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Haematobiochemical evaluation of levobupivacaine alone and in combination with fentanyl citrate and Butorphanol in goats

Sunil Oraon, AK Sharma, Reetu, Bidya Bhusan Kumar, Shraddha AB Minz, Vishwaranjan Kumar, Brajesh Verma, Mukesh Kumar and Indrajit Kumar

Abstract
The present study was conducted on 15 clinically healthy goats of either sex of 1-3 years of age and weighing between 11-15 kg. The animals were grouped randomly in to three, containing 5 animals in each subjected to different treatment. The animals of group 1received levobupivacaine @ 0.75 mg/kg alone while, animals of group 2 received fentanyl citrate @ 0.02 mg/kg b.wt alone with levobupivacaine @ 0.75 mg/kg b. wt. Animals of group 3 received butorphanol @ 0.04 mg/kg b.wt alone with levobupivacaine @ 0.75 mg/kg b.wt. The lumbosacral space was used for epidural injection of different drug combinations mentioned above. There were non-significant alterations in different haematobiochemical parameters within and among the groups. Hence, it is concluded that the administration of levobupivacaine did not produced deleterious effect on haematobiochemical profiles and considered to be safer analgesic agents for lumbosacral epidural administration in goats.

Keywords: Levobupivacaine, fentanyl citrate, Butorphanol, epidural analgesia, opioids

Introduction
The newer, long-acting, amide local anaesthetic Levobupivacaine, has been developed with less cardiotoxic potential than bupivacaine. Levobupivacaine is the pure S enantiomer of bupivacaine (Burlacu and Buggy, 2008) [4]. It has been found to be equally efficacious as bupivacaine, but with less cardiac and neurotoxic adverse effects. Levobupivacaine exerts its pharmacological action through reversible blockade of neuronal sodium channels. Specifically; the drug binds to the intracellular portion of sodium channels and blocks sodium influx into nerve cells, which prevents depolarization (Bajwa and Kaur, 2013) [3].
Fentanyl citrate is a potent opioid agonist with principle actions as therapeutic value is analgesia & sedation. Opioid like fentanyl have been used traditionally as an adjunct for epidural administration in combination with lower dose of local anaesthetic to achieve the desired anaesthetic effect (Benzon *et al.*, 1993) [6]. Butorphanol is a lipid-soluble narcotic with weak μ-receptor agonist and antagonist activity and strong k-receptor agonism. It has strong analgesic and sedative properties without respiratory depression. Butorphanol has been frequently used for post-operative analgesia and labor analgesia. The present paper deals the following administration of levobupivacaine alone or in combination with fentanyl citrate and butorphanol as lumbosacral epidural anaesthesia in goats.

Materials and Methods
The present experiment /study was conducted on 15 clinically healthy goats of either sex of 1-3 years of age and weighing between 11-15 kg. The goats were maintained in isomanagemental condition at Instructional Small Ruminants farm, RVC. All the goats were dewormed with broad spectrum anthelmentic (Panacur 150 mg) two weeks prior to the experiment. Frequent clinical examination of animals was done to rule out the possibility of any illness. The animals were grouped randomly in to three, containing 5 animals in each subjected to different treatment. The animals of group 1 received Levobupivacaine @ 0.75 mg/kg alone while, animals of group 2 received fentanyl citrate @ 0.02 mg/kg b.wt alone with Levobupivacaine @ 0.75 mg/kg b. wt. Animals of group 3 received butorphanol @ 0.04 mg/kg b.wt alone with Levobupivacaine @ 0.75 mg/kg b.wt. The lumbosacral space was used for epidural injection of different drug combinations mentioned above.

One goat was randomly selected from the group for the experiment to be performed next morning in the Department of Veterinary Surgery and Radiology, RVC. The lumbosacral space was used for epidural injection of different drug combinations mentioned above.Venous access were gained via the jugular vein with a 20 gauge winged needle to facilitate the collection of blood sample at different time intervals following epidural administration of analgesic agent. 5 ml of blood was collected on different time intervals 0, 5, 15, 30, 60, 90, 120 and 240 mins. Out of this 2 ml was collected in EDTA vial used for estimation of haematological parameter *viz*. Hb (g/dl), PCV (%), TLC (10^3/µl), DLC (%). Haematological parameters were recorded as per the method described by Schalm *et al*. (1975) [14]. whereas, remaining 3 ml of blood collected at 0,1,2, 4hrs and finally at 24 hrs was allowed to clot within the test tube in a slanting position for nearly 30 min and then centrifuged for 20 min at 3000 rpm. The supernatant serum will be collected in clean dry test tube by rubber bulb pipette, The separated serum will be used for estimation of various biochemical parameters by (ERBA Auto- analyzer Erba manhein chem – 5 plus V_2) using standard diagnostic kits.

1. Serum glucose (mg/dl) – GOD –POD method (Trinder, 1969) [13].
2. Serum glutamic pyruvic transaminase (SGPT) ((IU/L) – IFCC method (1986)
3. Serum glutamic oxaloacetic transaminase (SGOT) (IU/L) – IFCC method (1986)
4. Serum creatinine (mg/dl) Jaffe's method (Jaffe's 1886)
5. Blood urea nitrogen (gm/dl) – GLDH urease method (young 1990)
6. Total serum protein (mg/dl) – Biuret method (Tietz *et al*., 1976) [12].
7. Serum alkaline phosphates (IU/L)-Kind and king's method (1954).

The collected at different time intervals were subjected to statistical analysis using ANOVA and DMRT as per methods described by snedecor and Cochran (2004).

Results and Discussion

Haemoglobin in animals of different group did not show any significant differences at any intervals of observation (Table 1). PCV also showed the non – significant variations within and among the groups (Table1).Total erythrocyte count in animals of different group did not show any significant difference and the value remained within normal physiological limits(Table 1).Total Leucocyte Count was recorded respectively in group 1, 2 and 3 before epidural administration. The value of TLC at different interval of observation following epidural administration exhibited non–significant variations within and among the groups (Table 1). Similarly were also reported by Roonwal G. *et al.* for decrease non-significant change of Hb and PCV after administration of Levobupivacaine with and without fentanyl citrate in cow calves. (Roonwal *et al*. 2017) [8]. Korkmaz M. And Saritas Z. K. (2013) [9] reported that is no significant change in WBC, RBC, HCT and Hb value were observed during and after epidural administration of bupivacaine and Levobupivacaine in conscious dog. Turi *et al*. 2015 recorded a non-significant variation in Hb, PCV, TEC and DLC could be recorded at different intervals of observation. A transient increase in TLC and neutrophils at intial intervals could be recorded after epidural administration of butorphanol and alone in combination with lignocaine. Balage and Aher (2018) [1] recorded a decrease significant of Hb, PCV, TEC, and TLC during and after sedation after administration of dexmedetomidine in combination with Butorphanol.

Table 1: Mean (±SE) of haemoglobin (g/dl) and packed cell volume (%) total erythrocyte count (TEC), total leukocyte count (TLC), differential leukocyte count (DLC), at different time intervals in group 1, 2, and 3 in Goats

Period of Observation in (Min)	Haemoglobin			PCV		
	Group 1	Group 2	Group 3	Group1	Group 2	Group 3
0	9.00 ± 0.27	8.60±0.24	8.90±0.40	24.80±0.33	24.10±0.40	24.60±0.60
5	9.00±0.27	8.80±0.33	8.80±0.37	24.30±0.53	24.50±0.54	24.00±0.31
15	9.20±0.37	8.50±0.22	8.80±0.33	23.70±0.30	23.80±0.40	24.40±0.50
30	8.90±0.36	8.60±0.29	8.70±0.37	24.50±0.38	24.10±0.40	24.20±0.37
60	9.10±0.33	8.50±0.22	9.00±0.44	24.20±0.40	24.10±0.60	25.00±0.44
90	9.10±0.36	8.50±0.22	8.90±0.40	24.20±0.58	23.80±0.30	25.20±0.37
120	8.80±0.25	8.50±0.22	8.70±0.30	24.20±0.46	23.80±0.33	24.20±0.37
240	8.90±0.29	8.60±0.24	8.70±0.30	24.10±0.36	24.10±0.45	24.40±0.40

Period of Observation in (Min)	TLC			TEC		
	Group 1	Group 2	Group 3	Group 1	Group 2	Group 3
0	4.90±0.40	5.50±0.38	6.20±0.51	8.60±0.18	8.70±0.25	9.00±0.27
5	6.90±0.48	6.10±0.64	6.10±0.99	8.80±0.19	8.60±0.18	9.00±0.15
15	7.10±1.04	5.80±0.37	6.10±0.97	8.60±0.24	8.30±0.12	8.80±0.19
30	6.30±0.43	5.60±0.18	6.60±1.11	8.90±0.18	8.70±0.30	8.90±0.24
60	6.40±0.97	5.90±0.10	5.80±0.33	8.50±0.22	8.70±0.25	8.80±0.25
90	6.20±0.81	6.60±1.07	5.80±0.58	8.30±0.12	8.90±0.24	8.90±0.29
120	5.50±52	5.90±0.73	5.80±0.58	8.70±0.25	8.40±0.18	8.90±0.18
240	5.70±0.76	5.10±0.48	5.20±0.56	8.40±0.24	8.40±0.24	8.80±0.25

Table 2: Mean (±SE) of serum aspartate transaminase (IU/L), Serum glucose, SGPT, SGOT, Serum creatinine, blood urea nitrogen, total serum protein and alkaline phasphatase at different time intervals in group 1, 2, and 3 in goats.

Period of Observation in (hours)	AST			ALT			BUN		
	Group 1	Group 2	Group 3	Group1	Group 2	Group 3	Group 1	Group 2	Group 3
0	243.17±20.13	201.51±27.71	217.53±7.77	10.46±1.66	17.73±1.57	15.92±1.19	19.24±2.56	22.30±1.82	21.86±1.92
1	240.91±20.25	176.45±27.93	225.95±18.71	8.74±1.93	15.06±2.28	15.12±2.64	21.30±3.48	22.78±3.38	22.18±2.42

2	239.48±20.65	188.70±25.22	232.98±22.36	9.61±1.27	14.44±2.39	14.17±2.13	22.02±3.53	19.72±3.38	22.55±2.29
4	242.62±19.90	192.28±27.98	229.72±10.50	13.31±1.90	13.39±1.80	14.08±1.09	17.40±2.21	23.24±2.22	21.66±2.47
24	2.42±37.65	207.38±14.81	247.44±11.25	10.15±1.55	13.49±1.73	15.85±1.34	21.66±3.48	22.64±1.97	22.06±1.88

Period of Observation in (hours)	Glucose			ALP		
	Group 1	Group 2	Group 3	Group1	Group 2	Group 3
0	49.81±4.43	57.86±1.63	48.14±1.91	185.83±25.43	204.07±17.26	165.62±26.48
1	56.45±5.74	61.01±7.14	61.57±6.66	185.02±29.00	214.14±21.00	163.52±23.89
2	61.83±9.45	68.71±1.82	56.26±5.54	182.59±35.10	207.16±28.54	182.82±37.38
4	47.88±6.01	64.31±5.11	55.96±8.02	152.7±15.39	205.10±21.62	181.52±31.45
24	48.55±3.13	52.39±7.00	49.93±1.37	132.16±7.47	181.52±31.45	167.11±23.86
Period of Observation in (hours)	**Total protein**			**Creatinine**		
	Group 1	Group 1	Group 1	Group 1	Group 2	Group 3
0	7.19±0.28	1.36±0.13	1.36±0.13	1.36±0.13	1.22±0.14	1.41±0.15
1	6.77±0.22	1.38±0.16	1.38±0.16	1.38±0.16	1.13±0.09	1.29±0.11
2	6.50±0.42	1.29±0.10	1.29±0.10	1.29±0.10	1.18±0.09	1.45±0.15
4	7.27±0.22	1.40±0.15	1.40±0.15	1.40±0.15	1.25±0.13	1.54±0.09
24	7.25±0.31	1.30±0.16	1.30±0.16	1.30±0.16	1.27±0.15	1.44±0.12

The glucose level exhibited non- significantly increased (P>0.05) in all the groups at 1hr interval. A marked increase was noticed in group 3 followed by group 2 and group 1. Glucose level was non-significantly high (P>0.05) at different time intervals however the glucose levels were returned near to base line by the end of observations. The glucose level exhibited non- significantly increased (P>0.05) in all the groups at 1hr interval. A marked increase was noticed in group 3 followed by group 2 and group 1. Glucose level was non-significantly high (P>0.05) at different time intervals however the glucose levels were returned near to base line by the end of observations. AST activity estimated at different time intervals in all the groups were insignificant (P>0.05) and within normal physiological limits. AST activity in group 2 post induction showed the non-significant decrease from 1-4 hrs and after that the value showed the increasing trends as estimated on 24 hrs. ALP observed in all the groups were transiently variable and non- significant (P>0.05). Total protein different time interval in all three group were found within normal range and did not different significantly (P>0.05) within and among the groups. The value estimated at different intervals in all the groups showed insignificant variation (P>0.05). There was no definite trend of variations. The value also did not differ significantly (P>0.05) among the group at corresponding interval of observation. Creatinine estimated at different intervals in all the groups were within normal physiological limits and had non- significant alteration within and among the groups.

Hamad A.H. *et al.* (2016) [2] was also recoded of not any significant change of serum glucose after administration of fentanyl citrate. Roonwal *et al.* 2017 [8] was observed a non significant increase of serum alanine transaminase. the ALT increase significant between 1 hour to 6 hours and then again started decrease at 72 hours after administration of levobupivacaine and fentanyl in cow calves. Kumari *et al.* (2017) [11] was reported that the total serum protein showed a non-significant variation after administration of xylazine and Butorphanol Korkmaz and Saritas (2013) [9] was observed a epidurally administered BP and LP did not significantly alter the BUN.

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