Effects of Propofol-Sevoflurane Anesthesia on the Maternal and Fetal Hemodynamics Blood Gases, and Uterine Activity in Pregnant Goats

Kentaro SETOYAMA[1)], Takeshi SHINZATO[1)], Kazuhiro MISUMI[1)]*, Makoto FUJIKI[1)] and Hiroshi SAKAMOTO[1)]

[1)]*Department of Veterinary Medicine, Kagoshima University, 21–24 Korimoto 1-chome, Kagoshima 890–0065, Japan*

ABSTRACT. To determine the effects of propofol and sevoflurane on hemodynamics, acid-base balance and uterine activity in pregnant animals, a prospective experimental study was designed by use of ten pregnant goats. Propofol was intravenously administered at a bolus dose of 5 mg/kg and then infused a rate of 0.3 mg/kg/min for 5 min. Following the induction, the animals were incrementally inhaled 2.7 and 4.1% of end-tidal concentration of sevoflurane each for 30 min, and then recovered. The maternal and fetal heart rate (HR), arterial blood pressure (BP) and acid-base balance, the intrauterine pressure (IUP), and the uterine blood flow (UBF) were measured. Following the pre-anesthetic data, the parameters were measured 7 times throughout the anesthetic and recovering periods. The propofol infusion induced 1.37 times of HR increase and produced decrease in PO_2 and a relevant metabolic acidemia in the mother, with no effect in the fetus. Sevoflurane reduced BP in the fetus from 30 (2.7%) to 60 (4.1%) min of inhalation. The uterine contractions disappeared throughout sevoflurane inhalation, and then recurred within 15 min after the cessation of sevoflurane. Propofol injection increases HR, and induces a moderate hypoxemia and metabolic acidemia associated with the suppressed ventilation for pregnant goats, with less effect on the fetal hemodinamics. Sevoflurane causes minimal change in maternal hemodynamics, but induces significant hypotension in the fetus and reduction of uterine activity. These data may be useful in making anesthetic choices combined with analgesia for Caesarian section in goats.
KEY WORDS: fetus, pregnant goat, propofol, sevoflurane.

Anesthesia used for pregnant small ruminants should be taken care of the depressed blood volume (in particular, the placental blood flow) and hypoventilation in the mother. The higher blood volume that is 130 to 150% of normal near term, is meaningful to compensate the increased oxygen consumption in the developing fetus, placenta, uterus, and mammary tissue for the pregnant animals [3]. So, decreased cardiac output and subsequently utero-placental circulation, subsequent to analgesics, sedatives and anesthetics injections with cardiac depression [12, 15], would be unfavorable. Drug-induced uterine contraction is another factor to decrease utero-placental perfusion [27]. Hypoxemia and acidemia secondary to hypoventilation under anesthesia are also more serious, because of the decreased functional residual capacity (FRC, which is oxygen reserve in pulmonary capillaries between breaths) induced by the anterior displacement of the diaphragm due to the increased abdominal volume (that is the enlargement of gravid uterus) in the pregnants. In addition to such unfavorable effects, the placenta-transferred anesthetics could be increasingly complicated the fetal distress, and therefore, quickness of induction and recovery, and ease of anesthetic controllability are important in order to adopt in pregnant animals.

Propofol (2, 6-di-isopropylphenol compound), which has rapid onset and offset of action, is being used commonly as an induction drug for veterinary patients [4, 6, 19]. Due to the rapid emergence and disappearance of the anesthetic effect depending on a rapid redistribution of the drug from the central nervous system [18, 28], propofol can also be injected either continuously or repeatedly to maintain general anesthesia instead of the use of volatile anesthetics [21, 30]. Some reports on propofol in pregnant animal, have shown that continuous propofol anesthesia would not adversely affect maternal or fetal heart rate and blood pressure [2, 11], cause less decrease in uterine blood flow [2, 11], or suppress spontaneous uterine contraction [17]. Except for its less analgesic action, propofol could be safer for pregnant animals as compared with the other induction agents.

When we maintain the general anesthesia for Caesarean sections, inhalation anesthetics have been more often used than intravenous agents, because of the better and easier control of anesthetic depth. Sevoflurane is a newer volatile anesthetic in veterinary clinics [1, 7, 14, 23], with smooth and quick induction and recovery due to a low blood/gas partition coefficient (0.68) [18] and less accumulation (the 95% expired, and the 5% metabolized) [9]. To our knowledge, the physiological response to sevoflurane in pregnant animal has not yet been reported, except for analgesic enhancement related to pregnant hormones. The aim of this study was to look at the effects of propofol and sevoflurane on the hemodynamics and the acid-base balance in pregnant goat and the fetus.

MATERIALS AND METHODS

Experimental animals: This study was approved by Kagoshima University Institutional Animal Care and Use

* CORRESPONDENCE TO: MISUMI, K., Department of Veterinary Medicine, Kagoshima University, 21–24 Korimoto 1-chome, Kagoshima 890–0065, Japan.

Committee. The experiments were carried out on ten pregnant Japanese Saanen goats (26.3 to 39.9 kg; mean weight ± standard deviation, 31.1 ± 5.6 kg in body weight), between 125 and 135 days of gestation. The animals were healthy, as determined by pre-operative examinations, including physical examination, clinical laboratory evaluation, radiography of the thorax and abdomen, and ultrasonography of the fetus. The goats were kept without food or water for at least 24 hr before the operation. The goats were also fasted for at least 24 hr before the study. The surgical procedure was performed under oxygen-air-isoflurane following ketamine (10 mg/kg intravenously) induction. An incision was made in the peritoneum, and a blood flow meter with an inner diameter 2 mm (3S, Transonic Systems Inc, NewYork, U.S.A.) which was precedently calibrated in static water, was mounted on the middle uterine artery to evaluate uterine blood flow (UBF). The gravid uterus was then exposed, and the fetal head was exteriorized through a small hysterotomy incision. Three-point-eight French-scale (Fr) polyethylene catheters were inserted into the fetal carotid artery and jugular vein. Electrocardiogram electrodes were attached to the three subcutaneous points of the bilateral precordia and the dorsal neck. The fetus was returned and a 4.7-Fr polyethylene catheter was placed into the amniotic cavity, to measure intrauterine pressure (IUP), before the uterine incision was closed. After suturing the abdominal incision, 4.7-Fr polyethylene catheters were inserted into the femoral artery and vein of the mother. The catheters were filled with heparin added saline (10 IU/m*l* of saline) to prevent the obstruction due to blood coagulation. After the surgery, the animals were injected appropriate antibiotics and analgesics, and allowed to recover for at least postoperative 48 hr.

Experimental protocol: On the day of the experiment, while the animals were allowed to stay quietly in their cage, the data of maternal and fetal heart rate (HR), arterial blood pressure (BP), IUP, UBF, respiratory rate (RR) and arterial blood gas analysis were obtained as the baseline values. Five min after taking the baseline values, propofol was administered intravenously at a dose of 5 mg/kg [30] within 30 sec, and then infused continuously (0.3 mg/kg/min) for 5 min, according to previous reports [2]. The data were also obtained at 5 min following the first bolus injection of propofol. After obtaining the data, the goats were intubated and then exposed to oxygen-air-sevoflurane gas for 1 hr by using a semi-closed circuit system. The end-tidal sevoflurane concentration was set at 2.7% (1 × minimum alveolar concentration, MAC) for 30 min (MAC was assumed 2.7%) [7], after taking the 30 min measurements the end-tidal concentration was increased to 4.1% (1.5 × MAC). The inhaled sevoflurane (%) was monitored as the end-tidal anesthetics concentration in the gas mixture sampled at the rate of 200 m*l*/min, according to the infrared absorption method programmed in an anesthetic gas analyzer (BP-508, Colin Co., Komaki, Japan) which had been already calibrated by use of a standard gas. The goats were ventilated mechanically with a volume-limited respirator (ACE-3000, ACOMA medical industry Co., Tokyo, Japan) throughout the anesthesia. The

tidal volume and respiratory rate were set 15 m*l*/kg of body weight and 7 breaths/min, respectively. The oxygen flow was controlled between 2.5 to 4.0 *l*/min depending on their minute ventilation. Inspiratory oxygen concentration was monitored by use of an oxygen analyzer (FS-25II, oxygen monitor, ACOMA medical industry Co., Tokyo, Japan) and was at least 0.21. The catheters to measure the maternal and fetal BP and IUP were connected to sterile pressure transducers calibrated previously under the atmospheric pressure. The electrocardiogram electrodes were connected to a variability polygraph to monitor the fetal HR. UBF was measured by the flow probe connected to an electromagnetic blood flow meter (T206, 2 channel small animal blood flow meter, Transonic Systems Inc., NewYork, U.S.A.). Maternal and fetal HR, BP, IUP, and UBF were continuously recorded on the chart of the polygraph at the chart speed of 25 mm/min. At the given time periods (that is after 5 min of propofol infusion) at 15, 30, 45 and 60 min after sevoflurane inhalation, and 15 and 30 min after the cessation of sevoflurane, the chart was run at 25 mm/sec, and the values were measured and calculated after the each experiment. The maternal and fetal arterial blood pH, oxygen partial pressure (PO_2), and carbon dioxide partial pressure (PCO_2) were measured by a blood gas analyzer (Blood gas analyzer, AVL Scientific Co., U.S.A.), which was auto-calibrated by the specific standard liquids equipped in the instrument, and the measurements were corrected with the body temperature. The base excess was derived by means of the standard formula. To assess the uterine activity, the montevideo unit (MU) was calculated as follows [24, 26]: MU = {increased uterine pressure above baseline tone of a contraction (mmHg) × frequency}/10 min. The clinical findings including eyelid and corneal reflexes and reaction to painful skin pinch by a forcep were evaluated at the same period of anesthesia. The recovery findings were assessed according to a scoring system proposed by Valtonen *et al.* [32]: sedation (2-fully awake, 1-rousable, 0-not responding), ventilation (2-able to cough, 1-breathing easily, 0-airway require attention), movement (2-purposefully, 1-involuntarily, 0-not moving), Recovery scoring = sedation + ventilation + movement (maximum = 6 points). During the recovery, maternal spontaneous RR was also measured again.

Statistics: All values in the figures are expressed as the mean ± 1 standard deviation. The UBF was expressed as the percentage change from the baseline value. Statistical differences in the all parameters were analyzed by repeated measures analysis of variance, and Scheffe's method was used for simultaneous multiple comparisons. Differences in *p* value less than 0.05 were considered to be statistically significant.

RESULTS

The induction by propofol took 193 sec until the laryngeal reflex disappeared. And then, eyelid and corneal reflexes were lost and no movement for painful skin stimulation by clamp forceps was recorded throughout the anes-

Table 1. Recovery scoring assessment of sevoflurane anesthesia in pregnant goats

Time after the anesthesia off.	5 min	15 min	30 min	60 min
Sedation	1.3	1.7	2.0	2.0
Ventilation	1.4	2.0	2.0	2.0
Movement	0.6	1.0	1.4	2.0
Sum	3.3	4.7	5.4	6.0

The sum of the recovery score = sedation + ventilation + movement (max; 6 points); awakeness (2- fully awake, 1- rousable, 0- not responding), ventilation (2- able to cough, 1- breathing easily, 0- airway require attention), movement (2-purposefully, 1-involuntarily, 0-not moving). All data were presented as the averages.
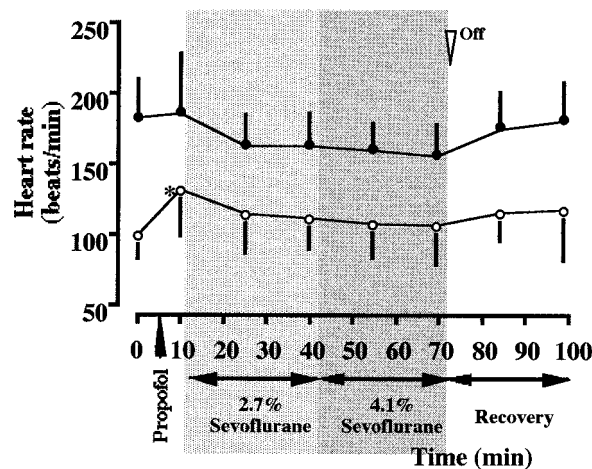

Fig. 1. Changes in the maternal and fetal heart rate during propofol-sevoflurane anesthesia in goats. The increased heart rate in the mother following propofol injection was statistically significant (*, p<0.05). The mothers' and fetuses data were expressed with the open and the closed circles, respectively. The baseline values were obtained at the time 0, and followed by propofol injection (black arrowhead) the 5 min later. The shaded area and the white arrow head indicate the inhalation period and the cessation of anesthesia, respectively.
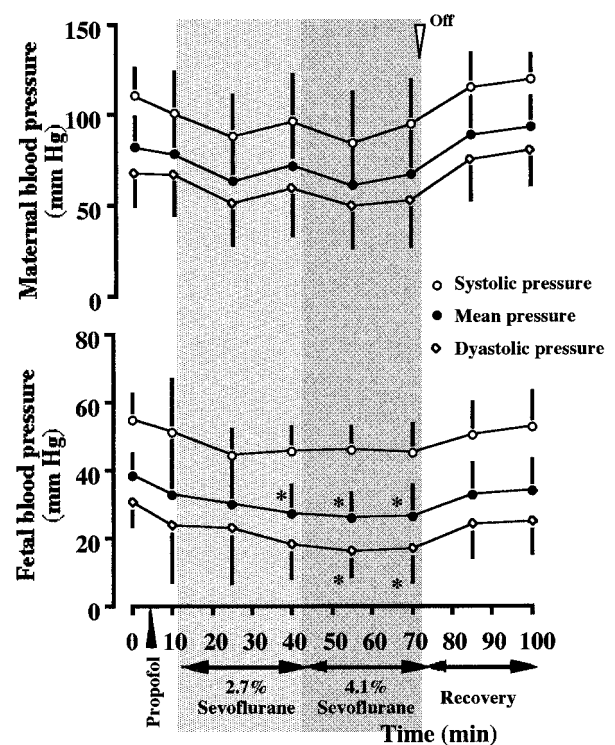

Fig. 2. Changes in the maternal and fetal arterial blood pressure during propofol-sevoflurane anesthesia in goats. Following sevoflurane inhalation, either the blood pressure decreased dose-dependently both in the mother and fetus. Significant differences in the fetus were seen at 2.7 and 4.1% of sevoflurane inhalation (*, p<0.05). The baseline values were obtained at the time 0, and then propofol injected (arrowhead) 5 min later. The shaded area and the white arrow head indicate the inhalation period and the cessation of anesthesia, respectively.

thesia. The majority of goats recovered at 30 min after the sevoflurane inhalation stopped, as shown in Table 1. In this study, a goat with postoperative leukocytosis was diagnosed as deglutition pneumonia after the study, and all fetuses aborted or were born prematurely with a difficult pregnancy.

Effects on maternal and fetal hemodynamics: The changes in HR and BP are presented in Figs. 1 and 2, respectively. At 5 min of propofol administration, the maternal HR significantly increased from 95 ± 15 (baseline value) to 130 ± 33 beats/min. Then, the maternal HR gradually decreased following sevoflurane inhalation. On the other hand, the fetal HR did not change significantly following to propofol infusion and sevoflurane inhalation. Propofol induced no statistical changes both in the maternal and fetal BP. Sevoflurane also induced no significant change in maternal BP, while fetal BP significantly decreased at 30

min (28 ± 9 mmHg) after inhaling 2.7% sevoflurane, and at 15 (27 ± 8 mmHg) and 30 min (27 ± 10 mmHg) after 4.1% inhalation, as compared with the baseline value (38 ± 7 mmHg). The depressed fetal BP recovered as soon as the cessation of sevoflurane.

Effects on uterine blood flow and intrauterine pressure: UBF showed no significant changes during propofol-sevoflurane anesthesia (Fig. 3). The IUP variability indicating uterine contraction, disappeared throughout propofol-sevoflurane anesthesia (Fig. 4), and then recurred within 15 min following the cessation of sevoflurane. The calculated MU values were 18.5, 0, 3.6, and 13.4 for the baseline value, during anesthesia, at 15 and 30 min of recovery, respectively.

Effects on maternal and fetal arterial blood pH and gases: Propofol injection induced significant decrease of maternal arterial blood PO_2 and pH, which respectively indicated hypoxemia and metabolic acidemia developing in the mother (Fig. 5). On the other hand, in the fetus, the decreased PCO_2 and base excess were seen at 15 and 45 min after sevoflurane inhalation (Fig 5). Maternal RR significantly decreased 5 min after propofol injection (11 ± 6.4
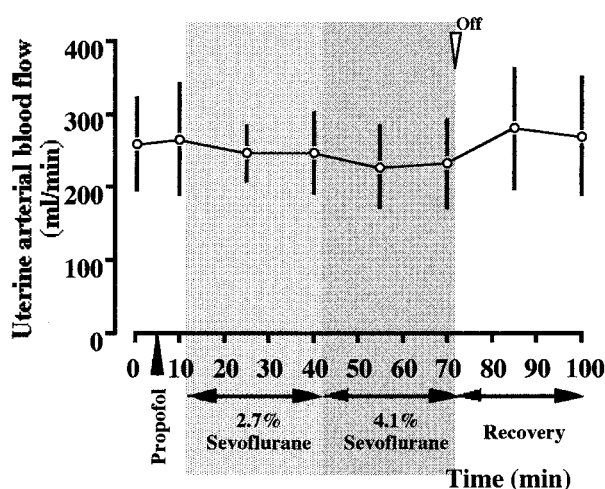
Fig. 3. Changes in the uterine blood flow during propofol-sevoflurane anesthesia in goats. The baseline values were obtained at the time 0, and then propofol injected (arrowhead) 5 min later. The shaded area and the white arrow head indicate the inhalation period and the cessation of anesthesia, respectively.

breaths/min), as compared with the baseline value (25 ± 8.2 breaths/min), and then recovered at 15 (26 ± 9.7 breaths/min) and 30 (28 ± 10.2) min after the cessation of sevoflurane anesthesia.

DISCUSSION

Drug applications for pregnant animals have often been investigated in ewe, since chronic catheterization and electronic monitoring techniques have been developed for this species. This has provided substantial physiological and pharmacological information from both the mother and fetus. Preliminarily, to determine the effective dose of propofol for goats, we intravenously injected 2.5 mg/kg of propofol that is a dose reported for pregnant ewes [32], but this dose did not allow intubation. Subsequently, 5 mg/kg of propofol was used. The dosage was associated with rapid loss of laryngeal, palperable, and corneal reflexes, and so 5 mg/kg of propofol could be enough for the anesthetic induction and intubation just like a result in non-pregnant goats by Pablo *et al.* [25]. Meanwhile, we needed a subsequent continuous infusion (at the rate of 0.3 mg/kg/min in this study) to take the hemodynamic and blood gas data after 5 min of propofol anesthesia, because the lost reflexes were recovered within 5 min after the bolus injection. Following this dose of propofol either 2.7% (1.0MAC) or 4.1% (1.5 MAC) sevoflurane of inhalation provided sufficient anesthetic depth for surgery, as shown in this paper. The MAC for the pregnant animal is normally between 60 and 70% of that for the non-pregnant animal [3], therefore < 1.0 MAC of sevoflurane might still maintain a surgical plane of anesthesia.

In pregnant ewes, a continuous propofol infusion did not have adverse effects on maternal or fetal heart rate and blood pressure [2]. Another report suggested that the maternal hemodynamics were less depressed with a continuous propofol infusion than with inhalation of isoflurane [11]. Consistent with these data, there was no finding indicating the hemodynamic suppression in this study. The maternal HR increased significantly after the 5 min of propofol induction in this study. Previously, the increase of maternal HR which could be ascribed to a decreased venous return caused by vascular dilation, has been seen transiently after propofol injection [5, 10, 30, 32]. Following the injection, we saw a transient decrease of PO_2 which could be associated with FRC and RR reduction due to the suppressive effect on the maternal breath. The decreased PO_2 might also
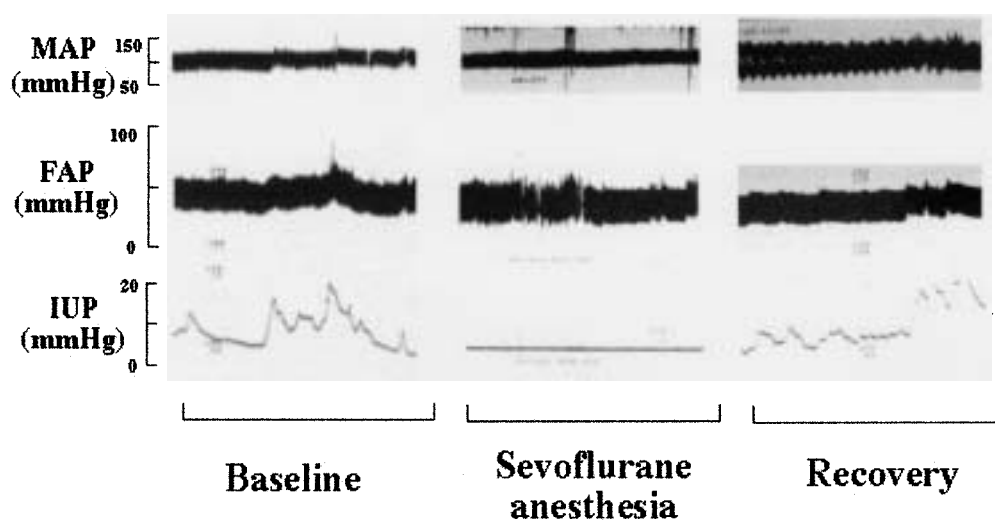

Fig. 4. A record of the maternal and fetal arterial pressure (BP, mmHg) and intra-uterine pressure (IUP, mmHg). The IUP variability disappeared throughout sevoflurane anesthesia, and then recurred after the cessation of anesthesia. The increased IUP was accompanied with the rise of FAP.
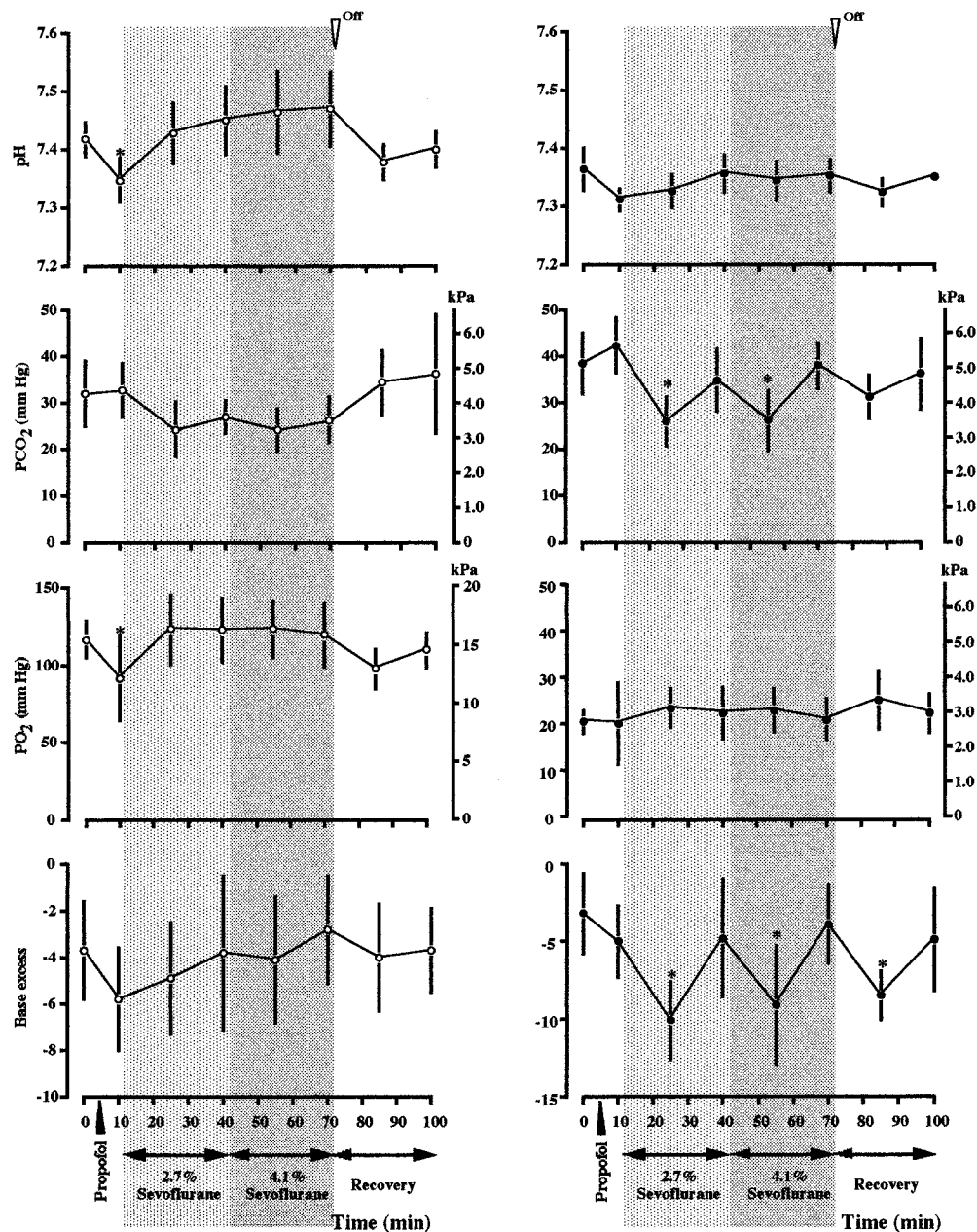
Fig. 5. Changes in the arterial blood pH and gases during propofol-sevoflurane anesthesia in goats. The maternal and fetal data were presented as the open (the left row of graphs) and closed circles (the right row of graphs), respectively. Decrease of arterial blood pH and PO_2, was induced following propofol injection in the mother, while the fetal PCO_2 and base excess decreased during sevoflurane inhalation. The baseline values were obtained at the time 0, and then propofol injected (arrowhead) 5 min later. The shaded area and the white arrow head indicate the inhalation period and the cessation of anesthesia, respectively.

contribute to decrease of pH via a mechanism of metabolic acidemia indicated by decreased base excess.

Generally, volatile anesthetics are negative chronotropes and inotoropes. Meanwhile, it has been suggested that sevoflurane has less affects on heart rate as compared with the earlier anesthetics [8]. According to previous studies on

sevoflurane anesthesia for pig or sheep, during the inhalation, the heart rate was in the normal range with no significant depression [13, 16, 22, 31] and also arterial blood pressure less decreased [1, 22, 31]. Our result that the changes of heart rate and blood pressure during sevoflurane inhalation were not statistically significant in the mother,

was consistent with the previous studies. In the fetus, the decrease of heart rate and arterial blood pressure during sevoflurane anesthesia were greater than in the mother. Since no significant change in the uterine blood flow was shown here, the depressed fetal hemodynamics could be predominantly due to placental transfer sevoflurane. Inhalant anesthetics are mainly eliminated from the lung with a minor amount of hepatic metabolism [7, 9]. In the fetus, which is unable to eliminate sevoflurane via the lung, the elimination of the inhalant anesthetic is mainly dependent on placental removal since hepatic enzyme are also immature in the fetus [20]. Thus, if the cumulative effects of inhalants could be more manifested in the fetus than adults, the decreased fetal HR as shown in this report could result from the depressed cardiac cycle due to the cumulated anesthetic.

In this study, propofol-sevoflurane anesthesia depressed uterine activity without changing uterine blood flow. It has been shown that propofol relaxes smooth muscle strain in the gravid uterus [29]. The effect of sevoflurane on spontaneous (naturally-occurring) contraction in the gravid uterus has not been studied although there are some data on the experimentally-induced contraction *in vivo* or *vitro*. Most of the inhaled anesthetics have a suppressive effect on gravid myometrium contractions. Isoflurane has a comparatively weak effect on uterine activity [26]. In present study, the IUP variability (an indicator of uterine contractions) completely disappeared throughout sevoflurane anesthesia; and then the activity recurred within 15 min after anesthesia. Despite of this muscle relaxation, there was no decrease in uterine blood flow. The quick reappearance of uterine contraction in the recovery phase would be an important advantage of this combination for obstetric anesthesia.

Based on the results shown here, we conclude as follows; 1) propofol injection can induce a transient tachicardia, decrease in PO_2 and pH in the mother, with minimal affects on either fetal heart rate or blood pressure, 2) oxygen-sevoflurane inhalation has minimal effects on maternal hemodynamics, and 3) the uterine relaxation occurs under sevoflurane anesthesia but activity reappeared quickly in the recovery phase. This data may be useful for choosing an anesthetic for obstetric surgery in goats.

REFERENCES

1. Aida, H., Mizuno, Y., Hobo, S., Yoshida, K. and Fujinaga, T. 1996. Cardiovascular and pulmonary effects of sevoflurane anesthesia in horses. *Vet. Surg.* **25**: 164–170.
2. Alon, E., Ball, R. H., Gillie, M. H., Parer, J. T., Rosen, M. A. and Shnider, S. M. 1993. Effects of propofol and thiopental on maternal and fetal cardiovascular and acid-base variables in the pregnant ewe. *Anesthesiology* **78**: 562–576.
3. Benson, G. J. and Thurmon, J. C. 1987. Special anesthetic consideration for caesarean section. pp. 337–348. *In*: Principles & Practice of Veterinary Anaesthesia (Short, C. E. ed.), Williams & Wilkins, Baltimore.
4. Bettschart-Wolfensberger, R., Freeman, S. L., Jaggin-Sch-mucker, N. and Clarke, K. W. 2001. Infusion of a al use of combination of propofol and medetomidine for long-term anesthesia in ponies. *Am. J. Vet. Res.* **62**: 500–507.
5. Bettschart-Wolfensberger, R., Semder, A., Alibhai, H., Demuth, D., Aliabadi, F. S. and Clarke, K. W. 2000. Cardio-pulmonary side-effects and pharmacokinetics of an emulsion of propofol (Disoprivan) in comparison to propofol solved in polysorbate 80 in goats. *J. Vet. Med. A* **47**: 341–350.
6. Branson, K. R., Quandt, J. E., Martinez, E. A., Carroll, G. L., Trim, C. M., Dodam, J. R., Hartsfield, S. M., Matthews, N. S., Mackenthun, A. and Beleau, M. H. 2001. A multisite case report on the clinic sevoflurane in dogs. *J. Am. Anim. Hosp. Assoc.* **37**: 420–432.
7. Clarke, K. W. 1999. Desflurane and sevoflurane. New volatile anesthetic agents. *Vet. Clin. North Am. Small Anim. Pract.* **29**: 793–810.
8. Ebert, T. J., Harkin, C. P. and Muzi, M. 1995. Cardiovascular responses to sevoflurane: a review. *Anesth. Analg.* **81**: S11–S22.
9. Fee, J. P. H. and Thompson, G. H. 1997. Comparative tolerability profiles of the inhaled anaesthetics. *Drug. Saf.* **16**: 157–170.
10. Gambling, D. R., Sharma, S. K., White, P. F., Van Beveren, T., Bala, A. S. and Gouldson, R. 1995. Use of sevoflurane during elective cesarean birth: a comparison with isoflurane and spinal anesthesia. *Anesth. Analg.* **81**: 90–95.
11. Gaynor, J. S., Wertz, E. M., Alvis, M. and Turner, A. S. 1998. A comparison of the haemodynamic effects of propofol and isoflurane in pregnant ewes. *J. Vet. Pharmacol. Ther.* **21**: 69–73.
12. Hall, L. W. and Clarke, K. W. 1991. Anaesthesia for obstetrics. pp. 355–362. *In*: Veterinary Anaesthesia, 9th ed. (Hall, L.W. and Clarke, K.W. eds.), Saunders, Philadelphia.
13. Halsey, M. J. 1981. Investigations on isoflurane, sevoflurane and other experimental anaesthetics. *Br. J. Anaesth.* **53**: S43–S47.
14. Hikasa, Y., Kawanabe, H., Takase, K. and Ogasawara, S. 1996. Comparisons of sevoflurane, isoflurane, and halothane anesthesia in spontaneously breathing cats. *Vet. Surg.* **25**: 234–243.
15. Hikasa, Y., Okuyama, K., Kakuta, T., Takase, K. and Ogasawara, S. 1998. Anesthetic potency and cardiopulmonary effects of sevoflurane in goats: comparison with isoflurane and halothane. *Can. J. Vet. Res.* **62**: 299–306.
16. Hikasa, Y., Saito, K., Takase, K. and Ogasawara, S. 2000. Clinical, cardiopulmonary, hematological and serum biochemical effects of sevoflurane and isoflurane anesthesia in oxygen under spontaneous breathing in sheep. *Small Rumin. Res.* **36**: 241–249.
17. Karsli, B., Kaya, T. and Cetin, A. 1999. Effects of intravenous anesthetic agents on pregnant myometrium. *Pol. J. Pharmacol.* **51**: 505–510.
18. Kuipers, J. A., Boer, F., Olieman, W., Burm, A. G. and Bovill, J. G. 1999. First-pass lung uptake and pulmonary clearance of propofol: assessment with a recirculatory indocyanine green pharmacokinetic model. *Anesthesiology* **91**: 1780–1787.
19. Lerche, P., Nolan, A. M. and Reid, J. 2000. Comparative study of propofol or propofol and ketamine for the induction of anaesthesia in dogs. *Vet. Rec.* **146**: 571–574.
20. Lerman, J., Sikich, N., Kleinman, S. and Yentis, S. 1994. The pharmacology of sevoflurane in infants and children. *Anesthesiology* **80**: 814–824.
21. Lin, H. C., Purohit, R. C. and Powe, T. A. 1997. Anesthesia in sheep with propofol or with xylazine-ketamine followed by

halothane. *Vet. Surg.* **26**: 247–252.

22. Manohar, M. and Parks, C. M. 1984. Porcine systemic and regional organ blood flow during 1.0 and 1.5 minimum alveolar concentrations of sevoflurane anesthesia without and with 50% nitrous oxide. *J. Pharmacol. Exp. Ther.* **54**: 640–648.

23. Matthews, N. S., Hartsfield, S. M., Mercer, D., Beleau, M. H. and MacKenthun, A. 1998. Recovery from sevoflurane anesthesia in horses: comparison to isoflurane and effect of postmedication with xylazine. *Vet. Surg.* **27**: 480–485.

24. Mosler, K. H. 1968. The dynamics of uterine muscle. *Bibl. Gynaecol.* **48**: 1–82.

25. Pablo, L. S., Bailey, J. E. and Ko, J. C. 1997. Median effective dose of propofol required for induction of anaesthesia in goats. *J. Am. Vet. Med. Assoc.* **211**: 86–88.

26. Paull, J. and Ziccone, S. 1980. Halothane, enflurane, methoxyflurane, and isolated human uterine muscle. *Anaesth. Intensive Care.* **8**: 397–401.

27. Sakamoto, H., Kirihara, H., Fujiki, M., Miura, N. and Misumi, K. 1997. The effects of medetomidine on maternal and fetal cardiovascular and pulmonary function, intrauterine pressure and uterine blood flow in pregnant goats. *Exp. Anim.* **46**: 67–73.

28. Servin, F., Desmonts, J. M., Haberer, J. P., Cockshott, I. D., Plummer, G. F. and Farinotti, R. 1988. Pharmacokinetics and protein binding of propofol in patients with cirrhosis. *Anesthesiology* **69**: 887–891.

29. Shin, Y. K., Kim, Y. D. and Collea, J. V. 1998. The effect of propofol on isolated human pregnant uterine muscle. *Anesthesiology* **89**: 105–109.

30. Short, C. E. and Bufalari, A. 1999. Propofol Anesthesia. *Vet. Clin. North Am. Small Anim. Pract.* **29**: 747–748.

31. Torri, G. and Casati, A. 2000. Cardiovascular homeostasis during inhalational general anesthesia: a clinical comparison between sevoflurane and isoflurane. On behalf of the Italian Research Group on sevoflurane. *J. Clin. Anesth.* **12**: 117–122.

32. Valtonen, M., Kanto, J. and Rosenberg, P. 1989. Comparison of propofol and thiopentone for induction of anaesthesia for elective caesarean section. *Anaesthesia* **44**: 758–762.