Egyptian Journal of Veterinary Sciences

https://ejvs.journals.ekb.eg/

Impact of Methanolic Extract of Pomegranate (*Punica granatum* L.) Seeds on Evaluation of Anaesthesia and Analgesia Produced using Lumbosacral Lidocaine, Tramadol and their Combination in Red Sokoto Bucks Undergoing Laparotomy

Abdulkadir Salman Zubairu[1,3], Abubakar Sadiq Yakubu[2], Adamu Abdul Abubakar*[2,3], Alimi Olawale Alimi[1,3], Aliyu Abdullahi[1] and Muhammad Salisu Abubakar[4]

[1]*Department of Veterinary Surgery and Radiology, University of Ilorin, Nigeria.*
[2]*Department of Veterinary Medicine, Collage of Applied Health Sciences, A'Sharqiyah University, Oman.*
[3]*Department of Veterinary Surgery and Radiology, Usmanu Danfodiyo University Sokoto, Nigeria.*
[4]*Department of Veterinary Pathology, Usmanu Danfodiyo University Sokoto, Nigeria.*

Abstract

SMALL RUMINANTS are easily managed for certain surgical procedures; they are less aggressive but cannot endure excessive manipulations without anaesthesia. Complications may arise when ruminants are placed under general anaesthesia, which is why regional anaesthetic techniques are commonly employed. Lidocaine alone does not provide adequate analgesia; therefore, combination with other drugs is frequently utilised to achieve sufficient analgesia. This study aimed to evaluate and compare the analgesic effects of lumbosacral lidocaine, tramadol, and their combination in Red Sokoto bucks. Fifteen (N=15) apparently healthy bucks weighing 10-12 kg were grouped into three (n=5); the lidocaine, tramadol and their combination groups. There was a significant difference in the duration of analgesia provided (p= 0.00218), with the lidocaine group exhibiting a longer duration of action. The combination of lidocaine with tramadol reduced the longer duration observed with lidocaine alone. A significant difference in standing time (p=0.0001) was observed, with tramadol alone having the shortest standing time and lidocaine the longest duration. The lidocaine alone group had the most rapid onset of action (p=0.0002) when compared to the other treatments. All animals in the lidocaine alone and combination groups lost locomotor control and were recumbent, but animals in the tramadol group maintained locomotor function and were not recumbent, despite exhibiting a degree of analgesia. In conclusion, lidocaine alone provides the most effective regional anaesthesia, while the combination of lidocaine with tramadol offers benefits in reducing post-operative patient recumbency time while maintaining quality regional analgesia. Epidural tramadol alone provided inadequate regional anaesthesia.

Keywords: Lumbosacral, Regional anaesthesia, Epidural analgesia, Lidocaine, Tramadol, Red Sokoto bucks.

Introduction

The epidural lumbosacral route is commonly employed for administering analgesic drugs to perform surgical interventions such as dystocia, ruminal impaction, uterine and/or vaginal prolapse, and other hindquarter surgical procedures [1,2], particularly in ruminant species. Numerous complications can arise when ruminants are placed under general anaesthesia, including but not limited to regurgitation of ruminal contents, pulmonary aspiration, and cardiopulmonary depression, depending on the agent used [3,4]. This is why regional anaesthetic techniques are often employed, especially in developing countries where there are fewer facilities for inhalant general anaesthesia and emergencies management drugs. Small ruminants are less aggressive and easier to handle; however, goats in particular cannot tolerate excessive surgical manipulations without anaesthesia [1,5].

*Corresponding authors: Adamu Abdul Abubakar, E-mail: adamu.abubakar@asu.edu.om, Tel.: Oman +96890717725
(Received 20 June 2024, accepted 05 November 2024)
DOI: 10.21608/EJVS.2024.298189.2188
©National Information and Documentation Center (NIDOC)

Local anaesthetic agents act either locally or regionally, and are one of the least frequently used for certain anaesthetic techniques. Most anaesthetic techniques utilising local anaesthetic agents are highly effective, inexpensive, and require minimal technical know-how for their use. Lidocaine as a local anaesthetic, acts as a blockade at voltage-gated sodium channels of neurons [6] and its analgesia is often not adequate for surgical procedures of longer duration greater than 45-60 minutes. Lidocaine is frequently combined with other drugs to achieve analgesia when performing surgeries on small ruminants [7]. Tramadol, a synthetic opioid, can be combined with lidocaine to achieve longer-lasting and more adequate analgesia in certain animal species [8,9]. The practice of inducing local anaesthesia to a surgical site or regions permits comfortable awakening from anaesthesia, thus, creating a sparing effect of other analgesic medications [9,10].

Laparotomy is indicated for many diagnostic and therapeutic purposes; for exploratory, diagnostic and curative purposes in both male and female animals [11,12]. We hypothesised that epidural administration of lidocaine and tramadol combination could have sufficient and longer analgesia greater than lidocaine alone and tramadol alone in goats. The study aims to evaluate and compare regional analgesic effects and their quality using lumbosacral lidocaine, tramadol and their combination in Red Sokoto bucks undergoing laparotomy.

Material and Methods

Experimental animals and ethical approval

This research work was carried out meticulously with standards by the Faculty Animal Research Ethics Committee of the Faculty of Veterinary Medicine, Usmanu Danfodiyo University Sokoto, Nigeria with approval number UDUS/FAREC/2019/AUP-R0-16. Furthermore, the study was carried out in compliance with the ARRIVE guidelines.

Fifteen (N=15) apparently healthy adult bucks weighing 10-12 kg were randomly grouped into three (n=5); lidocaine alone group, tramadol alone group and the combination of lidocaine and tramadol groups. The experimental animals were housed in a comfortable, germ-free ruminant pen with a normal light to dark cycle and acclimatised for two weeks, during which they received prophylactic treatment, comprising anthelmintic and antibiotics. They were provided water and fed a commercial diet concentrate with hay supplementation *ad libitum*. Feed and water were withdrawn prior to commencement of the epidural administration of the drugs, in accordance with the standard procedure described by [3, 13].

Epidural administration of anaesthetics

Each animal was placed in sternal recumbency with moderate physical restraint, and the lumbosacral area was located as described by [1,14,15]. The hair around the epidural injection site was clipped and prepared aseptically using chlorhexidine solution 0.3 m/v (Purit® Saro LifeCare Ltd, Apapa, Nigeria) and methyl-alcohol 70% (La Onyx® Samstella Pharm. Abule Oba, Nigeria) was used for final scrubbing of the site for epidural administration of these anaesthetic agents as shown in plates 1 and 2 respectively.

Lidocaine (Lignolab® 20mg/mL; Laborate Pharm. India) at a dose of 4 mg/kg was administered in animals in the lidocaine alone group (A). Tramadol (Pauco Tramadol® 100mg/2ml. Kwality Pharm. Amritsar, India) was administered at 3 mg/kg in tramadole alone group (B). A combination of lidocaine and tramadol was administered at 4 mg/kg and 3 mg/kg respectively in group (C). Drug administrations were performed slowly over a period of approximately 30 seconds according to a standard procedure described by [9,14].

Determination of depth of regional analgesia

The regional analgesia depth was determined by application of haemostatic forceps closed to the first ratchet at the interdigital space, perineal area and then cranially towards the thoracic region until response was observed as described by [7] this was performed to ascertain that there was no pain before commencement of exploratory laparotomy. The laparotomy procedure was performed according to standard procedure described by [12, 13]as shown in plates 3, 4 and 5, respectively.

Response to painful stimulus was ascertained by the buck's movement of head and neck towards the stimulus and attempt to kick using limbs; once this occurred, the source of mechanical stimulus was removed.

Assessment of anaesthetic and analgesic qualities

The following anaesthetic qualities were monitored and recorded during this experiment:

Onset of analgesia: this is the time interval (in minutes) between the administration of the anaesthetic agent to the disappearance of the pedal reflex.

Duration of analgesia: this is the time interval (in minutes) between the disappearance and return of the pedal reflex.

Standing time: this is the time interval (in minutes) between assumption of the sternal position and the ability of the buck to stand.

Vocalisation: this was evaluated and recorded to further ascertain the presence of pain in these animals while laparotomy is being carried out as described by [16], using the following scoring criteria; 0 = None (no vocalisation), 1 = Vocalising when touched, 2 = Intermittent vocalisation and 3 = Continuous vocalisation throughout the surgical procedure.

Ataxia; ataxia was noted, recorded and scored post administration when the onset of anaesthesia was established in each buck before being taken to the surgical table. A scale of 0 to 3 (16) was used for this study: 0 = Normal (walking without staggering), 1 = Mild (slightly staggering, easily able to walk), 2 = Moderate (markedly staggering, walking but very ataxic) and 3 = Severe (recumbent). All measurements and recordings were conducted at five-minute intervals until full recovery from the anaesthesia effect.

Data analysis

The generated data were tested for normality by constructing frequency histograms of the data series. All parametric, normally distributed data were expressed as mean ± SD and compared both for differences within and between treatments using repeated measures ANOVA and Tukey's test as post-hoc. Data generated from ataxia and vocalisation scores were expressed as median (minimum-to-maximum), Kruskal-Wallis test was used for the comparison of the data. All statistical analysis was performed using InVivoStat software version 4.2.0, and $p < 0.05$ was deemed significant.

Results

The onset of action, duration of action and standing time of all the treatment groups; lidocaine alone, tramadol alone and their combination is respectively presented in Table 1.

For the onset of action, there was a significant difference among the three groups (p=0.0002), with lidocaine alone exhibiting the most rapid onset,followed by the combination of lidocaine and tramadol. On Tukey's test, significant difference was observed between lidocaine alone groups and tramadol alone group, and between tramadol alone groups and the combination of the drugs (p=0.0002 and 0.0021) respectively. However, there was no significant difference observed between the lidocaine alone group and the combination of the drugs (p=0.2745).

Lidocaine alone appeared to have a longer duration of pain suppression when compared to tramadol and their combination. A significant difference was noted in the duration of action among the three groups (p=0.0218). Tukey's test performed showed significant difference between lidocaine alone groups with combination group (p=0.0176) but no significant differences were observed between lidocaine alone groups with tramadol alone group, there was also no significant difference observed between tramadol alone group with group treated with the combination (p=0.1715 and 0.4120) respectively.

There was significant difference in standing time among the three groups (p=0.0001) as tramadol was noted to have the shortest standing time and lidocaine alone with the longest duration. On Tukey's test, significant difference was seen between lidocaine alone groups with tramadol alone group. Equally, the lidocaine alone group and the combination group exhibited a significant difference (p= 0.0001 and 0.0001) respectively; however, no significant difference was observed between the tramadol alone groups and the combination group (p=0.1995).

The median ataxia score following epidural administration of the drugs is: in the lidocaine alone group [3.00 (3.00-3.00)], the tramadol alone group [1.00 (0.00-1.00)] and the combination group [3.00 (2.00-3.00)]. On the Kruskal-Wallis test, a statistical significance of p=0.0028 was observed, signifying great variation in the ataxia or mobility of the experimental animals after epidural drug administration.

The result of Vocalisation intra-operatively was presented in median (min-max), the lidocaine alone group [Lidocaine, 1.00 (1.00-3.00)], the tramadol alone group [Tramadol, 1.00 (1.00-2.00)] and the combination group [Lidocaine-Tramadol combination, 1.00 (1.00-1.00)]. The combination of lidocaine and tramadol had a lower vocalisation score when compared to the other groups as shown

in Figure 1. On the Kruskal-Wallis test, there was no significant difference among the three groups (p=0.282).

Discussions

In all the animals, the onset of action of regional analgesia was confirmed by the absence of sensation to application of Allis tissue forceps closed to the first ratchet at the interdigital web, perineal area and more cranially in the abdominal region. All animals in the lidocaine and the combination groups lost locomotor control and were recumbent, but the tramadol group had locomotor function and were not recumbent. The bucks in the tramadol groups were able to maintain standing and walking, even though there was a decrease regional pain perception around the affected area. The activities of local anaesthetics often affect both sensory and motor nerve fibres (2, 15) resulting in recumbency, this was evident as observed in the lidocaine alone and in the lidocaine-tramadol combination group as seen in this study.

Onset of action was faster in the lidocaine alone group (3.00 ± 0.71 min) than in the combination of both lidocaine and tramadol anaesthetic agents (4.60 ± 2.07 min) but was longer in the tramadol alone group (9.00 ± 1.58 min). These variations observed in the onset of action may be attributed to the penetrating ability of these anaesthetic agents into the nerve trunk and also their peak concentration which varies inversely with the size of the nerve trunk involved as stated by (16, 17). The findings of this study concur with the results of 18,19,20, 21) who also reported quicker onset of action in goats and other animals with lidocaine administration, and also the study of (19) conducted on the lamb revealed faster analgesic onset with lidocaine administration and that of (17) in a rabbits model undergoing knee surgery. This finding indicates that the use of tramadol alone as an epidural anaesthetic will not provide sufficiently rapid analgesia to commence surgery, especially in cases requiring immediate intervention. However, a combination with lidocaine has a relatively quicker onset, but lower than that of lidocaine alone. The slight delay in onset of action observed in the combination of lidocaine and tramadol group signifies its pre-emptive analgesic significance in bucks undergoing laparotomy procedure. The delay in analgesic onset may also suggest that tramadol acts competitively with lidocaine, thereby decreasing the local bioavailability of the lidocaine when combined together.

The duration of action of the lidocaine alone group was longer (55.60 ± 7.23 min) when compared to the tramadol alone group (46.80 ± 5.89 min) while their combination had the least duration of action (40.80 ± 8.25 min). With this finding, the sole advantage of the combination of lidocaine and tramadol over the use of lidocaine alone and tramadol alone is in the management of dystocia where caesarean section is to be performed, and the dam is expected to ambulate and nurse the neonate without a prolonged duration of recumbency. The combination of the two agents was observed to have the shortest duration, as reported by another study by (22,23) in dogs and sheep. Local anaesthetics such as lidocaine have sympathetic blockade activity resulting in vasodilation effect, thereby decreasing duration of analgesia (23), this could be the reason for antagonistic effect we observed in this study rather than synergism that was hypothesised. Contrary to longer duration of analgesia reported for the combination of the two agents in West African dwarf sheep reported by (23), in the water buffalo reported by (24), in donkeys reported by (25) and in camel as reported by (26). Perhaps, this could be the result of using lidocaine containing adrenaline for their studies, as well as possible breed and species differences. This finding suggests that the use of non-plain lidocaine may unnecessarily prolong the duration of recumbency and result in unwanted effects such as tympany, frothy bloat, regurgitation of ruminal content and aspiration pneumonia in ruminant species.

The standing time of lidocaine was longer in the lidocaine alone group (11.20 ± 2.39 min) compared with their combination (2.20 ± 1.09 min) while the tramadol alone group had the least standing time (0.40 ± 0.55 min). The combination of lidocaine and tramadol appeared to have merit over the use of lidocaine alone, as a reduced standing time was observed, which may help to reduce post-laparotomy monitoring time and possible ruminal bloating due to prolonged recumbency. Longer standing time of tramadol was also reported in another study by (21) in goats, but contrary to (23) in a study conducted using West African dwarf sheep, where a longer standing time for the combination of the two agents was reported, owing to the use of lidocaine containing adrenaline for their study, and also possible species difference might be the reason for the longer standing time that was recorded.

In this study, the ataxia score in the lidocaine alone group was 3 (severe) and all animals were

recumbent, while the tramadol-alone group only had mild ataxia (score of 1); that is, slight staggering was noticed but no recumbency. In the group with the combination of lidocaine and tramadol, three animals were recumbent (ataxia score of 3) and the remaining had marked staggering, that is, very ataxic (ataxia score of 2). Ataxia is anticipated following epidural administration of lidocaine, as the agent blocks both sensory and motor fibres. This study was not in agreement with (25) who observed that donkeys injected with lidocaine-tramadol combination were more ataxic compared to lidocaine alone but agrees with study of (25) performed on donkey and (9) who reported that there was severe ataxia in goats treated epidurally with lidocaine alone, mild ataxia in lidocaine-tramadol combination and no ataxia in goats treated with tramadol alone. Vullo et al. (27) also reported marked ataxia in a tom cat under epidural lidocaine-tramadol undergoing orchidectomy.

One limitation of this study is the inability to correlate the analgesic parameters with haematological and serum biochemical parameters to establish if the analgesia produced has any effect on the haemato-biochemical indices. The reason for this is that most of the blood samples collected were unsuitable for haemato-biochemical analysis, as only a few samples were successfully processed but wereinadequate for data analysis. Our future research will aim to focus on haemato-biochemical analysis and other vital parameters to strengthen the findings of this research.

Conclusion

In conclusion, lumbosacral administration of lidocaine alone at 4mg/kg induced superior regional anaesthesia and analgesia compared to tramadol alone and combination of the two agents. Lidocaine alone proved more effective in providing quality regional analgesia in Red Sokoto bucks compared to tramadol alone and the combination of lidocaine and tramadol. Meanwhile, vocalisation was more pronounced with lidocaine alone and least with its combination with tramadol, suggesting a deeper analgesia. It can be recommended that the use of epidural lidocaine alone and/or its combination with tramadol at the reported dose rates is safe for apparently healthy Red Sokoto bucks when undertaking laparotomy procedures.

Acknowledgements

We acknowledge Prof. Alhaji Aminu Muhammad, the Director of Veterinary Teaching Hospital, Usmanu Danfodiyo University Sokoto and Mr. Abdulmalik Shuaibu Bello for their efforts towards the success of this research.

Funding statement

This research study was not funded.

Conflicts of interest

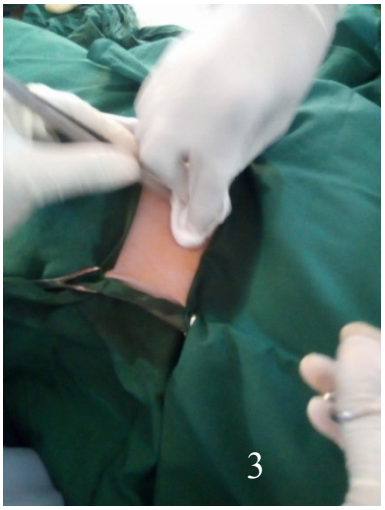
There are no conflicts of interest among the authors.

TABLE 1. The onset of action, duration of action and the lidocaine alone, tramadol and their combination administered epidurally to bucks

Parameter	A	B	C	P-value
Onset of Action (min)	3.00 ± 0.71^{a}	$9.00 \pm 1.58^{a, b}$	4.60 ± 2.07^{b}	0.0002
Duration of Action (min)	55.60 ± 7.23^{c}	46.80 ± 5.89	40.80 ± 8.25^{c}	0.0218
Standing Time (min)	$11.20 \pm 2.39^{d, e}$	0.40 ± 0.55^{d}	2.20 ± 1.09^{e}	0.0001

[a, b, c, d, e] Means ± SD with same superscript letters in the same row are significantly different at $p < 0.05$ (1-way ANOVA)

Plates 1 and 2: Advancing a hypodermic needle and injecting the agent into the epidural space



Plates 3, 4 and 5: Final scrubbing, skin incision and skin closure with Ford interlocking suture pattern respectively.

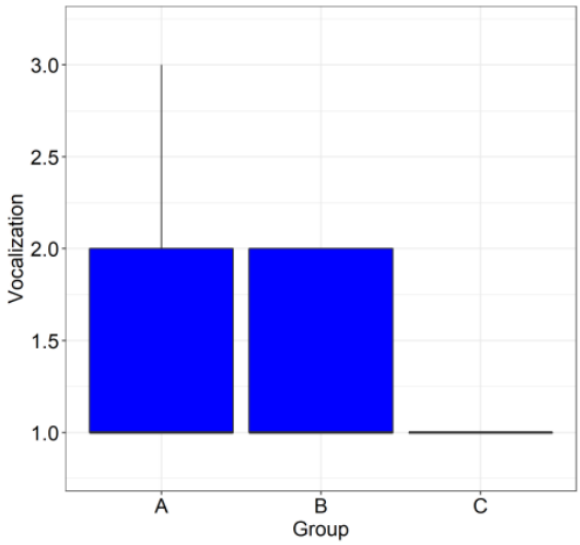


Fig. 1. Vocalisation score following lumbosacral epidural administration of lidocaine, tramadol and their combination in Red Sokoto bucks.

References

1. Ismail, Z. B. Epidural Analgesia in Sheep and Goats: A Review of Recent Literature. *Bulletin of University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca. Horticulture*, **73**(2), 197-202 (2016)
2. Shamsudeen, S., Idris, S. B., Abubakar, A. A. and Abubakar, M. M. Potentiating the Epidural Analgesic Effect of Lidocaine in Uda Sheep with Xylazine and Medetomidine. *Journal of Applied Veterinary Sciences*, **9**(2), 125-133 (2024). doi.org/10.21608/javs.2 024.275091.1323
3. Abubakar, A. A., David, G., Yakubu, A. S., Lawal, F. M. and Mamman Mustapha, O. Lumbosacral Epidural Analgesia with Ketamine Alone or in Combination with Xylazine in Dogs. *International Journal of Veterinary Science,* **4**(3), 111-117 (2015)
4. Zayed, M., Mahmoud, E., Khalil, A., Salah, M., Moustafa, M., Youssef, M. and Hassaneen, A. Lumbosacral injection of lidocaine, detomidine and lidocaine–detomidine in goats: anti-nociceptive effects and changes on haematobiochemical parameters. *Journal of Applied Animal Research*, **48**(1), 57-62 (2020)
5. Oguntoye, C.O., Olaifa, A.K., Olaifa, O.S. and Ayoade, O.E. Pentazocine As Adjuvant To Lidocaine Epidural Anaesthesia In Goats. *Nigerian Veterinary Journal*, **44**(4), 23-34. (2023). https://dx.doi.org/10.4314/nvj.v44i4.3
6. Tranquilli, W. J., Thurmon, J. C. and Grimm, K. A. *Lumb and Jones' Veterinary Anesthesia and Analgesia* (4th Edition). Blackwell Publishing, USA. Pp. 105-125 (2007)
7. Bigham, A., Habibian, D. and Ghasemian, F. Caudal epidural injection of lidocaine, tramadol, and lidocaine-tramadol for epidural anaesthesia in cattle. *Journal for Veterinary Pharmacology and Theriogenology*, **33**, 439-443 (2010)
8. Cassuto, J., Sinclair, R. and Bonderovic, M. Anti-inflammatory properties of local anaesthetics and their present and potential clinical implications. *Acta Anaestheesiol Scand*., **50**(3), 265-268 (2006).
9. Dehkordi, S. H., Bigham-sadegh, A. and Gerami, R. Evaluation of anti-nociceptive effect of epidural tramadol, tramadol-lidocaine and lidocaine in goats. *Veterinary Anaesthesia and Analgesia*, **39**(1), 106-110 (2012)
10. Cohen, S., Foss, E., Beths, T. and Musk, G.C. An Exploration of Analgesia Options for Australian Sheep. *Animals*, **14**(7), 990 (2024). https://doi.org/10.3390/ani14070990
11. Dreher, R. (2019). Development of Laparotomy as an Animal Model for Post-Operative Pain Enhancement by Morphine. University of Colorado Boulder. Master's degree thesis.
12. Acorda, J. A. and Cadoy, J. M. Surgical Analgesia, Physiological Responses and Cortisol Level in Goats Subjected to Exploratory Laparotomy under Distal Paravertebral Nerve Block, Conventional Needle Acupuncture and Aquapuncture. *Dairy and Veterinary Science Journal*, **5**(3), 1-7 (2018)
13. Abubakar, A. A., Andeshi, R. A., Yakubu, A. S., Lawal, F. M. and Adamu, U. Comparative Evaluation of Midventral and Flank Laparotomy Approaches in Goat. *Hindawi Journal of Veterinary Medicine,* **2014**, 1-7 (2014)
14. Lemke, K. A. Understanding the pathophysiology of perioperative pain. *Canadian Veterinary Journal*, **45**, 405-413 (2004)
15. Al-Ali, F.T., Almubarak, A.I., Marzok, M., El-Deeb, W.M. and El-Hawari, S.F. Evaluation of the anti-nociceptive effect of lidocaine-tramadol and lidocaine-medetomidine lumbosacral epidural anaesthesia: A cross-over comparative study in goats. *German Journal of Veterinary Research*, **3** (4), 20-24. (2023). https: //doi.org/10.51585/gjvr.2023.4.0066
16. Hendrickson, D. A. and Baird, A. N. *Turner and McIlwraith's Techniques in Large Animal Surgery* (4th Edition). Wiley-BlackWell, USA. Pp. 50-80 (2013)
17. Salem, M., Rizk, A., Mosbah, E., Zaghloul, A., Karrouf, G. and Abass, M. Antinociceptive effect of lidocaine, tramadol, and their combination for lumbosacral epidural analgesia in rabbits undergoing experimental knee surgery. *BMC Veterinary Research*, **18**(1), 252 (2022).
18. Mckune, C. M., Pascoe, P. J., Lascelles, B. D. X. and Kass, P. H. The challenge of evaluating pain and a pre-incisional local anaesthetic block. *Peer J.,* **10**(2), e341(2014). doi: 10.7717/peerj.341
19. Grubb, T. L., Riebold, T. W., Crisman, R. O. and Lamb, L. D. Comparison of lidocaine, xylazine, and lidocaine-xylazine for caudal epidural analgesia in cattle. *Veterinary Anaesthesia and Analgesia*, **29**, 64-68 (2002).
20. Torske, K. E. and Dyson, D. H. Epidural Analgesia and Anesthesia. *The Veterinary Clinics of North America: Small Animal Practice*, **30**(4), 859-874 (2000).
21. Ajadi, R. A., Owanikin, A. O., Martins, M. M. and Gazal, O. S. Effect of epidural tramadol and lignocaine on physiological and behavioural changes in goats subjected to castration with a high tension band. *New Zealand Veterinary Journal*, **60**(6), 344-384 (2012)

22. Go'mez de Segura I. A, Vasquez, I. and De Miguel, E. Antinociceptive and motor-blocking action of epidurally administered IQB-9302 and bupivacaine in the dog. *Regional Anesthesia Pain Med*., **25**, 522-528 (2000).

23. Ajadi, R. A., Sobanke, O. A., Adeniyi, A. A., Adeusi, A. A., Adebiyi, A. and Akinloye, A. K. Influence of Tramadol on Anaesthetic Indices and Physiological Parameters of Epidural Lignocaine in West African Dwarf Sheep Undergoing Laparo-Ovariectomy. *Nigerian Journal Physiological Sciences*, **32**, 165-170 (2017)

24. Ayman, A., Alan, G., Naglaa, G., Tarek, K. and Mustafa, S. Evaluation of analgesic effect of caudal epidural tramadol, tramadol-lignocaine and lignocaine in water buffalo (Bubalus bubalis). *Veterinary Medicine International*, **2015**, 1-6 (2015).

25. Marzok, M. A. and El-khodery, S. A. Comparative analgesic and sedative effects of tramadol, tramadol-lidocaine and lidocaine for caudal epidural analgesia in donkeys (Equus asinus). *Veterinary Anaesthesia and Analgesia*, **42**, 215-219 (2015).

26. Azari, O., Molaei, M. and Ehsani, A. Caudal epidural analgesia using lidocaine alone or combination with ketamine in dromedary camels (Camelus dromedarius). *Journal of South African Veterinary Association*, **85**, 1-4 (2014).

27. Vullo, C., Falcone, A., Marino, G., Monti, S., Tambella, A. M., Bufalari, A. and Catone, G. Comparison between the effects of epidural lidocaine, tramadol, and lidocaine–tramadol on postoperative pain in cats undergoing elective orchiectomy. *Acta Veterinary Scandinavia,* **65**, 33 (2023). https://doi.org/10.1186/s13028-023-00696-9