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Comparative evaluation of lignocaine and lignocaine-bupivacaine for lumbo-sacral epidural block in diazepam sedated West African dwarf goats

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Abstract

This study compared the onset of neural blockade, onset and duration of analgesia and duration of recumbency produced in five healthy West African Dwarf (WAD) goats by the lumbo-sacral epidural injections of a mixture of 2mg/kg lignocaine 2% solution and 0.95mg/kg bupivacaine 0.5% solution (LBM) and 4mg/kg lignocaine 2% solution. Associated changes in heart rate (HR), respiratory rate (RR) and rectal temperature (RT) were recorded at 10-min intervals in the initial 1 hour. The onset of neural blockade with LBM (9.6±2.7 min) was significantly ($p<0.05$) longer with LIG (2.8± 0.4 min) the onset (24.8 ± 3.8 min) and duration (113.8± 16.5 min) of analgesia with LBM were significantly ($p<0.05$) longer than the onset (11.6 ± 2.4min) and duration (68.6 ±14.9min) of analgesia with LIG respectively. The duration of recumbency with LBM (148.0 ± 9.7min) was also significantly ($p<0.05$) longer with LIG (81.6 ± 6.5). There were no significant differences ($p>0.05$) in the physiological parameters between the two groups. It was concluded that epidurally administered LBM had a slower onset of neural blockade but longer onset of analgesia, duration of analgesia and duration of recumbency than with LIG in diazepam-sedated goats. The epidural blockade also produced insignificant changes in the mean HR, RR, and RT responses of the experiment to both drug protocols.

Keywords: Bupivacaine, Epidural, Goats, Lignocaine; Loco-regional, Sedation

Introduction

In Nigeria, goat population estimate has been put at 34.5 million, compared to 22.2 million sheep and 13.9 million cattle (Ames, 2014). An increasing goat population naturally would lead to an upsurge in demand by goat producers for veterinary services necessitating the use of anaesthetics. Eze & Idowu (2002) reported that clinical procedures performed on goats ranked only second to those performed on dogs at a veterinary hospital in the south-eastern part of Nigeria. Surgical procedures carried out on goats include mastectomy, gastro-intestinal surgery, caesarean section and other reproductive tract surgeries, perineal surgeries and orthopaedics (Covino, 1986; Cruz *et al*., 1997).

The inherent hazards associated with the use of general anaesthesia in ruminants generally have led to the development of loco-regional anaesthesia provided by perineal or neuraxial blockade with drugs (Devendra, 1981; Eze & Idowu, 2002). Neuraxial blockade consists of subarachnoid or epidural administration of drugs resulting in anaesthesia of the animal's hindquarters. This anaesthetic technique offers the advantages of minimal equipment requirement, induction of awake

recumbency, and applicability to all animal patients, suitability for use under both field and hospital conditions at low cost (Fubini & Ducharme, 2004). However, the technique has certain drawbacks such as occasional technique failure, movements of the animal's forequarters necessitating additional restraints and possible arterial hypotension (Eze & Idowu, 2002).

In goats, lignocaine (LIG) and bupivacaine (BUP) are the two local anaesthetic agents commonly used to produce epidural blockade. The epidural administration of LIG is common in most animal species because of its penetrability, fast onset of action, production of excellent analgesia and muscle relaxation, as well as fast recovery from neural blockade (Devendra 1981; Eze & Idowu, 2002). However, the shortcomings of its use in the goat include short duration of action, the need for additional restraint and the toxic potential (Gray & McDonnell, 1986; Funicaine *et al*., 1987; Eze & Idowu, 2002; Fubini & Ducharme, 2004). Bupivacaine has also been epidurally administered to goats because of its long duration of action and excellent analgesia. The advantages associated with its use are slow onset of action, differential neural blockade at lower concentrations, the need for additional restraint, prolonged recovery from neural blockade and potential cardiotoxicity (Hall *et al*., 2001; Eze & Idowu, 2002; Gorgi *et al*., 2006).

The ideal epidural anaesthetic for the goat should combine the properties of rapid onset of action, long duration of action, good analgesia and muscle relaxation, fast recovery and minimal toxic effects. No single agent in current clinical use has these qualities. Consequently, there has been a practice of 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 goats (Gorgi *et al*., 2006) in order to utilize the beneficial properties of both drugs while minimizing doses. These authours recommended the adjunctive use of a sedative agent for the purpose of minimizing patient discomfort and frequent movements during the epidural blockade.

Increasing goat population should be expected to lead to an upsurge in demand for veterinary diagnostic, medical and surgical procedures necessitating the use of anaesthetics. For this purpose, epidural anaesthesia has several advantages over general anaesthesia including minimal equipment need, simplicity of technique, minimal systemic organ depression, eliminated risk of regurgitation and aspiration of ruminal contents, suitability for use under both hospital and field conditions (Hodgkinson & Dawson, 2007). In addition, the drugs under study are readily available for veterinary use in Nigeria. Hence the need for continued search for epidural anaesthetics of acceptable onset and duration of action, minimal toxicity and optimal patient comfort.

The aim of this study was to compare the efficacy and safety of epidurally administered 50:50 mixture of lignocaine and bupivacaine with lignocaine alone in diazepam-sedated goats. Specific objectives were to compare selected anaesthetic indices of both protocols and to compare selected physiological parameters of both protocols in the initial 60 minutes.

Materials and Methods

Study animals

The study was approved by Ethics Committee of University of Ibadan on animal research (UI-ACUREC/App/2015/004). Five West African Dwarf (WAD) goats, comprising 2 intact bucks and 3 intact non-pregnant, non-lactating does, aged between 1 and 1.5 years, having the mean body weight of 8±15kg were used for the study. They were purchased from a local goat market in Ibadan and selected from the herd on the basis of signalment and normal findings at general physical examination. The selected experimental goats were housed at the experimental unit of the department of Veterinary Surgery and Radiology of the University of Ibadan in a communal pen with concrete floor bedded with wood shavings. They were fed a basal diet of giant star grass (*Cyanodon alaniferensis*) and cassava/yam peelings, supplemented with a cereal-based concentrate ration at a rate of 50g/head/day. Salt lick and fresh clean water were provided *ad libitum* in the pen. The goats were allowed to get acclimatized to their new environment and feeding regimens for a period of 2 weeks during which they were dewormed with albendazole at an oral dose rate of 5mg/kg body weight. Prior to the start of the trials, the goats were confirmed to be in good general health based on normal haemogram and complete examination findings.

Study design

Each goat was sedated with diazepam (1mg/kg). Two epidural protocols were administered at one week interval. The first protocol consisted of 4mg/kg lignocaine 2% with adrenaline (LIG), the second protocol consisted of 2mg/kg lignocaine 2% mixed with 0.95mg/kg bupivacaine 0.5% in the same

syringe (LBM). The goats' heart rate (HR), respiratory rate (RR), and rectal temperature (RT) were measured immediately after the epidural injection of the drug and at 10-min intervals over 60-min period.

Experimental procedure

The sedated goats were placed restrained in sternal recumbency with their hind limbs pulled forward and spine flexed in the kyphotic position. An area of 5cm wide and 8cm long over the lumbosacral region was clipped and prepared for aseptic procedure after sedation to facilitate easy handling. The lumbosacral junction was located as described by Hall *et al*. (2001) and isolated with fenestrated sterile drape. A skin bleb was made over the identified injection site with 0.5ml lignocaine solution to facilitate a painless epidural puncture. An 18G × 3.2cm hypodermal needle was inserted through the skin and advanced into the epidural space. Correct needle placement in epidural space was confirmed by lack of resistance to the injection of 1ml of air. The syringe containing the calculated volume of drug solution was attached to the inserted needle and solution injected over a 30 second period. The development of neural blockade was confirmed on the basis of goats' inability to stand on its hindlimbs. Serial pinching of the goats' hindlimbs, perineum, flank and abdomen caudal to the umbilicus with a haemostatic forceps close to the first ratchet, as described in previous similar studies (Cruz *et al*., 1997) was used to determine the onset, extent and duration of analgesia on all or none basis.

Measurements

The goats' HR, RR, and RT were measured immediately after the epidural injection of drug at baseline and subsequently at 10-min intervals over the initial 1h of anaesthesia in the course of the trials. Heart rate was measured in beats per min with the aid of stethoscope. Respiratory rate in cycles per min was determined by visual observation of the thoraco-abdominal excursions. Rectal temperature in degrees celcius was determined with the aid of an electronic thermometer intermittently inserted into the goat's rectum.

Calculations

Onset of neural blockade: time interval (in min) from the epidural injection of drug to paralysis of the goat's hind limbs.

Onset of analgesia: time interval (in min) from the epidural injection of drug to loss of pedal reflex response.

Duration of analgesia: time interval (in min) between the loss and the return of pedal reflex response.

Duration of recumbency: time interval (in min) from onset of neural blockade to the goat's assumption of standing position.

Data analysis

All data are expressed as mean ± standard deviation (SD). Mean values of the indices for both drug protocols were compared using student's t-test for paired data. The physiological values (HR, RR, and RT) for both drug protocols were compared using analysis of variance (ANOVA) for repeated measures and least significant difference (LSD) was used as post-test. $p<0.05$ was accepted as significant for all data.

Results

The administration of diazepam at a dose rate of 1mg/kg IM consistently produced moderate sedation in all the experimental goats, which eventually assumed sterna recumbency. The sedated goats could be easily positioned with minimal resistance to handling for epidural puncture and also exhibited minimal struggling or obvious discomfort during trials.

The mixing of the LIG and BUP solutions in the same syringe did not result in visible colour change, haziness or gross precipitate formation. The epidural administration of either LBM or LIG solution consistently produced neural blockade in all the experimental goats. Some goats in the LBM-treated group developed a mild degree of ruminal tympany which was simply relieved by needle puncture of the rumen. In the course of the experiment, no signs of local anaesthetic toxicity such as tremors or convulsion, or respiratory paralysis, were observed. Aside a transient ataxic gait, recovery of the experimental goats from neural blockade was not complicated by any other disability or inappetence.

The onset of neural blockade with LBM (9.6 ± 2.7 min) was significantly ($p<0.05$) longer than with LIG (2.8 ± 0.4 min). The onset (24.8 ± 3.3 min) and duration (113.8±16.5 min) of analgesia with LBM were significantly ($p<0.05$) longer than the onset (11.6 ± 2.4min) and duration (68.6 ± 14.9 min) of analgesia with LIG, respectively. The duration of recumbency with LBM (148.0 ± 9.7min) was also significantly ($p<0.05$) longer than with LIG (84.6 ± 6.5 min).

The HR, RR and RT responses of the diazepam-sedated goats treated with epidural LBM and LIG are shown in tables 1 and 2, respectively.

The mean HR responses of the LBM-treated goats ranged between 84 and 106 beats/min (Table 1), while those of the LIG-treated goats ranged between 107 and 113 beats/min (Table 2). Mean HRs of the LBM group tended to be lower than those of the LIG group, but the differences between both groups were not significant ($p>0.05$).

The men RR responses of the LBM-treated goats ranged between 15 and 20 cycles/min (Table 1), while those of the LIG-treated goats ranged between 13 and 18 breaths/min (Table 2). Mean RRs of the LBM group appeared to be generally higher than those of the LIG group, but there were no significant ($p>0.05$) differences between both groups.

The mean RT responses of the LBM-treated ranged between 38.0 and 38.9ºC (Table 1), while those of the LIG-treated goats also ranged between 38.0 and 38.9 (Table 2). There were no significant ($p<0.05$) difference in the rectal temperature responses of goats in both treatment groups.

Discussion

The result of this study showed that the epidurally administered LMB had a slower onset of neural blockade but longer onset of analgesia, durations of analgesia and recumbency than with epidurally administered LIG in diazepam sedated goats. Furthermore, similar changes in mean HR, RR, and RT were recorded for both epidural protocols.

Obese, pregnant or aged goats were excluded from this study for certain reasons. It is known that the cranial spread of anaesthetic solution in the epidural space tends to be greater in obese subjects because of the increased fat deposits in the epidural space (Hodgkinson & Hussain, 1981). Similarly, there is a tendency for further cranial spread of epidural solutions in pregnant animals with smaller epidural space owing to engorgement of the epidural veins arising from raised intra-abdominal pressure (Park *et al*., 1980). A greater segmental spread of analgesia has also been documented in aged patients owing to the age-related progressive occlusion of the Intervertebral foramina and decreasing leakage from the epidural space (Funicaine *et al*., 1987). Thus, an attempt was made to control the confounding effects of such intrinsic factors by excluding these categories of goats from the experiment.

Whereas Taylor (1991) recommended that feed be withheld from small ruminants for 18h prior to anaesthesia, the goats used in this study were not fasted for any length of time since epidural neural

Table 1: Physiological responses of diazepam[a]-sedated goats to epidural blockade with 50:50 lignicaine-bupivacaine mixture[b]

Time Interval	HR (beats/min)	RR (cycles/min)	RT (˚C)
0	84.2 ± 7.8	20.2 ± 6.5	38.9 ± 0.9
10	97.4 ± 20.8	15.0 ± 4.7	38.9 ±0.9
20	97.6 ± 23.4	16.8 ± 3.1	38.0 ± 0.7
30	92.4 ± 18.3	16.6 ± 6.2	38.8 ±0.9
40	106.0 ± 22.8	17.8 ± 4.2	38.8 ±0.9
50	98.0 ±19.4	15.0 ± 2.9	38.5 ± 0.7
60	98.0 ± 23.0	17.8 ± 7.6	38.5 ± 0.7

Data are expressed as mean ± SD of 5 goats

a = 1mg/kg, 2% solution

b = 2mg/kg of lignocaine, 2% solution, 0.95mg/kg of bupivacaine, 0.5% solution

Table 2: Physiological response of diazepam[a]-sedated goats to epidural blockade with lignocaine[b]

Time Interval	HR (beats/min)	RR (cycles/min)	RT (˚C)
0	108.0 ± 37.9	17.0 ±3.3	38.7 ± 0.9
10	107.0 ± 32.8	16.2 ± 3.6	38.9 ± 0.7
20	107.0 ± 25.7	17.2 ± 5.3	38.0 ± 0.7
30	109.0 ± 27.2	14.4 ± 3.8	38.8 ± 0.4
40	108.0 ± 29.7	13.6 ± 3.8	38.8 ± 0.4
50	113.0 ± 24.0	15.8 ± 4.4	38.5 ± 0.4
60	108.0 ± 32.1	18.4 ± 3.8	38.5 ± 0.4

Data are expressed as mean ± SD of 5 goats

a = 1mg/kg, 2% solution

b = 2mg/kg of lignocaine, 2% solution, 0.95mg/kg of bupivacaine, 0.5% solution

blockade does not normally induce unconsciousness with its associated potential risks of regurgitation and aspiration of ruminal contents into the lung (Umar & Adetunji, 2000; Visser *et al*., 2008).

It is recognised that a full rumen would support increased rate of microbial fermentation with excessive gas production leading to the development of ruminal tympany. However, this was not considered to be a problem in the conscious, awake ruminant which still retains the ability to expel ruminal gases orally through eructation or aborally via flatulence.

In veterinary practice, loco-regional anaesthesia is preferably combined with sedation to provide a humane, stress-free chemical restraint of the animal patient for the intended procedure. The sedative agents often used in small ruminant include xylazine, acepromazine and diazepam (Taylor 1991; Hall *et al*., 2001). Xylazine, an alpha-2-agonist, is a potent sedative and analgesic but it causes profound cardio-respiratory depression and osmotic dieresis in the ruminant. Acepromazine, a phenothiazine tranquilizer produces only mild sedation, no analgesia and peripheral vasodilation with moderate hypotension (Hall *et al*., 2001). A consideration of such potentially confounding drug effects excluded the use of both sedative agents from the study.

Although diazepam, a benzodiazepine also produces mild sedation, it was the sedative of choice for this study because of its minimal cardio-respiratory effects and centrally-induced muscle relaxation (Hall *et al*., 2001). Whereas diazepam is preferably administered at a dose rate of 0.5mg/kg IV in the sheep and goat as it is poorly absorbed from the IM injection site (Taylor 1991), the latter route was employed in this study but at higher dose rate of 1mg/kg to improve its bioavailability. Furthermore, this option was chosen because of the convenience of IM injection and in order to prolong the drug's sedative effect.

The finding in this study that both LIG and BUP were completely miscible in the syringe is in accord with that in a previous similar study in the goats (Oguntoye & Adetunji, 2009). The miscibility may be explained by the the pKas of LIG (7.9) and BUP (8.1) which are rather similar (Covino, 1986), aside the fact that both local anaesthetics are aminoamides. The practice of mixing short and long-lasting anaesthetic agents with the aim of achieving rapid onset and long duration drug action is based on the premise there is no drug-drug interaction and that both agents behave as if the other agent were not present. Indeed, pharmacokinetic studies of such mixtures have established their safety based on their serum concentrations being in the same range as those of the component drugs injected (Seow *et al*., 1982).

Hall *et al.* (2001) argued that the drug mass (i.e volume × concentration) was probably the most important single determinant of the extent of spread of the epidural administered anaesthetic solution. A large volume produces a more cranial spread, while a higher drug concentration produces a more rapid onset and longer duration of blockade. For example, a dose rate of 4mg/kg lignocaine 2% solution completely desensitizes the rear limb and posterior abdomen caudal to the first lumbar vertebrae (Skarda & Tranquilli, 2007). This suggests that epidural drug doses should be as accurate as the parental drug doses. For this reason, already established drug dosages in goats of 4mg/kg (Nelson *et al*., 1979) and 1.9mg/kg bupivacaine (Trim, 1989) were employed in this study.

Local anaesthetic agents differ in terms of their onset and duration of action. These anaesthetic indices are determined by the physico-chemical properties of the drug, including lipid solubility, protein binding and pKa (Covino, 1986). Agents which are highly lipophilic will penetrate the nerve membrane more easily such that fewer drug molecules are required for conduction blockade. Highly protein-bound agents will remain at the receptor site for a prolong period of time, resulting in a long duration of anaesthetic action (Covino, 1986). This might explain why bupivacaine which is 96% protein-bound is longer lasting than lignocaine which is 64% protein-bound. In this study, the LBM was longer acting than LIG when used alone obviously because of the BUP component of the mixture.

In this study, the recorded range of mean HRs of the LBM-treated goats (84-106beats/min) appeared to be lower than those of the LIG-treated goats (107-113beats/min). It is likely that the slightly larger volume of the LBM than that of LIG resulted in more cranial autonomic blockade involved some cardiac accelerator fibers, causing vagal predominance with some decrease in HR.

The range of means RRs of the LBM-treated goats (15-20 beats /min0 and that of the LIG-treated goats (13-18 breath/min) are both slightly lower than the normal range 20-40 breath/min accepted for awake goats (Matthews, 1999). Considering that the level of neural blockade produced in these study is most unlikely to affect the intercostals and phrenic nerves so as to interfere with the bellows mechanism of the

goat's chest, the slightly low respiratory rate may relate to the sedative effects of diazepam.

The range of mean RTs (38.6-38.9°C) recorded in this study fell within normal range of 36.6-40°C accepted for goats (Matthews, 1999). In spite of the paralysis of the goats' hindquarters following epidural blockade, the recorded RTs were consistent with presence of an unimpaired thermoregulatory mechanism in conscious goats.

In conclusion, the epidurally administered LBM had a slower onset of neural blockade but longer onset of analgesia, duration of analgesia and recumbency than with the epidurally administered LIG in diazepam-sedated goats. The epidural blockade was also associated with a significant differences in mean HR, RR and RT produced by both drug protocols.

Conflicts of Interest

The authors declare no conflicts of interest.

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