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ORIGINAL ARTICLE

Pentazocine As Adjuvant To Lidocaine Epidural Anaesthesia In Goats

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ABSTRACT

The study evaluated the effect of pentazocine on lidocaine for epidural anaesthesia in goats. Four adult intact male West African Dwarf goats weighing 7.3 ± 0.5 kg (Means ± SD) were subjected to two sets of experiments in a crossover design at an interval of one week for drug washout. The experiments involved the epidural administration of lidocaine hydrochloride at 2 mg/kg and the epidural administration of lidocaine hydrochloride at 1 mg/kg combined with pentazocine at 0.5 mg/kg. Selected anaesthetic indices were calculated, and vital signs - heart rate, respiratory rate, and rectal temperature were taken before drug administration and at 10-minute intervals after that. Onsets of drug action and analgesia with lidocaine (1.67± 1.2 minutes; 3.7±0.6 minutes) were longer than with lidocaine- pentazocine (1.0± 0.1 minutes; 3.0± 1.0 minutes). Duration of analgesia with lidocaine (52.0 ± 6.9 minutes) was significantly longer ($p = 0.0021$) than with lidocaine-pentazocine (29.0 ±5.7 minutes). Duration of recumbency with lidocaine (55.0 ± 11.9 minutes) was also significantly longer ($p = 0.0001$) than with lidocaine - pentazocine (34.0 ± 1.2 minutes). There were no significant differences ($p \geq 0.05$) in the physiological parameters of the goats following the two treatments and were all within reference ranges.

In conclusion, epidural administration of lidocaine combined with pentazocine as an adjuvant produced a faster onset of analgesia than lidocaine alone but a shorter duration of analgesia and recumbency than lidocaine alone and did not enhance analgesia at the dosages employed for both drugs combination in this study.

Keywords: WAD goats, crossover design, epidural anaesthesia, analgesia, lidocaine, pentazocine, adjuvant, physiological parameters.

INTRODUCTION

Local anaesthesia is a popular and often preferred anaesthetic technique to general anaesthesia in ruminants. This is because of the unique challenges with the use of general anaesthesia in these species which include regurgitation and aspiration of ruminal contents with consequent pneumonia or immediate respiratory arrest with an unprotected airway (Wisner *et al*., 2014). Endotracheal intubation may be technically difficult especially in large goats and rams with large horns (Wisner *et al*., 2014). Other challenges of general anaesthesia in these species include ruminal tympany predisposing to respiratory acidosis and excess salivation not completely amenable to anticholinergics because of the production of viscid saliva with clinical doses. (Galatos, 2011). Epidural anaesthesia is a commonly used local anaesthetic technique in ruminant anaesthesia for surgical procedures caudal to the umbilicus. It is also useful for obstetrical manipulations. (Carpenter, 2004; Goncalves, 2011; Clarke *et al*., 2014).

Lidocaine hydrochloride is a widely used local anaesthetic agent in both human and veterinary patients because of its quick onset of action and excellent muscle-relaxing properties, analgesia provision and safety when used at recommended dosages (Wisner *et al*., 2014; Subramanian *et al*., 2016). However, when used for epidural anaesthesia the duration of analgesia obtained is usually short necessitating repeated administration or continuous epidural which may be associated with toxicity and sepsis (Sadegh *et al*., 2009; Shaikh and Atlapure, 2015; Subramanian *et al*., 2016). Various other drugs referred to as neuraxial adjuvants have therefore been combined with lidocaine to extend its duration of action for long-duration procedures. The use of adjuvants also helps in the dosage reduction of local anaesthetics (Delilkan and Vijayan, 1993; Kapral *et al.* 1999; Almeida *et al*., 2010) thus increasing the safety of these protocols. Opioids, midazolam, magnesium sulphate, neostigmine, epinephrine, sodium bicarbonate, steroids, alpha 2 agonists, benzodiazepines, and ketamine have all been used as adjuvants with local anaesthetics. (Lamonte and Lamke, 2008; Sadegh *et al*., 2009; Subramanian *et al*., 2016). The use of opioids as local anaesthetic adjuvants is usually associated with less cardiopulmonary depression than the alpha 2 agonists where some systemic uptake occurs (Tacke, 2011). Epidural opioid adjuvants to local anaesthetics also provide synergistic anaesthetic effects and superior analgesia, especially during activity (Kehlet and Dahl, 1993; Carpenter, 2004). The opioid prototype, morphine, extends the duration of action of local anaesthetics up to 24 hours (Lerche *et al*., 2016). Other opioids that have been used as neuraxial adjuvants in humans include buprenorphine, pethidine and tramadol (Carpenter, 2004; Girwalker-Bagle *et al*., 2015; Subramanian *et al*., 2016). Tramadol has been reported as local anaesthetic adjuvant in cats, horses, sheep and goats (Dehkordi *et al*., 2012; De-Rossi *et al*., 2012; Hermeto *et al*., 2015; Ajadi *et al*., 2017; Oguntoye and Olaifa, 2019). Methadone, fentanyl and hydromorphone have been reported in dogs (Almeida *et al*., 2007; Torske *et al*., 1999; Diniz *et al*., 2013; Lewis *et al*., 2014; Albuquerque, 2015). Some recent studies have also reported the use of butorphanol as an adjuvant with lidocaine and bupivacaine for epidural injection in goats (Turi *et al*., 2018; Haggag and Mahmoud, 2019). Most of these opioids are highly controlled and not readily

available in developing countries (Jong-pil Seo *et al*., 2011).

Pentazocine is an opioid with mixed agonist-antagonist actions like butorphanol. It is a benzomorphan derivative and has both agonistic action (Kappa opioid receptor) and weak antagonistic or, partial agonistic action (μ opioid receptor). Although, also a controlled drug, pentazocine is available in developing countries (Henderson, 2008). Pentazocine has been reportedly used for analgesia in dogs, rabbits, cattle, sheep and goats administered intravenously and intramuscularly (Adetunji *et al*., 2009; Kukanich and Wiese, 2015; Oguntoye *et al*., 2022).

A study in humans administered pentazocine via various routes and concluded that the epidural route was the most effective for analgesia provision compared with intramuscular, sublingual, intravenous bolus and infusion routes (Neeraj and Amit, 2016).

There is a paucity of information regarding the use of pentazocine with lidocaine for epidural analgesia in goats. The aim of this study, therefore, was to evaluate the analgesic efficacy and safety of the lidocaine–pentazocine combination for epidural anaesthesia in goats.

MATERIALS AND METHODS

Animals: Four clinically healthy, male adult West African Dwarf (WAD) goats weighing 7.3 ± 0.5 kg (Means± SD) were used for the study. The goats were housed together in a spacious, well-ventilated pen and fed with concentrates and cassava peels. Water was provided ad libitum in the pen.

Drugs: The drugs used were lidocaine hydrochloride (Glocain®, Vital Health Care PVT Ltd, India) supplied as 20mg per ml of colourless, aqueous solution with adrenaline in a 20-ml multidose vial and pentazocine hydrochloride (Pilat®, Belco pharmacy, India) available for parenteral injection supplied as 30 mg/ml solution for injection in 1ml ampoules).

Experimental Design: Each goat was randomly subjected to two trials carried out at a weekly interval in a simple randomized crossover design. The trials consisted of epidural administration of lidocaine hydrochloride (2mg/kg; LID group) and a combination of lidocaine/ropivacaine (1mg/kg and 0.5mg/kg respectively; LID-PEN group). One week was allowed for drug washout in between trials. Heart rate (HR), Respiratory rate (RR) and Rectal temperature (RT) were measured immediately after epidural injections and subsequently at 10-minute intervals over one hour.

Lumbosacral epidural procedure: The goats were manually restrained on sternal recumbency with their forelimbs extended cranially. The spine of the seventh lumbar vertebrae, wings of the ilium, and the crest of the sacrum were palpated and the lumbosacral space was located. The area was shaved and aseptically prepared. A skin bleb was made at the lumbosacral junction with 1ml of lidocaine to enhance a painless epidural puncture. An 18-gauge x 3.25 cm hypodermic needle was placed and correct needle placement was confirmed by loss of resistance to pressure on injection of 1ml of air. The appropriate local anaesthetic agent was then injected into the epidural space. The development of motor and sensory blockade was assessed by loss of motor function resulting

in the goats' inability to stand on its hind limbs. Analgesia was assessed by response to serial skin pinpricks of the areas caudal to the umbilicus (flank and ventral abdomen caudal, perineum and hind limbs) as described by Dehkordi *et al. (*2012).

Calculations:

a) Onset of action: Time interval (in minutes) between epidural drug administration and the first exhibition of wobbly gait by the goats.
b) Time to recumbency: Time interval (in minutes) between epidural injections of an anaesthetic solution to paralysis of the goat's hind limbs.
c) Time to onset of analgesia: Time interval (in minutes) between epidural injection of anaesthetic solution and loss of reflex response to serial skin pinpricks of areas caudal to the umbilicus.
d) Duration of analgesia: Time interval between loss and return of response to serial skin pricks.
e) Duration of recumbency: Time interval (in minutes) between the time of onset of hind limb paralysis and the time to return of spontaneous movements of the hind limbs.

Measurements of physiologic variables: Heart rate was measured in beats/minute with the aid of a precordial stethoscope. Respiratory rate in breaths/minute was determined by visual observation of chest movement. Rectal temperature was determined using a mercury-in-glass thermometer and measured in degrees centigrade (˚C).

Statistical Analysis: Data was expressed as Means ± SD. Anaesthetic indices were compared with student T-test while physiological variables were analyzed with repeated measures analysis of variance (ANOVA). Least square differences were used for post hoc analysis. All statistical analysis was performed using SPSS 17.0 software (SPSS Inc., Chicago IL, USA). A value of $p < 0.05$ was considered significant.

RESULTS

Observation: The lidocaine and pentazocine were miscible as their mixture did not show any sign of pharmacological incompatibility. The onset of drug action following epidural injections was ataxia then recumbency.

Anaesthetic indices: The anaesthetic indices calculated following the epidural injections of the drugs are shown in Table 1. Although the onset of drug action, time to recumbency and onset of analgesia with LID-PEN were shorter than with LID, the differences were not significant ($p>0.05$). However, durations of analgesia and recumbency with LID (52.0 ± 6.9 and 55.0±11.9 min) were significantly longer than the respective values of 29.0 ± 5.7 min ($p = 0.0021$) and 34.0 ± 1.2 min ($p = 0.0001$) with LID-PEN.

Table 1. Anaesthetic indices

	LID	LID-PEN
Onset of action (min)	1.67 ± 1.2	1.0 ± 0.1
Time to recumbency (min)	3.0 ± 1.7	1.7 ± 1.2
Onset of analgesia (min)	3.7 ± 0.6	3.0 ± 1.0
Duration of analgesia (min)	52.0 ± 6.9	29.0 ± 5.7*
Duration of recumbency (min)	55.0±11.9	34.0 ± 1.2*

Physiological parameters: The mean heart rates, respiratory rates and rectal temperature of the goats following epidural administrations of lidocaine and lidocaine - pentazocine combination are shown in Table 2.

Heart rate: There was no significant difference between the heart rate values of the goats at the various time following epidural administration of lidocaine and lidocaine - pentazocine combination except at the 20^{th} minute. Heart rate values were reduced from initial values with both treatments.

Respiratory rate: The respiratory rates of the goats showed fluctuating values with both treatments and no significant difference between the groups at any time (Table 2).

Temperature: There was no definite pattern in the temperature values of the goats following epidural administration of the trial drugs.

Table 2: Heart rate, respiratory rate and rectal temperature responses of the goats to epidural administration of lidocaine alone (LID) and combined with pentazocine (LID-PEN)

Time interval	HR (beats/min)		RR (breaths/min)		RT(^{0}C)	
(min)	LID	LID-PEN	LID	LID-PEN	LID	LID-PEN
0[a]	173.0 ±12.9	141.3±44.2	54.1± 6.1	39.0±17.1	39.0 ±0.6	38.6 ±0.5
10	224.0±36.7	159.3±63.9	44.7±4.2	42.0±23.9	39.2 ± 0.3	39.1 ± 0.7
20	169.3±10.1	126.7±3.6*	50.7 ±8.3	42.5 ±16.6	38.6±0.5	39.1±0.9
30	160.3±24.4	123.0±36.1	53.3±16.6	40.0±17.6	38.9±0.3	38.9±1.1
40	149.3±29.5	115.3±23.0	46.7±12.2	49.3±18.3	39.1±0.6	39.0±1.3
50	137.3±34.0	97.3±8.3	48.0±10.6	44.0±24.0	39.2 ±0.8	39.0 ±1.1
60	122.0±31.1	100.2±20.0	56.0±16.0	46.0± 23.2	39.0±0.9	38.5±1.3

Data were expressed as means ±SD

* $P \leq 0.05$

LID: epidural injection of Lidocaine (4mg/kg)

LID-PEN: epidural injection of Lidocaine (2mg/kg) and Pentazocine (2mg/kg)

[a] Initial data obtained immediately after epidural drug injection

DISCUSSION

Epidural analgesia was produced in all the goats following lidocaine alone or mixed with pentazocine evidenced by ataxia, recumbency and analgesia. Although pentazocine inclusion produced a faster onset of drug action, time to recumbency and onset of analgesia, it did not prolong the durations of analgesia and recumbency. On the contrary, the durations of analgesia and recumbency, with respective values of 29.0 ± 5.7 min and 34.0 ± 1.2 min, following epidural lidocaine-pentazocine administration were significantly shorter than the respective values of 52.0 ± 6.9 min (p= 0.0021) and 55.0 ± 11.9 min (p= 0.0001) following epidural lidocaine administration alone. This finding of a reduction in the analgesic duration and duration of recumbency by the lidocaine - pentazocine combination is at variance with similar work by Hagag and Mahmoud (2019) where butorphanol combined with bupivacaine for epidural injection in goats produced a longer duration of analgesia and recumbency than either drug alone despite administering the combination at half of the dosages used when bupivacaine or butorphanol was given singly. The expectation from this study was to have a longer duration of analgesia and recumbency with the lidocaine - pentazocine since both pentazocine and butorphanol have the same mechanism of action. They are both mixed agonist and antagonist opioids being an agonist at the kappa receptor and agonist with the mu receptor

(Wisner *et al*., 2014). However, this finding is somewhat similar to findings in sheep where lidocaine at half the dose when used singly was combined with tramadol epidurally for laparo-ovariectomy (Ajadi *et a*l., 2017). Another study in goats which employed tramadol as an adjuvant to lidocaine reported the longest duration of analgesia with tramadol alone, longer duration of analgesia with tramadol - lidocaine and the shortest duration of analgesia with lidocaine alone (Dehkordi *et al*., 2012). However, this study employed the full dose of lidocaine used alone as the dose combined with tramadol unlike the half dose used in the Ajadi sheep study (Ajadi *et al*., 2017) and the current pentazocine study which both employed half the lidocaine dose in the lidocaine - tramadol and lidocaine - pentazocine studies respectively. The behaviour of this opioid–local anaesthetic combination in the current study aligns with the observation of a shorter duration of analgesia with the long-acting bupivacaine when combined as a 50:50 mixture with shorter-acting lidocaine (Plumb, 2015). Local anaesthetic agents usually block both sensory and motor neurons thereby producing analgesia and hind limb paralysis leading to recumbency when administered into the epidural space. On the other hand, opioids usually block the sensory neurons alone thereby producing analgesia without recumbency (Lerche *et al.*, 2016). Indeed, the recent use of opioids as an adjunct to spinal or epidural anaesthesia is to reduce the dosage of local anaesthetics to improve ambulation following the procedure (Salinas, 2005). The reduction in the durations of analgesia and recumbency with the lidocaine - pentazocine group to about half of the same indices with lidocaine alone implies the pentazocine added had no synergistic action with lidocaine at half the dose of lidocaine. It may be possible to have an additive effect with pentazocine if both drugs are given at full doses of the individual drugs.

The epidural drugs in this study did not have any significant effects on the physiological parameters - respiratory rate and temperature of the goats. Although mean heart rates decreased from baseline values (Table 2) following epidural administration of both lidocaine alone and lidocaine - pentazocine combination, the mean heart rates of the goats still fell within the physiological range of 142 – 272 beats /min obtained in a study that assessed cardiac functions of healthy West African Dwarf goats (Azeez *et al*., 2018).

In conclusion, epidural administration of pentazocine combined with lidocaine as an adjuvant produced a faster onset of analgesia and reduced the duration of analgesia and recumbency but did not enhance analgesia at the dosages employed for both drugs in the combination in this study.

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