NOTE *Surgery*

Propofol-Ketamine Anesthesia for Internal Fixation of Fractures in Racehorses

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ABSTRACT. To assess the clinical usability of propofol-ketamine anesthesia for internal fixation of fractures in racehorses, hemodynamics, blood pH and gases, and vital responses to the continuous intravenous anesthesia in 7 surgical cases were analyzed. The quality of induction with propofol was variable for individual horses. The vital signs reflecting circulation, breath, and anesthetic depth wer e kept good without any troubles throughout the surgery. Mean time from the end of anesthesia to standing up was prolonged, however recovery from anesthesia was calm and smooth in all cases. Propofol-ketamine anesthesia may be a clinically usable technique for internal fixation of fractures in racehorses, however induction with propofol alone is not recommended.
KEY WORDS: internal fixation, propofol, racehorse.

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Propofol (2,6,-diisopropylphenol) is an injectable anesthetic agent characterized by rapid metabolism and short duration of action [2, 16]. Propofol has been widely used as a sole agent or as a part of total intravenous anesthesia (TIVA) for induction and maintenance of anesthesia in human beings and small animals [4, 5, 7, 13]. Our previous studies indicated that the use of propofol as a sole agent for intravenous anesthesia in racehorses was unsatisfactory, because analgesia was insufficient for orthopedic surgery [unpublished data]. Others reported that the use of propofol alone for the maintenance of surgical anesthesia in ponies was associated with cardiorespiratory depression [3].

Ketamine is a dissociative anesthetic agent, which produces strong analgesia and stable hemodynamics. This drug is also used as a part of TIVA, because it is rapidly cleared from the body [6, 19]. Intravenous anesthesia with propofol and ketamine has been reported to provide a good maintenance of anesthesia without remarkable cardiorespiratory depression in human beings [4, 5]. Thus, it was considered that this technique would be usable for racehorses undergoing prolonged, invasive surgery. To assess the clinical usability of propofol-ketamine anesthesia for internal fixation of fractures in racehorses, hemodynamics, blood pH and gases, and vital responses to the continuous intravenous anesthesia were analyzed.

Seven thoroughbred racehorses (2 females and 5 males) were used in this study. The horses ranged in age from 2 to 4 years old (mean, 2.8 years old) and in weight from 410 kg to 475 kg (mean, 446 kg). They underwent internal fixation to repair a simple longitudinal fracture of the proximal phalanx or the third metacarpus. Fractures were repaired with 2 or 3 lag screws. All of the horses were considered healthy on the results of preanesthetic blood examination and electrocardiography. Food was withheld for 12 hr before surgery, but water was freely accessible. All procedures were approved by the Experimental Animal Committee, Japan Racing Association.

A 14-gauge intravenous catheter was placed in the jugular vein under local analgesia, and then heart rate (HR), respiratory rate (RR), and rectal temperature were recorded as baseline values. Within 10 min of premedication with xylazine (1.0 mg/kg; Celactar, Bayer, Tokyo, Japan) and midazolam (50 μg/kg; Dormicum, Yamanouchi, Tokyo, Japan), 3.0 mg/kg of propofol (Rapinovet, Mallinckrodt Veterinary, Mundelein, U.S.A.) was administered intravenously via the catheter over 3 min. Horses were restrainted behind a swing gate with their heads controlled by a halter and a rope during induction. The time taken to lie still after propofol injection was recorded, and the behavior and clinical responses during the course of anesthetic induction were scored according to Mama's report [9].

After induction, the horses were intubated endotracheally and positioned in lateral recumbency on a padded surgical table with the fractured limb up. The endotracheal tube was connected to a large-animal breathing circuit (MOK 94, Silver Medical, Japan) and 100% oxygen was supplied at a rate of 5 *l*/min during anesthesia. Ventilation was mechanically controlled to maintain $PaCO_2$ between 35 and 45 mmHg. Anesthesia was maintained with propofol and ketamine infused by using volumetric infusion pumps (IVAC 599, Alaris Medical Systems, U.S.A.). Propofol infusion was started at the rate of 0.15 mg/kg/min and then adjusted to get an appropriate anesthetic restraint, while ketamine was administered at the constant rate of 50 μg/kg/min. The depth of anesthesia was assessed subjectively by two experienced anesthetists based on the vital signs. Ketamine was stopped before 20 min of the propofol off. Another 14-gauge intravenous catheter was placed in the jugular vein and lactated Ringer's solution was infused at a rate of 8 to 12 m*l*/kg/hr to support the circulating blood volume during anesthesia.

Electrocardiogram (base-apex lead) was monitored continuously by an anesthesia monitoring system (M1166A, Hewlett Packard, Palo Alto, U.S.A.). A 20-gauge catheter

was placed in the facial artery for measurement of systolic (SAP), diastolic (DAP), and mean arterial blood pressures (MAP) and for arterial blood sample collection. Arterial blood pressures were measured directly through the catheter by a pressure transducer system. HR, RR, SAP, DAP, MAP, and rectal temperature were recorded every 15 min from the beginning of propofol and ketamine administration. Arterial blood samples were collected every 15 min and immediately analyzed for PaO_2, $PaCO_2$, and pH by a blood-gas analyzer (860CO, Bayer Medical, U.S.A.).

At the end of the surgery, propofol infusion was stopped. Horses were immediately transported to a darkened recovery room and positioned in lateral recumbency. Oxygen was supplied via a demand valve until adequate spontaneous respiration appeared, at which time the endotracheal tube was removed. Horses were allowed to recover without assistance, and no additional drugs were administered. Times taken from the end of anesthesia (propofol infusion was discontinued) to extubation, first movement, sternal recumbency, first attempt to stand, and standing up were recorded. The behavior and clinical response during the course of recovery were scored according to Mama's report [9]. All horses were given cephalothin sodium (20 g/body/day; i.v.) and phenylbutazone (1.0 to 2.0 g/body/day; p.o.) for 3 to 7 days after surgery.

Analysis of variance was used to evaluate the variations in HR, SAP, DAP, MAP, body temperature, and blood gas data over time. If a significant difference was identified, paired t-test was used for further analysis. A value of $P<0.05$ was considered statistically significant. Data were expressed as mean ± s.d.

Mean time from the start of propofol administration to lateral recumbency was 2.5 ± 0.5 min. Scores for induction were variable: one was excellent, three were good, one was fair, and two were poor. Two horses paddled in the induction period. All horses became quiet within 1 min after lateral recumbency and easily intubated on the first or second attempt. One horse required additional propofol (1.0 mg/kg) to be hoisted onto the surgical table.

Propofol infusion rate and the total dose of propofol and ketamine infused for individual horses are shown in Table 1. The mean duration of propofol infusion was 124 ± 11 min (range from 112 to 140 min) and the mean duration of ketamine infusion was 105 ± 13 min (range from 90 to 121 min). The mean propofol infusion rate required for the enough anesthetic restraint to achieve the surgery was 0.16 ± 0.02 mg/kg/min. The vital signs reflecting circulation, breath, and anesthetic depth were kept good without any troubles throughout the surgery.

Mean values for HR, SAP, DAP, MAP, and rectal temperature are shown in Table 2 and those for RR, PaO_2, $PaCO_2$, and pH are shown in Table 3. HR significantly increased with duration of anesthesia. There was no significant change in arterial blood pressure over time. Body temperature significantly decreased with time. RR decreased immediately after induction and intermittent apnea (less than 2 breaths/min) was observed early in the anesthetic period in all horses. Intermittent positive pressure ventilation (IPPV) was initiated at approximately 5 min of anesthesia. RR was set between 6 and 10 breaths/min and inspiratory pressure was between 20 and 25 cmH_2O. $PaCO_2$ was slightly higher than the target value at 15 min of anesthesia, and then maintained between 35 and 45 mmHg at later times. PaO_2 did not change significantly throughout anesthesia; however, PaO_2 values for individual horses were variable (ranged from 179 to 565 mmHg).

Mean times from the end of anesthesia to extubation, first movement, sternal recumbency, first attempt to stand, and standing up were 6 ± 3 min, 20 ± 5 min, 45 ± 10 min, 66 ± 22 min, and 70 ± 23 min, respectively. Scores for recovery were good in five horses and fair in two horses. Two horses judged fair stood up on the second attempt with no exciting and struggling in the recovery period. No apparent complication was observed after anesthesia in all cases.

Propofol usually provides smooth induction with good muscle relaxation in human beings and small animals [2, 16]. However, increased spontaneous motor activity was also reported in a small number of individuals [8, 9, 12]. Premedication with xylazine or detomidine was reported to reduce muscular activity and improve the quality of propofol induction in small animals [17]. In Mama's study of adult horses, excitatory behavior and increased muscular activity were occasionally observed after propofol induction despite alpha2-agonist premedication (xylazine or detomidine) [8, 9]. Combination of alpha2-agonist and benzodiazepine provides better sedation than one of the drugs used on its own without further cardiovascular or respiratory depression [18]. Therefore, combination of xylazine and midazolam was administered to produce deeper sedation than that produced by xylazine alone in this study. In Matthews'

Table 1. Propofol infusion rate and the total dose of propofol and ketamine infused for individual horses

No.	Propofol Infusion rate (mg/kg/min) [Time (min)]	Total dose of propofol (mg/kg)	Total dose of ketamine (mg/kg)
1	0.15 [112]	16.80	4.50
2	0.15 [50] → 0.175 [13] → 0.20 [15] → 0.175 [20] → 0.20 [35]	23.28	5.75
3	0.15 [129]	19.35	5.60
4	0.15 [38] → 0.175 [12] → 0.20 [65]	20.80	4.70
5	0.15 [82] → 0.175 [34] → 0.20 [24]	23.05	6.05
6	0.15 [121]	18.15	5.20
7	0.15 [47] → 0.175 [26] → 0.15 [47]	18.65	4.90

Table 2. Values (mean ± SD) of heart rate (HR), systolic (SAP), diastolic (DAP), and mean (MAP) arterial blood pressures, and rectal temperature in 7 horses before and during propofol-ketamine anesthesia

	HR (bpm)	SAP (mmHg)	DAP (mmHg)	MAP (mmHg)	Rectal Temperature (°C)
baseline	34 ± 6 a				38.0 ± 0.3 a
15	29 ± 3 b	134 ± 14	86 ± 14	104 ± 12	38.0 ± 0.4 a
30	29 ± 3 b	129 ± 11	85 ± 12	101 ± 10	37.8 ± 0.5 a
45	29 ± 3 b	126 ± 9	83 ± 10	99 ± 9	37.7 ± 0.5 ab
60	32 ± 5 ab	130 ± 11	86 ± 10	101 ± 10	37.6 ± 0.5 abc
75	34 ± 5 ab	130 ± 11	86 ± 9	103 ± 11	37.5 ± 0.5 bc
90	37 ± 6 a	135 ± 13	88 ± 10	104 ± 10	37.3 ± 0.4 bc
105	36 ± 6 a	133 ± 9	86 ± 8	103 ± 10	37.2 ± 0.5 c
120 (n=5)	36 ± 5	135 ± 9	87 ± 7	104 ± 7	37.1 ± 0.5

Data with the same superscript are not significantly different from each other.

Table 3. Values (mean ± SD) of respiratory rate (RR), PaO_2, $PaCO_2$, and pH in 7 horses before and during propofol-ketamine anesthesia

	RR (bpm)	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	pH
baseline	14 ± 3 a			
15	8 b	357 ± 165	47 ± 6 a	7.39 ± 0.06 a
30	8 b	418 ± 141	41 ± 3 b	7.41 ± 0.03 a
45	8 b	428 ± 130	41 ± 3 b	7.42 ± 0.02 ab
60	8 b	413 ± 127	42 ± 3 b	7.43 ± 0.04 ab
75	8 b	411 ± 121	41 ± 4 b	7.45 ± 0.03 ab
90	8 b	414 ± 117	40 ± 4 b	7.45 ± 0.03 ab
105	8 ± 1 b	422 ± 128	41 ± 4 b	7.45 ± 0.03 ab
120 (n=5)	8	441 ± 59	41 ± 3	7.46 ± 0.03

Data with the same superscript are not significantly different from each other.

study of adult horses, administration of propofol over 2 min appeared to produce smoother induction than over 1 min administration [12]. A slower rate of administration seems to decrease the incidence of excitable inductions, therefore, propofol was administered over 3 min in this study. Although all horses seemed to be well sedated before induction, 3 of 7 horses had muscular rigidity during induction and 2 of them paddled during the transition to lateral recumbency. The quality of induction in this study was similar to those reported by Mama and Matthews [8, 9, 12]. Such excitatory behavior was unpredictable and harmful to both horses and handlers, so induction with propofol is not recommended if adequate restraint is not available. The use of guaifenesin with propofol is reported to reduce the frequency of violent anesthesia inductions and this technique appears to be suitable for horses, especially in easily excitable thoroughbred racehorses [1, 10, 12].

Cardiorespiratory depression, lack of inherent analgesia, and high cost prevent the routine use of propofol as a sole agent for anesthetic management in horses. Therefore, it would be advantageous to combine propofol with other anesthetic agents in order to improve the quality of anesthesia. Ketamine was chosen for this purpose, because it does not have marked depressant activity on cardiovascular or respiratory system and produces excellent analgesia in horses [11, 14]. Ketamine has been reported to have additive anesthetic effects when combined with propofol and to decrease the dose of propofol required to maintain surgical anesthesia in human beings and small animals [4, 5, 7]. In our previous study, 0.20 to 0.30 mg/kg/min of propofol was required to maintain surgical anesthesia when propofol was given alone [unpublished data]. Propofol infusion rate in this study was lower than these values, which would minimize the adverse effects of propofol and decrease the cost of anesthesia. The vital signs reflecting circulation, breath, and anesthetic depth were kept good without any troubles throughout the surgery, therefore, propofol infusion rate in this study was considered to be adequate.

HR often remains unchanged when anesthesia is maintained with propofol alone [2, 16]. HR did not change significantly during anesthesia in previous studies [8, 12, 15], whereas HR significantly increased with duration of anesthesia in our study. The increase in HR was probably due to the stimulatory effect of ketamine on the sympathetic nervous system or surgical stimuli. Propofol has been reported to decrease systemic arterial blood pressure as a result of peripheral vasodilation. Arterial blood pressure was well maintained in this study and it was also owing to the cardiovascular stimulating effects of ketamine or surgical stimuli, which counteracted the depressant effects of propofol. The

low propofol infusion rate might also play an important role in minimizing the adverse effects on cardiovascular system. MAP should be maintained above 70 mmHg to prevent postanesthetic complications such as myopathy, lameness, and colitis-X. In this study, MAP was maintained within an acceptable range without concurrent administration of inotropic agents (eg, dobutamine, dopamine)

The duration of recovery was not correlated to the duration of anesthesia and surgery. The total dose of propofol infused did not correlate to the time of recovery, either. Although recovery times in this study were slightly longer than those in previous reports, recovery from anesthesia was calm and smooth in all cases.

In conclusion, propofol-ketamine anesthesia may be a clinically usable technique for internal fixation of fractures in racehorses. However, induction with propofol is not recommended, because excitable inductions were observed in some cases.

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