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Original articles

Improved oxygen delivery to the fetus during cesarean section under sevoflurane anesthesia with 100% oxygen

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Abstract
Purpose. To assess the potential benefits of sevoflurane with 100% oxygen in cesarean section in terms of oxygen delivery to the fetus, neonatal depression, and uterine contractility.
Methods. Thirty-six patients undergoing elective cesarean section were enrolled. After thiamylal induction, 0.7% sevoflurane–60% nitrous oxide–40% oxygen anesthesia was administered in group G1 (n = 9), and 1.7% sevoflurane–100% oxygen anesthesia was administered in group G2 (n = 9). Spinal anesthesia under oxygen nasal prong was used in group SP (n = 18).
Results. At delivery, the Po_2 values in the maternal artery and the umbilical vein and artery (MA, UV, UA) of group G2 (474 ± 50, 43 ± 9, 32 ± 9 mmHg, respectively) were significantly greater than those in groups G1 (228 ± 46, 31 ± 4, 23 ± 5 mmHg, respectively) and SP (147 ± 21, 30 ± 7, 18 ± 7 mmHg, respectively). The So_2 in the UA of group G2 (56 ± 17 %) was also greater than that in groups G1 (34 ± 10 %) and SP (32 ± 10 %). The sevoflurane concentrations at delivery in the MA, UV, and UA in group G2 were almost threefold higher than those in group G1, whereas all the newborns in the three groups had Apgar scores of 8 or more at 5 min, and the intraoperative blood loss did not differ among the groups.
Conclusion. Sevoflurane anesthesia with 100% oxygen in elective cesarean delivery improves oxygen delivery to the fetus without severe neonatal depression, prolonged uterine relaxation, or increased blood loss.

Key words: Obstetric anesthesia, Cesarean section, Sevoflurane, Fetal oxygenation

Introduction

Sevoflurane has a lower blood/gas partition coefficient than halothane or isoflurane [1,2], suggesting that it should be easier to control the blood levels of this anesthetic. There are, therefore, a number of points that suggest that sevoflurane anesthesia should be suitable for cesarean section: (1) The rapid increase in blood concentration may depress uterine contraction with improved uterine blood flow and fetal oxygenation before delivery. (2) Rapid induction does not require supplementation with nitrous oxide, and 100% oxygen inhalation may help prevent fetal hypoxemia in emergency cesarean section. (3) Rapid elimination after delivery may reduce the potential for neonatal depression, prolonged uterine relaxation, and operative blood loss when its inspiratory concentration is controlled. (4) Rapid emergence from general anesthesia may allow the mother to protect her airway and to interact with her baby.

We therefore evaluated the usefulness of sevoflurane anesthesia with 100% oxygen for cesarean section in terms of placental transfer of oxygen and sevoflurane, neonatal depression, blood loss, and other complications.

Patients and methods

After obtaining approval from our institutional ethics committee on human research and written informed consent from each patient, we enrolled 36 parturient women undergoing elective cesarean section. The patients were assigned to one of three groups: 0.7% sevoflurane–60% nitrous oxide–40% oxygen anesthesia (G1), 1.7% sevoflurane–100% oxygen anesthesia (G2), and spinal anesthesia (SP). Patients were allowed to choose general or spinal anesthesia unless spinal anesthesia was contraindicated. The patients scheduled for general anesthesia were randomly assigned to group G1 or G2.

Two hours after oral administration of 10 mg famotidine to reduce gastric secretion, the patient was

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transferred to the operating room. Standard monitoring included electrocardiogram, automatic blood pressure recording, pulse oximetry, and bladder temperature. The radial artery was cannulated under local anesthesia for blood sampling.

In groups G1 and G2, intravenous 0.5 mg vecuronium bromide was given for precurarization during disinfection in the operating field and preoxygenation. One minute after precurarization, anesthesia was induced with 4 mg·kg^{-1} intravenous thiamylal sodium, and the trachea was intubated following 2 mg·kg^{-1} suxamethonium i.v. The operation was started immediately after tracheal intubation. Before delivery, we maintained anesthesia with 2 l·min^{-1} oxygen and 3 l·min^{-1} nitrous oxide and dialed 0.7% sevoflurane for group G1, and 5 l·min^{-1} oxygen and 1.7% sevoflurane for group G2. End-tidal carbon dioxide tension was kept at 28–32 mmHg with mechanical ventilation. The induction–delivery (I-D) time was recorded as the interval from the start of sevoflurane inhalation to delivery. The uterine incision–delivery (UI-D) time was also recorded. After delivery, anesthesia for both groups was maintained with 4 l·min^{-1} nitrous oxide, 2 l·min^{-1} oxygen, 0.5% sevoflurane, and 0.1–0.2 mg fentanyl i.v. Muscle relaxation was obtained with vecuronium bromide given at the umbilical clamp.

In group SP, a nasal prong was applied with 3 l·min^{-1} oxygen upon entering the operating room. With the patient in the right lateral position, the dura was punctured with a 25-gauge Quincke point needle at the L3–4 intervertebral space. Ten milligrams of tetracaine in 2.5 ml of 10% dextrose containing 0.1 mg morphine was administered intrathecally. The patient was then turned to the supine position with a right hip wedge to maintain left uterine displacement. Intravenous ephedrine 5–10 mg was used as a vasopressor agent as necessary. The operation was started when analgesia to pinprick reached T4 or 5. The I-D time was recorded as the interval from intrathecal injection to delivery.

At the umbilical cord clamp, maternal arterial blood (MA) was drawn from a radial arterial catheter, and umbilical venous and arterial blood (UV and UA) were simultaneously sampled by an obstetrician. From these samples, blood gas analysis with CO oximetry (ABL 620, Radiometer, Copenhagen, Denmark) and plasma cortisol assay (TDX Analyzer, Abbott Laboratories, North Chicago, IL, USA) were performed. The blood concentration of sevoflurane was measured in a 0.5-ml volume of these samples with the head-space sampling technique and gas chromatography (GC-14B and HSS-2B, Shimadzu, Kyoto, Japan) [3]. Intravenous 0.2 mg methylergometrine maleate was administered immediately after the delivery and followed by an infusion of 1 unit·h^{-1} oxytocin for augmentation of uterine contractility.

Intraoperative blood loss, including amniotic fluid, was estimated by counting the volume in the suction bottle and the weight of the swabs. After delivery, the obstetrician was asked to assess uterine contractility as follows: good, no additional treatment; fair, contraction recovered with uterine massage; and poor, supplementation of 0.5 mg prostaglandin $F_{2\alpha}$ in uterine muscle required. The same neonatologist and obstetrician, who had not been informed of the anesthetic methods, determined the Apgar score and uterine contractility, respectively. However, it was impossible for them to be blinded to the anesthetic method.

The patients were interviewed about intraoperative awareness on the day after the operation, when blood hemoglobin levels were checked to compare with preoperative values.

For statistical analysis, numerical variables were compared using one-way analysis of variance. When significance was observed, Student's *t*-test or paired *t*-test was used. The chi-square test was used to compare Apgar scores. A value of $P < 0.05$ was considered statistically significant. Data were expressed as means ± SD.

Results

The patients in the three groups were similar in age, weight, height, and gestational age (Table 1). The indications for cesarean section included previous cesarean section, breech presentation, and placenta previa. Two patients in group G1 suffered from idiopathic thrombocytopenic purpura. No patients had rupture of the membranes before the operation.

The duration of operation and UI-D time were similar in all of the groups, whereas I-D time was longest in group SP. Intraoperative infusion loading, estimated blood loss, urine output, fetal heart rate at entry to the operating room, and birth weight were similar in the three groups. The postoperative changes in blood hemoglobin were not significantly different among the groups (Table 1).

Po_2 in the MA, UV, and UA and So_2 in the UA were greater in group G2 than in groups G1 and SP (Table 2). The plasma cortisol levels did not differ among the groups, whereas in each group the maternal level was higher than the umbilical levels (Table 2). The sevoflurane levels in the MA, UV, and UA were almost threefold higher in group G2 than in group G1 (Table 3). Using the blood/gas partition coefficient of 0.63 at 37°C [2], the maternal alveolar concentration of sevoflurane at delivery was calculated as 0.36% in group G1 and 1.27% in group G2 . There were no significant differences among the groups in Apgar scores at 1 and 5 min.

Table 1. Demographic and surgical characteristics of groups SP (spinal anesthesia), G1 (0.7% sevoflurane–60% nitrous oxide–oxygen anesthesia), and G2 (1.7% sevoflurane–oxygen anesthesia)[a]

Characteristic	SP (n = 18)	G1 (n = 9)	G2 (n = 9)
Age (years)	31 ± 5	31 ± 4	29 ± 5
Weight (kg)	63 ± 11	58 ± 2	60 ± 8
Height (cm)	156 ± 6	155 ± 3	160 ± 6
Gestation (weeks)	37 ± 2	36 ± 2	36 ± 2
Blood hemoglobin ($g \cdot dl^{-1}$)			
Preoperative	10.3 ± 1.9	10.4 ± 1.6	10.6 ± 0.5
Postoperative	10.1 ± 2.1	9.8 ± 1.7	10.0 ± 2.1
Operation			
Duration (min)	32 ± 5	35 ± 12	38 ± 13
I-D time (min)	11 ± 2*	5 ± 2	8 ± 4
UI-D time (s)	75 ± 32	72 ± 44	56 ± 24
Infusion (ml)	1125 ± 310	975 ± 225	983 ± 288
Blood loss (g)	1107 ± 634	1229 ± 359	1189 ± 528
Urine output (ml)	141 ± 71	204 ± 82	166 ± 92
Birth weight (g)	2896 ± 493	2604 ± 290	2903 ± 566
Apgar score			
<7 at 1 min (no.)	0	1	0
<7 at 5 min (no.)	0	0	0

[a] Plus–minus values are means ± SD. Abbreviations: I-D time, induction to delivery time; UI-D time, uterine incision to delivery time.
* $P < 0.05$ versus groups G1 and G2.

Table 2. Blood gas data and plasma cortisol levels of the maternal artery (MA), umbilical vein and artery (UV and UA) in groups SP (spinal anesthesia), G1 (0.7% sevoflurane–60% nitrous oxide–oxygen anesthesia), and G2 (1.7% sevoflurane–oxygen anesthesia)[a]

Value		SP (n = 18)	G1 (n = 9)	G2 (n = 9)
pH	MA	7.44 ± 0.06	7.41 ± 0.04	7.41 ± 0.02
	UV	7.36 ± 0.04	7.35 ± 0.03	7.35 ± 0.01
	UA	7.41 ± 0.08	7.35 ± 0.03	7.35 ± 0.02
Pco_2 (mmHg)	MA	28.6 ± 3.7	30.9 ± 3.2	31.3 ± 2.7
	UV	40.1 ± 5.7	41.8 ± 2.5	41.6 ± 3.3
	UA	45.5 ± 5.3	42.3 ± 4.0	43.5 ± 4.0
Po_2 (mmHg)	MA	147 ± 21	228 ± 46**	474 ± 80‡
	UV	30 ± 7	31 ± 9	43 ± 9‡
	UA	18 ± 7	23 ± 5*	32 ± 9**
So_2 (%)	MA	99 ± 1	99 ± 1	99 ± 2
	UV	68 ± 25	67 ± 15	82 ± 15
	UA	32 ± 10	34 ± 10	56 ± 17†
HCO_3^- ($mM \cdot l^{-1}$)	MA	19 ± 1	20 ± 2	20 ± 2
	UV	23 ± 1	23 ± 1	23 ± 1
	UA	23 ± 2	23 ± 2	24 ± 2
BE ($mM \cdot l^{-1}$)	MA	−4.0 ± 1.5	−3.5 ± 1.6	−3.7 ± 1.5
	UV	−2.1 ± 1.2	−1.9 ± 1.0	−2.1 ± 1.0
	UA	−3.7 ± 2.3	−3.9 ± 1.8	−2.3 ± 2.1
Cortisol ($\mu g \cdot dl^{-1}$)	MA	38 ± 8	35 ± 6	40 ± 9
	UV	5 ± 2	6 ± 1	7 ± 3
	UA	6 ± 3	6 ± 2	7 ± 3

[a] Data are means ± SD.
* $P < 0.05$, ** $P < 0.01$ versus group SP.
† $P < 0.05$, ‡ $P < 0.01$ versus groups SP and G1.
BE, base excess

Table 3. Sevoflurane concentrations in the maternal artery (MA) and the umbilical vein and artery (UV and UA), and the concentration ratio in groups G1 (0.7% sevoflurane–60% nitrous oxide–oxygen anesthesia) and G2 (1.7% sevoflurane–oxygen anesthesia)[a]

Value	G1 ($n = 9$)	G2 ($n = 9$)
Blood concentration ($mg \cdot dl^{-1}$)		
MA	1.8 ± 0.5	6.3 ± 2.0 **
UV	1.1 ± 0.3	3.0 ± 0.9 **
UA	0.6 ± 0.3	1.4 ± 0.7 *
Concentration ratio		
UV/MA	0.58 ± 0.15	0.48 ± 0.14
UA/UV	0.56 ± 0.06	0.47 ± 0.19

[a] Data are means ± SD.
* $P < 0.05$, ** $P < 0.01$ versus group G1.

For uterine contractility after delivery, an assessment of "good" was made by the obstetricians in all the cases in the three groups. No case required uterine massage and supplementation with prostaglandin $F_{2\alpha}$. No intraoperative awareness or other complication was noted perioperatively.

Discussion

Low concentrations [< 1 minimum alveolar concentration (MAC)] of volatile anesthetics with 50–70% nitrous oxide are commonly used for general anesthesia in cesarean section [4,5]. The use of nitrous oxide affords a rapid increase in alveolar concentration of a volatile anesthetic with its second gas effect and reduces the possibility of maternal awareness during the first few minutes of anesthesia. If the highly blood-soluble anesthetics such as halothane are used without supplementation with nitrous oxide, the blood and brain concentrations will lag behind the inspired concentration. In cesarean section, the operation starts immediately after tracheal intubation in order to reduce the rate of anesthetic uptake by the fetus, but at this point the partial pressure of volatile anesthetics in maternal brain tissue may not have reached adequate levels. Such light anesthesia may accompany sympathetic stimulation, which induces uterine contraction and impairment of uteroplacental blood flow. Under the circumstances, an increase in maternal inspired oxygen concentration (F_IO_2 above 0.5–0.6) or in Pao_2 above 300 mmHg failed to produce a corresponding increase in the umbilical venous partial pressure of oxygen ($Puvo_2$) [6]. Recently, the use of 100% oxygen supplemented with halothane, enflurane, or isoflurane at a delivered concentration of 1.5 MAC, reduced to 1 MAC after 5 min, was shown to result in higher $PuvO_2$ and improved fetal oxygen delivery [7]. Piggott et al. [8] also reported that isoflurane anesthesia balanced in 100% oxygen gave higher $PuvO_2$ and Apgar scores, and less requirement for resuscitation than nitrous oxide and isoflurane in 50% oxygen anesthesia in emergency cesarean section. Thus, inhalation of 100% oxygen under an adequate depth of anesthetisia could be of benefit to a severely compromised fetus. McCrirrick et al. [9] recommended the "overpressure" technique, with 2% isoflurane balanced in oxygen for the first 5 min, 1.5% for the next 5 min, and 0.8% thereafter to reduce the risk of awareness during cesarean delivery.

Sevoflurane is a relatively new anesthetic, with a lower blood/gas partition coefficient than isoflurane, and its alveolar/inspiratory concentration ratio should rise more rapidly than those of the other volatile agents with the exception of desflurane. Therefore, sevoflurane anesthesia with 100% oxygen may not require the "overpressure" technique described above. The MAC for sevoflurane was reported to be 1.71% for healthy Japanese (mean age, 48 years) [10] and 2.05% for North Americans (mean age, 38 years) [11]. Although the mean age of approximately 30 years in our study population required over 2% sevoflurane, the MAC has been known to decrease by up to 40% during pregnancy in animal and human studies [12,13]. Therefore, we used inspired concentrations of 1 MAC (1.7% sevoflurane or 0.7% sevoflurane plus 60% nitrous oxide) from induction to delivery. Although only a small number of patients were involved in our study, no patients were conscious during the operation and there was no postoperative recall, indicating that the anesthetic effects of intravenous thiamylal appeared to persist until the partial pressure of sevoflurane and/or nitrous oxide reached sufficient levels above MACawake.

Oxygen delivery from mother to fetus appeared to be preserved at our anesthetic levels. The dialed 1.7% sevoflurane anesthesia with 100% oxygen (group G2) denoted higher $PuvO_2$, $PuaO_2$, and $SuaO_2$ than either spinal anesthesia or sevoflurane–nitrous oxide anesthesia (groups SP and G1). There was no ceiling in either $PuvO_2$ and $PuaO_2$ above PaO_2 of 300 mmHg, as described by Marx and Mateo [6]. However, in epidural anesthesia for elective cesarean section [14], an inspired oxygen concentration of 100% resulted in a slightly higher PuvO2 (47 mmHg) than the 43 ± 9 mmHg with our sevoflurane anesthesia with 100% oxygen. Furthermore, maternal PaO_2 was significantly higher in group G1 than in group SP, whereas $PuvO_2$ and $SuaO_2$ were almost identical in both groups (Table 2). These results may imply that sympathetic block with spinal or epidural anesthesia may afford more improvement in oxygen delivery to the fetus than general anesthesia. Although Shnider and Levinson reported that the fetal acid-base status in the UV and UA showed no clinically significant difference in general versus regional anesthesia

[15], nitrous oxide lacking in uterine relaxation action may not improve uteroplacental blood flow and fetal oxygenation. When regional anesthesia is not indicated for cesarean section, sevoflurane anesthesia with 100% oxygen will be useful to improve placental transfer of oxygen.

When improved oxygen delivery to the fetus is ensured under the appropriate depth of general anesthesia, exaggerated placental transfer of volatile anesthetics may cause marked fetal depression. Dwyer et al. [16] reported that isoflurane was more rapidly taken up by the mother during cesarean section than halothane, and that the rate of uptake by the fetus from the mother was the same for isoflurane and halothane. From our data, the maternal alveolar/inspired fraction ratio (F_A/F_I) of sevoflurane was 0.51 in group G1 (I-D time, 4.5 ± 2.0 min) and 0.74 in group G2 (I-D time, 7.6 ± 4.0 min), indicating the longer I-D time followed by the higher F_A/F_I ratio. These calculated F_A/F_I values at delivery were higher than that of isoflurane, which was 0.44 [15]. Because sevoflurane has a lower blood solubility, the F_A/F_I ratio of sevoflurane was more rapidly increased even in the shorter I-D time of our study. Satoh et al. [17] showed that when the mean I-D time was the same, the ratios of UV to MA concentrations of volatile anesthetics were similar with halothane, enflurane, sevoflurane, and isoflurane (0.4–0.5 for I-D time of 13 min). Although our I-D time was shorter than theirs, the UV/MA anesthetic ratio was similar. It may indicate that the UV/MA ratio was almost constant at the early phase of any volatile anesthetic inhalation. The alveolar concentrations of the neonate at delivery were calculated as 0.13% (range, 0.06–0.24%) in group G1 and 0.28% (range, 0.03–0.53%) in group G2 by using UA concentrations of sevoflurane. Such a partial pressure of sevoflurane in the brain tissue of the neonate may result in central nervous system depression in some cases. However, sevoflurane should be rapidly eliminated from the baby when respiration is established. In our study, only one newborn in group G1 had an Apgar score less than 7 at 1 min, and all of the scores at 5 min were normal. Even if neonatal depression or a sleeping baby immediately after cesarean delivery is correlated with sevoflurane, sevoflurane anesthesia with 100% oxygen will improve placental transfer of oxygen and possibly prevent neonatal hyoxemia, acid-base abnormality, and permanent brain damage, particularly in the severely compromised fetus.

We found that the plasma cortisol level, an indicator of nonspecific stress, did not differ between the spinal and general anesthesia groups. This may indicate that the stress of our sevoflurane anesthesia is not different from that in regional anesthesia.

This study involved only a small number of patients under general anesthesia. It would have been helpful to have performed a larger study. The 1.7% sevoflurane–40% oxygen group and the spinal anesthesia group under F_IO_2 1.0 should be included to compare the effects of nitrous oxide and sevoflurane on desirable uterine relaxation and to determine the effects of general and spinal anesthesia on oxygen delivery to the fetus, respectively. However, most of our patients chose regional anesthesia because of its wide use for cesarean section in our hospital. Further studies will be necessary to determine the neonatal safety of this technique and the incidence of intraoperative awareness.

In conclusion, 1.7% sevoflurane–100% oxygen anesthesia will improve placental oxygen transfer without severe neonatal depression, prolonged uterine relaxation, or increased blood loss in elective cesarean section.

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References

1. Malviya S, Lerman J (1990) The blood/gas solubilities of sevoflurane, isoflurane, halothane and serum constituent concentrations in neonates and adults. Anesthesiology 72:793–796
2. Strum DP, Eger EI II (1987) Partition coefficients for sevoflurane in human blood, saline and olive oil. Anesth Analg 66:654–656
3. Shim JC, Kaminoh Y, Tashiro C, Miyamoto Y, Yoo HK (1996) Solubility of volatile anesthetics in plasma substitutes, albumin, intravenous fat emulsions, perfluorochemical emulsion, and aqueous solutions. J Anesth 10:276–281
4. Warren TM, Datta S, Ostheimer GW, Naulty JS, Weiss JB, Morrison JA (1983) Comparison of the maternal and neonatal effects of halothane, enflurane and isoflurane for cesarean delivery. Anesth Analg 62:516–520
5. Gambling DR, Sharma SK, White PF, Beveren TV, Bala AS, Goulson R (1995) Use of sevoflurane during elective cesarean birth: a comparison with isoflurane and spinal anesthesia. Anesth Analg 81:90–95
6. Marx GF, Mateo CV (1971) Effects of different oxygen concentrations during general anesthesia for elective caesarean section. Can Anaesth Soc J 18:587–593
7. Bogod DG, Rosen M, Rees GAD (1988) Maximum F_IO_2 during caesarean section. Br J Anaesth 62:255–262
8. Piggott SE, Bogod DG, Rosen M, Rees GAD, Harmer M (1990) Isoflurane with either 100% oxygen or 50% nitrous oxide in oxygen for caesarean section. Br J Anaesth 65:325–329
9. McCrirrick A, Evans GH, Thomas TA (1994) Overpressure isoflurane at caesarean section: a study of arterial isoflurane concentration. Br J Anaesth 72:122–124
10. Katoh T, Ikeda K (1987) The minimum alveolar concentration (MAC) of sevoflurane in humans. Anesthesiology 66:301–303
11. Scheller MS, Saidman LJ, Partridge BL (1988) MAC of sevoflurane in humans and the New Zealand white rabbit. Can J Anaesth 35:153–156
12. Palahniuk RJ, Shnider SM, Eager EI II (1974) Pregnancy decreases the requirement for inhaled anesthetic agents. Anesthesiology 41:82–83
13. Chan MT, Mainland P, Gin T (1996) Minimum alveolar concentration of halothane and enflurane are decreased in early pregnancy. Anesthesiology 85:782–786

14. Ramanathan S, Gandhi S, Arismendy J, Chalon J, Turdorf H (1982) Oxygen transfer from mother to fetus during cesarean section under epidural anesthesia. Anesth Analg 61:576–581
15. Shnider SM, Levinson G (1993) Anesthesia for cesarean section. In: Shnider SM, Levinson G (eds) Anesthesia for obstetrics, 3rd edn. Williams & Wilkins, Baltimore, pp 211–245
16. Dwyer R, Fee JPH, Moore J (1995) Uptake of halothane and isoflurane by mother and baby during Caesarean section. Br J Anaesth 74:379–383
17. Satoh D, Iwatsuki N, Naito M, Sato M, Hashimoto Y (1995) Comparison of the placental transfer of halothane, enflurane, sevoflurane and isoflurane during cesarean section. J Anesth 9:220–223