

The analgesic, haematological and some physiological effects of extradural bupivacaine in healthy dogs

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Target Audience Veterinarians, Dog breeders and Pharmacologists

Abstract

The aim of this research is to investigate the analgesic, haematologic and some physiological effects of extradural bupivacaine on dogs using six clinically healthy adult male dogs. The method used is by obtaining baseline data for physiological variables from each dogs using the multiparameter patient monitors (GD3, GenaralMeditech, Inc, China). Blood sample were also collected from the cephalic vein after extradural administration of the drug. The onset of the analgesia was determined using pin prick and the quality of analgesia with pre scrotal urethrectomy. The physiologic variables, pulse and respiratory rate including temperatures, blood pressure and oxygen saturation were recorded. Blood samples for heamatology were collected at 30 minutes intervals after the drug administration with the dog simultaneously undergoing pre scrotal urethrectomy for bladder stones removal for one hour. The onset of the action was 29 ± 11.34 and the quality of analgesia was very good to excellent lasting for 128minutes. There was no significant difference in values of all the physiologic parameters except the ECG which showed significant level of arrhythmia 30 minutes after the drug administration. We therefore conclude that epidural bupivacaine produces very good regional analgesic for pre scrotal urethrectomy and safe in Nigerian local breeds of dogs.

Keywords: Analgesia, Extradural Bupivacaine, Haematology, Nigerian Local Dogs, Physiology

Description of the Problem

Although an animal unconscious during general anaesthesia is incapable of appreciating pain, there is evidence that the use of analgesic drugs before, during and after general anaesthesia assists in obtaining a smooth, pain-free recovery (1,2). Local analgesic can be used to

provide analgesia for a number of surgical procedures such as castration, tooth extraction, caesarian sectioning, removal of horn (3), obviating the need for general anaesthesia. Local anaesthetic agents can be defined as drugs which are used clinically to produce reversible loss of sensation in a

circumscribed area of the body (4). They are used widely to provide anaesthesia and analgesia both intra and post operatively (3). There are two classes of local anaesthetic drugs defined by the nature of the carbonyl-containing linkage group. The ester group and the amide group which include bupivacaine among others (5).

Bupivacaine, ($C_{18}H_{28}N_2O$) with a molecular weight of 288.43 g/mol, is generally considered a long-acting local anaesthetic that can provide anaesthesia for up to 4 hour after a single subarachnoid dose (Concepcion and Covino, 1984). It is indicated for local infiltration, nerve block, extradural, and intrathecal anaesthesia. Most of its adverse reactions relate to administration technique (resulting in systemic exposure) or pharmacological effects of anaesthesia. Systemic exposure to excessive quantities of bupivacaine mainly results in abnormalities of the central nervous and cardiovascular systems and it is related to the plasma concentrations (1, 6).

Propofol is a short acting intravenous anaesthetic agent primarily used as sedative to facilitate short period of restraint. It may be given by repeated injection or continuous infusion to maintain total intravenous anaesthesia (7). This study investigated the quality of analgesia, the haematological and physiological changes under bupivacaine extradural anaesthesia in this breed of dogs.

Materials and Methods

Six Nigerian local breed of dogs consisting mainly of intact males weighing between 10-15kg, aged between 1-1½ years were studied. The

animals were fasted overnight and the study was carried out as much as possible at the same time of the day for each dog at room temperature, ($29^{\circ}C$).

Venous access was secured at cephalic vein using 21G scalp vein (butterfly) needle, blood sample for haematological variables was collected in a potassium ethylene-diamine-tetraacetic acid (EDTA) bottle for baseline data. The haematological variables measured were PCV, RBC, WBC, monocyte, neutrophil, basophil, lymphocyte and eosinophil.

Induction was achieved with intravenous injection of propofol (Diprivan®, AstraZeneca, DE) at $6mgkg^{-1}$ and maintained by bolus injection of $2.5mgkg^{-1}$ at fifteen minutes interval. The dogs were allowed to breath spontaneously. Hartman's solution was infused at a rate of 10ml/kg/hour (1).

A lead II electrocardiograph (ECG) were attached at five locations (right fore and hind limbs, left fore and hind limbs and the right area of the chest) the right area of the chest was clipped to maintain proper contact.

The pulse rate was measured from the ECG and the pulse oximeter probe was attached to the tongue to measure the oxygen saturation and the respiratory rate, a temperature probe was inserted into the oesophagus to measure body temperature, blood pressure cuff, about 40% of the circumference of the radio-ulna bone was attached to the left fore limb of the dog for oscillometric blood pressure measurement, recorded values were taken from the multi-parameter patient monitor, (GD3, General Meditech, Inc, China), these served as baseline data for physiological

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variables.

The surgical site was aseptically prepared by clipping and disinfecting with 2% chlorhexidine. Each dog in sternal position received a 0.5% bupivacaine (Macaine®) at 0.5mg/kg administered extra-durally at L7-S1 intervertebral space using a 22gauge spinal needle(). The dog was left in this position for about 8minutes, onset of analgesia was determined by applying straight artery forceps (the first lachet) at the interdigital space of the paw by the same operator, loss of tone of the perineum and the tail, (8,9,10). The dog was placed in dorsal recumbency for pre-scrotal urethrotomy, surgical technique used for pre-scrotal urethrotomy was as described by Bray, (11) and was carried out on each dog to evaluate the quality of analgesia produced by extradural injection of 0.5mgkg⁻¹bupivacaine, the procedure lasted for 60minutes.

Blood samples were collected from the cephalic vein at 30minutes intervals for haematological variables for one hour and other physiological variables which included pulse and respiratory rates, blood pressure, oxygen saturation, the

ECG and temperature were measured from the patient monitor at 5minutes interval in the course procedure.

The time to return of response to noxious stimulus was assessed by restlessness and licking of the wound.

Statistical Analysis

The data obtained was analysed using one way ANOVA for repeated measures. Differences were significant at $p < 0.05$.

Results and Discussion

The onset of analgesia for dogs was found out to be 29 ± 11.34 minutes determined by loss of sensation to interdigital pressure applied by straight artery forceps.

The surgical procedure lasted for 50 ± 10.30 minutes and was carried out by student/surgeon in training. Duration of analgesia was 128 ± 13.98 minutes. The quality of analgesia determined by urethrotomy was very good in all the animals as there was no response to surgical stimulus throughout the course of the procedure.

There were no significant differences between the baseline values and values obtained in the haematologic variables studied, (Tables 1).

Table 1: Effects of extradural bupivacaine on the haematological variables (Mean \pm SD) of Dogs

Parameters	PCV%	RBC	WBC	Neut	Eosin	Mono	Lymp	Baso
CONTROL	31.83 \pm 11.3	4.49 \pm 2.17	22160 \pm 12773.98	84.17 \pm 4.88	1 \pm 1.10	1.67 \pm 1.37	12.5 \pm 5.32	0.67 \pm 0.82
30 MINUTES	29 \pm 11.64	3.85 \pm 2.27	21169.33 \pm 12900.44	84 \pm 6.8	1.17 \pm 0.98	2.17 \pm 3.43	11 \pm 5.33	1.67 \pm 1.86
60 MINUTES	29.5 \pm 10.50	4.48 \pm 1.93	22961.67 \pm 11255.09	86.67 \pm 6.15	0.83 \pm 1.33	1.5 \pm 1.52	10.33 \pm 6.65	0.33 \pm 0.52

P 0.05 level of significance.

There were no significant differences in some of the physiological variables studied these include the temperature, the blood pressure compared to the baseline values (Table 2) except the ECG. However, there was significant

decrease in the mean pulse rate 30 minutes post injection, 71.00 ± 34.5 . Increase was observed in respiratory rate with that of 30 minutes post administration slightly higher than that of 60 minutes

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postadministration. There was decrease in the observed oxygen saturation at both 30 and 60 minutes post administration when compared with the baseline value.

Table 2: Effects of extradural bupivacaine on some physiological variables (Mean ± SD) of dogs

Parameters	PR(BPM)	TEMP(°C)	RR(CPM)	SPO ₂ (%)	NIBP(mmHg)
CONTROL	86.33±36.95 ^b	36.87±0.33	26.17±5.91	95.17±3.92 ^c	97.33±26.55
30 MINUTES	71.00±34.55 ^a	38.85±0.25	35.33±17.97	67.17±38.37 ^a	99.00±39.12
60 MINUTES	86.83±66.45 ^b	38.90±0.24	36.17±17.30	81.83±25.79 ^b	109.50±25.19

PR- pulse rate, Temp - temperature, RR- respiratory rate, SPO₂- saturated partial pressure of oxygen and NIBP-non invasive blood pressure. a,b,c= mean values are significant

For the electrocardiographic findings only two values were significant and they were the values for the height of P wave at 30 minutes after administration and the R height, (QRS height) at 30 minutes after administration, (Table 3). A continuous decrease in the amplitude was observed for the mean value of the height of P wave with that of the 60 minutes being lower than that at 30 minutes. No changes were observed in

the duration of the P wave and the P-R interval. R waves showed a marked decrease in amplitude at 30 minutes with a slight increase in amplitude at 60 minutes after administration. There was slight increase in duration at both the 30 and 60 minutes for the QRS complex. Slight decrease in the duration of the Q-T interval. There was significant decrease and increase in the duration of the T wave at 30 minutes and 60 minutes respectively.

Table 3: Effects of extradural bupivacaine on ECG parameters (Mean ± SD) of dogs

Parameters	P-wave(h)/mV	R wave/mV	QRS complex/sec	QT interval/sec.	T-wave/mV
Control	0.23±0.15 ^b	1.18±0.21 ^b	0.03±0.01	0.12±0.03	0.18±0.02 ^b
30 Minutes	0.19±0.17 ^a	0.80±0.42 ^a	0.04±0.01	0.11±0.01	0.11±0.07 ^a
60 Minutes	0.15±0.07 ^a	1.22±0.29 ^b	0.04±0.01	0.11±0.02	0.20 ±0.22 ^b

Where h - height (amplitude), w - width (duration), and R - QRS height. NB: the paper speed was 50mV/s; calibration is 1cm by 1mV, a,b,c= mean values are significant

The quality of analgesia agrees with the findings of 3, 1 and Hall *et al* (8,2); Campoy; Boar, that say the onset of action of bupivacaine when administered epidurally is between the ranges of 20- 40 minutes but disagrees with their finding that says the duration of action is at least 6 hours because the mean value for durations obtained from the result is 128 ± 13.98minutes, this may be because the dose used in this study, 0.5mg/kg is lower than the dose, 1.0mg/kg used by these authors.

The decrease in the PCV value occur as a result of decrease in cardiac contractility caused by bupivacaine with no serious significant changes in the red blood cell concentration, this is in agreement with the discovery of Lefrant *et al.* (11).

The electrocardiographic result shows an increase in the P wave amplitude (atrial depolarization) for both the 30 and 60 minutes after induction that bupivacaine binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells thus

prevents depolarization. However, there was no effect on the duration of depolarization of sino atrial node of the atrium neither was the drug showing any effect on the conduction of impulses in AV node, bundle of His, bundle branches and the Purkinje system revealing that the conduction of impulses from the sino atrial node was not altered.

A marked decrease in the duration of QRS complex, the T-wave and R-wave at 30 minutes revealed that there was decrease in the size of the ventricle (preload), at this time agreeing with the findings recorded in Wikipedia, 2010, but a slight increase in the duration at 60 minutes showed that the size of the ventricle was restored back to normal at this time, this was thought to be as a result of positioning (dorsal recumbency) of the patient during surgery. A marked decrease in the amplitude of the T- wave at 30 minutes indicated a decrease rate of repolarization with a slight increase in the T- wave amplitude at 60 minutes revealed that there was an elevation in the rate of repolarization at this time.

Conclusion

In conclusion, this study showed that epidural bupivacaine produces very good regional analgesic effect when used as analgesic to carry out surgical procedure in the hind quarters of the Nigerian local dogs. However, it must be used where there is adequate ventilation because of its hypoxic effect. The clinical relevant is that extradural 5% bupivacaine at 1.0mg/kg can be used in anaesthetic technique as a part of multimodal approach to pain management in this breed of dogs..

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