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

Joon-ki Kim, Seong-mok Jeong¹, Na-Young Yi¹, Man-Bok Jeong¹, Eun-song Lee, Tchi-chou Nam¹, Kang-moon Seo¹*

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

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 baseline 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 rose the head. MAT 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.
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 $2.88 \pm 0.86$ min, $1.42 \pm 0.30$ min, and $0.19 \pm 0.05$ 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 $30.50 \pm 3.72$ min, $48.21 \pm 6.03$ min, and $47.92 \pm 5.10$ min in IT, IM, and IV group, respectively. MWT was $37.54 \pm 4.53$ min, $61.03 \pm 6.15$ min, and $70.95 \pm 8.10$ 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).

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

| Group | 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.

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

| Group | Pain* | Vomiting* | Head shaking* |
|-------|-------|-----------|---------------|
| 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; *Pain response at the time of injection; *Vomiting during the course of experiment; *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

This study was supported by the Research Institute for Veterinary Science, Seoul National University, Seoul, Korea.

References

1. Benson GJ, Thurmon JC, Tranquili WJ, Smith CW. Cardiopulmonary effect of an intravenous infusion of guaifenesin, ketamine, and xylazine in dogs. Am J Vet Res 1985, 46, 1896-1898.
2. Booker JL, Erickson HH, Fitzpatrick EL. Cardiodynamics in the Rhesus macaque during dissociative anesthesia. Am J Vet Res 1982, 43, 671-675.
3. Booth NH. Intravenous and other parenteral anesthetics. In: Booth NH, McDonald LE (eds.). Veterinary Pharmacology and Therapeutics. 5th ed. pp. 241-249. Iowa State University Press, Ames, 1982.
4. Booth NH. Nonnarcotic analgesics. In: Booth NH, McDonald LE (eds.). Veterinary Pharmacology and Therapeutics. 5th ed. pp. 311-320. Iowa State University Press, Ames, 1982.
5. Boothe HW. Surgery of the testis and scrotum. In: Birchard SJ, Sherdng RG (eds.). Small Animal Practice. pp. 882-886. Saunders, Philadelphia, 1994.
6. Clark DM, Martin RA, Short CA. Cardiopulmonary responses to xylazine/ketamine anesthesia in the dog. J Am Vet Med Assoc 1982, 18, 815-821.
7. England GCW. Orchidectomy. In: England GCW (ed.). Allen’s Fertility and Obstetrics in the Dog. 2nd ed. pp. 216-219. Blackwell Science, London, 1998.
8. Freire ACT, Gontijo RM, Pessoa JM, Souza R. Effect of xylazine on the electrocardiogram of the sheep. Br Vet J 1981, 137, 590-595.
9. Hall LW. General principles of anesthesia. In: Hilbery ADR (ed.). Manual of Anesthesia for Small Animal Practice. 3rd ed. pp. 11-16. British Small Animal Veterinary Association, Cheltenham, 1992.
10. Hedlund CS. Surgery of the reproductive and genital systems. In: Forssum TW, Hedlund CS, Hulse DA. Johnson AL, Seim HB, Willard MD, Carroll GL (eds.). Small Animal Surgery. pp. 619-622. Mosby, St. Louis, 2002.
11. Henry DP. Anaesthesia of boars by intratesticular injection. Aust Vet J 1968, 44, 418-419.
12. Kaplan B. A technique of canine castration using anatomic structures for hemostasis. Vet Med Small Anim Clin 1981, 76, 193-197.
13. Knight AP. Xylazine. J Am Vet Med Assoc 1980, 176, 454-455.
14. Kolata RJ, Rawlings CA. Cardiopulmonary effects of intravenous xylazine, ketamine and atropine in the dog. Am J Vet Res 1982, 43, 2196-2198.
15. Muir WW, Hubbell AE, Skarda RT. Anesthetic procedures and techniques in swine. In: Muir WW (ed.). Handbook of Veterinary Anesthesia. 2nd ed. pp. 320-325. Mosby, St. Louis, 1995.
16. Plumb DC. Ketamine HCl. In: Plumb DC (ed.). Veterinary Drug Handbook. 2nd ed. pp. 384-388. Iowa State University Press, Ames, 1995.
17. Plumb DC. Xylazine HCl. In: Plumb DC (ed.). Veterinary Drug Handbook. 2nd ed. pp. 707-710. Iowa State University Press, Ames, 1995.
18. Tabaru H, Ogawa H, Otsuka H, Ito K. Effects of xylazine on arterial blood pressure, heart rate and electrocardiogram in spinal dogs. Jpn J Vet Sci 1987, 49, 391-394.