RESEARCH ARTICLE

IJVAR *International Journal of Veterinary and Animal Research*
E-ISSN: 2651-3609 6(3): 77-82, 2023
DOI: 10.5281/zenodo.10440091

Comparison of The Efficacy of Intratesticular Lidocaine and Bupivacaine During Castration in Cats

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Received: December 29, 2022
Accepted: November 18, 2023

Abstract

In this study, it was aimed to evaluate the effectiveness of intratesticularly administered lidocaine and bupivacaine in castration in cats. 20 cats were divided into two groups regardless of breed and age. 80 microgram/kg medetomidine injection was administered for sedation. 4 mg/kg lidocaine or 1 mg/kg bupivacaine were injected intratesticularly in lidocaine and bupivacaine groups respectively. Castration was performed with routine methods. The reactions of the animals to the incision and the extraction of the funiculus spermaticus were recorded. After the operation, the animals were awakened by atipamezole. The pulse rate, respiratory rate and pain scores were evaluated for 6 hours at half-hour intervals. UNESP-Botucatu cat pain scale, Grimace cat pain scale and Glasgow cat pain scale were used to evaluate pain scores. A statistically significant difference was found between the groups in Grimace and Glasgow pain scores at the 150th min. and 180th min. postoperative evaluations ($p<0.05$). A statistically significant difference was found between the groups in Botucatu pain score at the 60th, 90th, 150th, 180th, 300th and 330th min. ($p<0.05$). No statistically significant difference was found in the pulse and respiration values ($p>0.05$). As a result, it was determined that bupivacaine should be preferred to lidocaine for long-lasting surgical procedures and postoperative analgesia due to its long duration of action.

Keywords: Analgesia, bupivacaine, castration, cat, lidocaine.

INTRODUCTION

In order to prevent uncontrolled pregnancies and inconvenient reproductive behaviors such as escaping from home, irritability, shouting, and marking with urine, can be eliminated by neutering cats (Baran et al., 2016).

General anesthesia and regional (local) anesthesia are used to create anesthesia in companian animals (Topal, 2005). Local anesthetics are the only class of drugs that can completely block nociceptive impulses from reaching the cerebral cortex, and therefore represent the only way to completely prevent the patient from perceiving a nociceptive stimulus (Barletta and Reed, 2019).

Lidocaine is the most widely used local anesthetic. It has excellent therapeutic uactivity, fast action (5-10 min.), and is suitable for almost every clinical use (Vardanyan and Hrub, 2006; Barletta and Reed, 2019; Grubb and Lobprise; 2020a). The approximate duration of action of lidocaine without epinephrine is 30 to 60 minutes. Besides its use as a local and topical anesthetic agent, lidocaine treats all ventricular arrhythmias, mainly ventricular tachycardia, and ventricular premature complexes (Grubb and Lobprise, 2020a). Conditions affecting the central nervous system such as nervousness, agitation, depression, lethargy, and convulsions may occur due to lidocaine administration (Grubb and Lobprise, 2020a).

Bupivacaine is another local anesthetic drugs used in small animal medicine. It blocks the formation and transmission of nerve impulses by blocking the Na+ channels in the nerve membrane (Grubb and Lobprise 2020a). The onset of action of bupivacaine is slower than lidocaine (20 minutes), but it is long-acting (6-8 hours) and is more potent than other local anesthetics (Papich, 2020). Bupivacaine can be used for both local and epidural analgesia/anesthesia. Side effects after local infiltration are rare. Signs of toxicity in cats include bradycardia, arrhythmias, tremors, muscle twitches, and seizures. (Vardanyan and Hrub, 2006; Papich, 2020; Grubb and Lobprise, 2020a).

Pain negatively affects the health and well-being of animals, so pain management should always be part of the postoperative treatment (Mathews et al., 2014; Grubb et al., 2020a). When postoperative pain cannot be prevented, it causes complications such as lactic acidosis, increased protein catabolism, gastrointestinal ileus, decreased or complete cessation of food intake, delayed wound healing and prolonged hospitalization. Cardiovascular, pulmonary, gastrointestinal, urinary, and metabolic changes occur due to the operation and the postoperative discomfort (Duncan and Lascelles, 2007; Epstein et al., 2015).

As animals cannot express themselves verbally, pain assessment is difficult especially for cats and requires good observation (Johnson et al., 1993; Mathews, 2000; Pekcan, 2005). Pain assessment scales can be used for this purpose; some of these are UNESP-Botucatu cat pain scale, Glasgow composite pain scale and Grimace cat pain scale (Steagall and Monteiro, 2020).

This study is aimed to comparatively evaluate the

Cite this article as: Tan B, Elma E, Pekcan Z. 2023. Comparison of The Efficacy of Intratesticular Lidocaine and Bupivacaine During Castration in Cats. International Journal of Veterinary and Animal Research, 6(3): 77-82. *DOI: 10.5281/zenodo.10440091*

effectiveness of intratesticular administered lidocaine and bupivacaine for the prevention of postoperative pain before castration operation in cats.

MATERIALS AND METHODS

Animal Material and Creation of Groups

Twenty adult male cats admitted for elective orchietomy at the Kirikkale University Faculty of Veterinary Medicine Department of Surgery were studied. Each animal was randomly assigned to one of two groups of ten. They were considered to be healthy based on physical and haematological examination. Animal owners were informed about the operation to be performed. All procedures were carried out with the permission of the Kirikkale University Animal Experiments Local Ethics Committee, dated 13.12.2022, and numbered E.40905.

Preparation for Operation

All cats were fasted at least 6 hours and water was withheld for 2 h prior to anesthesia**.** The cats were allowed to rest for at least one hour in order to calm down, enable them to adapt to the environment, and the researcher observe temperament-behavior of the cats before the operation. 20 mg/kg ampicillin (Vilamoks-LA, Vilsan) were administered once to prevent infection presurgically. In order to provide premedication, 80 microgram/kg (0.08 ml/kg) intramuscular (IM) medetomidine (Tomidin 10 ml, ProVet) was administered to all cats in the study. After the cats sedated, 4 mg/kg lidocaine without adrenaline (Jetokaine simplex 20 mg/ml, Adeka) or 1 mg/kg bupivacaine was injected intratesticularly to the lidocaine or bupivacaine (Marcaine 0.5%, Aspen) groups, respectively (Grubb and Lobprise, 2020a). A 22 gauge needle was inserted into the center of the testicles with the tip of the needle pointed toward the spermatic cord, half the the calculated dose was injected into each testicle. In both groups, some of the local anesthetics were left subdermally while exiting the testis to provide anesthesia of the skin. While waiting for the time required for the local anesthetic to take effect 15 minutes for lidocaine group and 30 minutes for bupivacaine group, the cats were routinely prepared for the operation.

Surgical Procedure

The open prescrotal castration method was preferred as the surgical procedure. During castration the responses of the animals to the incision retraction of the incision and funiculus spermaticus were recorded. After the end of the operation atipamezole (Reversal 10 ml, ProVet) was administered to antagonize the sedative effect of the medetomidine and pain scale evaluations were started. Pain was evaluted and recorded postoperative 6 hours by the same person (BT). 0.2 mg/kg meloxicam was administered after 6 hours and cats were discharged with the owner postoperative instruction forms.

Pain Scale and Measurement of Vital Functions

The heart rate and respiratory rate of all cats were measured and recorded before the operation. During the operation, the reactions to the incision and the extraction of the funiculus spermaticus were recorded. In the study, pain assessments were made using the UNESP-Botucatu cat pain scale, Grimase cat pain scale and Glasgow cat pain scale in order to obtain concrete data in determining the degree of pain at 0th, 30th, 60th, 90th, 120th, 150th, 180th, 210th, 240th, 270th, 300th, and 330th minutes in the postoperative period. Facial expressions, heart and respiratory rates were recorded to evaluate pain related physiological effects simultaneously (Figure 1, 2 and 3).

Figure 1. Ears forward, eyes open, mouth and mustache in a relaxed position and head above the shoulder line.

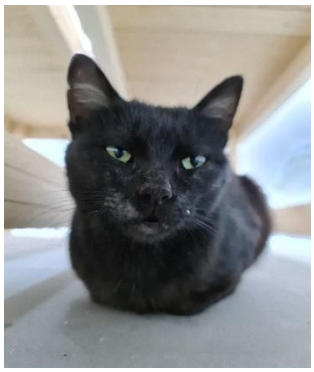

Figure 2. Ears slightly separated from each other, eyes half open, mouth position slightly tense, mustache position slightly curled or straightened, head in line with the shoulder line.

Figure 3. Ears outward, eyes closed, mouth stance taut, mustache stance straightened, head below shoulder line or slanted downwards.

Statistical analysis

In the study, the "Mann-Whitney U test" was used to compare groups at the same time, and the Friedmann test was used to compare different time periods in the same group. $p < 0.05$ was considered significant.

RESULTS

During incision increase in heart rate and movement of the hind legs recorded in two (L7 and L10) and three (B4, B8, and B10) cats in the lidocaine and bupivacaine group, respectively. One cat (B10) had a reaction to the

withdrawal of the funiculus spermaticus. Since the heart rates of these patients were recorded within the reference values, no other general anesthetic was added.

According to the results of the statistical analysis of the data; In the lidocaine group, changes in respiration and pulse over time were not significant in Grimace pain score, Glasgow pain score and Botucatu pain score ($p>0.05$). In the bupivacaine group, there were no significant changes in respiration and heart rate over time in the Grimace pain score, Glasgow pain score, and Botucatu pain score ($p>0.05$).

Table 1 and Table 2 show the time-dependent changes in respiration and pulse rate of cats treated with lidocaine and bupivacaine.

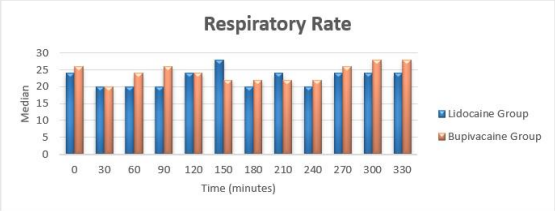

Table 1. Time-dependent variation of respiratory rate in cats treated with lidocaine and bupivacaine.

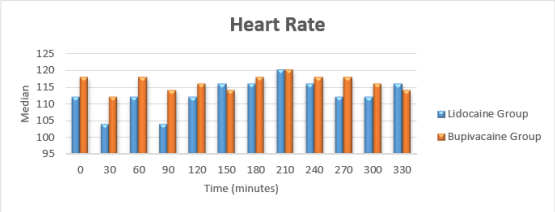

Table 2. Time-dependent variation of heart rate in cats treated with lidocaine and bupivacaine

In the intergroup comparisons, the Grimace pain score was recorded as 3 in the lidocaine group and 0.5 in the bupivacaine group at the 150th minute, and the median pain score was 2 in the lidocaine group at the 180th minute and 0 in the bupivacaine group. The pain score of the lidocaine group was higher than the bupivacaine group, and the difference was statistically significant ($p<0.05$) at 150th and 180th min. The median pain score of the lidocaine group was 3, while the median pain score of the bupivacaine group was 1 in the Glasgow pain score at the 150th and 180th minutes. It was determined that the pain score of the lidocaine group was higher than the bupivacaine group, and the difference was statistically significant ($p<0.05$) (Table 3 and 4).

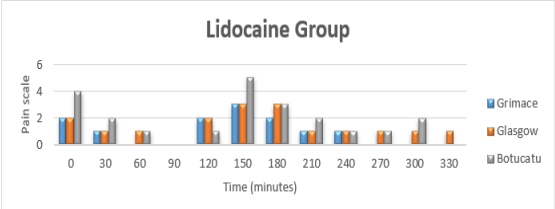

Table 3. Postoperative median pain scale values of cats treated with lidocaine

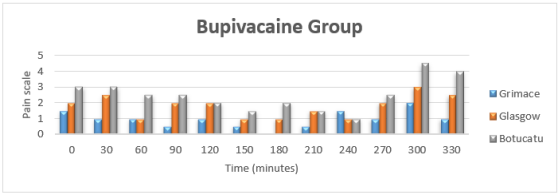

Table 4. Postoperative median pain scale values of cats administered bupivacaine.

The Botucatu pain scores at 60th, 90th, 300th, and 330th minutes, the medians were recorded as 1, 0, 2, 0 in the lidocaine group, and 2.5, 2.5, 4.5, and 4 in the bupivacaine group, respectively, and the pain score of the lidocaine group was lower than the bupivacaine group. The median scores of the lidocaine group were 5 and 3, respectively, and were 1.5 and 2 in the bupivacaine group, respectively. According to the pain scores at the 150th and 180th minutes, the bupivacaine group was found to be lower than that of the lidocaine group, and the difference was statistically significant ($p<0.05$) (Table 3 and 4).

Butorphanol was administered during postoperative period in three cats (L1, L5, and L10) in the lidocaine group and two cats (B6 and B10) in the bupivacaine group because of high pain scores and excluded from the study.

DISCUSSION AND CONCLUSION

In order to prevent uncontrolled reproduction and zoonotic diseases, as well as to prevent unwanted escape and urine marking in domestic cats, sterilization is frequently recommended. It is one of the most frequently performed operations in veterinary medicine. For the better surgical and postoperative period, researchers are still searching for better anesthetic combinations (Baran et al., 2016; Höglund et al., 2018).

Pain negatively affects recovery by causing stress in animals. Pain relief is important not only biologically and physiologically, but also ethically (Duncan and Lascelles, 2007; Gultekin, 2012). Pain can be prevented by several drugs like nonsteroidal antiinflamatory drugs, opioids, N-methyl-D-aspartat antagonists. Since the side effects of analgesics used in some animals are avoided, it has been suggested to use local anesthetics with fewer side effects instead (Barletta and Reed, 2019; Grubb and Lobprise 2020a). The aim of this study was to popularize the use of local anesthetics, which do not have many systemic side effects, for castration in cats.

Local anesthetic drugs like lidocaine and bupivacaine are one of the anesthetic drugs used for local blockage of motoric and sensoric function. It has been reported that high doses of lidocaine (toxic dose 8 mg/kg) and bupivacaine (toxic dose 5 mg/kg) cause complications such as ataxia, nystagmus, depression, seizures, bradycardia, hypotension and cardiovascular collapse (Barletta and Reed, 2019; Grubb and Lobprise, 2020a; Papich, 2020). In line with the drugs used in this study, no complications (respiratory arrest, cardiac arrest, death, etc.) or high-dose side effects occurred in any animal.

Evaluation of pain in animals can be difficult due to the inability to communicate verbally and the observers' lack of training and experience. In addition, animals may show different individual responses and behavior patterns to painful stimuli. While some animals show very severe pain symptoms for similar procedures, some may not (Mathews et al., 2000; Ansah et al., 2002; Pekcan, 2005; Gultekin, 2012). In this study, it was determined that 3 cats

in the lidocaine group and 2 cats in the bupivacaine group showed severe pain symptoms in the postoperative period, butorphanol was administered as a rescue analgesic and they were excluded from the study. This indicates that pain is an individual perception.

While assessing pain, it can be interpreted and evaluated differently by different observers. (Mathews, 2000; Dobromylskyj, 2001a). In an analgesia study conducted with 50 dogs, 3 different scoring systems were used by different observers and differences were observed in pain scores within the same hour (Holton et al., 1998; Pekcan, 2005). This creates difficulties in pain studies. In this study, scale interpretation was made by the same observer in 20 cats so interobserver differences were eliminated.

In most of the pain scales, the changes in behaviours while feeling pain are scored numerically and the total values are obtained from the pain scores (Mathews et al., 2014; Epstein et al., 2015;). There are no gold standard acute or chronic pain scoring systems for use in animals, but several scoring methods have become widely used around the world. All of these scales are largely based on analyzing behaviors (Holton, 1998; Steagall and Monteiro, 2019). In this study, the Botucatu cat pain scale, Grimace pain scale and Glasgow pain scales were used together to obtain accurate results. Each scale has both common and different components. Pain is more difficult to interpret in cats compared to dogs, so three scales were evaluated together. Arterial blood pressure assessment in the Botucatu pain scale could not be performed in some animals for technical reasons, although usage of the Botucatu scale was effective in determining and interpreting the presence of pain in cats, it was found not practical. Interpretation of the Glasgow cat pain scale was determined to be more practical in terms of its components and ease of application.

The average heart rate in cats is 110-140/minute (Fraser et al., 1991). Physiological parameters such as pulse, respiratory rate, and body temperature can be important indicators in terms of the presence and severity of pain. Even if a 20% change in physiological values is interpreted as the presence of pain, some other factors such as stress, fear, activity, anesthetic drug and other drugs can affect these physiological parameters (Pekcan, 2005). While other species show obvious symptoms such as vocalization in pain, this may not be the case in cats. Cats can show only postural changes against high-level pain, which creates difficulties during evaluation of pain (Glerum et al., 2001; Höglund et al., 2018; Er, 2019). In this study, there were also difficulties in the evaluation of pain from time to time. However, the pulse values remained within the reference limits during postoperative 6 hours in all cats.

Lidocaine, bupivacaine, and other local anesthetics are often administered to reduce the total dose of the general anesthetic drugs and also to provide some degree of postoperative analgesia. The approximate duration of action of lidocaine without epinephrine is 30 to 60 minutes. With epinephrine, this time can be extended to about 120 to 360 minutes. Bupivacaine has a duration of action of up to 8 hours when combined with epinephrine (Lim et al., 2021). The duration of conduction blockade, which is prolonged by at least 50% with the addition of epinephrine to lidocaine, it does not cause a clinical change in the blockade time when added to bupivacaine (Barletta and Reed, 2019; Grubb and Lobprise, 2020b; Bayram, 2020). Therefore, commercially produced bupivacaine preparations do not contain epinephrine.

The effects of lidocaine on the cardiovascular system are attributed to the blockade of sodium channels, which leads to a reduction in cardiac contractility at a rate proportional to their potential. Unfortunately, although the potency of bupivacaine is four times that of lidocaine, the potential for cardiac toxicity is also greater than that of lidocaine. Therefore, IV administration of lidocaine does not show any signs of toxicity, while IV administration of bupivacaine is contraindicated. Symptoms of toxicity in cats include bradycardia, arrhythmias, tremors, muscle twitches and seizures (Papich, 2020). In this study, in order to avoid any complications related to IV administration, the plunger of the injector was pulled back to prevent mislead IV injection and no cardiovascular complications were encountered.

When both active substances are compared, the onset of action of bupivacaine is four times longer than that of lidocaine, and the duration of action is also longer. This long duration of action is partially explained by the fact that the drug is very lipid soluble (Lim et al., 2021). When the onset times of lidocaine and bupivacaine were compared, it was determined that the operation was started earlier with a faster effect in cats using lidocaine, but when the increased rates and duration of the pain scales were examined, it was revealed that bupivacaine provided analgesia for a longer time.

Prolonging the presence of pain suppresses the immune system, causes the emergence of secondary diseases and delays the healing process by causing loss of appetite and cachexia. Insufficient food intake and loss of appetite cause hepatic lipidosis, especially in cats. (Mathews, 2000). With early postoperative food intake, catabolic protein metabolism is prevented and positive nitrogen balance is achieved. In this study, scale interpretations related to food intake were made in the postoperative period following the awakening of cats. Since the scale evaluations started from the 0th minute, the evaluations were interpreted as the cats' interest in food, and it was observed that the cats participating in the study were interested in food, 3 cats from the lidocaine group and 2 cats from the bupivacaine group were not interested in food.

The duration of anesthesia may be shorter when local anesthetics are applied to highly vascularized areas. It can also lead to direct intravascular injection, which carries the risk of incorrect infiltration technique and systemic toxicity (Lim et al., 2021). Although bupivacaine provides a longer duration of analgesia than lidocaine, some clinicians are more comfortable with lidocaine because the testicles are vascular and have a higher margin of safety if inadvertently injected IV (Grubb and Lobprise, 2020b). No complications were observed in our study. The local anesthetic given to the spermatic cord also moved upwards and relieved the pain caused by the surgical crushing of the cord and related vessels, and it was seen that the removed testes were anatomically larger than normal and haemorrhagic.

General anesthesia produces controlled and reversible loss of consciousness, sedation, analgesia and muscle paralysis however it has some morbidity and mortality side effects. In order to reduce these side effects, local anesthesia applications have recently gain popularity. Staying calm and still during operations is very important for the success rate of surgery. However animals may

become stressed and become active in unfamiliar environments such as the operating room for this reason local anesthesia without sedation is less preferred in veterinary medicine (Mathews, 2000; Grubb et al., 2020a;). In this study, medetomidine was preferred to provide either sedation and prevent the movement during the operation and no side effect was recorded related to the administration of medetomidine. Since our aim was to record postoperative pain after castration in cats, in order to eliminate the analgesic effect of medetomidine it was antagonized at the end of surgery.

Most of the anesthetic agents used in animals do not provide significant intra- and postoperative pain control, as they have little or no analgesic properties. (Lamont, 2008;). Medetomidine, a synthetic drug used both as a surgical anesthetic and analgesic, was preferred to provide preoperative sedation (Topal, 2005; Gultekin, 2012). As medetomidine is not enough for castration, local anesthetics were included in this study, and IV butorphanol was administered to cats whose pain score were higher than the acceptable score.

α2-adrenoceptor agonists, including medetomidine and dexmedetomidine, provide sedation, muscle relaxation and analgesia in cats (Robertson, 2018). The dose of medetomidine has been determined as 0.08 mg/kg (IV) and can be administered IM, IV, or SC. (Sinclair, 2003). With IV administration, medetomidine takes effect in 2 minutes, the sedative effect lasts for an average of 1-2 hours and can increase up to 6 hours depending on the dose given. The duration of the analgesic effect is approximately 1 hour and is shorter than the duration of sedation. The ability to reverse its effects with atipamezole is the major advantage of medetomidine, but this results in the reversal of analgesia in addition to sedation. (Topal, 2005; Çetinaslan and Apaydin, 2008; Robertson, 2018). In this study, the analgesic effect of medetomidine was eliminated by using atipamezole at the end of the operation to evaluate the analgesic efficacy of the applied local anaesthetics.

The onset of action of bupivacaine is 20-30 minutes, the duration of action is in the range of 3-10 hours, the onset of action of lidocaine is 5-10 minutes and the duration of action is in the range of 1-1.5 hours. The addition of epinephrine to lidocaine can extend this time to approximately 120-360 minutes (Lim et al., 2021). In the Botucatu, Grimace and Glasgow pain scales, in which the efficacy of lidocaine was evaluated, an increase in pain scores was detected at the 150th and 180th minutes, which was thought to be due to the shorter duration of action of lidocaine compared to bupivacaine. Likewise, the Botucatu pain score is 60., 90., and 300. It is thought that the increases in pain scores detected at 330 minutes are due to the effect duration of bupivacaine.

As a result, it was determined that lidocaine and bupivacaine can be used as safe local anesthetics in terms of the heart and respiratory parameters and pain scales examined. Bupivacaine should be preferred to lidocaine for long-lasting surgical procedures and postoperative analgesia due to its long duration of action.

Conflict of Interest

The authors declare that they have no competing interests.

Authorship contributions

Animal study and data collection: B.T., Analysis and interpretation: E.E., Statistical analysis and literatüre search: Z.P., Writing: B.T., Z.P.

Financial Support

This research received no grant from any funding agency/sector.

Ethical Approval

This study was conducted with the permission of the Kırıkkale University Local Ethics Committee for Animal Experiments with the decision No. E.40905. - 16 dated 13.12.2022.

REFERENCES

Ansah OB, Vainio O, Hellsten C, Raekallio M. 2002. Postoperative pain control in cats: Clinical trials with medetomidine and butorphanol. Vet. Surgery 31:99-103.

Baran A, Ozdaş OB, Sandal AI. 2016. Erkek Kedi ve Köpeklerde Üremenin Önlenmesi. Turkiye Klinikleri J Vet Sci Obstet Gynecol-Special Topics, 2(2): 9-18.

Barletta M, Reed R. 2019. Local Anesthetics: Pharmacology and Special Preparations. Veterinary Clinics of North America: Small Animal Practice, 49(6): 1109-1125.

Bayram A. 2020. Lokal Anestezik Toksisitesi. Aksaray Üniversitesi Tıp Bilimleri Dergisi, 1. Ulusal Multisentrik Multidisipliner Toksikoloji Sempozyumu, 23-27.

Çetinaslan M, Apaydın N. 2008. Köpeklerde medetomidin-ketamin-atipamezol anestezisinin hematolojik ve biyokimyasal parametrelere olan etkileri. Sağlık Bilim Derg, 17(2): 110-116.

Dobromylskyj P, Flecknell PA, Lascelles BD, Livingston A, Taylor P, Waterman-Pearson A. 2001. Pain assesment. Pain Management in Animals. Ed. Flecknell PA, Waterman-Pearson AWB. Saunders, London. p. 53-79.

Duncan B, Lascelles X. 2007. Supportive care for cancer patient. Withrow and Maceven's Small Animal Clinical Oncology. Ed. Withrow SJ, Vail DM, Missouri: Saunders. 4th.ed. p. 291- 307.

Epstein ME, Rodan I, Griffenhagen G, Kadrlik J, Petty MC, Robertson SA, Sġmpson W. 2015. 2015 AAHA/AAFP pain management guidelines for dogs and cats. Journal of Feline Medicine and Surgery, 17(3): 251-272.

Fraser CM, Bergeron JA, Mays A, Aiello SE. 1991. The Merk Veterinary Manual: A Handbook of Diagnosis, Theraphy and Disease Prevention and Control for the Veterinarian. Merck & Co. Rahway, N.J., USA. p. 965-970.

Glerum LE, Egger CM, Allen SW, Haag M. 2001. Analgesic effect of the transdermal fentanyl patch during and after feline ovariohysterectomy. Veterinary Surgery, 30(4): 351-358.

Grubb T, Sager J, Gaynor JS, Montgomery E, Parker JA, Shafford H, Tearney C. 2020 AAHA Anesthesia and monitoring guidelines for dogs and cats. Journal of American Animal Hospital Association, 56(2): 59-82.

Grubb T, Lobprise H. 2020a. Local and regional anaesthesia in dogs and cats: Overview of concepts and drugs (Part 1). Veterinary Medicine and Science, 6(2): 209-217.

Grubb T, Lobprise H. 2020b. Local and regional anaesthesia in dogs and cats: Descriptions of specific local and regional techniques (Part 2) Veterinary Medicine and Science 6(2): 218-234.

Gültekin Ç. 2012. Tümör cerrahisi uygulanan köpeklerde morfin ve tramadol'ün analjezik etkilerinin

karşılaştırılması. Doktora Tezi, Ankara Üniversitesi Sağlık Bilimleri Enstitüsü.

Holton LL, Scott EM, Nolan AM, Reid J, Welsh E, Flaherty D. 1998. Comparison of three methods used for assesment of pain in dogs. JAVMA, 212 (1): 61-66.

Höglund OV, Dyall B, Grasman V, Edner A, Olsson U, Höglund K. 2018. Effect of nonsteroidal anti-inflammatory drugs on postoperative respiratory and heart rate in cats subjected to ovariohysterectomy. Journal of Feline Medicine and Surgery, 20(10); 980-984.

Johnson CB., Taylor PM, Young SS, Brearley JC. (1993). Postoperative analgesia using phenylbutazone, flunixin or carprofen in horses, Veterinary Record, 133: 336-338.

Lamont LA. 2008. Adjunctive analgesic therapy in veterinary medicine. Veterinary Clinics of North America: Small Animal Practice, 38(6): 1187–1203.

Lim GFS, Huether M, Brodland D. 2021. Local anesthetics in comprehensive dermatologic drug therapy, 4th Ed. Editors; Wolverton SE, Wu JJ, p: 631-649.

Mathews K, Kronen PW, Lascelles D, Nolan A, Robertson S, Steagall PV, Yamashita K 2014. Guidelines for recognition, assessment and treatment of pain. Journal of Small Animal Practice, 55(6): E10-E68.

Mathews KA. 2000. Pain asesment and general appoach to management. Veterinary Clinics of North America Small Animal Practice, 30: 729-755.

Papich MG. 2020. Papich Handbook of Veterinary Drugs-E-Book. Elsevier Health Sciences.

Pekcan Z, Koç B. 2005. Köpeklerde epidural morfin ile fentanil bantların postoperatif analjezi üzerine etkileri. Doktora Tezi. Ankara Üniv. Sağlık Bilimleri Enstitüsü.

Robertson SA, Gogolski SM, Pascoe P, Shafford HL, Sager J, Griffenhagen GM. 2018. AAFP Feline Anesthesia Guidelines. Journal of Feline Medicine and Surgery, 20(7): 602-634.

Sinclair DM. 2003. A review of the physiological effect of α2- agonists related to the clinical use of medetomidine in small animal practice. Canadian Veterinary Journal, 44: 885-897.

Steagal PV, Monteiro BP. 2019. Acute pain in cats: Recent advances in clinical assessment, Journal of Feline Medicine and surgery, 21(1): 25-34.

Topal A. 2005. Veteriner Anestezi. Nobel Tıp Kitapevleri Ltd.Şti. İstanbul. p:3-4.

Vardanyan RS, Hruby V. 2006. Synthesis of Essential Drugs. Elsevier, 1st ed. 9-18.