

EFFECTS OF VARIOUS LOCAL ANALGESICS AND KETAMINE FOR CAUDAL EPIDURAL ANALGESIA IN BLACK BENGAL GOAT

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Abstract

The present study was conducted to find out the effect of analgesic and anaesthetic drugs for caudal epidural analgesia in Black Bengal goats. A series of thirty two (32) analgesic trails were conducted in goats age ranged from 8 to 12 months and with an average body weight of 8.1 kg. The animals were divided into four groups (n=4) and a replication of 8 trails was performed in each group at least one week interval. Two percent (2%) lidocaine hydrochloride (4 mg kg⁻¹), 2% lidocaine hydrochloride with adrenaline (4 mg kg⁻¹), 0.5% bupivacaine hydrochloride (1.0 mg kg⁻¹) and ketamine hydrochloride (4 mg kg⁻¹) were used to perform caudal epidural analgesia. The time of onset of anaesthesia, peak time of anaesthesia, area of desensitization and duration of anaesthesia were observed. 2% Lidocaine hydrochloride showed rapid onset of analgesia. 0.5% bupivacaine hydrochloride produced the highest area of desensitization in thigh region during caudal epidural analgesia. Perineal region and tail were totally desensitized during epidural analgesia. 0.5% bupivacaine hydrochloride prolonged the duration of analgesia during epidural analgesia. 2% Lidocaine hydrochloride and 2% Lidocaine hydrochloride with adrenaline showed no side effects whereas 0.5% bupivacaine hydrochloride showed shivering and drowsiness, ketamine hydrochloride excitement and drowsiness. It seemed that 2% Lidocaine hydrochloride is more effective whereas 0.5% bupivacaine hydrochloride is associated with side effects. Though ketamine hydrochloride is a dissociative agent, it could also be used in epidural analgesia.

Key words: Effects, local analgesics, ketamine, caudal epidural analgesia, Black Bengal goat

Introduction

Bangladesh is an agriculture based country. Livestock plays an important role in the economy of Bangladesh with a direct contribution of 2.95% of agricultural Gross Domestic Product (GDP) (Bangladesh Economic Review, 2006). Among ruminants, goats comprise 17.46 million (Agriculture sample survey, 2005) which occupies the second largest position in number in livestock. The leather and leather goods of Black Bengal goat has a supreme position in the international leather market which contributing about 6 to 7 percent of total export earnings (National Livestock Development Policy, 2007). Sometimes, epidural analgesia is needed to perform major surgical operations for correction of goat diseases. Anaesthesia is one of the miracles of medicine, without which modern surgical techniques would have been impossible. It was first developed to alleviate pain and provide relaxation for surgery. It is employed in animals for a wide variety of operative interventions. The choice of different types of anaesthesia, use of anaesthetic and analgesic agents, route of administration of anaesthetic agents all are depended on the animals as well as patients.

For correction of goat diseases, general anaesthesia often leads to tympanitis or regurgitation which is threatened for life (Hasim and Hossain, 1989). In ruminants the occurrence of regurgitation or gastro-esophageal reflux of rumen material and its subsequent inhalation during general anaesthesia has been widely reported (Boyd and Ducker, 1975). Since ruminants are amenable to physical restraint, majority of routine surgical procedures can be done using local analgesics (Kumar and Chouhan, 1996). These techniques are simple, safe, and economical and do not require sophisticated equipment. Among different types of local and regional analgesia, epidural analgesia has been used in veterinary practice for treatment of surgical interferences e.g. amputation of tail, removal of udder, examination of rectum, uterus, vagina, abscess opening and other operations.

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Injection of anaesthetics and analgesics within the canal but outside the dura mater is termed as epidural anaesthesia. Epidural anaesthesia was first reported in dogs by Cathelin in 1901, but due to the larger anaesthetic requirement and to the toxicity of cocaine, it was not used until 1921 (Lumb and Jones, 1984).

The drug so injected, temporarily paralyses the spinal nerve roots, its contacts, resulting in analgesia of tissues innervated by the nerves (Booth, 1988). It is classified according to the site at which the injection is made, i.e. Cranial (high) and Caudal (low). The use of epidural analgesia in veterinary medicine is most common in large animal practice. The method is also frequently used in small animals (Kinjavdekar *et al.* 1999).

Troncy *et al.* (2002) stated that use of epidural analgesia will depend on the medical problems of the patient, its temperament, the clinician's experience with epidural analgesia and the duration of surgical procedure. Theoretically, the technique may be used for any surgical procedure caudal to the diaphragm. Though a number of local analgesic agents are now available, lignocaine hydrochloride and bupivacaine hydrochloride are being mostly used for this purpose.

The local analgesic agents vary in their potency, duration of action and cost. Lignocaine is an amide type local analgesic and has a relatively rapid onset of action and an intermediate duration of about 1 to 2 hours (Lumb and Jones, 1996; Carpenter *et al.* 2004). Bupivacaine is a long acting local analgesic. It is about 4 times more potent than lignocaine and is used most commonly for regional and epidural nerve block (Eugene and Nicholas, 1995). The effect of a local analgesic is increased by addition of vasoconstrictor agents. Addition of adrenaline is a common practice for prolongation of the action of local analgesic drugs (Lumb and Jones, 1984). These drugs indiscriminately block the sensory, sympathetic and motor fibers (Dripps *et al.* 1988).

Ketamine hydrochloride, a dissociative agent has been used epidurally to relieve pre and post-operative pain in both man and animals. Spontaneous, unprovoked movements may occasionally be occurred in deeply anaesthetized patients (Brander *et al.* 1991).

As general anesthesia is not recommended for ruminants, local and regional anesthesia is performed with different types of local anesthetics and some general anesthetics. But all anesthetics are not suitable for different species and different operations. So, studying with different types of anesthetics for local and regional anesthesia in ruminants especially in goats is essential for different important operations. For example, Epidural analgesia is one of the regional analgesia. Thus, the aim of this study was to find out the effect of analgesic and anaesthetic drugs for caudal epidural analgesia in Black Bengal goats.

Materials and Methods

The research work was conducted in 8 goats (*Capra hircus*). The animals were apparently healthy especially during the experiment. The body weight of the animals ranged from 7.5 kg to 8.6 kg and their ages ranged from 8 months to 1 year. They were of both sexes. A total of 32 experimental trails were performed with the animals to investigate the effect of certain local anaesthetics in caudal (Sacro-coccygeal) epidural space. The work was carried out in the operation theatre of the veterinary clinics, Sylhet Agricultural University, Sylhet-3100. The period of experiment was 1 (one) year starting from March 2011 to March 2012.

Management of experimental animals

The animals were maintained in a room at the veterinary clinic of Sylhet Agricultural University, Sylhet collected from Sylhet Govt. goat farm. The animals were kept under good hygienic condition. They were allowed to graze in the open field for 6 hours every day and had a free access to water ad libitum. Standard concentrate feed was supplied. All animals were routinely dewormed and vaccinated against common infectious diseases. The animals were frequently examined to detect any pathological condition.

Preparation of the animals

The goats were taken to the operation theatre 20 to 30 minutes prior to administration of analgesic or anaesthetic agents. Age, sex and body weight were recorded before starting the experiment. The body weight of each of the animals was taken using weighing machine. The animals were then examined clinically to detect any pathological condition. The animals were placed on the operation table in lateral recumbency and were restrained physically by an assistant and also casting by ropes. The injection site was clipped, shaved and painted with tincture of iodine before any injection was administered. No premedicant was given prior to anaesthetic injection. The analgesia was always performed in the morning throughout the course of investigation.

Anaesthetic agents

2% Lignocaine hydrochloride

Lignocaine hydrochloride (Jasocaine[®], Jayson Pharmaceuticals Ltd.) is one of the most versatile and widely used local analgesic agents which is available in Bangladesh in 50 ml vial. Each milliliter contains 20 mg Lidocaine HCL (anhydd.).

2% Lignocaine hydrochloride with 0.0005% adrenaline

2% Lignocaine hydrochloride with 0.0005% adrenaline (Jasocaine[®], Jayson Pharmaceuticals Ltd.) is available in Bangladesh in 50 ml vial. Each milliliter contains 20 mg Lidocaine and 5 µg adrenaline.

0.5% Bupivacaine hydrochloride

Bupivacaine hydrochloride (Ultracaine[®], Jayson Pharmaceuticals Ltd.) is an amide type local analgesic available in Bangladesh in 30 ml vial. Each milliliter contains 5 mg Bupivacaine hydrochloride (anhydrous).

Ketamine hydrochloride (a dissociative anaesthetic agent)

Ketamine hydrochloride (G-KETAMINE[®], Gonoshasthaya Pharmaceuticals Ltd., Dhaka) is available in Bangladesh in 10 ml vial. Each milliliter contains 50 mg ketamine.

Methods of cranial epidural analgesia

Epidural analgesia is a useful technique in veterinary anaesthesia. Epidural analgesia is produced by injecting anaesthetic solution into the epidural space.

The goats were restrained on the operating table in lateral recumbency, the back was flexed and the hind limbs were held forward. The site of injection was immediately posterior to the last lumbar spine. The site of injection was clipped, cleaned and disinfected. A 3 inch, 18 gauge needle was inserted at the lumbo-sacral space and the analgesic solution was injected.

Experimental design

In this experiment a complete randomized design was used. The animals (n=8) were divided into 4 (four) different groups. In each group 8 (eight) experimental trials were accomplished (Table 1). To mitigate possible development of resistance to anaesthetic agents, a replication of the trails was made at least one week interval. Studies in these goats were carried out in the absence of surgical stress. The drugs were allocated for epidural analgesia as follows

Table 1. Experimental design

Groups	Types of analgesia	No. of trails	No. of animals	Site of injection	Concentration and doses of drugs
A	Caudal epidural	8	8	Sacro-coccygeal	2% Lignocaine hydrochloride 2 ml
B	Caudal epidural	8	8	Sacro-coccygeal	2% Lignocaine hydrochloride with 0.0005% adrenaline (Jasocaine [®]) 2 ml
C	Caudal epidural	8	8	Sacro-coccygeal	0.5% Bupivacaine hydrochloride (Ultracaine [®]) 2 ml
D	Caudal epidural	8	8	Sacro-coccygeal	Ketamine hydrochloride (G-KETAMINE [®]) 0.8 ml

Analgesic assessment

All animals were maintained on standing position during analgesic assessment. The state of analgesia was observed in every 5 minute with the help of a needle, by pricking the region. Analgesia was assessed as “+++” excellent (no response), “++” adequate (slight movement or reflex response), “+” poor (avoidance response) to needle pricking. Onset, peak point (time at which maximum area was desensitized) and the duration of analgesia were recorded. The desensitized area was measured by a scale and the progressions of analgesia at every 5 minutes were recorded. The measurement was carried out up to recovery. Tail movement, leg movement and any side effects were closely observed and recorded during the course of analgesia. Care was taken not to excite the animal before and during monitoring.

Statistical analysis

The data were analyzed statistically as follows:

- a. Student’s paired “t” test was performed to compare the obtained data before and after an anaesthesia.
- b. Analysis of Variance (ANOVA test) in completely randomized design was carried out according to Steel and Torrie (1980) to test significance variation among the effects in different time interval. The mean of data with its standard deviation (SD) and SEM were calculated.
- c. The results were analyzed by the Least Significant Difference test in “MSTAT” software.

Results and Discussion

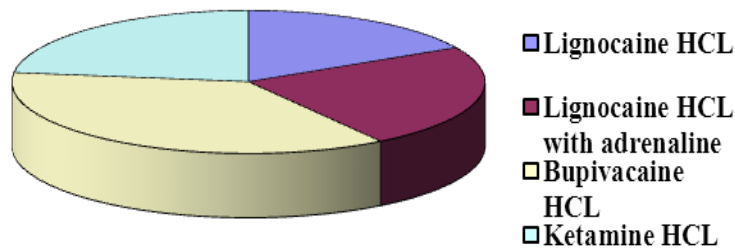
The onset of analgesia during caudal epidural analgesia

The mean value of onset was 3.63 ± 2.23 min in Group A and the onset occurred within 2-8 min. In Group B, the onset occurred within 3-8 min and the mean value was 5.0 ± 2.08 min (Fig. 1). The onset occurred within 6-10 min in all animals of Group C and the mean value of onset was 7.75 ± 1.62 min. In Group D, the mean value was 4.88 ± 1.77 min and the onset occurred within 3-7 min.

Table 2. Effects of various anaesthetic and analgesic drugs during caudal epidural analgesia in Black Bengal goat

Group	Amount of drugs ml (mg kg ⁻¹)	Onset of analgesia (min) Mean±SD	Peak point of analgesia (min) Mean±SD	Desensitized area at peak point (cm) Mean±SD				Duration (min) Mean±SD	Observations
				Hip region (cm)	Inguinal region (cm)	Perineal region (cm)	Tail		
A	2 (4)	2-8 3.63± 2.23e	5-12 7.88±2.38cd	8.9-22 14.81±4.79c	9.5-15 11.94±1.99c	Total	Total	28-50 37.0±7.59e	No side effects
B	2 (4)	3-8 5.0± 2.08c	7-12 9.13±1.72bc	8.5-15.4 12.1±2.29d	10-15 11.83±1.85c	Total	Total	35-64 42.88±9.88e	No side effects
C	2 (1)	6-10 7.75± 1.62b	9-18 14.38±2.73a	9.4-25 14.75±5.91c	10-15 12.08±1.85bc	Total	Total	20-42 49.06±10.90d	Muscle tremor
D	0.8 (4)	3-7 4.88± 1.77d	6-15 9.0±3.24bc	6.4-14.8 11.23±2.68d	10-15.5 12.3±1.82bc	Total	Total	35-66 48.5±9.3d	Excitement, drowsiness

In a column, mean values followed by common letter do not differ significantly from each other at 1% level of probability by LSD



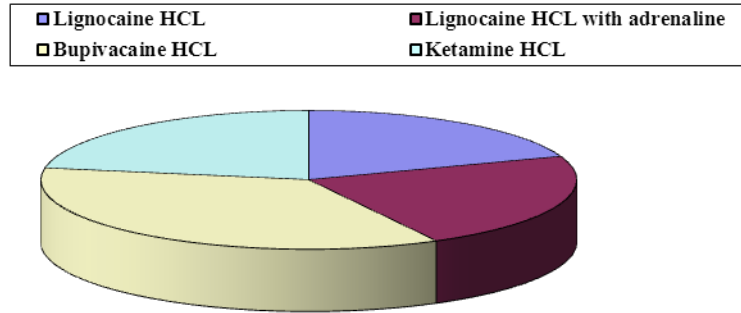
Onset of analgesia

Fig. 1. Comparison between the onset time of analgesia after caudal epidural administration of Lignocaine HCL, Lignocaine HCL with adrenaline, Bupivacaine HCL, Ketamine HCL

There were statistically significant ($p < 0.01$) variations between different groups in term of onset of anaesthesia. The onset of anaesthesia was significantly highest in Group C compared to other groups (Table 2).

The peak point of analgesia during caudal epidural analgesia

Anaesthetic agent exerted maximum effect within 5-12 min in all animals of Group A and the mean value was 7.88 ± 2.38 min. In all animals of Group B, peak point of anaesthesia was within 7-12 min and the mean value was 9.13 ± 1.72 min. In Group C, the mean value of peak point of anaesthesia was 14.38 ± 2.73 min and the peak point was within 9-18 minutes. Anaesthetic agent reached its peak point within 6-15 min in Group D and the mean value was 9.0 ± 3.24 min.



Peak time of analgesia

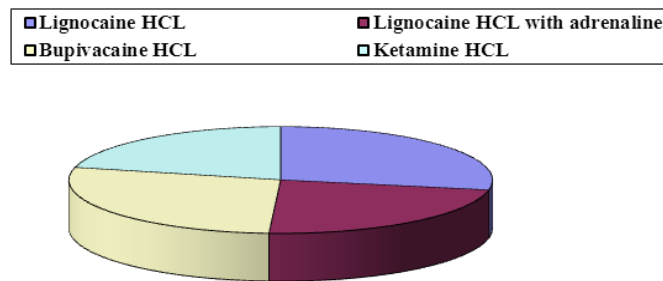
Fig. 2. Comparison between the peak points of analgesia after caudal epidural administration of Lignocaine HCL, Lignocaine HCL with adrenaline, Bupivacaine HCL, Ketamine HCL

There was not significant ($P > 0.05$) variation between Group B and D. Otherwise, there was statistically significant ($p < 0.01$) variations between different groups in term of extent of anaesthesia. The peak point of anaesthesia was significantly highest in Group C (Fig. 2).

The extent of analgesia

Area of desensitization in hip region

The area of desensitization was 14.81 ± 4.79 cm in Group A, 12.1 ± 2.29 cm in Group B, 14.75 ± 5.91 cm in Group C and 11.23 ± 2.68 cm in Group D.



Area of desensitization in hip region

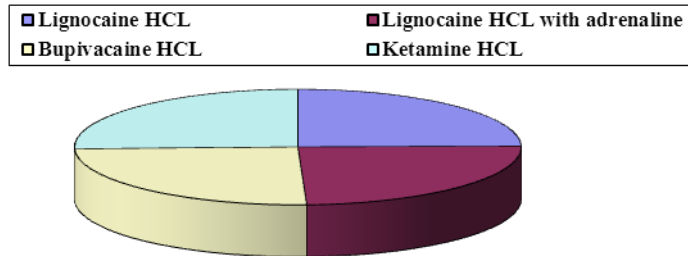
Fig. 3. Comparison between area of desensitization in hip region at peak point of analgesia after caudal epidural administration of Lignocaine HCL, Lignocaine HCL with adrenaline, Bupivacaine HCL, Ketamine HCL

There was not significant variation between Group A & C and between Group B & D (Fig.3). Otherwise, there was statistically significant difference among various groups in term of area of desensitization in hip region. The area of desensitization in hip region was significantly higher in Group A and C.

Area of desensitization in inguinal region

The area of desensitization was 11.94±1.99 cm in Group A, 11.83±1.85 cm in Group B, 12.08±1.85 cm in Group C and 12.3±1.82 cm in Group D.

There was not significant variation between Group C & D (Fig. 4). Otherwise, there was statistically significant difference among various groups in term of area of desensitization in perineal region. The area of desensitization in perineal region was significantly higher in Group A and B.



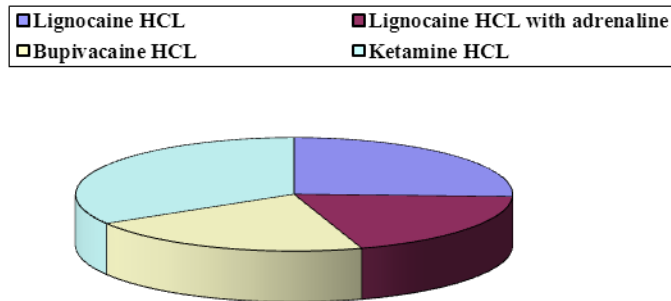
Area of desensitization in inguinal region

Fig. 4. Comparison between area of desensitization in inguinal region at peak point of analgesia after caudal epidural administration of Lignocaine HCL, Lignocaine HCL with adrenaline, Bupivacaine HCL, Ketamine HCL

Area of desensitization in perineal region and tail

In caudal epidural analgesia the area of desensitization from the site of injection to the perineal region upto tail was total in all animals. Similarly, the full length of tail was anaesthetized in all animals. So, there was no significant difference among them.

The duration of analgesia



Duration

Fig. 5. Comparison between duration time of analgesia after caudal epidural administration of Lignocaine HCL, Lignocaine HCL with adrenaline, Bupivacaine HCL, Ketamine HCL

The duration of anaesthesia was in between 28-50 min and the mean value was 37.0±7.59 min in Group A. The mean value of duration of anaesthesia was 42.88±9.88 min in Group B and the duration was in between 32-60 min (Fig. 5). In Group C, the duration was in between 35-64 min and the mean value was 49.06±10.90 min. In Group D, the mean value of duration of anaesthesia was 48.5±9.3 min and the duration was in between 35-66 min. These differences were statistically significant (p<0.01). The highest significant duration was found in Group C compared to other groups. There was not significant variation between Group A and B and between Group B and D. Otherwise, there were statistically significant (p<0.01) variations among different groups in term of duration of anaesthesia. The duration of anaesthesia was largest in Group C compared to other groups.

Other observations

Muscle tremor was found in Group C after using 0.5% Bupivacaine HCL. Excitement and drowsiness were observed in Group D after using Ketamine HCL. No side effects were found in Group A & B. In this experiment, no fatality was observed.

There were significant differences in different variance after epidural injection of same with same dose in different goats. Same amount of analgesic and anaesthetic drugs during caudal epidural analgesia showed different effects i.e. the onset of anaesthesia, peak time of anaesthesia, progression of analgesia or extent of analgesia from the site of injection at peak point and duration of analgesia were different when timing was considered. The findings were supported by Adetunji *et al.* (2002). The physical characteristics like body weight, length of the back of the animal, size of spinal canal, amount of epidural fat of the animals governed the distribution of injected drug in the epidural space (Lee, 2006).

Effects of various anaesthetic and analgesic drugs in same individual were different during epidural analgesia. It occurred due to intrinsic anaesthetic potency of different anaesthetic agents. The physiochemical properties such as lipid solubility, protein binding and P^{Ka} appear to be primary determinant of intrinsic anaesthetic potency (Wildsmith *et al.* 1985). Among them, the lipid solubility of anaesthetic drugs demonstrates local anaesthetic activity. Local analgesic agents which are highly lipid penetrate the nerve membrane more easily. The pronounced lipid solubility of anaesthetic agents causes low release of the drug from the lipid components of the spinal cord. These two aspects account for the change in the rate of access of anaesthetic with time to cerebrospinal fluid (CSF) and plasma and sustained concentrations in both fluids as well as redistribution of anaesthetic which in turn affect the duration of anaesthetic action (Perraz and Calvo, 1991). The protein binding characteristic of anaesthetic agents preliminary influence the duration of action of anaesthetic agents (Gissen *et al.* 1980).

The P^{Ka} of an anaesthetic agent may be defined as the p^H at which its ionized and nonionized forms are in equal concentrations. The unchanged base form of local anaesthetic agent is primarily responsible for diffusion, which is correlated with the amount of drug in the base form (Ritchie *et al.* 1965). Anaesthetic drugs whose P^{Ka} is closer to tissue p^H will have a more rapid onset time than the agents with high P^{Ka} .

In caudal epidural analgesia the onset was rapid in case of 2% lignocaine hydrochloride. On the contrary, the onset was slower in case of 0.5% bupivacaine hydrochloride and lignocaine hydrochloride with adrenaline. Kinjavdekar and Patap (2002), Howel *et al.* (1990), Mahale and Wakanker (1992), Hall and Clarke (1989) observed that in epidural nerve block the onset of analgesia was slow with 0.5% bupivacaine hydrochloride and the onset was more rapid with 2% lignocaine hydrochloride, while Trim (1989) and Norton *et al.* (1988) stated that lignocaine hydrochloride with adrenaline had a more rapid onset than bupivacaine hydrochloride. The onset of epidural analgesia is generally governed by the rate of disappearance of anaesthetic solution from the site of injection i.e. absorption of the drugs through blood and lymphatic channel, duramater, epidural fat (Hall and Clarke, 1989; Lee *et al.* 2001). The most important of these are extradural venous plexuses and epidural fat. 2% lignocaine hydrochloride is rapidly absorbed from tissues and mucous membrane into blood (Hall and Clarke, 1989). Moreover, 2% Lignocaine hydrochloride has P^{Ka} close to the tissue p^H which also responsible for its rapid action (Ritchie *et al.* 1965). Ketamine hydrochloride is highly lipid soluble drug. Its lipid soluble nonionized form is transferred rapidly to the CSF, nerve root and extradural root (Cousins and Mather, 1984). This physiochemical property might be responsible for the rapid onset of analgesia. During caudal epidural analgesia, the peak time of analgesia was high with 0.5% bupivacaine hydrochloride whereas the peak time of analgesia was low with 2% lignocaine hydrochloride in caudal epidural analgesia among different local analgesic agents. The time (the peak time of analgesia) at which maximum area was blocked and the progression of analgesia at peak time of anaesthesia were recorded to explain the extent of blockade of anaesthetic agents.

During caudal epidural analgesia, Lignocaine hydrochloride and Bupivacaine hydrochloride significantly produced higher desensitization area in thigh region than Lignocaine hydrochloride with adrenaline and Ketamine hydrochloride. Ketamine hydrochloride and Bupivacaine hydrochloride produced higher area of desensitization in inguinal region during caudal epidural analgesia. Both perineal region and tail was totally anaesthetized during analgesia in all animals. Singh *et al.* (2007) stated that Bupivacaine produced complete analgesia of tail, perineum, inguinal and thigh regions in all animals. The injection of 0.75-1 ml of lignocaine hydrochloride at sacrococcygeal space provides excellent analgesia for the docking of limb's tail (Hall and Clark, 1989).

The duration of analgesia with 0.5% bupivacaine hydrochloride was longer during caudal epidural analgesia than 2% lignocaine hydrochloride. This observation corresponds with the previous findings (Covino, 1986; Trim, 1989;

Howel et al. 1990 and Grubb et al. 1992). The protein binding characteristics of local analgesic agents influence the duration of action (Gissen et al. 1980). Agents such as bupivacaine, amethocaine and etidocaine are highly bound to proteins and display longest duration of anaesthesia. Besides this, rate of absorption, diffusibility of anaesthetic agents, speed of redistribution, all are responsible for duration of analgesia. If absorption is slow there will be an opportunity for more prolonged contact between solution and nerves, so that the intensity of spread is likely to be greater (Hall and Clarke, 1989). Lignocaine has intermediate duration of action. This observation was supported by Lemke and Dawson (2000). The duration of anaesthesia with ketamine hydrochloride was second highest during caudal epidural analgesia. But Lumb and Jones (1984) stated that it is difficult to undergo any surgical intervention with ketamine hydrochloride due to its brief anaesthesia. Rapid redistribution of this drug from nerves to other tissues might account for its short action. In caudal epidural analgesia, duration of analgesia was recorded higher with Lignocaine hydrochloride with adrenaline than Lignocaine hydrochloride. Aboud et al. (1985) reported that extradural adrenaline cause prolongation of analgesia. It is debatable that adrenaline increases the intensity of the block. But if so, it may produce this effect by direct action on adrenergic receptors, which mediate analgesia in the spinal cord (Carrie, 1990).

Muscle tremor was found during epidural analgesia with 0.5% bupivacaine hydrochloride. These findings are in agreement with the study reported by Walmsley et al. (1986) whereas Laishley et al. (1988) found drowsiness. Excitement and drowsiness were found during epidural analgesia with ketamine hydrochloride. A Baniadam et al. (1997) evaluated that caudal epidural ketamine administration induced analgesia with some degree of sedation and severe ataxia and recumbency in goats. In this experiment blood parameters were not analysed. So their effects on biochemical and haematological parameters should be conducted as research. Here, pinprick sensation (with a needle) was used in this experiment. Electromyography (EMG) and Electroencephalography (EEG) could have been given more accurate evaluation of analgesia.

In caudal epidural analgesia 2% lignocaine hydrochloride and ketamine hydrochloride produced rapid onset and peak time of analgesia compared to 0.5% bupivacaine hydrochloride and 2% lignocaine hydrochloride with adrenaline. Bupivacaine hydrochloride produced delayed onset and peak time of analgesia. 0.5% Bupivacaine hydrochloride produced the most extensive area of analgesia in hip region during analgesia. 0.5% bupivacaine hydrochloride and ketamine hydrochloride expressed extensive area of analgesia in inguinal region during analgesia. When adrenaline was combined with 2% Lignocaine hydrochloride, duration of analgesia was found to be prolonged during low epidural analgesia. 0.5% bupivacaine hydrochloride produced prolonged duration of analgesia.

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