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# Bupivacaine, Ketamine And Bupivacaine - Ketamine Epidural Anaesthesia In Bitches Undergoing Ovariohysterectomy

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## ABSTRACT

*This research was conducted to analyze the analgesic effects of bupivacaine, ketamine and bupivacaine–ketamine combination on bitches undergoing ovariohysterectomy, and determine a suitable regional anaesthesia. Fifteen (15) apparently healthy bitches, aged 8-12 months and weighing 10 - 15kg were procured within and around Zaria, Kaduna State for this experiment. The animals were grouped into three (3), A, B and C, screened and allowed to acclimatize to the new environment. Premedication was instituted with 0.02 mg/kg atropine sulphate and 1mg/kg Xylazine. Group A was administered an epidural injection of 0.5 % bupivacaine hydrochloride at 1 mg/kg, Group B was administered an epidural injection of 50 mg/ml ketamine hydrochloride at 2 mg/kg and Group C was administered an epidural injection of bupivacaine and ketamine combination at 0.5mg/kg and 1 mg/kg respectively. Analgesic indices determined were time to sphincter relaxation, the onset of action, duration of analgesia and duration of muscle relaxation. A standard ovariohysterectomy procedure was carried out at the onset of analgesia on each experimental animal, lasting an average of 45 minutes. Bitches in the bupivacaine group took a longer time (73 ± 18.0 secs) to sphincter relaxation which was significantly different from the other groups. Ketamine took the shortest amount of time (15 ± 3.0 secs) which was almost immediate. The onset of analgesia was the shortest (3 ± 1.0 mins) in group B with ketamine only. The combination of ketamine and bupivacaine produced a longer duration (121 ± 7.0 mins) of analgesia and significant muscle relaxation (110 ± 20.0 mins). The combination of bupivacaine and ketamine produced superior analgesic effects than those of bupivacaine or ketamine alone used for epidural injection, and sufficient for painful surgeries such as ovariohysterectomy in dogs.*

***Keywords:** Bupivacaine, Ketamine, Epidural, Dogs, Ovariohysterectomy*

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## INTRODUCTION

Nociception is the term for the physiological process of a pain receptor, or nociceptor, detecting pain and sending a signal of that pain to the brain [1]. Since recognizing pain is a crucial step in treating it, numerous subjective and objective assessment techniques have been researched, but none have yet been deemed to be the "gold standard."[2]. The numerous analgesic drugs and techniques currently available for the management of pain in animals pose a challenge to practising clinicians with regard to the choice of the appropriate drug and technique for optimal pain management in animals [3]

Canine ovariohysterectomy (OVH) is routinely carried out in veterinary clinics. Ovariohysterectomy is a common surgical treatment that is known to cause dogs to experience severe acute pain (4). Pain, according to [5], is an unpleasant feeling or sensation that is connected to real or potential tissue injury. The majority of pain is caused by surgical incision, manipulation of the abdominal viscera, and ensuing ligament stretching [6]. The multimodal and preventive analgesic strategy for postoperative pain treatment includes local anaesthetic methods [7; 8]. When it comes to therapeutic applications and delivery methods, local anaesthetics are exceedingly adaptable. Infiltration anaesthesia, field blocks, or spinal anaesthesia are common ways to give this class of medications to block the transmission of nociceptive sensations from the periphery to the spine [9]. The type of surgery, the surgeon's training, the doctor's familiarity with the procedure or medication, the drug's accessibility, any associated adverse effects, the cost, and occasionally predetermined clinic or hospital guidelines influence the decisions [10]. The management of postoperative pain by the use of epidural analgesia has developed over time as a critical part of the multimodal approach to achieve the goal of adequate analgesia with improved results [11]. The term 'epidural' refers to the space outside the dura mater and 'epidural analgesia' is used to describe the epidural administration of analgesics, such as opioids [12]. Epidural administration of drugs has been widely applicable in veterinary medicine practice for pain management [13; 14]. The merit of this route is its proximity to the spinal cord receptors concerned with the modulation and transmission of the nociceptive signal [12].

Bupivacaine is a long-acting amide anaesthetic mainly used for spinal anaesthesia [15] and is becoming widely used in clinical practice [16]. It is a long-acting and effective local anaesthetic usually administered via the epidural route for postoperative pain relief [17]. Anaesthetics like ketamine are used to induce and maintain anaesthesia during surgical procedures, including both elective and major surgery on local dogs in Nigeria. [18]. Ketamine is a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors in the spinal cord [19]. By blocking the sodium ion channels, Ketamine induces local analgesia. It also interacts with opioid centrally, monoaminergic and muscarinic receptors and voltage-sensitive calcium ion channels [19]. Ketamine has an anaesthetic effect when injected intrathecally and is synergic with bupivacaine [20].

## MATERIALS AND METHODS

Fifteen apparently healthy indigenous bitches aged 8-12 months and weighing 10-15kg were procured within and around Zaria, Kaduna State and used for this research. Two basic drugs were used; Bupivacaine Hydrochloride (Marcaine® *Spinal Heavy* 0.5%) injection (ADVANZ Pharma, London, United Kingdom) and Ketamine Hydrochloride injection (ROTEXMEDICA, Germany). The bitches were allocated at random into 3 groups, using a random number generator (RNG) and were anaesthetized epidurally with Bupivacaine HCl for group A, Ketamine HCl for group B and a combination of Bupivacaine HCl and Ketamine HCl for group C. Before

surgery, the bitches were fasted for up to 12 hours but with free access to water. They were premedicated with 0.02 mg/kg Atropine and sedated with 2 mg/kg xylazine hydrochloride. The surgical site (from the xiphoid cartilage to the umbilicus) was aseptically prepared with Povidone iodine. Prior to anaesthesia and surgery, an intravenous infusion line was placed via the cephalic vein, and maintenance fluid treatment with 0.9 per cent normal saline solution (Juhel®, Fabrique par Juhel Nig. Ltd/ Awka, Anambra State, Nigeria) was started. After identifying the lumbosacral space, 0.5 ml of 2% lidocaine was injected subcutaneously at the site of the spinal needle insertion to reduce epidural injection pain. A spinal needle was inserted into the epidural space and a syringe containing the drug was attached. The drug was injected slowly over one minute. Relaxation of the external anal sphincter and tail, hind limb ataxia, as well as a lack of response to the flexor pinch reflex of the pelvic limbs, develops at a successful injection.

Time to sphincter relaxation was recorded as the time between the epidural injection and the relaxation of the anal sphincter muscle recorded in seconds. The onset of action was the time between the epidural injection of the drug and the loss of reflexes in the hindlimbs. A pair of forceps was used by closing the hatchet while applying on the interdigital space of the foot and the absence of foot withdrawal was observed and recorded in minutes. Duration of analgesia was determined by observing the first sign of the return of stimulus in response to a pinprick stimulus on the limbs or lower abdomen from the onset of analgesia, recorded in minutes. Duration of muscle relaxation is the time between the onset of analgesia and the first sign of spontaneous movement by the experimental animal also recorded in minutes.

Data obtained from this study were analysed within groups using One-Way Repeated Measures ANOVA and between the groups by Two-Way Repeated Measures ANOVA with a Turkey Comparison post-hoc test, by comparing the periodic values for each group to its respective preliminary value. Column statistics were used to determine the M±SE of the groups. GraphPad Prism Version 9.0 (2020) software was used for the data analysis. Values of $P \leq 0.05$ were considered significant.

**RESULTS**

Bupivacaine had the longest mean time required for the anal sphincter to relax (73 ± 18.0 secs) and ketamine had the lowest (15 ± 3.0 secs). The mean time taken for the bupivacaine and ketamine combination was 25 ± 4.0. The onset of action of analgesia was fastest in the ketamine alone (3 ± 1.0 mins) and bupivacaine took the most time before onset (11 ± 1.0 mins). It took the combination group 5 ± 1.0 before onset. The mean analgesia duration lasted about 121 ± 7.0 mins in the bupivacaine-ketamine group which was the longest. It lasted about 115 ± 10.0 and 84 ± 12.0 in Bupivacaine and Ketamine alone groups, respectively. Duration of muscle relaxation also lasted the longest in the bupivacaine and ketamine combination group. Bupivacaine had the shortest (52 ± 15.0) while ketamine muscle relaxation lasted at 78± 19.0 (Table 1).

**Table 1 Mean ± (SEM) time to sphincter relaxation, onset of action, duration of analgesia and duration of muscle relaxation after epidural block using bupivacaine (n=5), ketamine (n=5) and a combination of bupivacaine and ketamine (n=5)**

| | Sphincter Relaxation (secs) | Onset of action (mins) | Duration of analgesia (mins) | Duration of muscle relaxation (mins) |
|---|---|---|---|---|
| A (Bup.) | 73 ± 18.0* | 11 ± 1.0* | 115 ± 10.0 | 52 ± 15.0 |
| B (Ket.) | 15 ± 3.0 | 3 ± 1.0* | 84 ± 12.0* | 78± 19.0 |
| C (Bup. + Ket. | 25 ± 4.0 | 5 ± 1.0* | 121 ± 7.0 | 110± 20.0* |

***Significant difference within groups (P<0.05)**

## DISCUSSION

The amount of sensory, motor, and autonomic blockade brought on by a lumbosacral epidural injection depends on the cranial distribution of the local anaesthetic in accordance with the anaesthetic volume, concentration, velocity of injection, amount of the epidural fat, epidural space size, posture, and gravity [21; 22; 23].

Among the three groups, bitches in the bupivacaine group took a longer time (73 ± 18.0 secs) to sphincter relaxation which differs significantly from the other groups. Ketamine took the least amount of time (15 ± 3.0 secs) which was almost immediate. The onset of analgesia was the shortest (3 ± 1.0 mins) in group B where ketamine was used alone. This was in line with the study [24] where ketamine when used alone for epidural analgesia produced the shortest onset of analgesia as compared with ketamine and xylazine combination. However, ketamine/xylazine produced a longer duration (60 ± 12.23 mins) as compared to ketamine alone (50 ± 7.07 mins) [22]. In this study also, ketamine when combined with bupivacaine produced a longer duration (121 ± 7.0 mins) of analgesia than the drugs used alone. [25] also reported a similar outcome when bupivacaine was combined with lidocaine for epidural anaesthesia. Duration of muscle relaxation was also significantly longer when bupivacaine and ketamine were combined for epidural regional anaesthesia (110 ± 20.0 mins)

## Conclusion

The combination of bupivacaine and ketamine produces superior analgesia and muscle relaxation and offers an advantage over bupivacaine or ketamine alone used for epidural injection, and is sufficient for painful surgeries such as ovariohysterectomy in bitches.

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