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Comparison of Intraoperative Effects of Intratesticular Lidocaine and Procaine on Hemodynamic Responses in Male Cats Undergoing Routine Castration

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ABSTRACT

This study was aimed to compare the effects of intratesticularly administered lidocaine and procaine on perioperative nocifensive responses in cats undergoing elective castration. Sixteen male cats (weighing between 2.3 and 6.7 kg, and 8 mounths to 3 years of age) were received for planned castration and suitable for inclusion. Cats were incidentally divided to 2: the lidocaine (group 1) and the procaine (group 2) groups. In group 1, lidocaine (1 mg/kg) was slowly injected to the right testis of the cats with a hypodermic syringe. In group 2, 1 mg/kg procaine was slowly injected to the right testis with the same technique. Besides to objective follow-up clinical monitoring, heart rate, electrocardiogram, respiration frequency, pulse oximetry, rectal temperature and blood pressure were traced during surgery with a bedside monitor. Respiration frequency values were significantly higher than before surgey at the first prescrotal incision and the clamping of the left testicular pediclein group 1 ($p < 0.05$). BP diastolic values significantly increased from before surgeryat the clamping of right testicular pedicle in the procaine group ($p < 0.05$). These findings suggested that intratesticular procaine is a beneficial analgesic technique in cats undergo planned castration and should be considered as an adjunct to standard anesthetic practice with lidocaine.

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INTRODUCTION

Castration is one of the widespread surgerie in veterinary practice and is considered a rather stinging operation (Hewson et al 2006, McMillan et al 2012). One noted that only 30% of veterinary surgeons administered analgesic drugs in castration of dogs (Capner et al 1999). Nearly all analgesic drugs are systemic, an opiod is used only in 50% of the cases, a nonsteroidal anti-inflammatory drug is used in 27% of the cases, and combined analgesics are employed in 23% of the cases. In human medicine, local anesthetics has been proven to have a positive impact on pain management (Bonnet and Marret 2005). Various articles demonstrated that lidocaine in either the funiculus spermaticus or testes reduced nocifensive answers to pain related with castration in lambs (Wood et al 1991, Dinnis et al 1997, Molony et al 1997), piglets (Mcglone and Hellman 1988, White et al 1995, Haga and Ranheim 2005), calves (Satfford et al 2002), horses (Haga et al 2006, Portier et al 2009), and dogs (McMillan et al 2012). However, no previous research compared the impact of intratesticular lidocaine and procaine application in routine castration in cats. Our hypothesis was that intratesticular lidocaine and procaine would provide effective intraoperative surgical pain relief.

This study was aimed to compare the effects of intratesticularly administered lidocaine and procaine on perioperative nocifensive responses in cats undergoing elective castration.

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MATERIALS AND METHOD

Sixteen male cats (weighing between 2.3 and 6.7 kg, and 8 mounths to 3 years of age) were received for planned castration and suitable for inclusion. During the study, the breeds of the cats were determined as follows: 10 domestic short hair, 3 domestic long hair, 1 Angora, 1 Russian blue, 1 Persian. This study was done in small animal clinic of Kyrgyz Turkish Manas University, Faculty of Veterinary Medicine in 2017 and 2018 years. Animals were judged healthy based on the objective checking conducted by the supervisor researcher and joined in the study (ASA classification I or II). Owners were inquired to fast cats after 24.00 on the day of the operation, but water was provided ad libitum. Body condition score, bodyweight (BW), and age of each cat was registered. Exclusion criteria covered the presence of aggressive temperament, many anxiety, previous adverse reaction to NSAIDs, and pre-existing behavior that indicated pain. All cats were treated as outpatients, and received before 08:30 and discharged between 17:30 and 18:30 on the same day.

Carprofen (Rimadyl, New Jersey, USA, 4 mg/kg, IV) was injected to all cats for analgesia. Thereafter, cats were premedicated with 2 mg/kg xylasine (Alfazin, İzmir, Turkey) intramuscularly (IM). After 15 min, 10 mg/kg ketamine (Alfamine, İzmir, Turkey) was IM administrated. Serum physiologic solution (Eczacıbaşı, İstanbul, Turkey) was applied (10 ml/kg/hr, IV) during the operation.

Besides to objective follow-up clinical monitoring, HR, ECG, *f*R, pulse oximetry (SPO_2), body temperature (BT) and BP were traced during surgery with a bedside monitor (G9000, Guoteng, China). Prior to the start of the experiment, the monitor was adjusted based on the manufacturer's directions. Measurements were registered at all the times.

The initial physiologic parameters (HR, *f*R, BP, BT, SPO_2) were saved before premedication. Said tense was enumerated as the baseline (T0 time point). Cases were prepared since prescrotal castration with a common aseptic method, including the scrotum. The closed scrotal castration technique was employed. Cats were incidentally divided to 2: the lidocaine (group 1) and the procaine (group 2) groups.

In group 1, lidocaine (1 mg/kg) (Lidocain, Lake Forte, USA) was slowly injected to the right testis of the cats with a hypodermic syringe (Bıçakçılar, Samsun, Turkey). Lidocaine 2% was used by 0.05 ml/kg/testis for this dosage. In group 2, 1 mg/kg procaine (Novocain, Lake Forte, USA) was slowly injected to the right testis with the same technique. Similarly, the injection was adjusted to 0.25 ml/5 kg BW/testis procaine solution (2%). In digital palpation, if the strain within the testis was roughly noted to be extreme, the local anesthesic injection was stopped. Five minutes after the injection of lidocaine, the right testicle was surgically removed. The local anesthesic wasn't applied in the left testis. Left testes are removed before 5 min from right testes, in either group. Left testes represented the control group.

Based on the regular examination of control of eye position, jaw tone, and palpebral reflex, suitable deep anesthesia was ensured. Statistical collation measurements (*f*R HR, BP, BT, and SPO_2) were received at 5 time points during anesthesia: T0: the baseline, T1: the first prescrotal incision, T2 and T3: the clamping of left and right testicular pedicles respectively, and T4: the completion of the operation.

Tukey's multiple range test and ANOVA were employed to determine intergroup differences (SPSS Inc., Chicago, USA). Approval of the study was obtained from Manas University, Animal Experiments Local Ethics Committee (2016-03/2) Number Ethics Committee Decision.

RESULTS AND DISCUSSION

No significantly differences were among the groups based on BW, BCS, age and baseline *f*R, HR, BP, SPO_2, and RT measurements (Table 1). The duration of surgery was between 17-21 minutes. The duration of surgery was no statistically different between the groups ($p > 0.05$).

Table 1. *Animal data and baseline (T0) physiological variables for both groups (Mean±SE).*

Patient variable	Lidocaine group (N=8)	Procaine group (N=8)	p
Age (years)	1,7±0,8	1,5±0,3	NS
Body weight (kg)	3.5±0.2	3,9±0,5	NS
Body condition score	2.8±0.3	2,5±0.2	NS
Baseline heart rate (beats/minute)	106.6±20.4	116.5±37.3	NS
Baseline respiration frequency (breaths/ min)	11.8±1.3	12.6±0.7	NS
Baseline blood pressure (mmHg)	121.4±1.4	111.7±7.1	NS
Baseline SPO_2 (mmHg)	92.0±1.2	91.7±6.6	NS
Baseline rectal temperature (mmHg)	38.7±0.2	37.9±0.5	NS

SPO_2: Oxygen saturation, NS ($p > 0.05$).

There were no statistically significant differences between group 1 and group 2 *f*R values at the baseline (T0), the first prescrotal incision, the clamping of the left testicular pedicles, the clamping of the right testicular pedicles, or the completion of the operation. (Table 2). *f*R values were significantly higher than baseline at the first prescrotal incision and the clamping of the left testicular pedicle in group 1 ($p < 0.05$). There was no statistically significant difference between baseline and the first prescrotal incision, the clamping of the left testicular pedicles, the clamping of the right testicular pedicles, and the completion of the operation *f*R values in the procaine group.

There were no significantly significant differences between group 1 and group 2 in HR values at the baseline, the first prescrotal incision, the clamping of the left testicular pedicles, the clamping of the right testicular pedicles, or the completion of the operation (Table 2). There were not statistically significant differences between baseline and the first prescrotal incision, the clamping of the left testicular pedicles, the clamping of the right testicular pedicles, or the completion of the operation HR values in either group.

Table 2. *Distribution of intraoperative monitoring values in cats (Mean±SE)*

Parameters/Groups		T0	T1	T2	T3	T4	p
SPO_2 (%)	Lidocaine (N=8)	$92.0±1.2^{y}$	$93.7±0.8^{xy}$	$94.0±0.7^{xy}$	$94.1±1.0^{xy}$	$95.2±1.1^{x}$	*
	Procaine (N=8)	91.7±6.6	89.5±4.2	90.0±3.1	93.1±1.8	92.7±1.8	-
	P	NS	NS	NS	NS	NS	
Respiration frequency	Lidocaine (N=8)	$11.8±1.3^{y}$	$15.2±0.8^{x}$	$14.7±0.9^{x}$	$11.0±0.8^{y}$	$12.5±0.8^{xy}$	*
	Procaine (N=8)	12.6±0.7	13.5±0.8	15.3±1.1	13.0±1.7	14.3±1.1	-
	P	NS	NS	NS	NS	NS	
Heart rate	Lidocaine (N=8)	106.6±20.4	117.7±18.4	131.2±18.1	96.4±6.3	97.1±7.0	-
	Procaine (N=8)	116.5±37.3	94.7±10.9	94.4±10.9	93.1±1.8	104.3±9.9	-
	P	NS	NS	NS	NS	NS	
Blood pres. *(sistolic)*	Lidocaine (N=8)	143.0±4.3	149.7±8.5	147.2±9.3	146.0±2.8	145.0±2.7	-
	Procaine (N=8)	136.6±6.5	155.3±7.3	139.3±5.7	143.6±2.9	147.6±2.9	-
	P	NS	NS	NS	NS	NS	
Blood pres. *(mean)*	Lidocaine (N=8)	121.4±1.4	119.2±10.7	112.4±14.7	114.6±8.3	122.5±3.2	-
	Procaine (N=8)	111.7±7.1	119.4±7.3	119.4±4.5	128.5±2.5	128.5±2.4	-
	P	NS	NS	NS	NS	NS	
Blood pres. *(diastolic)*	Lidocaine (N=8)	106.2±6.1	105.0±11.7	90.5±22.2	101.0±7.1	101.0±9.2	-
	Procaine (N=8)	$91.3±15.2^{yz}$	$111.0±6.4^{xy}$	$101.3±11.1^{xy}$	$108.6±14.8^{x}$	$104.6±10.1^{xy}$	*
	P	NS	NS	NS	NS	NS	

^{xyz} means with different superscripts within one row differ significantly ($p < 0.05$), NS: Non significant ($p > 0.05$): row comparison
*: ($p < 0.05$): row comparison; SPO_2: Oxygen saturation.

There were no statistically significant differences between the lidocaine group and procaine group BP diastolic values at any time point (Table 2). There were no significant differences between baseline and the first prescrotal incision, the clamping of the left testicular pedicles, the clamping of the right testicular pedicles, or the completion of the operation BP diastolic values in the lidocaine group. BP diastolic values significantly increased between baseline and the clamping of the right testicular pedicles in the procaine group ($p < 0.05$).

One cat's *f*R, BP mean and HR values were increased by 20% in the lidocaine group after the clamping of the left testicular pedicles (T2 time point, controls). Additionally, two cats' *f*R, one cat's BP mean, and two cats' HR values increased by 20% in the procaine group after the clamping of the left testicular pedicles (T2 time point, controls). An increase by 20% in *f*R, BP mean and HR values was not observed in both groups at the clamping of the right testicular pedicles (local anesthetic applied).

Certain adverse effects were determined after intratesticular injection; however, none was of clinical importance. Althhough no increase was observed in regional hemorrhage, a spot of blood on the scrotal skin and an injection mark

that did not close due to extreme intratesticular pressure after injection were observed in every case. Furthermore, testical or tunical hemorrhage and/or mild hematoma formation were determined in 4 out of 14 (28.5%) injected testes.

It was planned that the present study would include an anesthetic regime that has been commonly adopted in general practice. Xylazine is an α2 adrenergic receptor agonist, and it was first produced in 1962 as an antihypertensive; however, it was later determined to have potent sedative effects in animals (Lemke 2004). Ketamine, a derivative of phencyclidine and cyclohexamine, is an NMDA antagonist often employed to induce feline anesthesia (Khenissi et al 2017). Time points were determined based on the time of maximal surgical stimulation and nociceptive response and the beginning and end of the surgical stimulus (Taylor and Weary 2000).

To wield the antinociceptive influence, local anesthetic should be dispensed in the location of the noxious stimulus, to the ligation of the funiculus spermaticus. It was indicated that lidocaine dispenses in testis quickly through the testicular pedicle of the horse (Haga et al 2006) and an observable anti-nociceptive impact could be observed within 10 min of introduction in piglets (Haga and Ranheim 2005). Thus, the top of local anesthetic impact may have been missedin the present research. For this reason, we think that the analgesia observed with this method be obtained in engaged general practice conditions, since lidocaine or procaine could be applied during aseptic preparation of the surgical site and the clipping.

The opioid and NSAID mixture administered during the anesthesia was regarded by the researches as an efficient combination of analgesic drugs for transactions characterized by minimal to moderate pain; thus, it could be suggested that application of the local anesthetic led to a discrepancy in monitored data. Minimal adverse effects were recorded after intratesticular administration; hemorrhage or hematoma development was moderate and wasn't objectively important since the testes were planned for rustication. These findings suggested that this application could provide a statistically and clinically important addition to intraoperative control of the pain.

There are several limitations in the present study. Individual sensitivity to ketamine or xylazine may have been translated into deeper anesthesia in one cat when compared to the others. Clinically, every animals seemed to be at a uniform level of anesthesia, but this is a qualitative analysis. Nevertheless, similar monitoring values across the groups at the first prescrotal incision suggested that the depth of anesthesia was similar in all cases and at the graderequired to inhibit autonomic nocifensive answeres and noxious stimuli to within the 10% of baseline. Thus, we determined that there was little distinction between the anesthesia levels of the animals.

Another limitation of the study was the fact that the lead researcher was not blind to the experimental groups. The baseline assure the anesthetist unawareness of the topic assignment, one choice would be for the lead researcher to leave of the operation theatre during the commencement of each application. This was not feasible since all cats that were anesthetized locally had a single drop of blood on the skin surface, which could be clearly observed when the researcher returned. Another possible option would be to inject an intratesticular placebo of 0.9% NaCl of an equal volume to mimic the application of local anesthetics. This option was considered by the researchers; however, it would not used the singular animal. Third limitation of the study was the fact that systemic effects of local anesthetics were not analyzed for the groups. Previous articles reported that local anesthetics had certain sytemic effects on central nervous system and heart. The central nervous system is more sensitive to the effects of local anesthetics when compared to the cardiac system and will generally manifest signs/symptoms of toxicity first. The initial central nervous system symptoms include tinnitus, blurred vision, dizziness, tongue paratheses, and circumoral numbness. These effects could affect monitorized physiological parameters in the cases.

The administration of intratesticular procaine and lidocaine decreased the nociceptive stimulation of cats that underwent castration in the present study. There was reduced nociceptive stimulation in the right testes in groups after the primary skin incision, which was unpredictable since intratesticular procaine and lidocaine are unlikely to desensitize the prescrotum skin. A rise in nociceptive stimulations were observed after the removal of the left testicles (control, T2) in both lidocaine and procaine group. Respiration rate, HR, RR, SPO_2, BP systolic, BP mean, and BP diastolic values were not significantly different at any time points between the groups. This suggested that intratesticular procaine is equally potent at blocking nocifensive autonomic response (right testis, T3) to testicular removal with lidocaine.

CONCLUSION

In conclusion, these findings suggested that intratesticular procaine is a beneficial analgesic technique in cats that undergo planned castration and should be considered as an adjunct to standard anesthetic practice with lidocaine. Further studies are required to determine any long term benefits of this practice.

ETHICAL STATEMENT

During the writing process of the study titled "Comparison of intraoperative effects of intratesticular lidocaine and procaine on hemodynamic responses in male cats undergoing routine castration", scientific rules, ethical and citation rules were followed; No falsification has been made on the collected data and this study has not been sent to any other academic media for evaluation. The study protocol was addmitted by the local ethics committee (Ethic Committe of Manas University) (approval number: 2014-12).

CONFLICT OF INTERESTS

The authors declared no conflict of interest.

AUTHORS CONTRIBUTION

All authors contributed equally

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