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# Clinico physiological Evaluation of Levobupivacaine with and without Fentanyl Citrate in Cow Calves.

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## Abstract

A study was planned to evaluate the efficacy of Levobupivacaine as an epidural analgesia, with and without Fentanyl Citrate and to evaluate the clinico-physiological changes. The study was conducted on 12 healthy cow calves, weighing between 50 to 70 kg. The animals were divided into two groups of six animals each. The animals of group 1 received Levobupivacaine (@ 0.8 mg/kg body wt.) in sacrococcygeal space, while animals of group 2 received Levobupivacaine (@ 0.8 mg/kg. body wt.) and Fentanyl Citrate (@ 2 µg/kg body wt.) simultaneously in the sacrococcygeal space. The clinico-physiological changes were recorded at different time intervals in both treatments. The animals of treatment II showed longer duration and good depth as compared to animals of treatment I. The recovery was smooth in both groups. Rectal temperature, respiration rate and heart rate showed non-significant decrease in their values in both the groups.

**Key Words**: Levobupivacaine, Fentanyl citrate, epidural analgesia, opioids.

## Introduction

The quest for searching newer and safer anesthetic agents has always been one of the primary needs in anesthesiology practice. Levobupivacaine is the pure S enantiomer of bupivacaine (Burlacu and Buggy, 2008). Levobupivacaine 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). On the other hand Fentanyl citrate is a potent, synthetic opioid analgesic with a rapid onset and short duration of action. Fentanyl is commonly used for analgesia and as a component of balanced sedation and general anaesthesia in animal patients. Thus it was thought worthwhile to use levobupivacaine and fentanyl as an epidural analgesia in cow calves to evaluate the efficacy of Levobupivacaine as an epidural analgesia, with and without Fentanyl Citrate and to study the clinico–physiological changes.

## Material and Methods

The study was conducted on 12 apparently healthy young cow calves of either sexes weighing approximately 50-100 Kg at the Department of Surgery and Radiology, Teaching Veterinary Clinical

Complex of the College of Veterinary Science and Animal Husbandry, MHOW. Animals were divided into two groups (I, II) of 6 animal each. **Group I:** Levobupivacaine 0.50% @ 0.8 mg/kg body weight in sacrococcygeal space. **Group II:** Levobupivacaine 0.50% @ 0.8 mg/kg body weight along with Fentanyl Citrate @ 2µg/kg body weight in sacrococcygeal space. Rectal temperature (ºF), Respiration rate (per min.), Heart rate (per min.) were recorded at 0, 30, 60, 90 minutes, 3 hours and 6 hours. Time taken for loss of reflex was noticed in seconds/minutes for following areas of hind limb: Tail, Anal sphincter, Vulva ( in case of female animal), Perineum, Posterior Vagina (in case of female animal), Upper Thigh, Lower Thigh. Time taken for reappearance of reflex was noticed in minute/hours for the same area as for loss of reflex but in the reverse order as: Lower thigh, Upper thigh, Posterior vagina (in case of female animal), Perineum, Vulva (in case of female animal), Anal sphincter and, Tail. On the basis of above observations induction and duration of analgesia were also ascertained.

**Results and Discussion**

Results of the present study are depicted in tables 1 to 3. Time from injection to loss of reflexes at tail region was considered as time of onset of analgesia. The onset of analgesia was almost similar in both the treatment which was 1.66 ± 0.21 in treatment I and 2.33 ± 0.61 in treatment II. The onset was smooth without any side effects in both the groups. Foster and Markham (2000) reported that the onset of action is < or = 15 minutes with Levobupivacaine.

**Table 1: Observation in minutes (Mean ± SE) on loss of body reflexes after epidural administration of Levobupivacaine alone and with Fentanyl citrate in cow calves.**

| Body reflexes | Treatments | |
|---|---|---|
| | Treatment I | Treatment II |
| Tail | 1.66 ± 0.21 | 2.33 ± 0.61 |
| Anal sphincter | 5.1 ± 1.1 | 4.5 ± 0.84 |
| Perineum | 9.5 ± 2.65 | 6.83 ± 1.04 |
| Upper Thigh | 21.33 ± 5.4 | 15.33 ± 2.7 |
| Lower Thigh | 29.16 ± 5.97 | 28 ± 4.81 |

The epidural administration of Levobupivacainealone and its combination with Fentanyl citrate induced duration of analgesia of 163.34 ± 4.14 and 212.67 ± 1.21 in treatment I and treatment II respectively. There was a significant difference between two treatments. The combination in treatment II prolonged the duration significantly. Lejus *et al.* (2001) observed a significant prolongation in the duration of analgesia due to epidural Bupivacaine in combination with Fentanyl Citrate. Ghanem *et al.* (2013) inferred that epidural administration of morphine-fentanyl shorten the onset of analgesia and increases the duration of action because fentanyl is a lipophilic µ-receptor agonist opioid, when administer depidurally rapidly absorbed into epidural fat and the systemic circulatory system, resulting in minimal contact time with spinal opioid receptors. These results supports the prolonged duration of analgesia in our study after epidural injection of Levobupivacaine-Fentanyl treatment in comparison with Levobupivacaine alone treatment.

**Depth of analgesia (minutes):** In treatment I mild to moderate analgesia between 2 to 5 minutes and moderate analgesia between 5 to 10 minutes at perineum and tail was observed. In treatment II moderate analgesia between 1 to 5 minutes and moderate to strong analgesia between 5 to 10

**Table 2: Observation in minutes (Mean ± SE) on return of body reflexes after epidural administration of Levobupivacaine alone and with Fentanyl citrate in cow calves**

| Body reflexes | Treatments | |
|---|---|---|
| | Treatment I | Treatment II |
| Lower Thigh | 105 ± 6.70 | 148.33 ± 2.7 |
| Upper Thigh | 121 ± 8.29 | 168 ± 4.77 |
| Perineum | 137 ± 2.85 | 181.5 ± 2.75 |
| Anal Sphincter | 144 ± 2.22 | 202.5 ± 2.5 |
| Tail | 165 ± 10.11 | 215 ± 1.82 |

minutes at tail and perineum region was observed. Analgesia at upper and lower thigh was mild between 20 to 25 minutes and moderate analgesia was observed between 25 to 30 minutes in treatment I while in treatment II strong analgesia was induced at upper and lower thigh between 25 to 30 minutes. In treatment II strong or complete analgesia was produced between 35 to 150 minutes and moderate analgesia persisted upto 180 minutes at perineum region and upto 200 minutes at tail region whereas in treatment I moderate analgesia persisted upto 165 minutes at tail region. Luck et al. (2008) concluded that Levobupivacaine alone produced complete analgesia of the tail, perineum, inguinal region and upper parts of hind limbs for 5 hours. In the present study more depth of analgesia was observed in treatment II animals than treatment I animals due to addition of Fentanyl Citrate. Therefore surgeries of longer duration and of more depth can be performed using treatment II.

**Incoordination in gait (minutes):** Animals of both treatments i.e. Levobupivacaine alone and Levobupivacaine with Fentanyl Citrate did not become recumbent, however standing analgesia was produced with some degree of incoordination.

**Rectal temperature (°F):** After epidural administration of Levobupivacaine in treatment I, rectal temperature decreased non significantly from 100.75 ± 0.62 to 99.8 ± 0.72 between 30 minutes to 90 minutes and minimum value (99.8 ± 0.72) was observed at 90 minutes thereafter the value again started increasing and reached towards the baseline value at 360 minutes. In treatment II, rectal temperature decreased non significantly from 99.7.39 ± 0.80 to 98.81 ± 0.74 between 30 minutes to 90 minutes and minimum value 98.81 ± 0.74 was observed at 90 minutes, thereafter value started increasing and reached towards the baseline value at 360 minutes. The decrease in body temperature may be due to the peripheral vasodilation in area of block. Hall and Clark, (1989) suggested that spinal nerves always carries sympathetic fibres and peripheral nerve block always produces vasodilation.

**Heart rate (per minute):** The heart rate also did not vary significantly in both treatments and there was non significant decrease in value of heart rate upto 90 minutes which then increased and approached the base value towards 360 minutes. The minimum value of heart rate was 50.5 ± 2.77 and 50 ± 2.30 in treatment I and II respectively. Foster and Markham (2000) reported that the advantage of Levobupivacaine over Bupivacaine is this that unlike bupivacaine, it is not cardiac toxic. Thus after administration of Levobupivacaine no significant changes were found in heart rate.

**Respiration rate (per minute):** The respiration rate showed non significant decreasing pattern in both treatment between 30 minutes to 90 minutes and minimum value 14 ± 1.26 and 12.66 ±

1.42 in was observed at 90 minutes in treatment I and II respectively and then gradually approached towards basal value at 360 minutes. Gill *et al.* (1984) reported significant decrease in respiration rate after epidural administration of bupivacaine in cattle. Korkmaz and Saritas (2013) reported a slight decline in respiratory rate after epidural administration of levobupivacaine in conscious dogs.

**Table 3: Mean (±SE) of Rectal Temperature (°F), Heart Rate and Respiration Rate at different time intervals in treatment I and II in cow calves**

| Time of observation (minutes) | Rectal temperature | | Heart Rate | | Respiration Rate | |
|---|---|---|---|---|---|---|
| | Treatment I | Treatment II | Treatment I | Treatment II | Treatment I | Treatment II |
| 0 | 100.75 ± 0.62 | 99.7 ± 0.80 | 52.66 ± 2.61 | 54 ± 1.93 | 15.66 ± 1.20 | 14.33 ± 1.20 |
| 30 | 100.33 ± 0.69 | 99.4 ± 0.74 | 52 ± 2.46 | 50.66 ± 2.45 | 15. ± 1.43 | 14± 1.36 |
| 60 | 100.28± 0.65 | 99.23 ± 0.72 | 51.66 ± 2.75 | 50.66 ± 2.23 | 14 ± 1.46 | 12.66 ± 1.42 |
| 90 | 99.8 ± 0.72 | 98.81 ± 0.74 | 50.5 ± 2.77 | 50 ± 2.30 | 14 ± 1.26 | 12.66 ± 1.42 |
| 180 | 100.35 ± 0.62 | 100.33 ± 0.47 | 52.66 ± 2.10 | 52.66 ± 2.44 | 14.66 ± 1.33 | 14.66 ± 1.33 |
| 360 | 100.56 ± 0.61 | 99.61 ± 0.76 | 52.5 ± 2.70 | 53.66 ± 2.02 | 15.33± 1.33 | 14.33 ± 1.20 |

Levobupivacaine was efficacious in producing caudal epidural analgesia and its combination with fentanyl Citrate produced longer duration of action than Levobupivacaine alone thus use of combination of Levobupivacaine with Fentanyl Citrate can be safely advocated in clinical cases where longer duration of analgesia is required

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**Conflict of Interest:** All authors declare no conflict of interest.

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