Case Report

Clinical Consideration in Total Intravenous Anesthesia Using Xylazine and Propofol in Calves

Keita Tokimitsu[1] Momoko Yachida[1] Wataru Miki[2] Tadashi Kuramoto[2] Nanako Mochizuki[2] Sakura Yoshida[2] Tadahiro Goto[3] Yasuhiro Morita[1,4]*

Abstract

Surgery must often be performed in fields where only simple equipment and facilities are available for cattle practice, and anesthesia with minimal procedures should be improved for sufficient surgery in the field and on farms. The study aimed to investigate total intravenous anesthesia (TIVA) using xylazine and propofol to improve the anesthesia protocol for field surgeries in calves on farms. Fourteen calves undergoing laparotomy (every seven cases of herniorrhaphy for umbilical hernia repair and cryptorchidectomy) were assigned to this experiment and randomly divided into two groups using TIVA: continuous intravenous infusion with only xylazine (XY, 0.24-0.26 mg/kg/h), and xylazine and propofol (XYP, 0.24 mg/kg/h and 12 mg/kg/h, respectively). The respiratory rate (RR), heart rate (HR), body temperature, saturation of percutaneous oxygen (SpO_2), blood pressure, and frequency of body movement (FBM) were recorded and compared between the two anesthesia protocols during laparotomy. Spontaneous respiration was maintained during surgery in all cases. RR was significantly decreased, and FBM slightly decreased in XYP, whereas SpO_2 and HR in XYP were significantly higher than in XY. The results indicated that TIVA with xylazine and propofol could provide stable vital signs under anesthesia while maintaining spontaneous respiration, which could help field surgery more safely and accurately.

Keywords: calves, TIVA, propofol, anesthesia, field surgery

[1]*Department of Clinical Veterinary Sciences, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido, 080-8555, Japan*
[2]*Veterinary clinic, Obihiro University of Agriculture and Veterinary Medicine, Inada-cho, Obihiro, Hokkaido, 080-8555, Japan*
[3]*Hokkaido Agricultural Mutual Aid Association, 92 Shin-eidai, Ebetsu, Hokkaido, 069-0806, Japan*
[4]*Department of Bioresource Sciences, Graduate School of Bioresource and Environmental Sciences, Kyushu University, 744 Motooka, Nishi-ku, Fukuoka, Fukuoka, 819-0395, Japan*
***Correspondence**: morita.yasuhiro.362@m.kyushu-u.ac.jp* (Y. Morita)

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Introduction

Surgery must often be performed in fields where only simple equipment and facilities are available for cattle practice, depending on veterinarian visits to the farms. Therefore, the use of inhalation anesthesia and other opioid drugs can be restricted, and a combination of sedation with xylazine and local anesthesia is the first choice for surgery. However, the combination of xylazine and local anesthetic is insufficient for sedation, analgesia, and muscle relaxation (Lin *et al.*, 2022). Therefore, anesthesia with minimal procedures should be improved for sufficient surgery in the field and on farms. Total intravenous anesthesia (TIVA) is an intravenous anesthesia protocol that involves repeated bolus administration of one or more anesthetic drugs. TIVA is generally used to achieve more stable patient vitals, lower drug doses, and better control of anesthetic depth (Araújo *et al.*, 2014; Picavet *et al.*, 2004). Several protocols have been considered for small ruminants (Izer *et al.*, 2023; Vieitez *et al.*, 2017), and TIVA should be applied and modified in field cattle practices for sufficient field surgery.

Propofol has been used for induction and intravenous anesthesia in ruminants such as sheep (Lin *et al.*, 1997; Musk, 2024), goats (Velázquez-Delgado *et al.*, 2021), and cattle (Deschk *et al.*, 2016; Lima *et al.*, 2022). Reid et al. (1993) described the pharmacokinetics of propofol in goats; the mean elimination half-life was short (15.5 min), the volume of distribution at steady state was large (2.56L/kg), and the clearance rate was rapid (275 mL/kg/min) (Reis *et al.*, 1993), similar to that in other ruminants (Riebold, 2015). With propofol, induction is rapid and smooth, the duration of action is short, and recovery is good quality (Riebold, 2015). Xylazine is an α_2-adrenergic receptor agonist with potent sedative, analgesic, and muscle relaxant activity and provides desirable restriction in livestock (Greene and Thurmon, 1988), especially ruminants assume recumbency with a dose of moderated sedation (Brearley *et al.*, 1990). A combination of propofol and xylazine has been shown to provide a better quality of anesthesia and recovery than the combination of xylazine, ketamine, xylazine, and acepromazine in equine (Valverde *et al.*, 2013; Wagnar *et al.*, 2011).

This study focuses on TIVA and aims to investigate the combination of TIVA with xylazine and propofol, which is characterized by a short onset time and rapid awakening, with the conventional combination of xylazine and local anesthesia with lidocaine.

Materials and Methods

Fourteen calves in Holsteins, Japanese Black, and their crossbreds (67-252 days old, 80-246 kg) undergoing laparotomy (every seven cases of herniorrhaphy for umbilical hernia repair and cryptorchidectomy; Table 1) were assigned to this experiment and randomly divided into two group using total venous anesthesia methods: continuous intravenous infusion with only xylazine (XY, Selactar; Bayer Healthcare, Leverkusen, German, 0.24-0.26 mg/kg/h), and xylazine and propofol (XYP, 2% propofol; Maruishi Pharmaceutica, Tokyo, Japan, 0.24 mg/kg/h and 12 mg/kg/h, respectively). Both anesthesia procedures were performed after sedation with XY 0.1 mg/kg, IV, followed by tracheal intubation to prevent pulmonary aspiration. For central analgesia, IM butorphanol (Vetorphale; Meiji Seika Pharma, Tokyo, Japan) 0.01 mg/kg, IM was administered to both groups at the beginning of surgery and when body movements were observed, and lidocaine (less than 6mg/kg, xylocaine 2%; AstraZeneca K.K., Osaka, Japan) was used for local analgesia to produce pain relief.

The surgery time was defined as the time point of local anesthesia before the skin incision. The anesthesia time was defined as time points from the start of TIVA to the emergence from anesthesia and extubation. The age and body weight of animals, as well as the entire operative and anesthesia time, were analyzed using Welch's t-test between the two anesthesia methods. The evaluation parameters were respiratory rate (RR), heart rate (HR), body temperature (T), saturation of percutaneous oxygen (SpO_2), blood pressure (BP), and frequency of body movements (FBM). The entire operative and anesthesia time in each case varied, and statistical differences in each vitals (RR, HR, T, SpO_2, BP) were analyzed using two-way repeated measures ANOVA with post hoc Holm's procedure with two anesthesia methods and the part of the operative time (0-75 minutes from the start of each surgery, 15-minute intervals). FBM was defined as the number of butorphanol administrations per hour during surgery, and it was analyzed using Welch's t-test between two anesthesia methods. All analyses were performed using js-STAR XR+ release 1.7.1 (https://www.kisnet.or.jp/nappa/software/star/).

Result and Discussion

In both anesthesia groups, the age and body weight of animals, as well as the entire operative and anesthesia time, were not statistically different (Table 1). In addition, the total volume of lidocaine administered for local anesthesia was within the safe dose, reported at 13mg/kg (Lin *et al.*, 2022), and was not different between both groups (Table 1). Spontaneous breathing was maintained the entire operation time in all patients, although the operation time in some cases was more than three hours (Table 1). In addition, all animals showed a smooth emergence from anesthesia. Figure 1 showed profiles of the vitals at 15-minute intervals intraoperatively in each anesthesia group of TIVA with xylazine only (XY, n=7) and that of with xylazine and propofol (XYP, n=7), respectively, of RR (64.7 ± 13.7 vs. 44.3 ± 10.7, XY vs. XYP, mean ± SD, during surgery), SpO_2 (94.4 ± 3.87 vs. 96.6 ± 2.09), HR (66.8 ± 10.7 vs 74.9 ± 9.8), BP (103.9 ± 14.5 vs 107.0 ± 19.6), and T (38.4 ± 0.87 vs 39.6 ± 0.98). The change in the RR was significantly lower in the XYP group than in the XY group after the first 15 min of surgery (Figure 2A). The change in SpO_2 remained between 96-97% in the XYP group and was maintained intraoperatively higher than in the XY group (Figure 2B). Changes in HR were significantly higher in the XYP group than in the XY group at 15, 30, and 60 min after the beginning of surgery (Figure 2C). Both groups showed no significant differences in the changes in T and BP, and both parameters were maintained within the normal ranges intraoperatively (Figure 2D, E).

There was no significant difference in FBM between the two groups intraoperatively (0.61 ± 0.44 vs 0.33 ± 0.25, mean ± SD). However, patients with XYP showed smaller movements that could not disturb the operation, such as cramps, than patients with XY.

Table 1 Summary of cases assigned to the experiment.

Anesthesia	Cases	Breed*	Sex	Age (day)	Body weight (BW, kg)	Operation	Lidocaine administration for local anesthesia (total, [mg, mg/BW])	Operative time† (min)	Anesthesia time# (min)
XY	1	H	male	97	97.8	cryptorchidectomy, left	480, 4.9	90	135
	2	H	male	91	106	cryptorchidectomy, right	540, 5.1	122	165
	3	H	male	124	143	cryptorchidectomy, left	250, 1.7	209	254
	4	JB	female	242	246	herniorrhaphy	800, 3.3	115	197
	5	JB	male	130	136.5	herniorrhaphy	500, 3.7	133	219
	6	H	male	89	97	herniorrhaphy	200, 2.1	119	145
	7	H	male	63	80	herniorrhaphy	400, 5.0	140	170
XYP	8	H	male	89	101	herniorrhaphy	200, 2.0	87	117
	9	H	male	119	166	cryptorchidectomy, right	400, 2.4	77	95
	10	H	male	107	132	cryptorchidectomy, left	500, 3.8	113	154
	11	H	male	99	128	herniorrhaphy	500, 3.9	147	176
	12	H	male	87	108.5	herniorrhaphy	480, 4.4	155	188
	13	H	male	106	130	cryptorchidectomy, left	400, 3.1	210	225
	14	H	male	67	97.2	herniorrhaphy	500, 5.1	130	208
XY	(mean±SD)			119±54	129.5±52		452.9, 3.7	132.6	183.6
XYP	(mean±SD)			96±16	123.2±22		425.7, 3.5	131.3	166.1

*H: Holstein calves; JB: Japanese Black calves
†defined as time points from local anesthesia for skin incision to finish of skin suture
#defined as time points from the start of TIVA to emergence from anesthesia and extubation

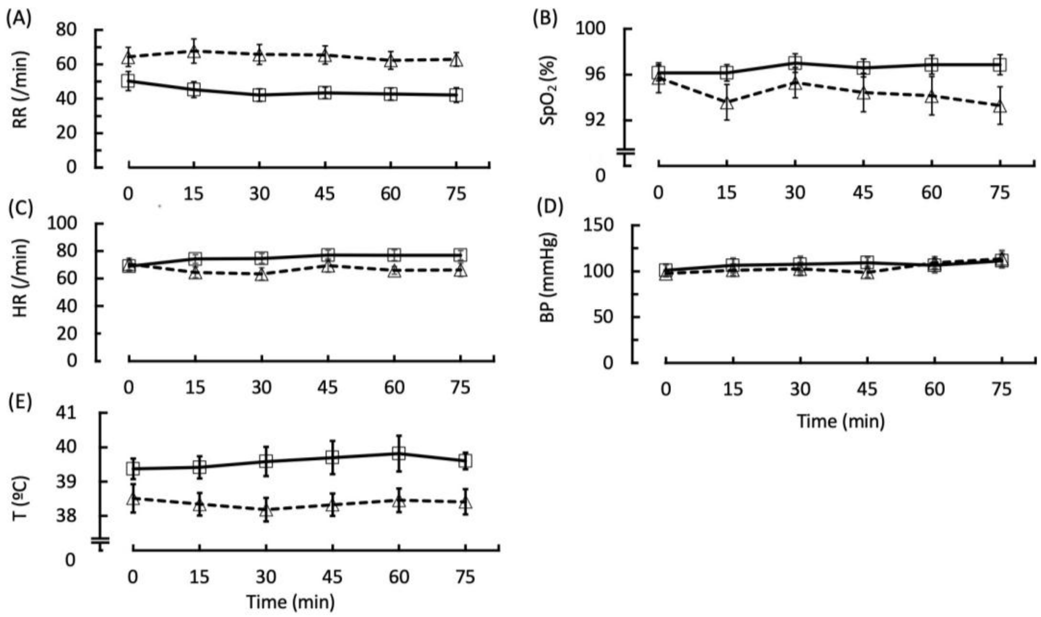

Figure 1 Profiles of the vitals at 15-minute intervals during surgery in each anesthesia group (n=7) of (A) respiratory rate, RR, (B) saturation of percutaneous oxygen, SpO2, (C) heart rate, HR, (D) blood pressure, BP, and (E) body temperature; T, solid and dashed lines indicate cases of TIVA with xylazine and propofol and that with xylazine only, respectively (mean ± SD).

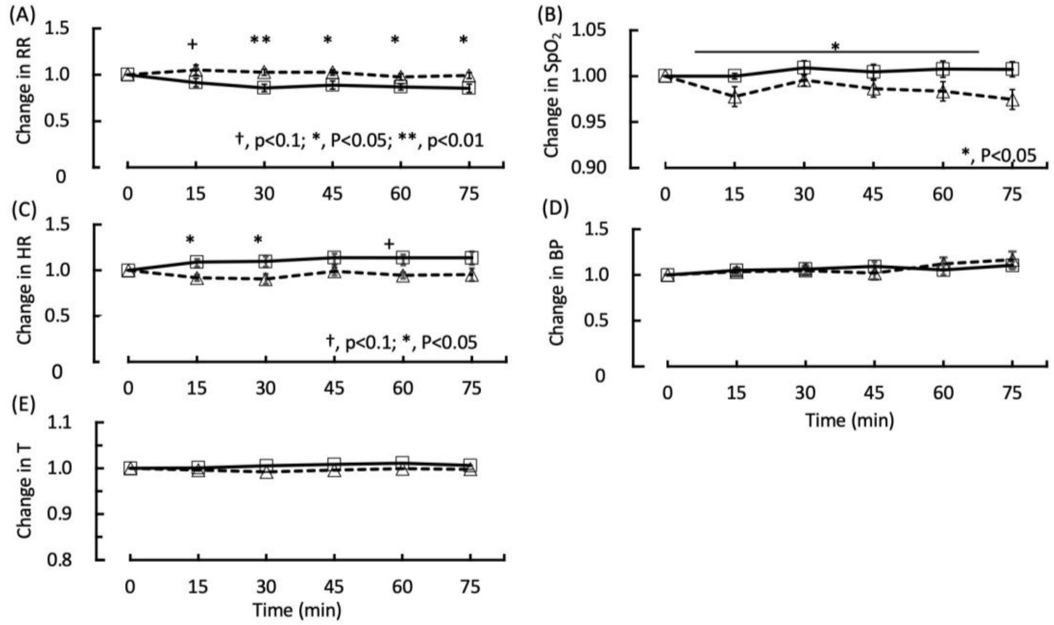

Figure 2 Profiles of changes in the vitals based on the start of the surgery at 15-minute intervals during the surgery in each anesthesia group (n=7) of (A) respiratory rate, RR, (B) saturation of percutaneous oxygen, SpO2, (C) heart rate, HR, (D) blood pressure, BP, and (E) body temperature, T, solid and dashed line indicate cases of TIVA with xylazine and propofol and that of with xylazine only, respectively (mean ± SD).
†, *, ** indicates significant differences ($p < 0.1$, 0.05, 0.01, respectively) as determined by two-way ANOVA post hoc Holm's procedure with anesthesia method and operative time (0-75 minutes, 15-minute intervals)

The RR in calves is approximately 24-36 per minute (Dißmann *et al.,* 2022), and many reports suggest that sufficient anesthesia requires more than 90% SpO_2 (Lin *et al.,* 2022). Propofol decreases respiratory rate by approximately 20% (Kumar *et al.,* 2014). However, in this study, the respiratory rate did not decrease below the normal range, and SpO_2 remained stable at 96-97%, even when propofol was used. Therefore, the anesthesia method used in this study may have been sufficient for gas exchange.

The HR under anesthesia in calves ranges from 70 to 90 beats per minute, and the normal average blood pressure is 90-120 mmHg (Lin *et al.,* 2022). Propofol increases the heart rate in calves (Deschk *et al.,* 2014); however, in this study, only a mild increase under TIVA using xylazine and propofol was observed. In addition, propofol decreases blood pressure in goats (Kumar *et al.,* 2014); however, in the present study, blood pressure was maintained within the normal range. Therefore, blood circulation could be maintained under TIVA with xylazine and propofol.

A previous study in goats indicated that combining dexmedetomidine and propofol abolished jaw laxity and reflex movements (Kumar *et al.*, 2014). In addition, adequate muscle relaxation was obtained in buffalo calves after propofol induction (Potliya *et al.*, 2015). In the present study, muscle relaxation was observed in a way similar to previous reports. Only smaller body movements were observed during TIVA using xylazine and propofol, and the degree of body movement was minor compared to TIVA using xylazine alone. These results suggest that combining xylazine and propofol suppresses body movements and provides sufficient muscle relaxation for laparotomy in calves.

In addition, side effects of propofol are reported, such as post-induction apnea, increased susceptibility to microbial infection, arrhythmia, circulation insufficiency, hypotension, and respiratory insufficiency (Guo and Ma, 2020; Lima *et al.,* 2022). However, in the present study, these clinical side effects were not observed. In the present study, we used 2% propofol for the prevention of abnormal body movement and consideration of the patient's body weight; 1% propofol requires twice the dose, and the rate of administration should be increased. However, other studies used 1 % propofol because of the prevention of side effects (Deschk et al. 2016; Lin HC et al. 2022), and patients' statuses, such as body weight and general appearance before surgery should be considered when selecting the type of vials.

In the present protocol, only two drugs are used, and the dose of propofol was low compared to previous studies (Reis *et al.,* 1993; Riebold, 2015). In addition, combination anesthesia can provide spontaneous breathing with sufficient gas exchange, blood circulation, less body movement, and sufficient muscle relaxation. Moreover, one of our surgery records provides the efficiency of the present protocol for a severe clinical case: intestinal torsion applied anastomosis in a calf, the patient's vitals were stable, and spontaneous breathing was maintained with sufficient saturation during surgery. Although further studies are needed to evaluate TIVA using xylazine and propofol for long-time surgery and severe clinical cases, the present protocol of TIVA has the potential to easily perform laparotomy with smaller equipment and facilities.

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Ethical statement: Ethical review and approval were waived for this study because it was a case report, and all examinations and treatments were performed on the patient. Informed consent was obtained from all owners who approved this study.

Authors contribution:
Keita Tokimitsu: Conceptualization, Methodology, Investigation, Data curation, Writing- Original draft preparation, Project administration
Momoko YACHIDA: Investigation, Data curation, Writing- Reviewing and Editing
Wataru MIKI: Investigation, Data curation
Tadashi KURAMOTO: Investigation, Data curation
Nanako MOCHIZUKI: Investigation, Data curation
Sakura YOSHIDA: Investigation, Data curation
Tadahiro GOTO: Methodology, Investigation, Data curation)
Yasuhiro MORITA: Conceptualization, Methodology, Investigation, Data curation, Formal analysis, Writing- Original draft preparation, Writing- Reviewing and Editing, Visualization, Project administration, Funding acquisition

List of abbreviations:
TIVA: Total intravenous anesthesia
RR: Respiratory rate
HR: Heart rate
SpO_2: Saturation of percutaneous oxygen
IV: Intravenous injection
IM: Intramuscular injection
ANOVA: Analysis of variance
SD: Standard deviation

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