockade and potential cardiotoxicity (2).

The ideal agent for central neural blockade in goats should combine the properties of rapid onset of action, long duration of action and fast recovery, good analgesia and muscle relaxation with minimum of toxic effects to the animal (6). No single

agent that is currently available for clinical use combines these properties. Consequently, there has been considerable interest in mixing two local anaesthetic agents in order to meet these requirements. Indeed, the use of a 50:50 mixture of LIG and BUP has been reported in humans (7, 8) and dogs (9, 10) to utilize the beneficial properties of both agents.

The purpose of this study was to compare the anaesthetic indices produced by the lumbosacral extradural injection of a 50:50 mixture of LIG and BUP with those of either agent alone in goats. The heart rates (HR), respiratory rates (RR) and rectal temperatures (RR), including associated side effects were monitored as indicators of safety of the blockade during the trials.

### MATERIALS AND METHODS

#### Animals

Fifteen healthy West African Dwarf (WAD) goats of both sexes (8 intact bucks and 7 intact does), aged 1.5 to 2.5 years and weighing  $10.1 \pm 2.1$  kg (mean  $\pm$  sem) were used. They were housed in two communal pens and fed on maintenance diet based on giant star grass (*Cynodon alenifuensis*) and yam peelings, supplemented with a cereal-based concentrate ration at a rate of 0.5 kg/head/day. Salt lick and fresh clean water were provided free choice in the pens.

The study protocol was approved by the faculty ethical committee on the use of animals for research.

### Drugs

The anaesthetic drugs used in this study included:

- Lignocaine hydrochloride (Glocain, Vital Health Care PC Ltd, India), which was supplied as 20 ml multidose vial.
- Bupivacaine hydrochloride (Marcain Astra Pharmaceuticals Ltd), which was supplied as a 5 mg/ml of aqueous solution for injection in 10 ml ampoule.
- A 50:50 mixture of lignocaine 2% solution and bupivacaine 0.5% solution compounded on the basis of the recommended doses of the component drugs.

### Experimental Design

The goats were randomly allocated to three groups each of five animals. Each group received respectively lumbosacral extradural injections of 4 mg/kg lignocaine 2% (LIG group), 1.9 mg/kg bupivacaine 0.5% (BUP group) and 2 mg/kg lignocaine 2% combined with 0.95 mg/kg bupivacaine 0.5% (LBM group). The goats' HR, RR and RT were measured immediately after the extradural puncture and thereafter at 10-minute intervals over a period of 60 minutes.

### Experimental Procedure

With the goat restrained manually in ventral recumbency and its hind limbs directed cranially, the lumbosacral junction was located as described by Hall and Clarke(1) and then surgically prepared. A skin bleb was made over the injection site with 0.5 ml lignocaine solution to achieve a relatively painless extradural puncture with an 18 gauge x 3.25 cm hypodermic needle. Placement of the needle in the extradural space was confirmed by lack of resistance to the injection of 2 ml of air. The appropriate local anesthetic solution was then administered over a period of 30 seconds. The development of motor and sensory blockade was assessed by the goat's inability to stand on its hind limbs. Serial pinching of the skin of the goat's hind limbs, perineum, flank and ventral abdomen caudal to the umbilicus with an artery forceps closed to the first ratchet was used to determine the onset and extent of analgesia produced.

### Calculations

Time to reumbency (in minutes) was defined as time interval between extradural injection of anaesthetic solution to paralysis of the goat's hind limbs. Time to onset of analgesia was calculated (in minutes) from the time of extradural injection of anaesthetic solution to loss of reflex response to pinching with artery forceps. Duration of analgesia (in minutes) was determined by return of response to pressure with artery forceps. Duration of recumbency (in minutes) was recorded from the time of the block to spontaneous movements of the hind limbs.

### Measurements

The HR was measured in beats/minute with the aid of a precordial stethoscope. The RR was determined in breaths/minute by visual observation of the thoraco-abdominal excursions. The RT was measured in degrees centigrade using a mercury-in-glass clinical thermometer.

### Data Analysis

All data were expressed as means  $\pm$  sem. Mean values of the anesthetic indices were compared using students' t test for unpaired data. Analysis of variance (ANOVA) with repeated measures was used to detect significant differences of mean values of HR, RR and RT from baseline. Dunnet's t-test was used to detect the time at which treatment response differed from baseline. A value of  $p > 0.05$  was considered significant.

## RESULTS

### Observations

Solutions of LIG and BUP appeared to be completely miscible in the same syringe, with no evidence of pharmaceutical incompatibility such as visible colour change, haziness or frank precipitate formation.

The non-sedated goats did not seem to tolerate extradural puncture in spite of the skin bleb made over the puncture site. Extradural neural blockade was consistently achieved in all the goats. They needed to be firmly restrained for extradural puncture. The onset of neural blockade was marked by the goats' assumption of a sitting posture with splayed hind limbs. Motor blockade (muscle relaxation) in the hindquarters preceded sensory blockade (analgesia) in all treated goats. Areas of analgesia included both the hind limbs, perineum, left and right flanks, and ventral abdomen just caudal to the umbilicus.

Two of the goats in the LBM group resisted being positioned in ventral recumbency in preference to lateral recumbency. In the course of the trials both goats developed a mild ruminal tympany which could be relieved simply by needle puncture of the rumen.

In all the series of trials, neither respiratory paralysis nor signs of toxicity were observed. Apart from a transient ataxic gait, recovery of the goats from the neural blockade was not complicated by inappetence or any other disability.

### Extadural Anaesthetic Indies

Mean time to recumbency with the mixture ( $3.2 \pm 0.8$  min) compared well to that with bupivacaine alone ( $3.7 \pm 0.7$  min) but was significantly longer than with lignocaine alone ( $1.8 \pm 0.5$  min). Mean time to onset of analgesia with the mixture ( $4.8 \pm 0.9$  min) compared well to that with lignocaine alone ( $4.2 \pm 0.8$  min) but was significantly shorter than with bupivacaine alone ( $14.4 \pm 1.4$  min). Mean duration of analgesia with the mixture ( $130.0 \pm 20.6$  min) was significantly longer than with lignocaine alone ( $69.3 \pm 7.2$  min), but significantly shorter than with bupivacaine alone ( $197.0 \pm 94.4$  min). Mean duration of muscle relaxation with the mixture ( $114.4 \pm 19.5$  min) was significantly longer than with lignocaine alone ( $64.7 \pm 6.4$  min) but was significantly shorter than with bupivacaine alone ( $145.0 \pm 7.2$  min).

**Table 1:** Side effects of the extradural injections of LIG<sup>a</sup>, BUP<sup>b</sup>, and LBM<sup>c</sup> in goats.

Side effects	Observed			Number of goats with		
	LIG <sup>a</sup>	BUP <sup>b</sup>	LBM <sup>c</sup>	LIG <sup>a</sup>	BUP <sup>b</sup>	LBM <sup>c</sup>
Phonation	Yes	Yes	Yes	1	2	1
Attempts to stand	Yes	Yes	Yes	5	5	5
Ruminal tympany	No	No	Yes	0	0	2
Urination	Yes	Yes	Yes	4	3	1
Ataxic gait	Yes	Yes	Yes	5	5	5

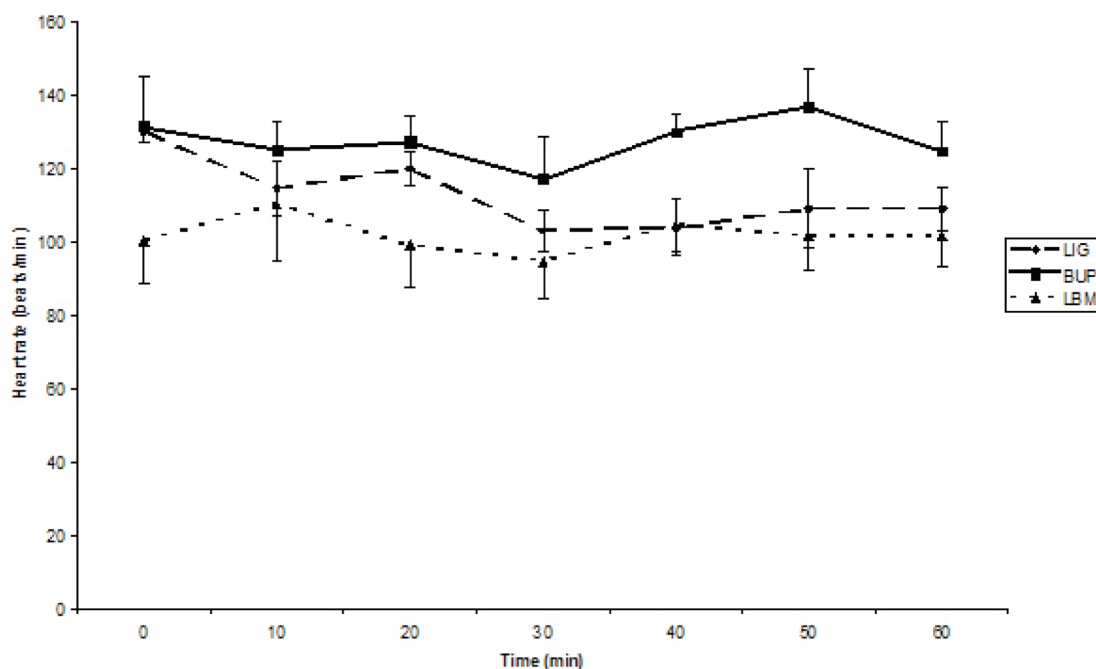
<sup>a</sup> at the dose rate of 4mg/kg<sup>b</sup> at the dose rate of 1.9 mg/kg<sup>c</sup> at the dose rate of 2/0.95 mg/kg

\* observed in the immediate recovery period

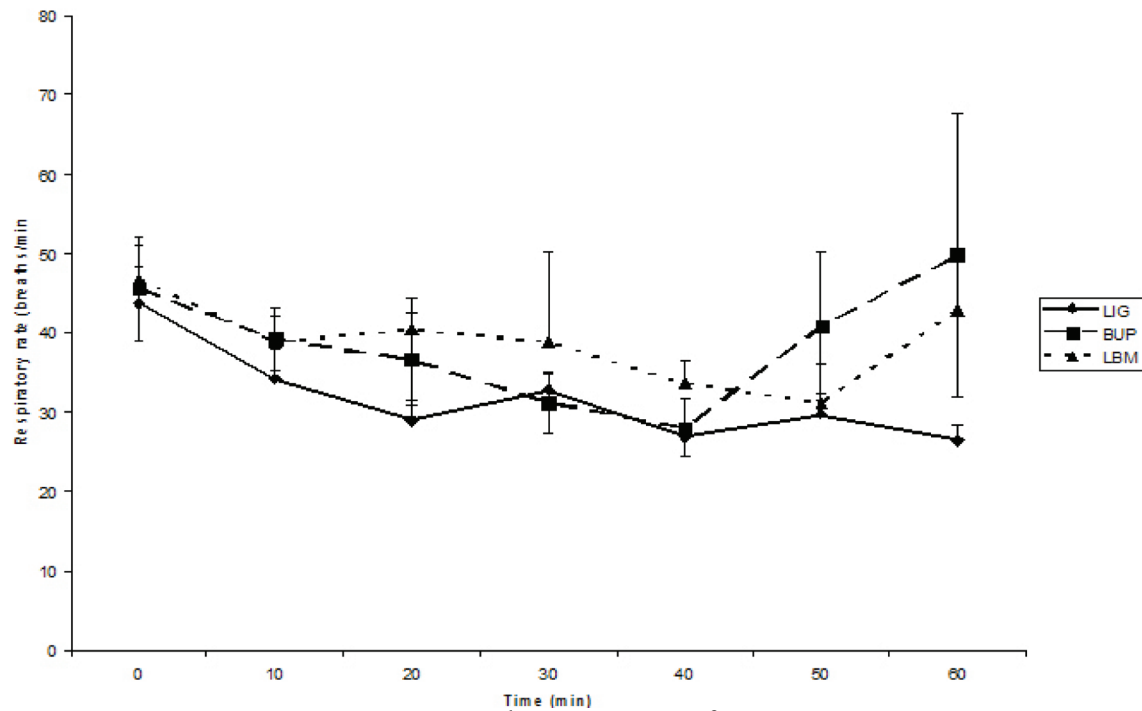
LIG - Lignocaine

BUP - Bupivacaine

LBM - Lignocaine/bupivacaine mixture

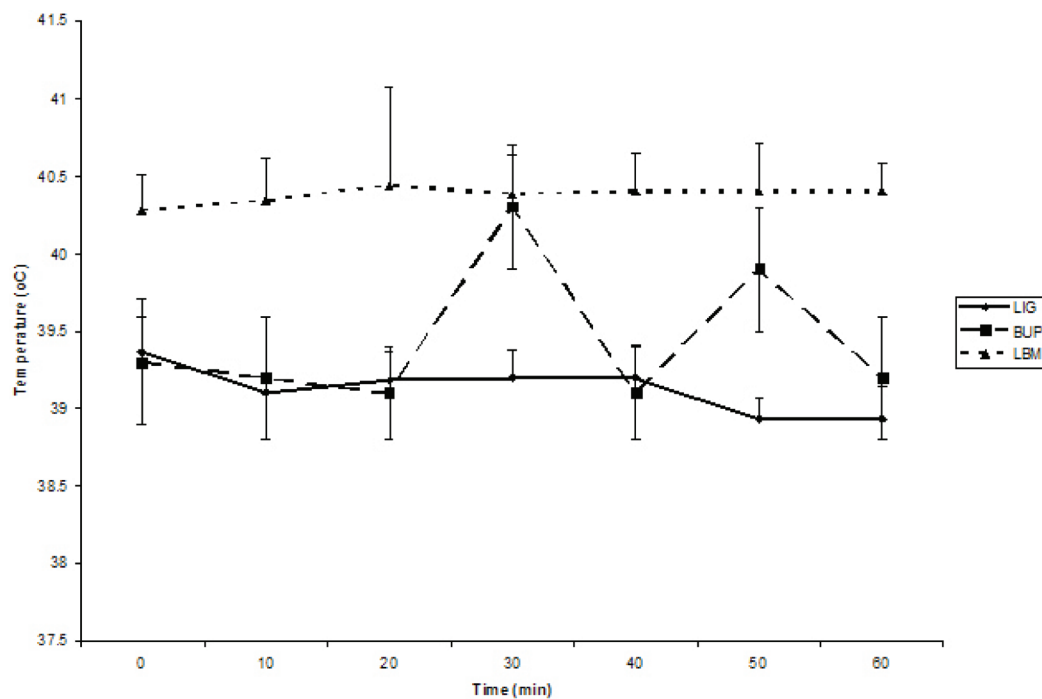
**Fig 1:** Heart rate responses of goats under extradural injections of LIG (4mg/ kg), BUP (1.9mg/ kg) and LBM (2mg/ kg LIG/0.95mg/ kg BUP)Data are expressed as means  $\pm$  sem of 5 goats.

**Fig 2:** Respiratory rate responses of goats under extradural injections of LIG (4mg/ kg), BUP (1.9mg/ kg) and LBM (2mg/ kg LIG/0.95mg/ kg BUP)



Data are expressed as means  $\pm$  sem of 5 goats.

**Fig 3:** Temperature responses of goats under extradural injections of LIG (4mg/ kg), BUP (1.9mg/ kg) and LBM (2mg/ kg LIG/0.95mg/ kg BUP).



Data are expressed as means  $\pm$  sem of 5 goats.

### Physiological Variables

The responses of the experimental goats to extradural blockade in terms of HR, RR and RT are shown in figures 1, 2 and 3 respectively.

Mean HR of the treated goats ranged between 94 and 136 beats/min. This variable was highest in the BUP group, lowest in the LBM group and intermediate in the LIG group. However, differences among the groups were not significant ( $P>0.05$ ). Mean RR of the treated groups decreased from 45 breaths/min early in the trials to 26 breaths/min at the 40th min interval. There were no significant ( $P>0.05$ ) differences among the three treatment groups. Whereas mean RT remained above 39°C in all the treatment groups, this variable was significantly ( $P<0.05$ ) higher in the LBM group than in either the LIG group or BUP group.

### Side Effects

The side effects of the extradural blockade observed in the course of the trials are given in Table 1. Whereas all the treated goats exhibited periodical premature attempts to stand, as well as ataxic gait in the immediate recovery period, only a number of goats in each of the three groups additionally exhibited phonation and urination. A mild degree of ruminal tympany occurred in two goats only in the LBM group.

## DISCUSSION

The results of this investigation showed that, in spite of its longer time to recumbency, the mixture had similar onset of analgesia, longer duration of analgesia and of muscle relaxation than with lignocaine alone. Negligible changes in physiological variables and a few side effects of some clinical concern were also associated with the extradural blockade.

In veterinary clinical practice, the use of local anaesthetic techniques is frequently combined with sedation to provide humane, stress-free restraint for the procedure. However, the use of sedative was deliberately omitted in this study to avoid its possible confounding effects on the physiological variables being measured. Besides, domestic goats are generally believed to be placid animals of manageable size.

The observation in this study that both lignocaine and bupivacaine were completely miscible in the syringe is in accord with that in previous similar studies in humans (7, 8) and dogs (9, 10). The miscibility may be explained by the  $pK_a$ s of lignocaine (7.9) and bupivacaine (8.1) which are rather similar (11), apart from the fact that both agents are amide-type local anaesthetics.

Local anaesthetic agents differ in terms of their onset and duration of action. These anaesthetic properties are essentially determined by physio-chemical characteristics which include lipid solubility, protein binding and  $pK_a$  (11). Agents which are highly lipophilic will penetrate the nerve membrane more easily such that fewer molecules are required for conduction blockade. Highly protein bound agents will remain at the receptor site for a prolonged period of time, resulting in long duration of anaesthetic activity (11). This explains why bupivacaine, which is 90% protein bound is longer acting than lignocaine which is

only 64% protein bound. In this study, the anaesthetic mixture appeared to have intermediate activity probably because the concentration of bupivacaine in the mixture was 0.25% as against 0.5% of the control concentration.

The obtained range of mean HR (94-136 beats/min) for the experimental goats appeared to be higher than the normal range of 70 – 94 beats/min accepted for the resting goats. This more likely reflects the anxiety of the manually restrained non-sedated goats, rather than the direct effect of extradural blockade.

The range of mean RR (26 – 45 breaths/min) obtained in this study also compared well with the normal range of 20 – 40 breaths/min accepted for this species (12). This was not unexpected considering that extradural anaesthesia does not cause a central depression of respiration as do general anaesthetics. Moreover, the level of blockade produced in this study is most unlikely to include intercostal and phrenic nerves, thereby interfering with the bellows mechanism of the chest.

The range of mean RT (39 – 40.40°C) recorded fell within the normal range of 38.6-40.0°C accepted for the goat (12). Regardless of thermal effects of the stress of manual restraint and the denervation of animals' hindquarters following extradural blockade, the recorded temperatures were consistent with the presence of an unimpaired thermoregulatory mechanism in the non-sedated goats.

It was interesting to note that two goats in the mixture group developed ruminal tympany (Table 1). Since general anaesthesia was not used, these two cases of ruminal tympany were certainly related to the lateral recumbency assumed by the goats.

A notable feature of the lumbosacral extradural blockade in the non-sedated goats was periodical attempts by the animals to stand and walk (Table 1). This is not beneficial because periodical gross movements are not compatible with the performance of sterile, safe and efficient surgical operation. Therefore, the adjunctive use of a tranquillizer or sedative would appear to be necessary in order to make use of the surgical anaesthesia produced by the extradural neuronal blockade.

Urination observed in some of the goats (Table 1), after the epidural blockade may cause a break in aseptic surgical technique when surgery is on. This urination may relate to paralysis of the sympathetic fibres with consequent predominance of parasympathetic activity and loss of the goat's ability to retain urine in the bladder. Alternatively the urination may relate to anxiety in the goats.

It was not surprising that all the experimental goats exhibited rear limb ataxia early in the recovery period (Table 1), because paralysis of the rear limb is a normal sequel of lumbosacral extradural block.

The extradural block produced in these trials desensitized areas of the body caudal to the umbilicus of the goats. This certainly would allow surgical procedures to be performed on the abdomen, pelvic cavity, perineum and the hind limbs.

In conclusion, despite its similar time to recumbency to bupivacaine alone, the mixture had similar onset of analgesia

to, and longer duration of analgesia and of muscle relaxation than lignocaine alone. The extradural blockade was associated with insignificant changes in heart rate, respiratory rate and rectal temperature, as well as a few side effects that were of some clinical concern. The adjunctive use of a tranquillizer or sedative would be necessary to provide an effective restraint for surgical procedures in goats.

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