Research Article
Volume 15:3, 2024

Journal of Veterinary Science & Technology

ISSN: 2157-7579 Open Access

Anesthetic Efficacies of Epidurally Administrated Lignocaine-Hcl and Bupivacaine-Hcl Alone and their Combinations in Rabbits

Roshik Shrestha*

International Veterinary Student's Association, Nepal

Abstract

Aim: The current study aimed to evaluate the anesthetic efficacies of epidurally administered lignocaine-HCl and bupivacaine-HCl alone and their combinations in rabbits.

Materials and methods: A total of 15 rabbits weighing 1.8 to 2.3kg was allocated equally into three groups. Rabbits in Group A received epidural injection of 4 mg/kg 2% lignocaine-HCl; Group B received epidural injection of 1 mg/kg 0.5%, bupivacaine-HCl. However, the rabbits of Group C received epidural injection of combined solution of 2 mg/kg of 2% lignocaine-HCl and 0.5mg/kg of 0.5% bupivacaine-HCl. Physiological parameters such as Heart Rate (HR), Respiratory Rate (RR) and Rectal Temperature (RT) were recorded 10 minutes before and then after epidural anesthesia at every 10 minutes intervals over a period of 120 minutes. Similarly, the onset and duration time of anesthesia, onset and duration time of loss of weight bearing ability and flaccid paresis were recorded after epidural administration of analgesia.

Results: The onsets of anesthesia were 8.0 ± 0.354 min, 12.5 ± 0.224 min 10.1 ± 0.272 min in rabbits those received, lignocaine, bupivacaine and lignocaine + bupivacaine epidurally, respectively. The duration of anesthesia was higher ($P<0.01$) in rabbits of Group B (138.00 ± 5.15 min) than those of Group A (50.60 ± 1.60) and Group C (87.20 ± 5.05). The onset of loss of weight bearing ability, duration of loss of weight, onset of flaccid paralysis and duration of flaccid paralysis were higher ($P<0.05$) in Group B (17.6000 ± 0.245 min) as compared to Group A and Group C. There were no significant changes in heart rate, respiration rate and temperature were found among the groups.

Conclusion: The lumbosacral epidural administration of combination of lignocaine and bupivacaine provided superior anesthetic effects over lignocaine and bupivacaine.

Keywords: Analgesia • Local anesthetics • Lumbosacral • Rabbits

Introduction

Lumbosacral anesthesia resulted in effective analgesia due to its proximity to the spinal cord receptors responsible for the regulation and transmission of nociceptive signals [1,2]. The epidural administration of local anesthetic is relatively a safe and provides effective anesthesia and post-operative analgesia. The several drugs and their combinations have been used to induce epidural analgesia [3,4]. The ideal epidural local anesthetic should have a rapid onset of action, a long duration of action, good analgesia and muscular relaxation [5]. There is no single anesthetic that possess all of these qualities. Although lignocaine has a short latency period for epidural anesthesia, its effectiveness becomes limited for longer surgical procedure [6]. Bupivacaine lasts longer but it takes more time to onset and its muscular relaxation is also poor [5-7]. Therefore, an agent with a rapid onset and a sufficient duration of action would be ideal. It can be obtained with local anesthetic mixtures which combine the desirable properties of each component drug. So far any study has been performed with epidural administration of lignocaine and bupivacaine combination in rabbit.

The present study aimed compares the effects of lignocaine, bupivacaine alone and their combinations for epidural anesthesia considering the onset and duration of analgesia in rabbits.

***Address for Correspondence:** Roshik Shrestha, International Veterinary Student's Association, Nepal, Tel: + 9847483301; E-mail: sthroshik@gmail.com*

Received: 29 May, 2024, Manuscript No. jvst-24-137544; **Editor Assigned:** 31 May, 2024, PreQC No. P-137544; **Reviewed:** 12 June, 2024, QC No. Q-137544; **Revised:** 17 June, 2024, Manuscript No. R-137544; **Published:** 24 June, 2024, DOI: 10.37421/2157-7579.2024.15.241

Materials and Methods

Study location

This study was done from August, 2023 to October, 2023 in NPI college research unit.

Experimental rabbits

Fifteen apparently healthy rabbits weighing 1.8 ± 2.3 kg were used in this study. They were purchased from local rabbit market in Bharatpur. The rabbits were housed in a 12-h light dark cycle in 3 different cages of the research laboratory of NPI College. They were fed normally available grass, concentrates and water ad libitum. The rabbits were kept for 2 weeks for acclimatization in in laboratory environment. The experimental protocol was approved by the Nepal veterinary council on animal research (Ref. no. 35/2080/81).

Study design

Food was withheld from the rabbits for 8 hours (i.e. overnight) prior to the experiments, while water was allowed freely. The body weight of each rabbit was determined using weighing balance. The injection site was located and the hair of the lumbosacral region was shaved and the skin cleansed and the epidural puncture was performed using 26*5/8" needle. A total of 15 rabbits were allocated equally in LIG, BUP and LIG+BUP groups. The rabbits of LIG, BUP and LIG+BUP groups received the lumbosacral epidural administration of 2% lignocaine (4 mg/kg) 0.5% bupivacaine (1mg/kg) and 1:1 mixture of 2% lignocaine and 0.5% bupivacaine (2 mg/kg and 0.5 mg/kg). Physiological parameters were recorded 10 minutes before the epidural anesthesia and then after anesthesia at every 10 min intervals over a period of 120 min.

Assessment of epidural anesthesia

Onset of anesthesia was assessed by observing the reflexes to needle pinprick stimulation to the hind paddle or toe web. It was performed at one-minute interval until anaesthetization. However, the duration of anesthesia was determined by return of response to bipedal pinprick stimuli. Loss of weight-bearing was detected when rabbits did not stand on its hind limbs. The recovery was confirmed when the rabbits became stable. The flaccid paralysis was confirmed when no measurable tone in both hind limbs. The heart rate (HR), respiratory rate (RR) and rectal temperature (RT) were recorded appropriately 10 minutes then after at every 10 minutes intervals over a period of 120 min of epidural injections of local anesthetics.

Statistical analysis

The data are expressed as mean ± SEM. The data was analyzed in Minitab version 17 software. Data were analyzed using one way ANOVA followed by post hoc Tukey's test. However, the physiological variables were compared using for repeated measures in each group. The P value less than 0.05 was considered significant.

Results

The onset of anesthesia with LIG-Group (8.0 ± 0.354 min), BUP-Group (12.5 ± 0.224 min) and LIG-BUP combination- Group (10.1 ± 0.272 min) was significantly different (P<0.05) from each other among the three groups. The mean duration of anesthesia of LIG group (50.60 ± 1.60), BUP group (138.00 ± 5.15), LIG+BUP group (87.20 ± 5.05) differs highly significant (P<0.01) from each other. Mean onset of loss of weight bearing ability was significant (P<0.05) in BUP group with (17.6000 ± 0.245). Mean duration of loss of weight bearing ability was highly significant (P<0.05) in BUP group (76.80 ± 3.57) compared to LIG group and LIG+BUP which also differs from each other significantly (P<0.05) with values of (24.000 ± 0.949) and (49.00 ± 2.74). The mean onset of flaccid paresis in BUP group (19.600 ± 0.927) was highly significant (P<0.05) as compared to LIG group and LIG+BUP group with values of (23.900 ± 0.400) and (24.600 ± 0.927) respectively. The mean duration of flaccid paresis was highly significant (P<0.05) in LIG group (10.900 ± 0.332) compared to BUP group and LIG+BUP group which also differs from each other significantly (P<0.05) with values of (50.20 ± 2.22) and (19.00 ± 1.52) respectively. There were no significant changes in heart rate, respiration rate and temperature (Tables 1-4).

Discussion

None of the rabbits died or showed any side effects during and after anesthesia until one week period. In this study, the rabbits were gently restrained for injection of epidural anesthesia with short needles which produced no apparent discomforts. The lumbosacral epidural anesthesia technique in rabbits and ferrets is identical to dogs and cats, with the exception that the rarely definitive popping sensation when the intervertebral ligament is punctured [8]. The spinal cord continues caudally into the sacral vertebrae in rabbits and thereby the increased risk of puncture of both the dura and arachnoid membranes during lumbosacral epidural injection [9]. To overcome this situation, the anesthesia was administered once cerebrospinal fluid was seen in the hub of the needle. In this study, solutions of lignocaine and bupivacaine were observed to be dispersed in the syringe, showing pharmacological compatibility which is similar to previous studies [10]. The doses of LIG 0.2 ml/kg i.e. (4 mg/kg) and BUP 0.2 ml/kg i.e. (1 mg/kg) were used in this study following the doses of prior studies [11]. The combination of lignocaine and bupivacaine exhibited longer onset of action (P<0.05) than lignocaine but shorter (P<0.05) than that of bupivacaine. This result is similar to findings done by Cruz M, et al. [12]. Onset of action of local anesthetics differs due to pka (acid dissociation constant or pH at which the non-ionized and ionized fractions are at equilibrium) values when pH value of tissue remains constant. Local anesthetics can exist in both unionized and ionized forms in tissue pH, according to the Henderson-Hasselbalch equation. Drugs with a high unionized form rapidly diffuse through biological membranes and provide a rapid beginning of action. Local anesthetics with a low pka of 7.6-7.9 have a rapid onset of action because 30% to 40% of these medicines exist in the unionized state at pH 7.4 of which lignocaine has pka value of 7.9. Lignocaine has a faster onset time than drugs with a high pka because its pka is closer to tissue pH [6]. On the contrary, local anesthetics with high pka of 8.0 - 8.9 are slow acting agents because only 15% or less of these medicines is unionized at pH 7.4 of which bupivacaine hold value of 8.1.

Table 1. The mean ± SEM of onset time of anesthesia (min), duration of anesthesia (min), onset and duration of loss of weight bearing ability (min), onset and duration of flaccid paresis (min).

Parameter	LIG	BUP	LIG+BUP
Time of onset of anesthesia	8 ± 0.354 [a]	12.5 ± 0.224 [b]	10.1 ± 0.272 [c]
Duration of anesthetic effect	50.60 ± 1.60 [a]	138.00 ± 5.15 [b]	87.20 ± 5.05 [c]
Onset of loss of weight bearing ability	16.00 ± 0.707 [a]	17.60 ± 0.245 [b]	16.00 ± 0.274 [a]
Duration of loss of weight bearing ability	24.00 ± 0.949 [a]	76.80 ± 3.57 [b]	49.00 ± 2.74 [c]
Onset of flaccid paralysis	23.90 ± 0.400 [a]	19.60 ± 0.927 [b]	24.60 ± 0.927 [a]
Duration of flaccid paresis	10.90 ± 0.332 [a]	50.20 ± 2.22 [b]	19.00 ± 1.52 [c]

Table 2. The mean ± SEM of HR (beat/min) measured at different times 10 minutes prior and then after anesthesia at every 10 minutes intervals over a period of 120 min post injection.

Time	LIG	BUP	LIG+BUP
-10	232.60 ± 9.79	225.4 ± 10.3	222.80 ± 4.79
10	218.60 ± 7.61	242.8 ± 15.2	215.60 ± 6.18
20	200.40 ± 8.18	213.80 ± 9.68	200.00 ± 5.67
30	208.40 ± 7.28	206.2 ± 10.8	208.40 ± 5.61
40	234.40 ± 6.76	203.2 ± 13.8	210.00 ± 7.13
50	225.2 ± 11.9	197.4 ± 12.1	208.40 ± 3.82
60	203.6 ± 12.3	204.60 ± 9.91	204.40 ± 2.99
70	203.4 ± 13.2	205.00 ± 7.63	221.60 ± 2.64
80	218.80 ± 7.71	209.80 ± 8.32	212.2 ± 10.1
90	216.40 ± 4.30	210.00 ± 6.88	218.40 ± 2.66
100	215.80 ± 4.61	203.60 ± 8.19	221.60 ± 3.06
110	219.80 ± 6.00	207.6 ± 13.7	223.20 ± 1.53
120	214.00 ± 6.03	211.4 ± 11.1	225.20 ± 2.71

Table 3. The mean ± SEM of RR (breaths/min) measured at different times 10 minutes prior and then after anesthesia at every 10 minutes intervals over a period of 120 min post injection.

Time	LIG	BUP	LIG+BUP
-10	129.60 ± 3.83	148.6 ± 11.8	143.2 ± 12.6
10	127.40 ± 4.49	159.6 ± 7.46	135.20 ± 6.21
20	123.40 ± 7.70	147.40 ± 7.40	141.40 ± 6.66
30	125.00 ± 7.30	138.4 ± 10.2	144.20 ± 6.33
40	122.6 ± 13.2	142.6 ± 10.9	145.20 ± 9.09
50	131.2 ± 14.6	134.0 ± 12.0	142.80 ± 8.55
60	142.4 ± 16.0	137.8 ± 12.6	149.60 ± 9.10
70	149.8 ± 15.5	136.8 ± 10.8	138.40 ± 7.09
80	140.0 ± 12.7	143.0 ± 12.3	146.60 ± 7.24
90	138.4 ± 11.0	146.6 ± 15.3	135.60 ± 7.30
100	134.20 ± 8.01	144.0 ± 17.2	135.60 ± 6.56
110	131.60 ± 9.05	146.4 ± 13.3	139.60 ± 8.42
120	129.40 ± 6.46	149.0 ± 10.8	137.00 ± 6.71

Table 4. The mean ± SEM of RT (°F) measured at different times 10 minutes prior and then after anesthesia at every 10 minutes intervals over a period of 120 min post injection.

Time	LIG	BUP	LIG+BUP
-10	101.76 ± 0.129	101.68 ± 0.0583	101.84 ± 0.211
10	101.56 ± 0.0510	101.46 ± 0.0872	101.60 ± 0.0600
20	101.54 ± 0.0510	101.32 ± 0.0735	101.42 ± 0.121
30	101.56 ± 0.103	101.40 ± 0.268	101.52 ± 0.0583
40	101.60 ± 0.0707	101.30 ± 0.103	101.36 ± 0.354
50	101.72 ± 0.116	101.34 ± 0.103	101.42 ± 0.0840
60	101.64 ± 0.0748	101.38 ± 0.0800	101.32 ± 0.371
70	101.50 ± 0.0707	101.42 ± 0.180	101.46 ± 0.0812
80	101.40 ± 0.0949	101.34 ± 0.121	101.34 ± 0.206
90	101.70 ± 0.210	101.38 ± 0.185	101.38 ± 0.273
100	101.7 ± 0.169	101.40 ± 0.0949	101.70 ± 0.0949
110	101.65 ± 0.150	101.48 ± 0.107	101.52 ± 0.0663
120	101.68 ± 0.133	101.48 ± 0.0374	101.50 ± 0.134

Moreover, the duration of analgesia was significantly longer with lignocaine and bupivacaine combination ($P<0.01$) than lignocaine alone and significantly shorter than bupivacaine alone ($P<0.01$), indicating that adding bupivacaine to lignocaine accelerates and prolongs the duration of anesthesia. Similar findings were reported in a previous study conducted on dogs [13]. Duration of action of lignocaine is intermediate according to Best CA, et al. [14]. The longer duration of action of bupivacaine is due to which it is highly protein bound [6].

The mean duration of loss of weight bearing ability was significantly high in lignocaine bupivacaine combination group ($P<0.05$) than in lignocaine alone indicating that adding bupivacaine to lignocaine accelerates and prolongs the quality of analgesia. Onset of flaccid paresis is significantly rapid ($P<0.05$) in bupivacaine group. The mean duration of flaccid paresis was significantly longer in the lignocaine bupivacaine combination group ($P<0.01$) than in lignocaine alone. This finding can be attributed to a synergistic effect between lignocaine and bupivacaine. According to Best CA, et al. [14] combining the two drugs can decrease the side effects of each drug and increase the duration of flaccid paresis and analgesia. No any significance differences were observed in heart rate, respiration rate and temperature between three groups.

Conclusion

The combination of lignocaine and bupivacaine mixtures showed an ideal anesthetic effect over lignocaine or bupivacaine alone having shorter onset and prolonged duration of action with good analgesia. None of the treatments induced significant changes in heart rate, respiration rate and temperature in this rabbit. Further research is needed to investigate the analgesic effect of lignocaine and bupivacaine combination in rabbit under surgical conditions.

Acknowledgement

None.

Conflict of Interest

None.

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How to cite this article: Shrestha, Roshik. "Anesthetic Efficacies of Epidurally Administrated Lignocaine-Hcl and Bupivacaine-Hcl Alone and their Combinations in Rabbits." *J Vet Sci Technol* 15 (2024): 241.