

Comparison of lidocaine and its combination with ketamine for distal intravenous regional anesthesia (DIVRA) in bovines

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ABSTRACT

The hoof diseases of cattle can be managed surgically under intravenous regional anesthesia (IVRA). For routine induction of IVRA, a tourniquet is placed circumferentially at the metacarpus/metatarsus. In the present study, hoof diseases of cattle were corrected using a modified IVRA technique. The cattle with hoof ailments were randomly divided into two groups and a tourniquet was placed just distal to the dew claws instead of at the metacarpus/metatarsus in order to decrease the dose of anesthetic. In group I lidocaine (2mg/kg) and in group II a mixture of lidocaine and ketamine (2mg/kg+1.5mg/kg) was injected into the axial digital vein to induce distal intravenous regional anesthesia (DIVRA). The heart rate, respiration rate, systolic and diastolic pressure were unaffected in both groups. Oxygen saturation was significantly ($P<0.05$) lower between 5 and 60 minutes in group I and between 15 and 40 minutes in group II animals. The sensory and motor block onset time was shorter, and the sensory and motor block recovery time was longer in group II animals as compared to group I animals. It was concluded that the DIVRA technique using lidocaine alone and lidocaine admixed with ketamine are suitable for hoof examination and surgery.

Key words: distal IVRA; lidocaine; ketamine; cattle

Introduction

Local and regional anesthesia is an integral part of performing minor and major surgical operations on large animals for economic and practical reasons. Biers block was first implemented by August Bier in 1908 by injecting procaine into the subcutaneous veins that were exposed between two tourniquets

(ABDEL-RAHMAN et al., 2012). For patients at high risk, Intravenous Regional Anesthesia (IVRA) is an alternative method for general anesthesia (MOHR, 2006). It is a regional anesthetic technique with success rates of 94% to 98%, and the primary advantages of IVRA are its simplicity, reliability

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and cost effectiveness. Moreover, sophisticated anesthetic instruments are not available at rural veterinary hospitals, so it may be a popular choice for veterinarians to correct surgical ailments of bovine extremities. Proximal intravenous regional anesthesia is an ideal method for digital surgery in bovine. Generally a tourniquet is applied above the elbow or hock joint for occluding the arterial circulation of the limb by applying pressure >150 mm Hg. The amount of bleeding at the surgical site is thereby considerably reduced. In this technique, a large amount of local anesthetic is required which may cause local anesthetic toxicity during tourniquet release (SKARDA, 1987).

Claw surgeries are painful for affected cows and require adequate pain management, including local anesthesia (LA) and analgesic application to control postoperative pain. The ideal local anesthetic for IVRA should have properties such as short onset, long lasting anesthesia with a low dose, and minimal side effects. Lidocaine remains the standard local anesthetic agent, but it causes tourniquet pain and postoperative analgesia is absent. To overcome these drawbacks of lidocaine various studies have been conducted to find a local anesthesia mixture in combination with opioids (fentanyl, pethidine, tramadol), NSAIDs (ketorolac, acetylsalicylate, lornoxicam) and other analgesics, that allows relief from tourniquet pain and prolonged duration of analgesia after tourniquet release. Local anesthetic toxicity may be noted in proximal IVRA due to leakage past the tourniquet because of high venous pressure or tourniquet failure (REUBEN et al., 2002). KUMAR et al. (2020) developed a distal intravenous regional anesthesia for management of claw diseases in bovines.

Ketamine, a phenyl-piperidine derivative, is used as an anesthetic agent. At sub-anesthetic doses, ketamine exerts a noncompetitive blockade of *N*-methyl-aspartate (NMDA) receptors. NMDA receptors play a major role in synaptic plasticity, and are specifically implicated in central nervous system facilitation of pain processing. NMDA receptor antagonists have been used in perioperative pain management (ELMETWALY et al., 2010). Ketamine also has local anesthetic qualities, and it has been studied as a sole agent for IVRA

(LAURETTI et al., 1999). In addition to the spinal cord, NMDA receptors have also been identified on peripheral unmyelinated sensory axons. This is the reason that ketamine as an NMDA receptor antagonist attenuates the tourniquet pain.

The present study was conducted with the intention of reducing doses of local anesthetics to a non toxic level for inducing IVRA to manage major surgical interventions on claws, or resection of the distal interphalangeal joint.

Materials and methods

The present study was performed on crossbred cattle of both sexes, aged between 1-2 years, having hoof/claw pathologies such as heel erosions, digital dermatitis, sole ulcers and claw amputation. The bovines with foot disease(s) were randomly divided into two groups with six animals in each group. The affected animals were fasted for 48h and the area below the pastern joint was aseptically prepared for distal intravenous regional anesthesia (DIVRA). No premedication was administered in either group of animals before casting. The animals were casted and restrained in lateral recumbency with the affected limb uppermost. For DIVRA, the elastic tourniquet was applied just below the pastern joint and distal to the dew claws. Thereafter, the axial digital vein was catheterized using a butterfly cannula no. 22 and, under gentle flexion of the fetlock joint, blood was drained through the needle until the pressure dropped, as indicated by slow dripping rather than blood running out of the hub. In group I, lidocaine alone (2mg/kg) and in group II a mixture of lidocaine and ketamine (2mg/kg+1.5mg/kg) was injected into the axial digital vein to induce lower intravenous regional anesthesia (IVRA). The injection site was compressed with a povidone iodine-soaked cotton swab for about 1 minute after removing the needle, to avoid unintended drainage of the local anaesthetic from the punctured vein or formation of a hematoma. The anesthetic potency was monitored by observing the following parameters at different time intervals:

Heart rate. Heart rate may vary according to the body's physical needs. Heart rates were taken preoperatively and at 5, 10, 15, 20, 30, 40, 50 and 60 min. / until recovery after the administration

of anesthesia and just after the release of the tourniquet.

Respiration rate. Pulse rates were taken preoperatively and at 5, 10, 15, 20, 30, 40, 50 and 60 min. / until the recovery after the administration of anesthesia and just after the release of the tourniquet.

Peripheral oxygen saturation (SPO2). This was measured by pulse oximetry (Marketed by-Dr. Trust, Model No. DR50D, Nectar Life science Limited Works, Saidabad, Mohali, Punjab). Measurements were taken preoperatively and at 5, 10, 15, 20, 30, 40, 50 and 60 min. / until recovery after the administration of anesthesia and just after the release of the tourniquet.

Systolic pressure. This was measured by a non-invasive blood pressure monitoring unit (Romsons BPX automatic BP monitor) in mmHg. It was taken preoperatively and at 5, 10, 15, 20, 30, 40, 50 and 60 min./ until recovery after the administration of anesthesia and just after the release of the tourniquet.

Diastolic pressure. This was measured by a non-invasive blood pressure monitoring unit (Romsons BPX automatic BP monitor) in mmHg. It was taken preoperatively and at 5, 10, 15, 20, 30, 40, 50 and 60 min./ until recovery after the administration of anesthesia and just after the release of the tourniquet.

Sensory block onset time. This was taken preoperatively and at 5, 10, 15 and 20 min. after administration of anesthesia as per the method described by KOGNOLE et al. (2004). The loss of sensation of the skin distal to the dew claw region was ascertained by superficial pin-pricks, and the time taken for the induction of anesthesia was noted.

Motor block onset time. This was taken preoperatively and at 5, 10, 15 and 20 min. after administration of anesthesia, as per the method described by MANOHAR et al. (1971) with some modifications. Briefly, with the animal in a standing position, the time at which no weight was being borne by the affected limb and when no response to hypodermic needle pricks in deep tissues, were recorded for each animal separately.

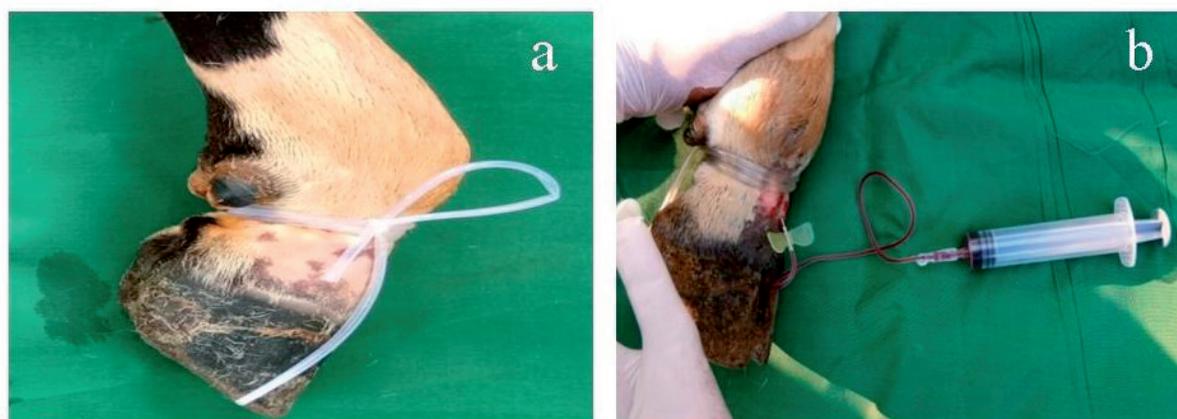


Fig. 1. Application of a tourniquet just distal to the dew claws (a) and injection of anesthetic in the axial digital vein for lower IVRA (b)

Sensory block recovery time. This was measured 30 minutes after administration of anesthesia at 10 min intervals until recovery after the administration of anesthesia, as per the method described by KOGNOLE et al. (2004). During surgery the recovery of sensation distal to the dew claw region was noted.

Motor block recovery time. This was measured 30 minutes after administration of anesthesia at 10 min intervals until recovery after the administration of anesthesia, as per the method described by MANOHAR et al. (1971), with some modifications. Briefly, with the animal in a standing position, the time at which the animal could bear weight without stumbling on the affected limb was noted.

Complication. Any signs or symptoms of local anesthesia toxicity, such as perioral numbness, regurgitation, pain, skin rashes, bradycardia, hypotension and convulsion, were vigilantly observed.

Statistical analysis. SPSS software version 17.0 (SPSS, Inc., Chicago, IL) was used for data analysis. One-way ANOVA (Analysis of variance) was used to compare the mean values at different intervals with their base values. The independent “t” test was used to compare the mean values between groups at different intervals.

Results

Heart rate. Mean \pm SE values of the heart rate in both groups of animals at different intervals are presented in Table 1. No significant changes in heart rate in either group of animals at different time intervals shows minimum tourniquet pain. It was highest at 30 minutes in group I animals. Comparison between groups revealed a significant ($P < 0.05$) difference in heart rate between the two of animals at 30, 40, 50 and 60 minutes. However, the values were within the normal range.

Table 1. Mean \pm SE of heart rate (per minute), pulse rate, respiration rate, peripheral oxygen saturation (%) and systolic pressure (mm of Hg) of animals in different groups at different time intervals, and after removal of the tourniquet (ROT)

Time interval	Heart 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
0	76.00 ± 1.03	74.00 ± 0.73	27.00 ± 0.42	25.00 ± 0.85	92.33 ± 0.21	93.33 ± 0.84	124.00 ± 0.98	124.00 ± 1.86	95.00 ± 1.12	94.33 ± 0.61
5	76.33 ± 0.95	74.33 ± 0.95	26.66 ± 0.42	26.00 ± 0.51	88.33 $\pm 1.11^*$	79.33 ± 8.01	124.00 ± 0.51	124.33 ± 0.61	96.00 ± 0.73	94.66 ± 0.42
10	77.33 ± 1.22	74.33 ± 0.80	26.33 ± 0.95	28.00 ± 1.03	82.66 $\pm 1.47^*$	75.66 ± 6.85	124.00 ± 0.51	124.33 ± 0.61	95.00 ± 0.85	94.00 ± 0.73
15	78.66 ± 1.83	75.00 ± 1.43	25.00 ± 0.85	27.33 ± 0.98	75.33 $\pm 3.31^*$	75.66 $\pm 4.98^*$	125.00 ± 0.68	125.00 ± 0.44	94.66 ± 0.98	94.33 ± 0.80
20	80.00 ± 1.71	75.66 ± 0.02	24.33 ± 1.08	26.00 ± 1.03	84.33 $\pm 3.29^*$	74.33 $\pm 3.60^*$	125.33 ± 0.42	124.66 ± 0.42	95.33 ± 0.66	96.33 ± 0.33
30	81.00 ± 1.52	75.00 ± 1.84	24.00 ± 1.03	26.33 ± 1.08	80.00 $\pm 2.75^*$	80.00 $\pm 2.63^*$	123.66 ± 0.61	122.66 ± 0.66	96.00 ± 0.51	95.33 ± 0.44
40	79.66 ± 1.20	75.66 ± 1.20	24.33 ± 0.95	26.66 ± 0.66	86.66 $\pm 1.64^*$	81.33 $\pm 3.65^*$	123.33 ± 0.66	124.00 ± 0.73	96.00 ± 0.51	95.00 ± 0.44
50	80.00 ± 1.26	75.33 ± 0.66	26.00 ± 1.03	27.66 ± 0.95	87.00 $\pm 1.26^*$	86.00 ± 2.52	124.33 ± 0.61	125.33 ± 0.42	94.00 ± 0.89	94.33 ± 0.61
60	79.00 ± 1.43	74.33 ± 1.40	25.66 ± 0.80	28.00 ± 1.15	89.00 $\pm 0.73^*$	85.66 ± 3.39	125.00 ± 0.68	125.00 ± 0.44	94.33 ± 0.61	93.66 ± 0.61
ROT	75.66 ± 0.95	75.00 ± 1.43	26.33 ± 0.51	24.33 ± 0.61	90.66 ± 0.80	92.33 ± 0.40	125.00 ± 0.66	125.00 ± 0.44	95.00 ± 0.51	95.33 ± 0.44

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

Respiration rate. Mean \pm SE values of the respiration rate in both groups of animals at different intervals are presented in Table 1. There was no significant change in respiration rate in either group at different time intervals even after removal of the tourniquet. Comparison between groups also revealed no significant change.

Peripheral oxygen saturation (SPO_2). Mean \pm SE values of peripheral oxygen saturation (SPO_2) at different intervals in both groups of animals are presented in Table 1. Peripheral oxygen saturation significantly ($P < 0.05$) decreased at 5, 10, 15, 20, 30, 40, 50 and 60 minutes in group I animals. However, the lowest value was observed at 15 minutes. In group II oxygen saturation was significantly lower ($P < 0.05$) at 15, 20, 30 and 40 minutes. Thereafter, oxygen saturation increased towards the base value.

Systolic pressure. Mean \pm SE values of systolic pressure at different intervals in both groups of animals are presented in Table 1. There was no significant change in systolic pressure in group I or II animals at different time intervals even after removal of the tourniquet.

Diastolic pressure. Mean \pm SE values of diastolic pressure at different intervals in both groups of animals are presented in Table 1. There was no significant change in diastolic pressure in either group of animals at different time intervals even after removal of the tourniquet. None of the cattle needed treatment for hypotension or bradycardia.

Sensory block onset time (SBOT). Mean \pm SE values of SBOT at different intervals in both groups of animals are presented in Fig. 2. Sensory block onset time was significantly ($P > 0.05$) shorter in group II (3.33 ± 0.33 minutes) when compared to group I (5.00 ± 0.36 minutes).

Motor block onset time (MBOT). Mean \pm SE values of MBOT at different intervals in both groups of animals are presented in Fig. 2. Motor block onset time was significantly ($P > 0.05$) shorter in group II (4.50 ± 0.42 minutes) as compared to group I (6.00 ± 0.25 minutes).

Sensory block recovery time (SBRT). Mean \pm SE values of SBRT at different intervals in both groups of animals are presented in Fig. 3. Sensory block recovery time was significantly ($P > 0.05$) longer

in group II (64.20 ± 1.05 minutes) as compared to group I (60.83 ± 2.41 minutes).

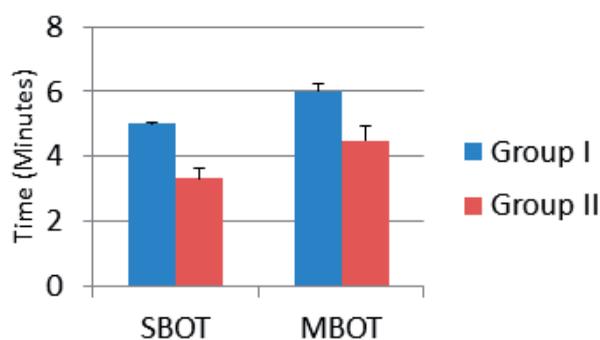


Fig.2. Mean \pm SE of sensory block onset time (SBOT) and sensory block recovery time (SBRT) in animals in different groups

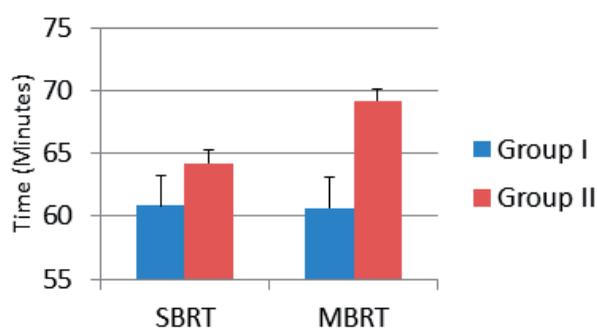


Fig.3. Mean \pm SE motor block onset time (MBOT) and motor block recovery time (MBRT) in animals in different groups

Motor block recovery time (MBRT). Mean \pm SE values of MBRT at different intervals in both groups of animals are presented in Fig. 3. Motor block recovery time was significantly ($P > 0.05$) longer in group II (69.16 ± 0.98 minutes) when compared with group I (60.66 ± 2.38 minutes).

Postoperative complications after release of the tourniquet. None of the animals in either group showed any signs of cardiovascular or CNS toxicity after the release of the tourniquet. Just after recovery, the animals returned from lateral recumbency to standing and stumbling for a very short period - about 1-2 minutes was noted in group II animals.

Discussion

Claw diseases are common in cloven footed animals and are mainly caused by claw horn lesions, such as sole ulcers and white line disease, or by inflammatory alterations of the adjacent soft tissues (COOK et al., 2016). Claw horn lesions are commonly treated in their early stages by therapeutic claw trimming (THOMAS et al., 2016). Claw surgery of delayed or complicated cases is painful for the injured animal, and requires appropriate pain management, including local anaesthesia and analgesic to control pain (JANSSEN et al., 2016). Lidocaine alone does not produce postoperative analgesia. Ketamine, when used in combination with a local anesthetic, has been shown to be very effective in reducing the incidence of tourniquet pain (ABDEL-GHAFFAR et al., 2014). Ketamine is added to a lower dose of lidocaine in order to reduce the lidocaine associated complications (YAGHUBI et al., 2016).

In general, intravenous regional anesthesia is achieved by placing a tourniquet above the elbow or hock joint, for management of surgical affections distal to the elbow or hock joint. A large amount of local anesthetic is required to achieve regional anesthesia, which may lead to local anesthetic toxicity (LUMB and JONES, 1984). For management of claw diseases, the area to be sensitized is decreased many times. So, in the present study the dose of local anesthetic was decreased to a non-toxic level by applying the elastic tourniquet just below the pastern joint and distal to the dew claws for inducing DIVRA for the management of claw disease in cattle. The dose of ketamine was also reduced to half. The decrease in the dose of LA lowered toxicity during tourniquet release. In routine IVRA, toxicity during removal of the tourniquet is prevented if the tourniquet is released for 10 to 15 seconds and placed again for 2 to 3 minutes, repeating this process many times (SKARDA, 1987). In a lower IVRA technique, the tourniquet may be released immediately without any signs of local anesthetic toxicity.

There fact that there was no significant change in heart rate in either group of animals at different time intervals demonstrates there was minimum tourniquet pain. Heart rates may increase due to

tourniquet pain (TERKELSEN et al., 2005). A significant ($P < 0.05$) increase in heart rate was also noted after IVRA (YAVARI et al., 2017). Ketamine has well known hemodynamic effects (hypertension and tachycardia), but it did not show any of these effects during the study period in either group when given as an adjuvant in IVRA. Small doses of ketamine (≤ 0.1 mg/kg) did not show any significant hemodynamic changes or clinical side effects (ELIWA, 2018). After removal of the tourniquet no significant ($P > 0.05$) change in heart rate was observed in either group of animals. However, a significant decrease in heart rate over time after the removal of the tourniquet from IVRA using 2% procaine was observed by YAVARI et al. (2017).

There was no significant change in respiration rate in either group at different time intervals, even after removal of the tourniquet. Comparison of the groups also revealed no significant change. A significant decrease in respiration rate over time after removal of the tourniquet from IVRA using 2% procaine was observed by YAVARI et al. (2017).

Peripheral oxygen saturation significantly ($P < 0.05$) decreased at 5, 10, 15, 20, 30, 40, 50 and 60 minutes in group I animals. However, in group II, oxygen saturation was significantly lower ($P < 0.05$) at 15, 20, 30 and 40 minutes. Significantly lower peripheral oxygen saturation might be due to lateral recumbency, as the rumen was pressing on the lungs and diaphragm. Lateral recumbency also impairs respiration in cows, leading to a moderate increase in arterial $p\text{CO}_2$ and a decrease in $p\text{O}_2$ (YAVARI et al., 2017). There were no statistical differences between the groups given lidocaine alone and in combination with ketamine in peripheral arterial oxygen saturation at any intra-operative time interval (ESMAT and KASSIM, 2015). After removal of the tourniquet, no significant change in oxygen saturation was observed in any of the animals in the different groups, and pulse rates were nearly normal.

There was no significant change in systolic or diastolic pressure in either group of animals at different time intervals, even after removal of the tourniquet. No significant differences were observed

in the mean intraoperative systolic and diastolic blood pressure values between the lidocaine and lidocaine+ketamine groups (ABDEL-GHAFFAR et al., 2014). None of the cattle needed treatment for hypotension or bradycardia. The significantly higher MAP in the IVRA cows may indicate a stress response induced by tourniquet pain YAVARI et al. (2017). No significant change in blood pressure was observed after using lidocaine or its combination with ketamine as an IVRA (HAIDER and MAHDI, 2013).

Sensory block onset time was measured by the pin prick method. Needle pricks to the interdigital space, as a common nociceptive test for checking desensitization after LA and before surgical interventions (HUDSON et al., 2008). Sensory block onset time was significantly ($P>0.05$) shorter in group II (3.33 ± 0.33 minutes) when compared to group I (5.00 ± 0.36 minutes) animals. These results were in accordance with the findings of SHETH et al. (2015). MIR et al. (2007) also observed a rapid onset of sensory block when 1% ketamine was added to lidocaine. KOGNOLE et al. (2004) observed a lower mean time (1.53 ± 0.33 minutes) required for the onset of anesthesia when a bupivacaine HCl - ketamine HCl combination was used as IVRA. Lidocaine IVRA is effective but is associated with slightly delayed onset of anesthesia as compared to a lidocaine and ketamine combination (VISCOMI et al., 2009).

Motor block onset time was significantly ($P>0.05$) shorter in group II (4.50 ± 0.42 minutes) as compared to group I (6.00 ± 0.25 minutes) animals. Addition of ketamine to lidocaine leads to rapid onset of motor block (MIR et al., 2007). Application of a tourniquet just proximal to the elbow joint of buffalo calves meant it took more than 15 minutes for anesthesia to develop in the region below the carpus (MANOHAR et al., 1971). Complete analgesia, with adequate muscular relaxation and motor block, was achieved with complete desensitization of the limb below the tourniquet, and the limb was carried in a posture simulating radial paralysis (TYAGI et al. 1973)

Sensory block recovery time was significantly ($P>0.05$) longer in group II (64.20 ± 1.05 minutes) as compared to group I (60.83 ± 2.41 minutes)

animals. These results were in accordance with the findings of KOGNOLE et al. (2004). Sensory block recovery time was prolonged after lidocaine combined with ketamine as compared to lidocaine alone (ELMETWALY et al., 2010). In the present study, the combination of lidocaine with ketamine gave excellent results with prolonged post operative analgesia. A mixture of local anesthetic agents for IVRA gave more profound analgesia and a successful block, and a low incidence of complications compared with individual drug alone (HAIDER AND MAHDI, 2013).

Motor block recovery time was significantly ($P>0.05$) longer in group II (69.16 ± 0.98 minutes) when compared with group I (60.66 ± 2.38 minutes) animals. Motor block recovery time was prolonged after lidocaine combined with ketamine as compared to lidocaine alone (ELMETWALY et al., 2010). Recovery from the anesthetic effect after release of the tourniquet consistently took 14 to 15 minutes for the return of sensation, and 106 minutes for the return of moderate function of the limb (TYAGI et al., 1973). However, in the present study recovery from the anesthetic effect after release of the tourniquet was earlier, which may be due to the lower dose of lidocaine used in DIVRA.

None of the animal in either group showed sign of cardiovascular or CNS toxicity after release of the tourniquet. Just after recovery, the animals returned from lateral recumbency to standing, and stumbling was noted for a very short period (about 1-2 minutes) in group II animals. Approximately 70% of lidocaine remains within the tissues of the previously isolated limb following tourniquet release, with the remainder entering the general circulation in the subsequent 45 minutes (TUCKER and BOAS, 1971).

Conclusions

Distal intravenous regional anesthesia (DIVRA) was achieved using lower doses of lidocaine and ketamine as compared to the established IVRA technique, without causing significant adverse effects. This modified IVRA technique may be used only for the management of claw affections of dairy cattle.

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SAŽETAK

Bolesti papaka u goveda mogu se kirurški liječiti pod intravenskom regionalnom anestezijom (IVRA). Za rutinsko uvođenje u IVRA-u postavlja se kružno čvrsti zavoj na metakarpus/metatarzus. U ovom su istraživanju bolesti papaka u goveda liječene modificiranom IVRA metodom. Istražene životinje nasumično su podijeljene u dvije skupine a zavoj kojim se samnjuje doza anestetika postavljen je, umjesto na metakarpus/metatarzus, distalno od rudimentiranih papaka. U skupini I primijenjen je lidokain (2 mg/kg), a u skupini II kombinacija lidokaina i ketamina (2 mg/kg + 1,5 mg/kg). Za uvođenje u distalnu intravensku regionalnu anesteziju (DIVRA) anestetici su aplicirani u aksijalnu digitalnu venu. Srčana frekvencija, frekvencija disanja, sistolički i dijastolički tlak u obje su skupine bili nepromijenjeni. Zasićenost kisikom bila je znakovito niža ($P < 0,05$) između 5. i 60. minute u skupini I te između 15. i 40. minute u skupini II. Vrijeme pojave senzornih i motoričkih blokova bilo je kraće, a vrijeme oporavka tih blokova dulje u životinja u skupini II u usporedbi sa skupinom I. Zaključeno je da je DIVRA, uz upotrebu i samog lidokaina i lidokaina u kombinaciji s ketaminom, prikladna metoda za pregled i obavljanje kirurških zahvata na papcima goveda.

Ključne riječi: distalna IVRA; lidokain; ketamin; goveda

