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Comparative evaluation of lignocaine hydrochloride alone and its combination with pentazocine lactate for intravenous regional anaesthesia in cattle

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Abstract
The cattle having different surgical ailments of hoof/digit were divided in to two groups including 6 cattle in each group. Lignocaine hydrochloride (@ 4 mg/kg b.wt) and combination of lignocaine HCl + pentazocine lactate (4 mg/kg b.wt. + 1.0 mg/kg b.wt.) was injected in the radial vein in group I and II animals, respectively for inducing IVRA. In group I the HR and PR increased significantly ($P < 0.05$) at 20 minutes. The RR increased at 10 minutes in group I and between 30 and 60 minutes in group II. Oxygen saturation significantly ($P < 0.05$) decreased between 5, 10, 15, 20 and 30 minutes interval. Systolic pressure significantly increased between 15 and 30 minutes in group I animals. SBOT was less and SBRT was significantly ($P < 0.05$) more in group II as compared to group I. MBOT was similar in both group I and II animals. Efficacy of lignocaine in combination with pentazocine for producing IVRA was more as compared to lignocaine alone.

Keywords: Claw diseases, Lignocaine, IVRA, Bovine

Introduction
Distal limb and hoof/claw deformities such as fracture, interdigital fibroma, overgrown hoof, white line disease and sole ulcers are common disorders in cattle (Solano *et al.*, 2016) [18]. Claw trimming is the only method of treatment of early stages claw horn lesions (Thomas *et al.*, 2016) [20]. Cows with necrotic claw lesions represent a major welfare concern like chronic lameness for weeks and treatment of cases without necessary local anaesthesia. The more severe cases in which the inflammation and purulent infection reaches the pododerm, and inner structures of the horn shoe, leads to purulent arthritis of the coffin joint, osteomyelitis or necrosis of tendons and ligaments, amputation of claw or resection of the coffin joint under local anaesthesia (LA) is the only treatment of choice. Adequate pain relieving agents like lignocaine hydrochloride (2%) and non-steroidal anti-inflammatory drugs (NSAIDs) should be administered to control postoperative pain as claw surgeries are painful for diseased cattle (Janssen *et al.*, 2016) [10].

Intravenous regional analgesia is a safe and most commonly used technique with success rates between 97-98% (Charath *et al.*, 2014) [4]. Also this technique can be performed with minimum instruments and there is minimal bleeding at the surgical site (Reuben *et al.*, 2002) [16]. This technique provides analgesia of the limb or digits for short surgical procedures. Intravenous regional anesthesia is particularly advantageous to use in critically ill patients that are not fit for general anaesthesia. Being a regional technique it avoids all the complications of general anesthesia. It works through the retrograde diffusion of the local anaesthetic along and then out of the veins running adjacent to nerves within neurovascular bundles. Standard IVRA involves administration of 0.5% lidocaine solution. The disadvantages include local anesthetic (LA) toxicity, inadequate muscle relaxation, pain at the tourniquet site and minimal postoperative analgesia (Muhammad and Muhammad, 2012) [13]. Lignocaine remains the standard local anesthetic agent and most often used for IVRA. Advancement in the field of IVRA aimed at reducing the tourniquet pain increasing tourniquet tolerance improving the chances of intra operative and post-operative analgesia and decreasing the drug related adverse

effect. Lignocaine is a pharmacologically more desirable drug due to its quicker onset of action, increased potency and wider diffusion throughout tissues when compared with procaine (Edmondson, 2016) [5]. Opioids are most commonly used as adjuncts in IVRA along with local anesthetics (Bansal *et al*., 2011) [3]. Vasantha *et al*. (1988) [21] used bupivacaine HCL in veterinary practice there after Kognole *et al.* (2004) [11] used a combination of bupivacaine hydrochloride, pentazocine lactate, ketamine hydrochloride and buprenorphine to compare the anesthetic effects of these drugs in forelimbs of calves. Pentazocine is synthetic opioid analgesic. We combined pentazocine lactate, a synthetic opiate, with lignocaine hydrochloride in IVRA and compared it with IVRA using lignocaine only.

Materials and methods

The cattle having distal limb affections were distributed in to two groups having 6 cattle in each group. The affected animals were off fed for 48h. Animals were casted and restrained in right lateral recumbency with affected limb upper most. The anesthesia administration site and surgical field was shaved, scrubbed and painted with betadine lotion (5%). Intravenous regional anesthesia was achieved using standard technique as described by Yavari *et al.*, (2017) [23]. Briefly, tourniquet was applied at the middle (minimum circumference) of the metacarpus (Fig. 1). Butterfly canula was fixed in the radial vein to exsanguinate the area properly. Thereafter, lignocaine hydrochloride (@ 4 mg/kg b.wt) and combination of lignocaine HCl + pentazocine lactate (4 mg/kg b.wt. + 1.0 mg/kg b.wt.) was injected in the radial vein through the prefixed canula in group I and II animals, respectively. After removing the needle, injection site was compressed with povidone iodine soaked cotton swab for about 1 minute to avoid unintended drainage of the local anaesthetic from the punctured vein or formation of a haematoma. The anaesthetic potency was monitored by observing the following parameters:

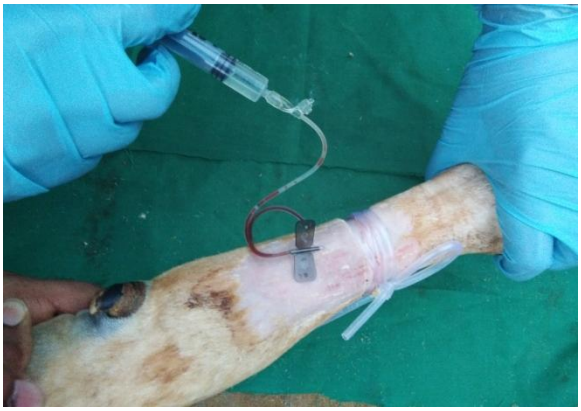

Fig 1: Application of tourniquet at mid metacarpus for IVRA

Heart rate

Heart rate is measured by the frequency of heart contractions per minute. It may vary in accordance with physical condition of the body. Heart rate was recorded preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Pulse rate

Pulse rate is the tactile arterial palpation of the heart beat and can be recorded as beat per minute (bpm) by palpating middle coccygeal artery by fingers. Pulse rate of animals was recorded preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Respiration rate

It is measurement of frequency of breathing per minute. It was taken preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Peripheral oxygen saturation (SPO2)

It is percentage of haemoglobin binding site occupied by oxygen and recorded using pulse oxymetry device (*Dr. Trust, Model no. DR50D, Nectar Life science Limited Works, Saidabad, Mohali, Punjab*). The device was fixed at the tip of the ear pinna and the values were recorded preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Systolic pressure

It is pressure within the major arteries in systolic phase of cardiac cycle and recorded by non invasive blood pressure monitoring unit (*Romsons BPX automatic BP monitor*) in mmHg. It was taken preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Diastolic pressure

It is the pressure within arteries in diastolic phase of cardiac cycle. It was also recorded by non invasive blood pressure monitoring unit (*Romsons BPX automatic BP monitor*) and is measured in mmHg. It was taken preoperatively, 5, 10, 15, 20, 30, 40, 50, 60 minutes or till recovery and just after release of tourniquet.

Sensory block onset time

It is the time from drug injection to sensory block achieved in all dermatomes. It was recorded at 5, 10, 15 and 20 minutes after the administration of drugs as per method described by Kognole *et al.* (2004) [11]. Briefly, sequential loss of reflexes was recorded by making repeated pin pricks over the skin distal to tourniquet at specific time intervals (not more than 2 to 3 times at a given space).

Motor block onset time

It is measurement of motor blockade. It was taken preoperatively and at 5, 10, 15 and 20 minutes after the administration of anesthesia as per method described by Kognole *et al.* (2004) **[11]**.

Sensory block recovery time

It was measured after 30 minutes of administration of anesthesia at every 10 min interval till the recovery after the administration of anesthesia as per method described by Kognole *et al.* (2004) [11]. Briefly, the return of reflexes was ascertained by pricks of Robert-Jones towel clamp.

Motor block recovery time

It was measured after 30 minutes of administration of anesthesia at every 10 min interval till the recovery after the administration of anesthesia as per method described by Kognole *et al.* (2004) [11].

Complication

Any complication related to local anesthesia like regurgitation, pain, skin rashes, bradycardia, tachycardia, hypotension, prostration, stumbling after release of tourniquet

and convulsion was vigilantly looked.

Statistical analysis

One way ANOVA (Analysis of variance) was used to compare the mean values at different intervals with their base values. Independent "t" test was used to compare the mean values between groups at different intervals.

Results and Discussion

Intravenous regional anaesthesia is found very suitable for regional anaesthesia of the limb in various ruminant species (Vasantha *et al.*, 1988) [21]. The more severe cases in which the inflammation and purulent infection reaches the pododerm, and inner structures of the horn shoe, leads to purulent arthritis of the coffin joint, osteomyelitis or necrosis of tendons and ligaments, amputation of claw or resection of the coffin joint under local anaesthesia (LA) is the only treatment of choice. (Heppelmann *et al.*, 2009) [9]. Pain relieving agents like lignocaine hydrochloride (2%) and non-steroidal anti-inflammatory drugs (NSAIDs) are used to control postoperative pain as claw surgeries are painful for affected cattle (Janssen *et al.*, 2016) [10]. For local anesthesia of the distal limb, IVRA is recommended (Anderson and Edmondson, 2013) [1]. For intravenous regional anaesthesia of the distal hind limb, a tourniquet is applied around the middle of the metatarsus and local anaesthetia is injected into a vein. Intravenous regional anesthesia is advantageous because of reduced bleeding at the surgical site during surgery, which improves the visibility of structures at the operating field.

Mean ± SE values of heart rate at different intervals in various groups are shown in table 1. In group I the heart rate increased significantly ($P < 0.05$) at 20 and 30 minutes as compared to base value and it was maximum at 30 minutes (82.83±0.66). Thereafter, the heart rate was more or less similar to base value. No significant change in heart rate was noted in the animals of group II at any interval of time. The heart rate was more or less similar to base value. Significantly ($P < 0.05$) increased heart rate in group I cattle might be due to pain sensation produced by tourniquet. Some researchers opined that acute pain increases heart rate (Terkelsen *et al.*, 2005) [19]. A significant ($P < 0.05$) increase in heart rate was also noted after IVRA (Yavari *et al.*, 2017) [23]. Increase in heart rate may be due to restraining of animals in lateral recumbency. Restraining of the animal induces stress response as indicated by an increased heart rate (Rizk *et al*., 2012) [17]. Contrary to the present results there was no significant change in heart rate during IVRA of bovine foot with lignocaine (Prentice *et al.* 1974) [15]. No significant change in heart rate was noted in the animals of group II at any interval of time. The heart rate was more or less similar to base value. The results of group II were in accordance with the findings of Patel *et al.* (2005) [14]. The IVRA tourniquet was removed just after recovery and the animals were returned from lateral recumbency to standing. Heart rate was significantly ($P < 0.05$) increased after removal of tourniquet in group II animals. Heart rate was decreased non-significantly ($P > 0.05$) after removal of tourniquet in group I animals. Decrease in heart rate over time after removal of tourniquet from IVRA using 2% procaine was also observed by Yavari *et al.* (2017) [23]. However, it was increased significantly ($P < 0.05$) in group II animals. The possible reason may be the systemic absorption of pentazocine after release of tourniquet, which acted upon opioid receptors in the central nervous system (Bansal *et al.*, 2011) [3]. Significant increase in heart rate in group II may be attributed to high dose rate of pentazocine which was used in the study. Pentazocine is expected to cause tachycardia in high doses. The intravenous administration of pentazocine reportedly increases heart rate. It increases plasma catecholamine levels, accompanied by marked elevations in both blood pressure and heart rate (Küukhüseyin, 2003) [12]. Pentazocine was also shown to antagonize the myotropic effect of histamine and acetylcholine via its local anesthetic-like action (Fogarty *et al.*, 1970) [6].

Mean ± SE values of pulse rate at different intervals in various groups are shown in table 1. In group I pulse rate increased significantly ($P < 0.05$) at 20 minutes (72.33±0.55) as compared to base value. Thereafter, the value decreased towards the base value. However, no significant ($P > 0.05$) change in pulse rate was noted in group II animals at any time interval. Significant increase in pulse rate in group I might be due to tourniquet pain caused by stimulation of sympathetic (autonomic) nervous system by electrical pain signals that reach the central nervous system. Tourniquet pain is one of the major disadvantages of IVRA and thought to be mediated by impulse propagation via small, unmyelinated, slow conducting C fibres (Gielen and Stienstra, 1991) [7]. No significant change in pulse rate in group II might be due to analgesic effect of pentazocine. Addition of butorphanol to the lignocaine did not significantly alter the baseline pulse rate (Bansal *et al.*, 2011) [3]. Tourniquet was removed just after recovery and the animals were returned from lateral recumbency to standing. After removal of tourniquet, the pulse rate increased significantly ($P < 0.05$) in group II animals. It may be due to sudden increase in pentazocine concentration in blood circulation after release of tourniquet. The IVRA tourniquet was removed just after recovery and the animals were returned from lateral recumbency to standing. No significant change in pulse rate was observed in none of the animals of different groups and pulse rate was nearly normal.

The respiration rate was increased at 10 minutes of interval in group I animals. Early increase in respiration rate in group I animals might be due to tourniquet pain. In group II, there was no significant change ($P > 0.05$) in respiration rate up to 20 minutes interval, but a significant decrease in respiration rate was noted from 30 minutes to 60 minutes and it was minimum at 60 minutes of interval. Lateral recumbency impairs respiration in cows which may lead to a moderate decrease in respiration rate (Yavari *et al*., 2017) [23]. Respiration rate was significantly decreased after removal of tourniquet in both groups of animals. A significant decrease in respiration rate over time after removal of tourniquet from IVRA using 2% procaine as in group I animals was also observed by Yavari *et al.* (2017) [23]. Significant decrease in respiration rate in group II animals might be due to respiratory depressant effect of pentazocine (Zeng *et al.*, 2015) [25]. The decreased respiration rate is related to the inhibition of the medullary respiratory centre by pentazocine (Küukhüseyin, 2003) [12].

Oxygen saturation significantly ($P < 0.05$) decreased at 5,10,15,10 and 30 minutes interval and it was minimum at 30 minutes. Thereafter the value continuously increased significantly ($P < 0.05$) up to 60 minutes (90.00±0.96). There was no significant ($P < 0.05$) change in peripheral oxygen saturation of group II. Addition of butorphanol to the lignocaine did not significantly alter the baseline peripheral oxygen saturation (Bansal *et al.*, 2011). Respiration in

ruminants is affected by the recumbency position and leads to moderate increase in arterial pCO_2 and a decrease in pO_2 (Yavari *et al.*, 2017) [23]. After removal of tourniquet, no significant change in oxygen saturation was observed in none of the animals of different groups and peripheral oxygen saturation was nearly normal. Zancy *et al.* (1998) [24] observed decrease in arterial oxygen saturation after injection of pentazocine in human beings.

Systolic pressure significantly increased between 15 and 30 minutes in group I animals and it was maximum (143.66±4.07) at 30 minutes of interval. Systolic pressure started to decrease towards the base value up to 60 minutes. Mean arterial pressure (MAP) significantly decreased over time after removal of tourniquet (Yavari *et al.*, 2017) [23]. There was no significant (P > 0.05) change in MAP from the baseline value in group II animals. Addition of butorphanol to the lignocaine did not significantly alter the baseline systolic pressure (Bansal *et al.*, 2011) [3]. After removal of tourniquet, no significant change in systolic pressure was observed in group I animals. A significant increase in systolic pressure in group II might be due to increase in the level of pentazocine in circulation which may increase the systolic pressure. Zancy *et al.* (1998) [24] also observed significant increase in systolic pressure at 5 min post injection.

A non significant (P > 0.05) increase in diastolic pressure was noted in both groups up to 60 minutes. After removal of tourniquet, diastolic pressure significantly ($P < 0.05$) increased in group II. A significant increase in diastolic pressure in group II might be due to increase in the level of pentazocine in circulation which may increase the systolic pressure. However, no significant (P > 0.05) change in diastolic pressure was observed in group I. Addition of butorphanol to the lignocaine did not significantly change the baseline diastolic pressure (Bansal *et al.*, 2011) [3]. Diastolic pressure was not altered after injection of pentazocine in human beings (Zancy *et al.*, 1998) [24].

Table 1: Mean ± SE of heart rate (per minute), pulse rate, respiration rate, peripheral oxygen saturation (%), systolic pressure (mm of Hg) and diastolic pressure (mm of Hg)of animals of group I and II at different time intervals, and after removal of tourniquet (ART)

Time interval	Heart rate (per minute)		pulse rate (per minute)		Respiration rate (per minute)		Peripheral oxygen saturation (%)		systolic pressure (mm of Hg)		Diastolic pressure (mm of Hg)	
	I	II	I	II	I	II	I	II	I	II	I	II
0	77.16 ±0.60	75.16 ±0.90	70.83 ±1.27	69.16 ±1.68	25.83 ±0.47^{a}	27.33 ±0.49^{b}	93.33 ±0.49^{a}	96.16 ±0.83^{b}	135.3 ±2.40	133.3 ±1.40	104.7 ±2.51^{a}	96.33 ±1.56^{b}
5	73.50 ±0.67^{a}	77.16 ±0.79^{b}	66.66 ±1.11	71.16 ±2.40	26.50 ±0.42	28.33 ±0.55	92.00 ±0.36^{a*}	95.00 ±0.77^{b}	139.0 ±1.52^{a}	135.5 ±1.36^{b}	110.7 ±4.94^{a}	98.50 ±2.20^{b}
10	76.00 ±0.44	78.00 ±1.15	66.33 ±1.30^{a}	73.83 ±1.60^{b}	27.83 ±0.30*	26.83 ±0.94	88.16 ±1.10^{a*}	94.33 ±1.60^{b}	137.5 ±2.17	136.3 ±0.61	103.3 ±4.99	101.2 ±2.19
15	77.83 ±2.35	79.66 ±2.12	68.33 ±1.58	73.83 ±2.03	27.83 ±0.60	26.66 ±1.58	86.16 ±0.47*	92.50 ±2.26	138.5 ±1.78*	139.2 ±4.62	106.7 ±5.23	101.0 ±1.82
20	81.83 ±0.30*	80.00 ±2.76	72.33 ±0.55*	72.83 ±1.02	26.16 ±0.40	26.33 ±1.25	83.66 ±1.54*	91.66 ±2.27	142.2 ±2.78*	137.2 ±3.59	109.0 ±9.24	103.2 ±2.67
30	82.83 ±0.66*	80.66 ±2.59	71.16 ±0.95	71.50 ±1.87	26.33 ±0.33	23.83 ±1.68*	82.50 ±1.64^{a*}	93.66 ±2.64^{b}	143.7 ±4.07*	137.3 ±1.99	108.5 ±6.18	100.6 ±3.01
40	76.33 ±1.42^{a}	79.33 ±1.66^{b}	71.66 ±1.16	72.50 ±1.47	24.50 ±0.22^{a}	24.50 ±0.76*	85.00 ±1.09^{a*}	93.66 ±2.80^{b}	138.0 ±3.86	137.5 ±1.60	108.0 ±5.95	99.50 ±2.34
50	77.50 ±0.99	78.16 ±1.44	70.00 ±1.69	73.50 ±2.01	25.66 ±0.66	24.83 ±0.60*	87.50 ±1.28^{a*}	94.33 ±2.21^{b}	136.2 ±2.58^{a}	138.7 ±0.55^{b}	100.8 ±3.60	98.83 ±1.62
60	77.76 ±1.11	77.33 ±1.68	70.83 ±1.40	71.50 ±2.17	24.50 ±0.76	23.16 ±0.79*	90.00 ±0.96^{a*}	95.00 ±1.36^{b}	135.3 ±3.25^{a}	137.8 ±1.70^{b}	104.2 ±6.44	99.33 ±1.78
ART	76.00 ±1.15^{a}	82.00 ±3.65^{b*}	71.16 ±0.95	74.83 ±0.23*	22.14 ±0.12*	22.46 ±0.33*	92.50 ±2.26	91.66 ±2.27	136.33 ±0.21^{a}	142.66 ±0.55^{b*}	104.33 ±1.24	101.26 ±1.17*

*Differ significantly ($P < 0.05$) from day 0 values

^{ab}Value with different alphabets differ significantly ($P < 0.05$) between groups at particular time interval

Sensory block onset time was earliest in group II (4.50±0.42 minutes) as compared to group I (4.66±0.33 minutes). Early onset of sensory block was also observed after addition of butorphanol in lignocaine (Bansal *et al.* 2011) [3], nalbuphine in lignocaine (Bakri *et al.*, 2016) [2] as compared to lignocaine alone for IVRA. Kognole *et al.* (2004) [11] conducted a study on IVRA using bupivacaine in combination with pentazocine and sensory block onset time for this combination was 0.17±0.03 min. Early onset of sensory block in group II might be due to synergism between lignocaine HCl and pentazocine. Patel *et al.* (2005) [14] opined that the mean time required to achieve complete anesthesia was minimum for lignocaine-pentazocine combination for IVRA. Parentral administration of pentazocine produces analgesia and peak value occurs within 15 min to 1 hr which might be responsible for rapid onset of action during IVRA. When used alone, lignocaine took greater time for the complete induction of anesthesia. Lidocaine IVRA is effective and is associated with slightly delayed onset (4.5 ± 0.3 minutes) of anesthesia (Viscomi *et al.*, 2009) [22].

Sensory block recovery time was longest in group II (64.50±1.70 minutes) as compared to group I (61.33±2.18 minutes). Kognole *et al.* (2004) [11] conducted a study on IVRA using bupivacaine in combination with pentazocine and sensory block recovery time for this combination was 110.00±6.57 min. Bansal *et al.* (2011) [3] also observed delayed recovery from sensory block after addition of butorphanol in lignocaine as compared to lignocaine alone for IVRA. Patel *et al.* (2005) [14] also observed SBRT more than 1 hour after using combination of lignocaine-pentazocine. In present study combination of lidocaine with pentazocine give excellent results by prolonged post operative analgesia. Mixture of local anaesthetics agent for IVRA had more profound analgesia and successful block and low incidence of complication compared with patient who received individual drug only (Haider and Mahdi, 2013) [8]. Sensory block recovery time was longer after addition of nalbuphine in lignocaine as compared to lignocaine alone for IVRA (Bakri

et al., 2016) [2].

Motor block onset time was earliest in group I as compared to group II animals. These results were in accordance with the findings of Kognole *et al.* (2004) [11]. Early onset of motor block was also observed after addition of nalbuphine in lignocaine as compared to lignocaine alone for IVRA (Bakri *et al.*, 2016) [2].

Motor block recovery time was more in group II as compared to group I animals. Kognole *et al.* (2004) [11] conducted a study on IVRA using bupivacaine in combination with pentazocine and sensory block recovery time for this combination was longer. Motor block recovery time was longer after addition of nalbuphine in lignocaine as compared to lignocaine alone for IVRA (Bakri *et al.*, 2016) [2].

The tourniquet was removed just after recovery and the animals were returned from lateral recumbency to standing. The animals in which IVRA was induced by combination of lignocaine and pentazocine (group II) were in prostration for 5-6 minutes. Slight decrease in heart rate (bradycardia) and stumbling was observed in this group of animals. This change was within the normal range. Animals of groups I did not show such types of signs. Side effects and complications due to the drugs used were not serious in nature.

Table 2: Mean ± SE of sensory block onset time (SBOT), sensory block recovery time (SBRT), motor block onset time (MBOT) and motor block recovery time (MBRT) (in minutes) of animals of different groups.

Groups	Sensory block onset time (SBOT)	Sensory block recovery time (SBRT)	Motor block onset time (MBOT)	Motor block recovery time (MBRT)
I	4.66±0.33	61.33±2.18[a]	5.16±0.30	62.50±1.17
II	4.50±0.42	64.50±1.70[b]	5.16±0.47	61.50±2.14

Conclusion

Intravenous regional anesthesia (IVRA) technique using lignocaine HCl alone and combination with pentazocine was found suitable for hoof examination and surgery but lignocaine admixed with pentazocine was safe as compared to lignocaine alone.

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