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Effect of intratesticular injection of xylazine/ketamine combination on canine castration

Joon-ki Kim, Seong-mok Jeong[1], Na-Young Yi[1], Man-Bok Jeong[1], Eun-song Lee, Tchi-chou Nam[1], Kang-moon Seo[1,*]

Department of Veterinary Medicine, Kangwon National University, Chuncheon 200-701, Korea
[1]Department of Veterinary Surgery, College of Veterinary Medicine, Seoul National University, Seoul 151-742, Korea

This study was performed to compare the effect of intratesticular (IT) injection of xylazine/ketamine combination for canine castration with those of intramuscular (IM) or intravenous (IV) injection. Xylazine and ketamine was administered simultaneously *via* intratesticularly (IT group), intramuscularly (IM group) or intravenously (IV group) at doses of 2 and 10 mg/kg, respectively. Pain response at the time of injection, mean induction time, mean arousal time, mean walking time and cardiopulmonary function during anesthesia were monitored after the xylazine and ketamine administration. In IV and IM groups, heart rates were significantly decreased 30 and 45 min after xylazine and ketamine administration, respectively ($p < 0.05$). Respiratory rates were significantly decreased in the IV group ($p < 0.05$). In the IT group, there was no significant changes in heart and respiratory rates. The occurrence of cardiac arrhythmias was less severe in IT group compared with those in IM and IV groups. The route of administration did not affect rectal temperature. Mean induction time was significantly ($p < 0.05$) longer in IT group than in IM and IV groups. On the contrary, mean arousal time and mean walking time were shortened in IT group. Clinical signs related to pain response at the time of injection and vomiting were less observed in IT group than in IM group, and head shaking was less shown in IT group than in IM and IV groups during recovery period. These results indicated that intratesticular injection of xylazine/ketamine for castration has several advantages such as less inhibition of cardiopulmonary function and fast recovery from anesthesia without severe complications, and would be an effective anesthetic method for castration in small animal practice.

Key words: canine, castration, intratesticular injection, ketamine, xylazine

*Corresponding author
Tel & Fax: +82-2-880-1258
E-mail: kmseo@snu.ac.kr

Introduction

Xylazine has been widely used in veterinary practice as a sedative agent. Cardiopulmonary effects of xylazine have been widely reported in the dog and other species. A bradycardic effect of xylazine can be seen with some animals developing a second-degree heart block or other arrhythmias [4,8,13-15,17,18]. Ketamine increases cardiac output, heart rate, mean aortic pressure, pulmonary arterial pressure and central venous pressure. Ketamine does not induce respiratory depression at usual dosages [2,3,6,15,16]. Xylazine is commonly used in combination with ketamine for reduced muscle tonicity. The combination of xylazine/ketamine produces a good general anesthesia and has several advantages such as an easy administration, rapid onset/termination of anesthesia and few apparent clinical complications [1]. Benson *et al.* [1] investigated that heart rate, mean arterial pressure, systemic vascular resistance and arterial oxygen tension were not significantly altered from base-line values by induction and maintenance with guaifenesin-xylazine-ketamine mixture. Kolata and Rawlings [14] reported that heart rate was increased at 5 minutes after atropine, ketamine, and xylazine injection and returned to near baseline by 45 minutes after injection time.

Castration is indicated for reproductive neutering, modification of behavior patterns, testicular neoplasia, severe testicular or scrotal trauma, refractory orchitis, benign prostatic hyperplasia, perianal gland adenoma, perineal hernia, and scrotal urethrostomy in dogs [5,7]. There is no specific anesthetic method for castration. Routine general anesthesia or local anesthesia has been used for castration [10,12,15]. One of the disadvantages of injected general anesthesia for castration was long recovery time from anesthesia in spite of short operation time. Depth or level of anesthesia was less readily controlled with injected anesthesia compared to inhalation anesthesia. Intramuscular and/or intravenous anesthesia was easy to inject an overdose. Once anesthetics administered intramuscularly or intravenously could not be recovered from body and its

elimination depends on detoxification and/or excretion into bile or urine [3,9].

Intratesticular injection was attempted for castration in boars [11]. Castration was usually attained within ten minutes, and the excess anesthetic was removed with the testis, eliminating the risk of overdose. However, intratesticular injection for castration has not been reported in dogs. We make assumption that intratesticular injection for canine castration can eliminate excess anesthetics as soon as the testicles are removes, therefore fast recovery from anesthesia without complication after xylazine/ ketamine administration.

This study was conducted to compare the anesthetic effect of intratesticular injection of xylazine and ketamine with intramuscular or intravenous injection for canine castration and examine the practical applicability of intratesticular injection of general anesthetics for castration in small animal practice.

Materials and Methods

Twenty-one male dogs, weighing 2.5 to 27.0 kg (18.5 ± 16.0 kg) were presented. They were determined to be healthy by physical examination, electrocardiogram (ECG), complete blood count, and serum chemical profiles. Dogs were fasted for 12 hours before the anesthesia. Control values for heart rate, respiratory rate, rectal temperature, and ECG (lead II) were obtained before the administration of anesthetics.

Twenty-one dogs were divided randomly into three groups: intratesticular (IT), intramuscular (IM) and intravenous (IV) groups (Table 1). Each group was composed of 7 dogs. Xylazine (Rompun®, Bayer Korea, Korea) and ketamine (Ketamine 50®, Yuhan, Korea) were mixed in the same syringe at doses of 2 mg/kg and 10 mg/ kg, respectively. The administration sites were parenchyma of left testis in IT group, biceps femoris muscle in IM group and cephalic vein in IV group.

Heart rate, respiratory rate, rectal temperature and ECG were monitored every ten minutes from the time of injection for thirty minutes, and then every fifteen minutes for additional thirty minutes. Mean induction time (MIT), mean arousal time (MAT) and mean walking time (MWT) were recorded after combined administration of xylazine/ ketamine. MIT means that time from injection of xylazine/ ketamine combination until the dogs fell down. MAT represents that time from injection of xylazine/ ketamine combination until the dogs rose the head. MWT means that time from injection of xylazine/ketamine combination until the dogs could stand and walk unaided. Pain response at the time of anesthetic administration, vomiting, and head shaking during recovery from anesthesia were observed through the anesthetic period.

Intratesticular injection and castration procedure were performed as follows. Left testis was held firmly in the hand and the skin was tensed over the testis. Needle was inserted into the middle of testis and all dosages of xylazine/ ketamine were injected. Left testis was removed first to prevent further absorption of excessive anesthetics, and then right testis was removed. Castration was performed following routine procedure through prescrotal incision. In all experimental groups, castration was started immediately after the dog fell down.

All the parameters were compared with control values obtained before the injection of anesthetics. Treatment effect in each parameter was analyzed by repeated measured ANOVA and significant difference among the treatment groups were compared by Tukey's studentized range test (SAS, ver. 6.12). The significance level was $p < 0.05$.

Results

The effects of xylazine/ketamine on heart rate, respiratory rate, rectal temperature and anesthetic parameters after administration *via* intratesticularly, intramuscularly and intravenously were compared.

Heart rates

After administration of xylazine/ketamine, heart rate was gradually decreased in all groups (Fig. 1). Heart rates were significantly decreased from 45 min after administration of xylazine/ketamine in IM group, and from 30 min in IV group compared that of preanesthetic period ($p < 0.05$). However, there was no significant decrease in heart rate in IT group.

Respiratory rates

Respiratory rate was significantly decreased from 10 min after administration of anesthetics in IV group, whereas there was no significant change in IT and IM groups compared with control values ($p < 0.05$) (Fig. 2).

Table 1. Design of experiments

Group*	Treatment	No. of dogs	Site of administration
IT	Xylazine 2 mg/kg + Ketamine 10 mg/kg	7	Parenchyma of left testicle
IM	Xylazine 2 mg/kg + Ketamine 10 mg/kg	7	Biceps femoris muscle
IV	Xylazine 2 mg/kg + Ketamine 10 mg/kg	7	Cephalic vein

*IT: intratesticular, IM: intramuscular, IV: intravenous.

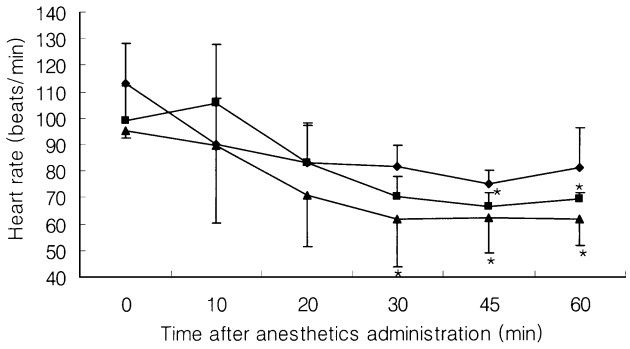

Fig. 1. Heart rate after xylazine/ketamine administration in dogs. *p<0.05, ◆ : IT (intratesticular), ■ : IM (intramuscular), ▲ : IV (intravenous).

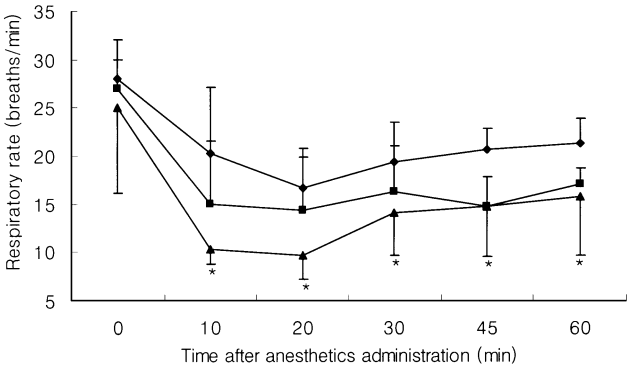

Fig. 2. Respiratory rate after xylazine/ketamine administration in dogs. *p<0.05, ◆ : IT (intratesticular), ■ : IM (intramuscular), ▲ : IV (intravenous).

Rectal temperature

Rectal temperature tended to decrease slightly from 20 min after the injection of xylazine/ketamine in all groups, but not significant (Fig. 3).

Mean induction time (MIT), mean arousal time (MAT), and mean walking time (MWT)

MIT was 2.88 ± 0.86 min, 1.42 ± 0.30 min, and 0.19 ± 0.05 min in IT, IM, and IV group, respectively. MIT of IT group was significantly longer than those of IM and IV groups ($p < 0.05$). MAT was 30.50 ± 3.72 min, 48.21 ± 6.03 min, and 47.92 ± 5.10 min in IT, IM, and IV group, respectively. MWT was 37.54 ± 4.53 min, 61.03 ± 6.15 min, and 70.95 ± 8.10 min in IT, IM, and IV groups, respectively. MAT and MWT of IT group were significantly decreased in IT group than those of other groups ($p < 0.05$) (Fig. 4).

Electrocardiogram

Following the administration of xylazine/ketamine combination, several kinds of arrhythmias were observed including sinus arrest, first-degree heart block, and second-degree heart block (Table 2, Fig. 5).

Sinus arrest was detected in 5 dogs in IT group.

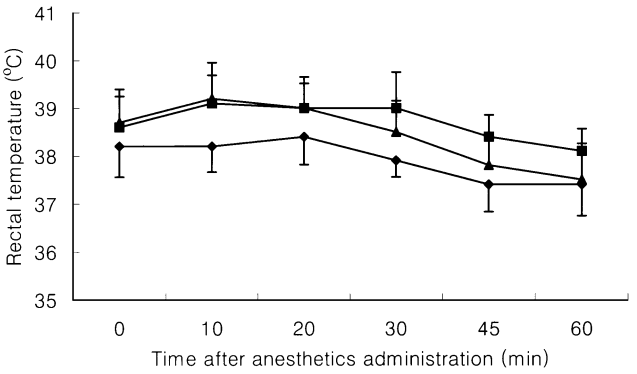

Fig. 3. Rectal temperature after xylazine/ketamine administration in dogs. ◆ : IT (intratesticular), ■ : IM (intramuscular), ▲ : IV (intravenous).

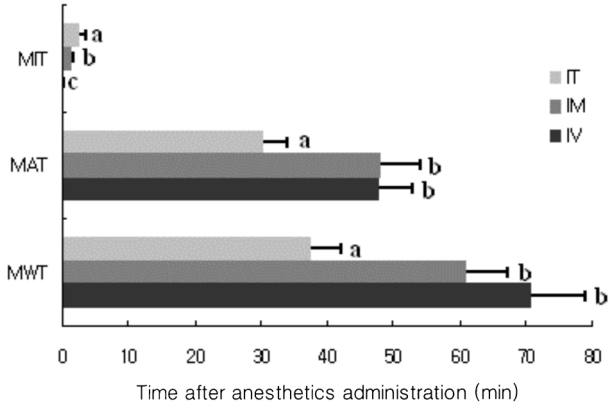

Fig. 4. Mean induction time(MIT), mean arousal time (MAT) and mean walking time (MWT) after xylazine/ketamine administration in dogs. a,b,c: Different scripts in the same parameter differ significantly at p=0.05 level by Tukey's studentized range test.

Nonetheless in IM and IV groups, it was shown in all dogs. First-degree heart block was observed in 2 dogs in IT group, whereas, it was observed in 5 dogs in IM and IV groups. Second-degree heart block was shown in 2 dogs in IT group, 3 dogs in IM group and 5 dogs in IV group. The overall presence of cardiac arrhythmias in IT group was lower than that of other groups.

Clinical signs

At the time of injection pain responses were observed in 4 dogs in IT group and all dogs in IM group. Vomiting was shown in 1 dog in IT group, 4 dogs in IM group and 3 dogs in IV group. During recovery period, the sign of head shaking was observed in all groups, but the frequency of the sign in IT group was lower than those in IM and IV groups (Table 3).

Discussion

After injection of xylazine/ketamine combination

Table 2. Cardiac arrhythmias observed after administration of xylazine/ketamine in dogs

Group*	Cardiac arrhythmias[#]		
	Sinus arrest	First-degree heart block	Second-degree heart block
IT	5/7	2/7	2/7
IM	7/7	5/7	3/7
IV	7/7	5/7	5/7

*IT: intratesticular, IM: intramuscular, IV: intravenous
[#]No. of dogs showing arrhythmia/No. of dogs tested.

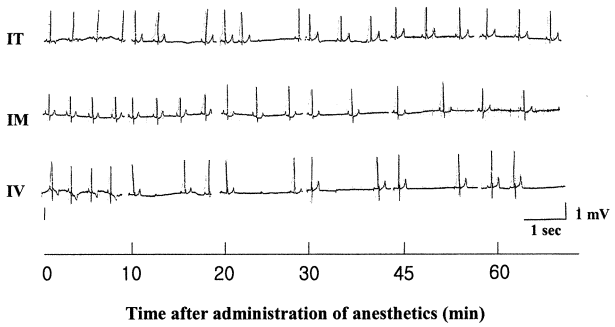

Fig. 5. Electrocardiogram after xylazine/ketamine administration in dogs. IT: intratesticular, IM: intramuscular, IV: intravenous.

cardiopulmonary depression was observed in all groups. However, the degree of depression was less severe after intratesticular injection than that of after intramuscular or intravenous injection. MAT and MWT were significantly shortened in IT group compared with other groups. These results suggest that intratesticular administration of general anesthetics be the more effective and safer method than IV or IM injection for canine castration.

Heart rate was significantly decreased 30 and 45 min after IM and IV injection of xylazine/ketamine, respectively. Irrespective of route of administration, injection of xylazine/ketamine combination caused several types of cardiac arrhythmias in all groups, but first and second-degree heart blocks were observed more frequently in IM and IV groups than in IT group. Inhibited cardiac function shown in this study was likely due to xylazine, which was similar with the previous reports that xylazine inhibited cardiopulmonary function even when administered together with ketamine by increasing vagal tone occurring in response to hypertension [4,6,8,13-18]. However, cardiac function was not severely affected by anesthetics in IT group. The left testis, injected with anesthetics, was removed approximately within 5 min after anesthetic injection, which might prevent excessive absorption of anesthetics. Atropine is routinely administered before injection of general anesthetics to reduce the cardiac arrhythmia and excessive salivation caused by anesthetics [3,6]. To examine the net pharmacological effect of xylazine/ketamine on cardiac function atropine was not premedicated in this study and cardiac function was severely affected.

Respiratory function was significantly depressed by IV injection of xylazine/ketamine but no significant change was found in IM and IT groups. Plumb [17] suggested that the effect of xylazine on respiratory function was usually insignificant, but at high dosages, it could cause respiratory depression with decreased tidal volume and respiratory rate. In the present study, higher dosage of xylazine than recommended for IV injection was administered intravenously, and this resulted in the decrease in respiratory rate in IV group.

Mean rectal temperature was not significantly affected by xylazine/ketamine in all groups, which is in agreement with the observation of Clark *et al.* [6]. It has been reported that xylazine depress thermoregulatory mechanisms and body temperature can be affected by ambient air temperature [17]. It seems that rectal temperature, in this study, was not affected by ambient temperature because castration was performed in a confined operation room where airflow and fluctuation of room temperature was minimized.

MIT depends on the absorption rate of anesthetics from the site of injection and absorption rate is partly related with distribution of blood vessels or blood supply. MIT was longer in IT group than in IV and IM groups. It is probable that absorption of injected anesthetics might have been

Table 3. Clinical signs after xylazine/ketamine administration in dogs

Group*	Clinical signs[#]		
	Pain[a]	Vomiting[b]	Head shaking[c]
IT	4/7	1/7	2/7
IM	7/7	4/7	7/7
IV	0/7	3/7	7/7

*IT: intratesticular, IM: intramuscular, IV: intravenous; [#]No. of dogs showing clinical sign/No. of dogs tested; [a]Pain response at the time of injection; [b]Vomiting during the course of experiment; [c]Head shaking during recovery period.

delayed in IT group due to fewer blood vessels in the testicular parenchyma than in biceps femoris muscle. MAT and MWT are probably affected by the blood concentration of circulating anesthetics. MAT and MWT in the IT group was shorter than in IM and IV groups. It is considered that anesthetics were not further absorbed due to immediate removal of left testis after induction of anesthesia, which in turn reduced the concentration of circulating anesthetics.

Only 4 dogs out of 7 appealed pains at the time of anesthetic injection in IT group but all dogs injected intramuscularly revealed pain response. This finding is supported by the fact that nerves are less distributed in the testicular parenchyma than in muscles. Clinical signs around the time of induction and recovery period were observed. Less vomiting and head shaking were observed in IT group than in IM and IV groups. Faster absorption of anesthetics in IM group than in IT group at the time of induction might stimulate vomiting in IM group, and sustained high concentration of anesthetics in IM and IV groups might result in the sign of head shaking at recovery periods.

In conclusion, the present results indicated that intratesticular injection of anesthetics for castration has several advantages such as less inhibition of cardiopulmonary function and fast recovery from anesthesia without severe complications. These advantages may be attributed to prevention of absorption of excessive anesthetics by fast removal of testis injected with anesthetics immediately after the induction of anesthesia. Therefore, intratesticular administration of xylazine/ketamine can be an effective anesthetic method for castration in small animal practice.

Acknowledgments

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