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Anesthetic management with sevoflurane combined with alfaxalone-medetomidine constant rate infusion in a Thoroughbred racehorse undergoing a long-time orthopedic surgery

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A three-year old Thoroughbred racehorse was anesthetized with sevoflurane and oxygen inhalation anesthesia combined with constant rate infusion (CRI) of alfaxalone-medetomidine for internal fixation of a third metacarpal bone fracture. After premedication with intravenous (IV) injections of medetomidine (6.0 µg/kg IV), butorphanol (25 µg/kg IV), and midazolam (20 µg/kg IV), anesthesia was induced with 5% guaifenesin (500 ml/head IV) followed immediately by alfaxalone (1.0 mg/kg IV). Anesthesia was maintained with sevoflurane and CRIs of alfaxalone (1.0 mg/kg/hr) and medetomidine (3.0 µg/kg/hr). The total surgical time was 180 min, and the total inhalation anesthesia time was 230 min. The average end-tidal sevoflurane concentration during surgery was 1.8%. The mean arterial blood pressure was maintained above 70 mmHg throughout anesthesia, and the recovery time was 65 min. In conclusion, this anesthetic technique may be clinically applicable for Thoroughbred racehorses undergoing a long-time orthopedic surgery.

Key words: *alfaxalone, medetomidine, sevoflurane, Thoroughbred*

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In equine practice, a long-time orthopedic surgeries are usually performed under inhalation anesthesia. Among inhalation anesthetic agents, sevoflurane has the advantages of rapid induction, easy control of anesthetic depth, and rapid recovery because of its low blood solubility [4, 17, 23]. However, sevoflurane is known to induce both dose- and time-dependent cardiopulmonary depression, which could increase the risk of postanesthetic mortality and death [2, 6, 12, 24]. The important issues in relation to the anesthetic management for a long-time orthopedic surgery are maintenance of adequate cardiopulmonary function and achievement of safe recovery.

Most balanced anesthetic techniques include the use of an α_2-adrenoceptor agonist because of its potent sedative and analgesic effects [21]. The short half-life of medetomidine and its selectivity and potency make it suitable for use as a constant rate infusion (CRI) for balanced anesthesia in horses [3, 5, 11]. In our previous study [20], medetomidine (3.0 µg/kg/hr) CRI reduced the sevoflurane requirement for arthroscopic surgery by approximately 10% in Thoroughbred racehorses, resulting in good maintenance of cardiopulmonary function, and improved the quality of recovery from anesthesia.

Alfaxalone (3α-hydroxy-5α-pregnane-11, 20-dione), a new injectable anesthetic agent, is a synthetic neuroactive steroid that acts on the gamma aminobutyric acid $(GABA)_A$ receptors in the central nervous system and produces unconsciousness and muscle relaxation. Several experimental trials of alfaxalone in horses have been reported [7–9, 14, 15, 18, 22]. In our previous study [22], alfaxalone showed similar effects in relation to anesthetic induction, recovery quality, and cardiopulmonary responses compared with ketamine and thiopental in Thoroughbred horses. Others reported that alfaxalone has a number of pharmacological properties that are desirable for CRI in horses [7, 8]. In our pilot study (unpublished data; n=25), alfaxalone-medetomidine CRI

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reduced the sevoflurane requirement for a short-time (60–90 min) arthroscopic surgery by approximately 23–25% and resulted in almost the same recovery quality compared with medetomidine CRI. Therefore, further reduction of the sevoflurane requirement is expected by applying this anesthetic technique for a long-time orthopedic surgery in the same way as applied for a short-time arthroscopic surgery. In this report, we describe the anesthetic management with sevoflurane combined with alfaxalone-medetomidine CRI in a Thoroughbred racehorse undergoing a long-time (over 3 hr) internal fixation surgery.

A three-year old male Thoroughbred racehorse weighing 450 kg developed a medial condylar fracture of the right third metacarpal bone during exercise. The fracture line extended proximally for more than 1/3 of the total length of the third metacarpal bone. Internal fixation surgery using a 10-hole locking compression plate (LCP) was performed on the day after fracture. A 14-G catheter (BD Angiocath 14G 5-25", Nippon Becton Dickinson, Tokyo, Japan) was placed in the right external jugular vein under local anesthesia. Ten min after premedication with medetomidine (6.0 μg/kg; Dorbene, Vetcare Oy, Salo, Finland), butorphanol (25 μg/kg; Vetorphale, Meiji Seika Pharma Co., Ltd., Tokyo, Japan), and midazolam (20 μg/kg; Dormicum, Astellas Pharma Inc., Tokyo, Japan), anesthesia was induced with 5% guaifenesin (500 m*l*/head; 5% Guaifenesin, Shinyo Pure Chemicals Co., Ltd., Osaka, Japan) followed immediately by alfaxalone (1.0 mg/kg; Alfaxan, Jurox Pty Ltd., New South Wales, Australia). The horse was restrained behind a swing gate with its head controlled by a halter and a rope during the induction phase. After induction of anesthesia, the horse was intubated endotracheally and positioned in left lateral recumbency on a padded surgical table. Anesthesia was maintained with sevoflurane (Sevofrane, Maruishi Pharmaceutical Co., Ltd., Japan) and oxygen (approximately 5 *l*/min) in combination with alfaxalone (1.0 mg/kg/hr) and medetomidine (3.0 μg/kg/hr) CRI throughout the maintenance period. Anesthetic depth was adjusted by altering inspired sevoflurane concentration to be maintained at an adequate level for the surgical procedure. Respiration was controlled by using intermittent positive pressure ventilation (MOK 94, Silver Medical Co., Tokyo, Japan) at a rate of 8–12 breaths/min to maintain arterial carbon dioxide tension ($PaCO_2$) between 45 and 55 mmHg. Lactated Ringer's solution (Lactec Injection, Otsuka Pharmaceutical Co., Ltd., Tokyo, Japan) was infused at a rate of approximately 10 m*l*/kg/hr during anesthesia. Dobutamine (Dobutrex, Shionogi & Co., Ltd., Osaka, Japan) was infused to maintain mean arterial blood pressure (MAP) above 70 mmHg. Four-point high palmar nerve block was performed using mepivacaine (3 m*l*; Carbocaine Injection 2%, AstraZeneca K. K., Osaka, Japan).

A base-apex lead electrocardiogram was used to monitor heart rate (HR) and rhythm. A 20-gauge catheter (Surflo 20G 2", Terumo Corporation, Tokyo, Japan) was placed in the facial artery for measurement of systemic arterial blood pressure and for arterial blood sample collection. Arterial blood pressures were measured directly through the catheter by a transducer system. Respiratory gas was collected continuously, and end-tidal sevoflurane (ET_{SEVO}) concentration was determined by infrared absorption. The ET_{SEVO} concentration was recorded throughout anesthesia, and HR, systolic arterial blood pressure (SAP), diastolic arterial blood pressure (DAP), and MAP were recorded every 5 min by an anesthesia monitoring system (BP608, Omron Colin Co., Ltd., Tokyo, Japan). Arterial blood samples were collected at 30, 60, 90, 120, and 180 min, and $PaCO_2$, arterial oxygen tension (PaO_2), and pH were immediately analyzed by a blood-gas analyzer (ABL800 FLEX, Radiometer Co., Ltd., Tokyo, Japan).

Two cortex screws were inserted in lag fashion at the distal part of fracture. Then a 10-hole LCP was inserted according to the method previously described by James *et al* [13].

After surgery, the horse was transported to a darkened recovery room and positioned in left lateral recumbency. Respiration was assisted by pressure support ventilation via a demand valve until adequate spontaneous respiration appeared, and then the endotracheal tube was removed. During the recovery period, spontaneous respiration appeared at 10 min (time from the end of inhalation anesthesia), and the endotracheal tube was removed at 15 min. The horse was resedated with medetomidine at 15, 20, and 25 min (2.0 μg/kg IV). Recovery was assisted with the horse's head and tail controlled by a halter and ropes.

The scoring scale of 1–5 (1, poor; 2, marginal; 3, fair; 4, good; 5, excellent) previously reported by Mama *et al.* was used for subjective assessment of induction [16]. The horse showed a smooth transition to lateral recumbency with good muscle relaxation, and the induction quality in this case was scored 5. Goodwin *et al.* reported that premedication with romifidine (100 μg/kg IV) followed by alfaxalone (1.0 mg/kg IV) induction resulted in excited and uncontrolled induction in their preliminary trials [7]. In our previous study, 2 of 6 horses administered alfaxalone (1.0 mg/kg IV) showed slight muscular rigidity or limb movement during the transition to lateral recumbency, although all horses seemed to be well sedated with medetomidine (6.0 μg/kg IV) and midazolam (20 μg/kg IV) before induction [22]. Previous studies suggested that including guaifenesin might improve induction quality [9]. Therefore, guaifenesin was combined with alfaxalone in this case, and this might have contributed to smooth induction.

The total surgical time was 180 min, and the total inhala-

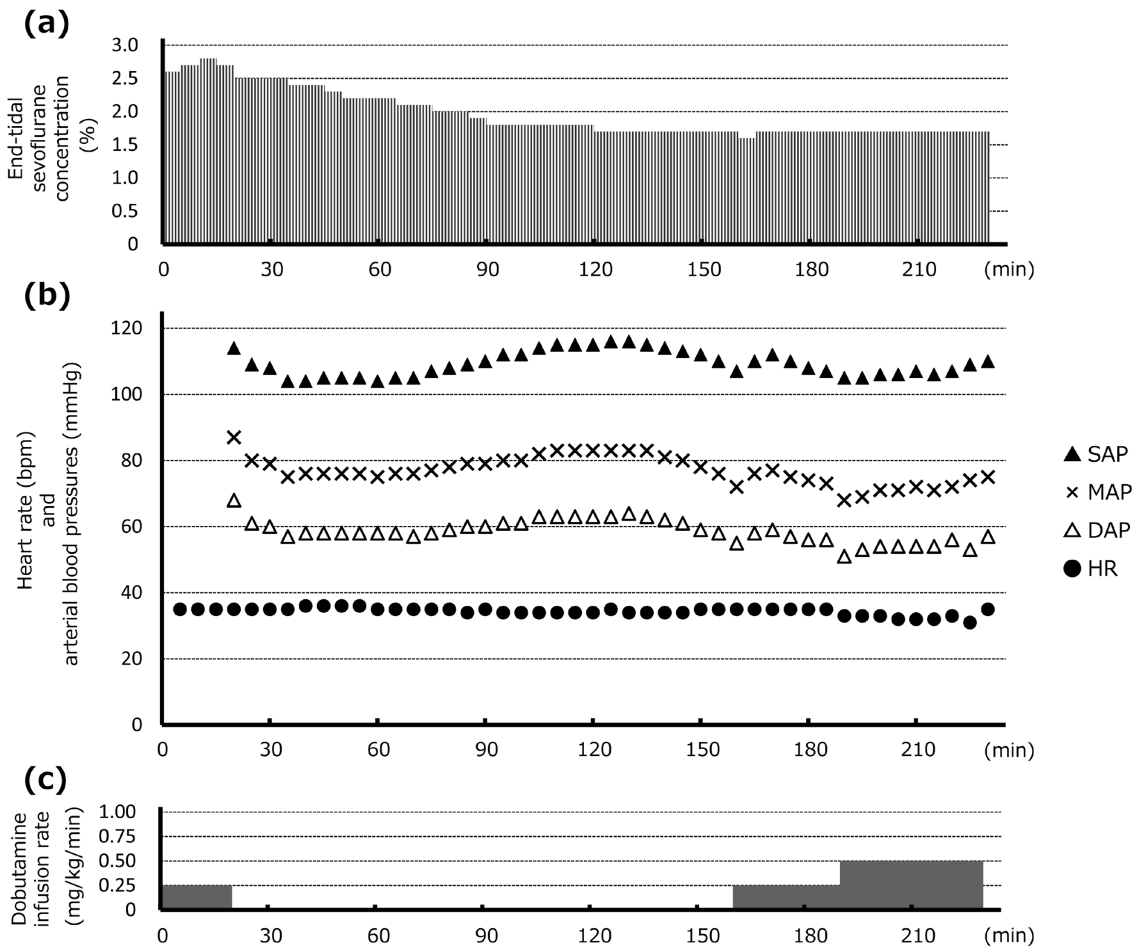

Fig. 1. Time course changes in end-tidal sevoflurane concentration (a), heart rate and arterial blood pressures (b), and dobutamine infusion rate (c) during the anesthetic period.

tion anesthesia time was 230 min. The ET_{SEVO} concentrations recorded during anesthesia are shown in Fig. 1a. We previously reported that the mean ET_{SEVO} concentrations required for arthroscopic surgery and internal fixation were 2.8 ± 0.1% [20] and 3.0 ± 0.3% [19], respectively, when anesthesia was maintained with sevoflurane alone. We have also reported that medetomidine CRI reduced the mean ET_{SEVO} concentrations required for arthroscopic surgery by approximately 10% [20]. In this case, the average ET_{SEVO} concentrations during surgery was 1.8%, which was equivalent to approximately 80% of the minimum alveolar concentration of sevoflurane in horses (2.31 ± 0.11%) [1]. It was suggested that the potent anesthetic effect of alfaxalone compensated for the reduction of sevoflurane. Granados *et al.* reported that alfaxalone CRI (0.42 mg/kg/hr) reduced the requirements of desflurane by 22% in sheep undergoing experimental orthopedic surgery [10], and these results support our current study. Further study is needed to determine the actual sevoflurane sparing effect of alfaxalone-medetomidine CRI in horses.

The HRs and blood pressures recorded during anesthesia are shown in Fig. 1b. HR was stable and maintained at an adequate value during anesthesia. MAP was maintained above 70 mmHg throughout anesthesia. We previously reported that the mean dobutamine infusion rate required for keeping MAP between 60 and 80 mmHg was 0.90 ± 0.16 μg/kg/hr when anesthesia was maintained with sevoflurane alone for internal fixation [19]. The dobutamine infusion rate required for keeping MAP within the target value was much lower in the current case (Fig. 1c). Goodwin *et al.* reported that the average MAP during alfaxalone-medetomidine anesthesia for field castration was 104–112 mmHg [9]. Combination with alfaxalone-medetomidine CRI might have minimized the cardiovascular depression as a result of sevoflurane reduction. Results for respiratory values are shown in Table 1. $PaCO_2$ was maintained within the target

Table 1. Time course changes in arterial oxygen tension (PaO_2), arterial carbon dioxide tension ($PaCO_2$), and blood pH during the anesthetic period

Time (min)	30	60	90	120	180
PaO_2 (mmHg)	546	541	549	541	527
$PaCO_2$ (mmHg)	57.1	52.3	52.6	50.0	50.6
pH	7.35	7.38	7.39	7.41	7.40

value throughout anesthesia except at 30 min.

The horse stood quietly with some ataxia in the second trial at 65 min. The quality of recovery was a clinically acceptable level. In our pilot study (the above-mentioned unpublished data), the mean time to standing after 60–90 min of sevoflurane anesthesia in combination with alfaxalone-medetomidine CRI was 72 min. Although the anesthesia time exceeded 3 hr and the horse was resedated with medetomidine three times for prevention of rough recovery, the time from the end of inhalation anesthesia to standing was not prolonged. It was considered that both alfaxalone and medetomidine did not accumulate and were rapidly cleared from the body. No complications were observed after surgery. The fracture was successfully repaired, and the LCP was removed under sedation and local anesthesia at 85 days after surgery.

In conclusion, alfaxalone-medetomidine CRI reduced the sevoflurane requirement, providing good maintenance of cardiopulmonary function. We consider that sevoflurane in combination with alfaxalone and medetomidine CRI can be a clinically effective anesthetic technique for Thoroughbred racehorses undergoing a long-time orthopedic surgery. Further studies are needed to accurately evaluate whether this anesthetic technique is applicable for various types of equine surgery.

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