Sevoflurane Anesthesia for Elective Cesarean Section

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Sevoflurane anesthesia was given to sixteen women who had been scheduled for elective cesarean section. The maternal systolic blood pressure significantly decreased during the anesthesia induction. Both the anesthesia induction and emergence were smooth and rapid. These findings were supported partially by the pharmacokinetic analysis of sevoflurane concentration in the maternal artery and expired gas mixture. Spontaneous uterine contractions were good in 12 patients, fair in two and poor in two. The measured blood loss was 752 ± 257 ml including amniotic fluid. No blood transfusion was given to any patient. The median value of the Apgar score at one minute was seven (range three to nine). No neonate was intubated for resuscitation. No abnormal maternal laboratory data were found, including liver and kidney function tests and blood cell counts one week after the operation. No adverse effect of sevoflurane on the neonate was found one week after the delivery and three months after the discharge. (Key words: Sevoflurane, Cesarean section, Pharmacokinetics)

(Asada A, Fujimori M, Tomoda S et al.: Sevoflurane Anesthesia for elective cesarean section. J Anesth 4: 66–72, 1990)

Sevoflurane is a new inhalaltion anesthetic with rapid induction and emergence because of its low blood gas coefficient[1,2]. Several clinical studies have been reported[3–8], but the effects of sevoflurane on parturient women or fetuses have not been examined. The present study was undertaken to evaluate the clinical application of sevoflurane for elective cesarean section.

Methods and Subjects

Sixteen women who had been scheduled for elective cesarean section were studied with their informed consent. Their mean age was 32.1 ± 4.9 years, height 155.3 ± 5.5 cm, body weight 60.3 ± 5.7 kg, respectively and they were within the 38th to 39th week of pregnancy. Their ASA physical status was one for fifteen patients and two for one patient who had mild anemia of serum hemoglobin 9.9 g/dl and hematocrit 29.7%. The indication for elective cesarean section was previous cesarean section in thirteen patients, placenta previa in one, previous myomectomy in one and breech presentation with cephalopelvic disproportionality in one. Those patients with severe toxemia or in pregnancy of less than 35 weeks were excluded from this study. Patients were premedicated only with 0.4 to 0.5 mg atropine sulfate one hour before induction. The radial artery was cannulated, after Allen's test, for measuring the maternal blood pressure and for sampling blood. Anesthesia was induced slowly with 60% nitrous oxide and 3 to 4% sevoflurane in all patients. Tracheal

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intubation was facilitated with 1 $mg \cdot kg^{-1}$ succinylcholine. The blood pressures were continuously monitored throughout the sevoflurane induction by one of the authors. The maternal systolic blood pressures gradually and steadily decreased with the increased inspired sevoflurane concentration in most patients. The lowest value of maternal systolic blood pressure occurring during the induction of anesthesia was recorded. The electrocardiogram was monitored throughout the anesthesia for every patient. Anesthesia was maintained with 60% nitrous oxide and 0 to 3% sevoflurane and all the anesthetics were discontinued and 100% oxygen was administered when the myometrium was incised. After the fetus was delivered and the umbilical cord was clamped, 60% nitrous oxide and 0.5 to 4.0% sevoflurane were given to mothers. The sevoflurane concentration was adjusted to maintain the maternal spontaneous respiration. Supplemental succinylcholine was given if the patient began to move during delivery. Apgar score was assessed by a pediatrician one and five minutes after delivery.

Oxytocin was infused in all patients after delivery and in some patients ergometrine and/or prostaglandin F2 alpha were added. Spontaneous contractions and the response of the myometrium to these drugs were assessed by an obstetrician. The spontaneous contractions were regarded as good when the myometrium began to contract by itself, as fair when it felt soft but resistant, and as poor when it felt relaxed and soft. The response of myometrium to oxytocin and other drugs was evaluated in the same manner as mentioned above. Sevoflurane was discontinued at the end of the operation and then nitrous oxide was discontinued. The times from discontinuation of sevoflurane and nitrous oxide to emergence were recorded for each patient.

Samples for blood gas analysis, serum electrolytes, hematocrit, hemoglobin and blood glucose were drawn from 15 mothers, before induction and at delivery, except one patient who was positive for hepatitis B antigen. The sample from one patient could not be measured because of blood coagulation. Umbilical venous blood could be drawn at delivery to measure pH, P_{O_2}, P_{CO_2}, BE, serum electrolytes, blood glucose, hematocrit and hemoglobin from twelve neonates. The samples from three neonates coagulated, and the sample from one neonate whose mother was positive for hepatitis B antigen was not drawn. Before and after the operation the screening tests were done on the serum of parturients for evaluation of hepatic and renal functions and blood cell counts on the following day and one week later. Hepatic function tests were as follows: GOT, GPT, LDH, total bilirubin, alkaline phosphatase, total protein and albumin. Renal function tests were as follows: BUN, serum creatinine, sodium, potassium, chloride in serum and urinalysis. Blood cell counts were as follows: red cells, white cells with differential, platelets, hematocrit and hemoglobin.

Blood sevoflurane concentration was measured with a Shimadzu 6APTF (Kyoto, Japan) gas chromatograph with a FID detector. We modified the analytical method that Kudo and Oyama[9] reported about enflurane. Sevoflurane concentrations of the maternal arterial blood and the expired gas were measured in fourteen patients five minutes after induction, at the start of operation, at delivery, at 30 and 40 min after induction and immediately before extubation. Sevoflurane concentrations of the maternal arterial blood also was measured just before leaving the recovery room. Sevoflurane concentration of the umbilical venous blood was measured in fourteen neonates. The maternal cardiac output and heart rate were non-invasively monitored by an impedance cardiograph (NCCOM3, BoMed, Irvine, CA) in two patients before and during anesthesia. Cardiac output was measured four to five times every minute. The data were averaged every minute. During induction the inspired concentration of sevoflurane was increased from 0.0 to 4.0% stepwise by 0.5 or 1.0% increments each 45 to 60 seconds. Thus the data for cardiac output during the induction were expressed by averaging the values taken during each increment of inspired concentra-

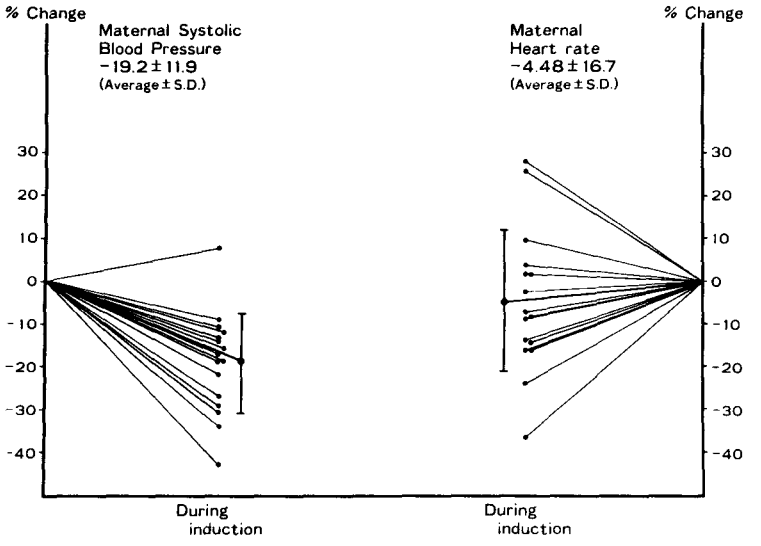

Fig. 1.

tion of sevoflurane.

The patients were asked by questionaire within 24 to 48 hours following the operation if they experienced any smell during induction, and had a sore throat after the anesthesia or if they had awareness during the anesthesia. The neonatal physical status was observed in the nursery. A follow-up study was conducted to seek any abnormalities in growth such as body weight, height or other physical conditions, for at least three months after discharge from the hospital.

Statistics: A paired t-test and Spearman rank correlation coefficient test were used to analyze the data. A P value less than 0.05 was considered as significant. The data are expressed as mean ± standard deviation of the sixteen patients or neonates (n = 16) if not otherwise mentioned.

Results

The times from induction to intubation, from induction to delivery, and from incision to delivery were 7.3 ± 2.0 min, 19.4 ± 6.5 min, and 2.8 ± 1.4 (n = 9) min, respectively. The duration of anesthesia was 1.6 ± 0.3 hours and duration of the operation 1.2 ± 0.3 hours. The time of emergence from discontinuing sevoflurane was 6.4 ± 4.0 min and the time of emergence from discontinuing nitrous oxide was 3.7 ± 2.1 min. Spontaneous uterine contractions were good in 12 patients, fair in two patients and poor in two. The response of myometrium to oxytocin and other drugs was good in 15 patients and poor in an acidotic patient. The measured blood loss was 752 ± 257 ml which included amniotic fluid. No blood transfusion was given to any patient. The median value of the Apgar score at one minute was seven (range three to nine). The median value of the score at five minutes was 10 (range four to 10).

No remarkable change was found on the electrocardiogram during anesthesia. Maternal systolic blood pressure significantly decreased during the induction (fig. 1). The decrease of the maternal heart rate during induction was not significant. The sevoflurane concentration in the maternal expired gas increased to 1,528 ± 369 micromole·L^{-1} (3.8 ± 0.9 vol%, n = 14) five minutes after induction while the patients were inhaling 3 to 4% of sevoflurane (table 1). It decreased to 284 ± 138 micromole·L^{-1} (0.7 ± 0.3 vol%) at delivery. It was 77 ± 28 micromole·L^{-1} (0.2 ± 0.1 vol%) just before extubation while all the anesthetics were discontinued and 100% oxygen was being given to the patients. The sevoflurane concentration in the maternal arterial blood increased to 684 ± 181 micromole·L^{-1} (1.7 ± 0.5 vol%) five minutes after the start of induction. It decreased to 192 ±

Table 1. Sevoflurane concentration

Time or events after induction	Expired gas (Maternal)	Radial artery (Maternal)	Umbilical vein (Fetal)
5 min	1528 ± 369 (3.8 ± 0.9)	684 ± 181 (1.7 ± 0.5)	
Delivery	284 ± 138 (0.7 ± 0.3)	192 ± 98 (0.5 ± 0.3)	186 ± 59 (0.5 ± 0.1)
Extubation	77 ± 28 (0.2 ± 0.1)	79 ± 38 (0.2 ± 0.1)	
Recovery room		35 ± 32 (0.1 ± 0.1)	

mean ± SD, n = 14* micromole·L^{-1} (vol%, 37°C)
*Two patients are excluded from the data in the table. See text.

Table 2. Blood gas data for maternal arterial and umbilical venous blood at delivery

		pH	P_{O_2} (mmHg)	P_{CO_2} (mmHg)	BE (mEq·L^{-1})
Maternal artery	Before induction (FI_{O_2} 0.21)	7.43 ± 0.03	102 ± 4	31 ± 2	−3 ± 2
	At delivery (FI_{O_2} 1.0)	7.43 ± 0.06	309 ± 96	30 ± 5	−4 ± 2
Umbilical vein		7.35 ± 0.07	43 ± 11	42 ± 8	−3 ± 3

All values are expressed as mean ± S.D. n = 11*
*Three samples could not be measured. One sample was not drawn. See text. The sample of neonate from an acidotic mother was measured but excluded from this table because the mother had metabolic acidosis before induction.

98 micromole·L^{-1} (0.5 ± 0.3 vol%) at delivery. The sevoflurane concentration in the umbilical venous blood was 186 ± 59 micromole·L^{-1} (0.5 ± 0.1 vol%). The concentration ratio of the umbilical venous blood to the maternal arterial blood was 0.97 at delivery. The maternal arterial concentration of sevoflurane decreased to 79 ± 38 micromole·L^{-1} (0.2 ± 0.1 vol%) immediately before extubation. It decreased further to 35 ± 32 micromole·L^{-1} (0.1 ± 0.1 vol%) just before the patients left the recovery room. The representative change of sevoflurane concentrations was shown in figure 3.

No remarkable changes were seen in blood gas analysis, serum electrolytes, hemoglobin, hematocrit, blood glucose (table 2) of maternal blood at delivery except an acidotic patient. No remarkable changes were seen in blood gas analysis, serum electrolytes, hemoglobin, hematocrit, and blood glucose level of umbilical venous blood except a baby from an acidotic mother. No abnormalities were found in the patients in the data of screening tests of hepatic and renal functions and blood cell counts on the following

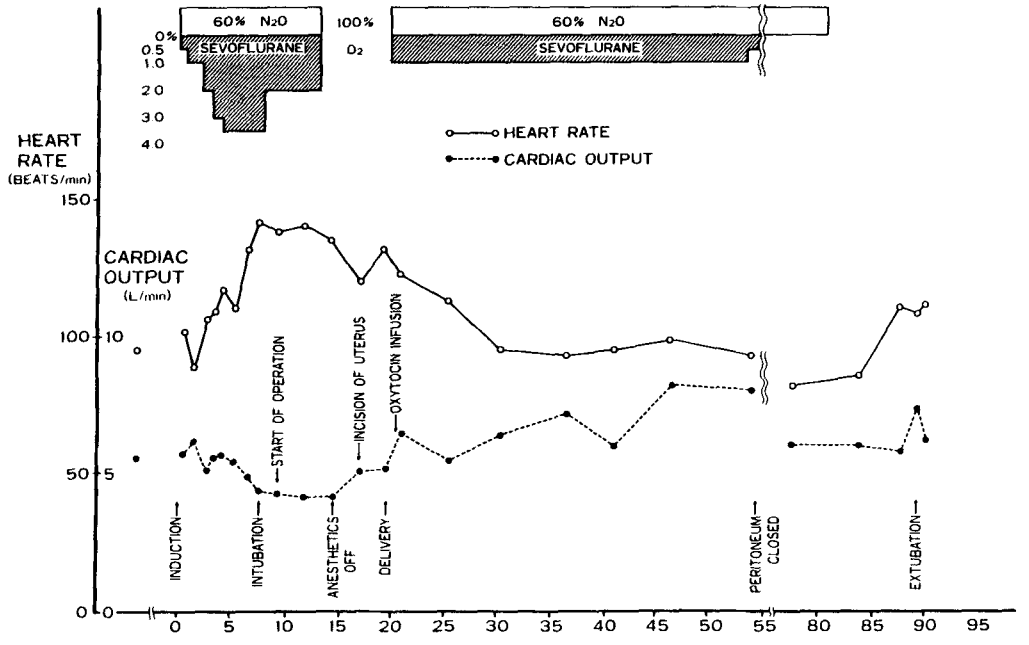

Fig. 2.

day and one week later. The follow-up study three months after discharge did not show any significant abnormalities in body weight, height or other physical conditions in the neonates. Seven of 16 mothers complained of sore throat postoperatively. Twelve patients experienced some smell like a disinfectant during the induction and one during emergence. No one had awareness during the operation, but one patient remembered the events during emergence prior to extubation.

Discussion

The MAC for sevoflurane is reported to be 1.71% for the healthy Japanese (mean age 48)[3] or 2.05% for North Americans (mean age 38)[4]. Three to four per cent of sevoflurane was well tolerated by the patients during anesthesia induction in this study which would be equivalent to 1.8 to 2.3 MAC according to the former report[3]. No coughing, breath holding, laryngospasm or excitement was noticed during induction period although twelve patients were aware of the smell of the anesthetic. The smooth induction with sevoflurane can decrease the possibility of regurgitation and aspiration of gastric contents. An inhalation induction rather than a rapid-sequence induction was chosen as the method in this study to allow straightforward evaluation of the pharmacological effects of sevoflurane. An intravenous anesthetic such as thiobarbiturate which is commonly used for a rapid sequence induction has the depressant effects on cardiovascular, respiratory and central nervous systems of the patients and the fetuses as well. We can not correlate the values of the measurements such as maternal blood pressure, blood gas analyses of the mother and neonate, and Apgar's score directly with the sevoflurane concentrations in the maternal arterial or umbilical venous blood samples if we use an intravenous induction agent.

The decrease of maternal blood pressure was treated by increasing the infusion rate of lactated Ringer's solution or by decreasing the inspired sevoflurane concentration. Holaday et al.[5] showed a 24% decrease of the systolic blood pressure during the sevoflurane induction in six healthy young volunteers, which was similar to our finding. The decrease of maternal blood pressure is assumed to be due mainly to the decrease in cardiac output because the percent decrease in the maternal systolic blood pressure was well

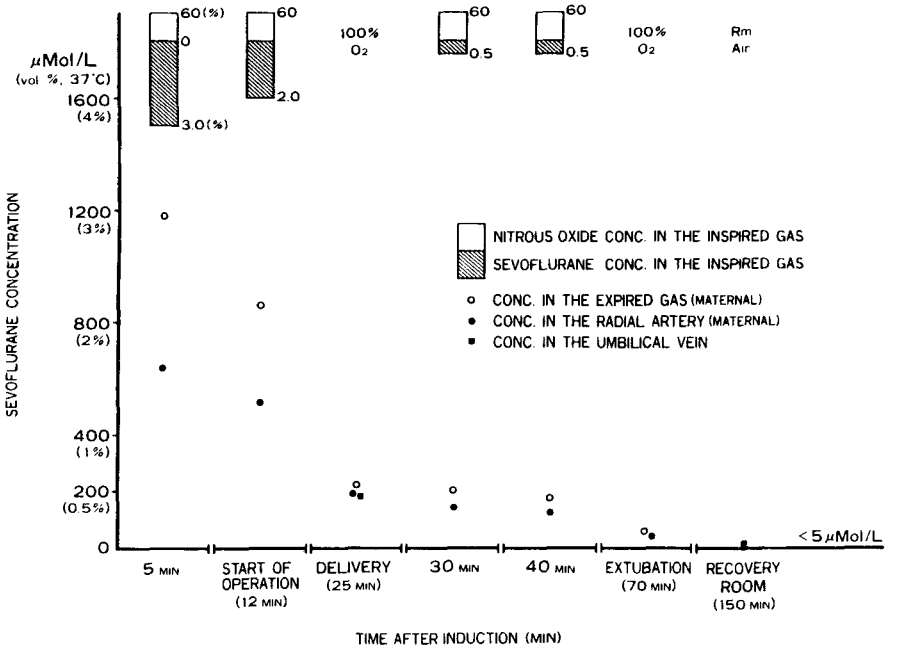

Fig. 3.

correlated with the reduction of the maternal cardiac output (fig. 2).

The data for pH, P_{CO_2} and BE in the umbilical venous blood were comparable to those that Abboud et al.[10] reported about nitrous oxide, halothane or enflurane. Our data are also comparable to those that Warren et al.[11] and Ghaly et al.[12] reported about isoflurane. On the other hand the P_{O_2} level (43 ± 11 mmHg) in this study was higher than those that Abboud et al.[10] reported about nitrous oxide, halothane or enflurane and Warren et al.[11] and Ghaly et al.[12] reported about isoflurane although the inspired oxygen concentration during deliveries in their mothers differed from ours. The P_{CO_2} level in the maternal arterial blood at delivery did not differ significantly from that before induction. Spontaneous respiration was permitted as a rule during anesthesia maintenance because a maternal P_{CO_2} less than 20 mmHg may cause fetal hypoxemia and acidosis[13]

One patient showed metabolic acidosis before the anesthesia induction; pH 7.37, P_{O_2} 96 mmHg, P_{CO_2} 22 mmHg, BE −10 $mEq \cdot L^{-1}$. Her neonate showed metabolic acidosis in the umbilical venous blood; pH 7.24, P_{O_2} 27 mmHg, P_{CO_2} 41 mmHg, BE −10 $mEq \cdot L^{-1}$. The Apgar score was six and nine at one and five minutes respectively. The metabolic acidosis in the mother and neonate was not corrected because the information for the blood gas analysis was not available at that time. Not only were the spontaneous uterine contractions poor in this patient, but also the response of uterine muscle to oxytocin, ergometrine and prostaglandin F2 alpha were poor. The response gradually improved without any further treatment.

The amount of estimated blood loss in this study was 752 ± 257 ml. Although the amount cannot be compared directly with that in epidural anesthesia or in general anesthesia by other inhalation anesthetics, the amount of blood loss in this study is more than that in epidural anesthesia[14], and comparable to that in general anesthesia by nitrous oxide, halothane or enflurane[10,14]. These findings suggest that uterine contractions might be depressed by sevoflurane as much as by the other inhalation anesthetics as mentioned above.

Dick et al.[15] showed that the concen-

tration ratio of enflurane in the umbilical venous blood to that in the maternal arterial blood was 0.6 after 17 min following rapid sequence induction. The blood gas coefficient of enflurane is higher (1.8) than that (0.6) of sevoflurane. It takes longer time for enflurane in the alveolus to equilibrate with that in the blood of the mother and thus with that of umbilical venous blood. The sevoflurane concentration ratio of the umbilical venous blood to maternal arterial blood was 0.97 at delivery (table 1 and fig. 3).

The neonates with a poor Apgar score were treated with oxygen by mask, by suctioning the oral cavity and stimulating the baby on the back by rubbing gently with a pediatrician's hand. The neonates did not fall asleep again once they began physical activity. No neonate was intubated for resuscitation in this study. This suggests that sevoflurane is rapidly eliminated through the neonatal lung after delivery.

The authors gratefully acknowledge the review of this paper made by Harry W Linde, Ph. D., Professor of Anesthesia, Northwestern University Medical School. The authors also wish to thank Junko Abe and Noriko Kusunoki for technical assistance.

(Received Oct. 11, 1988, accepted for publication Jul. 24, 1989)

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