

Over Half MAC Sevoflurane in Cesarean Section

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Half MAC (minimal alveolar concentration) of volatile anesthetics has been commonly used with nitrous oxide for cesarean section which could occur intraoperative awareness. Over half MAC or more than 1% sevoflurane was studied on 65 parturients who came for either elective or emergency operations. The patient characteristics were age $31.00 \pm 5.67(21-41)$ years, BW $72.37 \pm 10.51(52.6-117)$ kg, and ASA physical status I, 52% for elective and 73% for emergency cases. The indications for operations were mostly CPD, fetal distress and previous cesarean sections. The anesthetic time was $59.19 \pm 17.35(35-145)$ minutes while the induction-delivery time was $12.72 \pm 5.66(3-28)$ minutes. General anesthesia was rapid sequence induction with propofol or thiopental and tracheal intubation under succinylcholine with the application of cricoid pressure. The depth of anesthesia was maintained with 1.5-3% sevoflurane until delivery and the volatile agent was lowered to 0.4-1%, adjusted to clinical manifestation. Midazolam and morphine were added postdelivery. Data of hemodynamic changes during delivery, neonatal outcome and intraoperative blood loss were analyzed without any remarkable note. The postoperative interview on recalls confirmed adequate depth of anesthesia. It was concluded that sevoflurane at more than 1% concentration could be used predelivery in cesarean sections on the issues of awareness, hemodynamics and fetal conditions but caution was suggested in terms of uterine relaxation effect which was dose-dependent.

Keywords: Sevoflurane, Obstetrics, Cesarean section, Uterine atony, Neonatal outcome, Awareness

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Awareness is apparently a problem in general anesthesia for cesarean section, apart from difficult airway and pulmonary aspiration. The incidence is around 0.4%, compared with 0.1%-0.2% in non-parturient patients^(1,2). Anesthesiologists tend to give light anesthesia for fear of neonatal depression and uterine atony by less supplement of volatile anesthetic agents. Sevoflurane is a new inhalation agent with rapid onset and recovery but the information in safe obstetric use is lacking⁽³⁾. 1% or half MAC of sevoflurane was reported for use before newborn delivery because at this concentration it did not cause significant myometrial relaxation and consequently postpartum hemorrhage. But over half MAC of volatile agents is recommended to assuredly suppress intraoperative awareness⁽⁴⁾. This is equivalent to the bispectral index score (BIS) lower than 60. Gender plays

some role in risk of awareness, for female patients are likely to recall during surgery and require more anesthetics than male counterparts. The induction technique in cesarean section is rapid sequence with cricoid pressure and it was found that unless enough bolus dose of induction agent was given, parturients could remember the tube put in their windpipes. It is hard to maintain anesthetic depth by narcotics or benzodiazepines, thereafter, until delivery, therefore the mainstay is volatile agents at the concentration of which awareness has to balance with hypotension, uterine atony and fetal depression. The purpose of the present study was to ensure that 1.5-2% sevoflurane can be used safely for cesarean section.

Material and Method

The design was a prospectively descriptive study on 65 parturients who were either electively or urgently enrolled for cesarean section under general anesthesia. The protocol was approved by the Ethics Committee of Ramathibodi Hospital, Faculty of

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Medicine, Mahidol University. The inclusion criteria were: parturients with ASA 1-3, either primipara or multipara, who chose general anesthesia for cesarean section as an elective or emergency case. Exclusion criteria were patients allergic to sevoflurane, preterm or multiple gestation, and medical conditions that required modification of the anesthetic protocol. Indications for cesarean section were notified and consent obtained from the patient. The patient characteristics such as age, body weight, coexisting disease, etc were recorded. The patients were preoxygenated for at least 3 minutes or took 4 deep tidal breaths, then after obtaining baseline hemodynamic variables, rapid sequence induction and intubation were performed under propofol 2-2.5 mg/kg or thiopental 3-5 mg/kg and succinylcholine 1-2 mg/kg with the application of cricoid pressure. Anesthesia was maintained by O₂:N₂O 1:1, atracurium 0.5 mg/kg or rocuronium 0.6 mg/kg or pancuronium 0.08 mg/kg or vecuronium 0.1 mg/kg, morphine 0.1-0.15 mg/kg or fentanyl 1-2 µg/kg and sevoflurane from 1.5 - 2% until delivery according to the anesthesiologist. The authors' institutional practice for cesarean section is to perform surgical skin preparation and draping before induction of anesthesia. Patients' lungs were mechanically ventilated with a tidal volume of 10 ml/kg and rate 10-12 breath/min. Sevoflurane was lowered to 0.4-1% after delivery and adjusted to the patient's clinical hemodynamics and supplemented with intravenous midazolam 1.5-2 mg. Apgar scores or neonatal conditions were recorded together with birth time and weight. Following delivery and clamping of the umbilical cord, oxytocin (Syntocinon) 10 units was added to 1 L intravenous fluid and methylergometrine maleate (Methergin) 0.2 mg was bolused for uterine contraction. The amount of blood loss was recorded after delivery and at the end of the operation. Intraoperative hypotension was treated with crystalloid, or colloid and ephedrine, if not better, where necessary. Volumes and types of intravenous fluids and amount of blood loss were noted. Immediately following skin closure, administration of sevoflurane and nitrous oxide ceased and the patient was ventilated with 100% oxygen at 6 L/min. Prostigmine 2.5 mg and atropine 1.2 mg were used to reverse residual paralysis at the end of the case and the patient was extubated. Arterial blood pressure and heart rate were recorded at 1 min-intervals from induction to delivery of the neonate and at 3-min intervals thereafter. Patients were interviewed regarding intraoperative recall upon discharge from the

postoperative care unit and on the first postoperative day.

Statistics

Assuming the null hypothesis of the incidence of awareness in cesarean section is 0.4% while the alternative one is 0%, and the standard deviation of the population is 1, the significance level is 0.05 and the power is 80% in 2-sided test⁽⁵⁾, the sample size was calculated to be at least 51. Continuous data were reported as mean ± SD while ordinal data as counts and percentage.

Results

Most of the patients were ASA physical status I in either elective (52%) or emergency (73%) cases. One case was diabetic, hypertensive and morbid obesity who accounted for BW 117 kg and then classified as status II-III. More than half of emergency cases were CPD, fetal distress (tachycardia or bradycardia) and abnormal placenta. The characteristics are presented in Table 1.

Patients came for cesarean sections with diagnoses of CPD (44%), previous cesarean operations (26%) and fetal distress as in Table 2.

One parturient was diagnosed as PIH with systolic BP over 170 mmHg in the theater. After tracheal intubation, BP went up to 220/130 but came down after 2% sevoflurane to normal level. The outcome of both mother and neonate was uneventful. The average anesthetic time was 1 hour and the induction-delivery time ranged from 3 to 28 minutes, the maximum of which was due to surgical delay (Table 3). Intravenous induction agents were mainly propofol or thiopental, while nondepolarizing muscle relaxant was mostly atracurium. Midazolam and morphine were supplemented after delivery and sevo-

Table 1. Patient characteristics (n = 65)

	Mean ± SD	(Range)
Age (years)	31.00±5.67	(21-41)
BW (kg)	72.37±10.51	(52.6-117)
Physical status		
Elective (n = 42)		
I	23	
II	19	
Emergency (n=23)		
I	17	
II	5	
III	1	

Table 2. Indications for cesarean section (n = 65)

CPD	28
Previous cesarean	17
Fetal distress	5
Abnormal placenta	4
Elderly primigravida	4
Abnormal presentation	4
PIH	1
Herpes vaginalis	1
Oligohydramnios	1

* CPD = cephalopelvic disproportion, PIH = pregnancy induced hypertension

flurane turned down to 0.4-1% according to hemodynamic responses of the patients. All neonates were active with good crying and apgar scores. The post-operative interviews revealed none of recalls. Intra-operative fluid was given approximately 1 L as crystalloids; it was more than 2 L in one patient who weighed

more than 100 kg. Her hemodynamics were stable throughout the operation. The other patient with placenta previa totalis bled about 1,200 ml and was resuscitated by colloid towards the end of the operation; the total amount of fluid was 2,100 ml.

Hemodynamic changes during delivery are presented in Table 4 and Fig. 1. Data were not completely analysed because in some cases the induction-delivery time was earlier than 15 minutes.

Discussion

Traditionally, anesthesiologists tend to give general anesthesia as light as possible such as 0.5% halothane, isoflurane or sevoflurane in 50% N₂O for cesarean section to avoid fetal depression and uterine atony. This half MAC concept is believed to reduce the incidence of awareness but does not suppress totally intraoperative recall, especially in the period before delivery. Chin et al revealed EC₅₀ (end-tidal concentration at which 50% patients have

Table 3. General anesthetic data as mean ± SD (range)

Anesthetic time (min)	59.19±17.35	(35-145)
Induction-delivery time (min)	12.72±5.66	(3-28)
Anesthetic agents		
propofol (mg)	91.06±22.74	(60-160)
thiopental (mg)	240.78±34.57	(100-250)
succinylcholine (mg)	106.26±11.98	(100-150)
sevoflurane predelivery (%)	1.98±0.18	(1.5-3)
sevoflurane postdelivery (%)	1.10±0.40	(0.4-1.5)
atracurium (mg)	31.89±9.10	(25-60)
rocuronium (mg)	37.57±8.67	(30-75)
midazolam (mg)	1.98±0.33	(1-2.5)
morphine (mg)	9.77±1.08	(4-13.5)
Intraoperative fluid (ml)	1,121.42±330.77	(550-2,100)
Blood loss (ml)	496.03±191.19	(250-1,200)
Newborn weight (g)	3,261.19±492.71	(1,610-4,210)
Apgar scores (1,5 min)	9,10	
Intraoperative recalls	none	

Table 4. Hemodynamic data during delivery as mean ± SD

	Blood pressure (mmHg)	Heart rate (beat/min)
Predelivery		
15 min	136.82 ± 21.17/ 80.48 ± 13.27	91.46 ± 11.51
10	138.84 ± 21.30/ 81.78 ± 13.89	92.77 ± 10.04
5	129.69 ± 17.75/ 75.83 ± 12.51	91.41 ± 10.42
Delivery	125.48 ± 18.97/ 73.15 ± 14.11	90.07 ± 12.24
Postdelivery		
5 min	121.29 ± 19.05/ 69.93 ± 13.99	88.17 ± 11.89
10	115.18 ± 15.52/ 66.17 ± 13.72	86.06 ± 11.52
15	114.15 ± 13.64/ 68.23 ± 13.09	84.67 ± 11.22

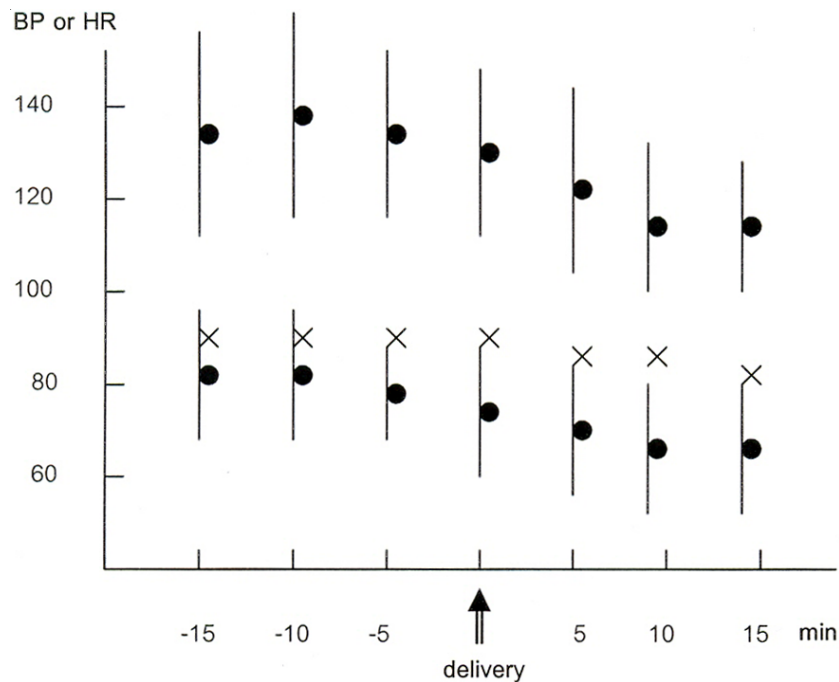


Fig. 1 Hemodynamic changes during delivery: mean \pm SD of systolic and diastolic BP were plotted as dots and whiskers respectively. Heart rate was shown as crosses

bispectral index score or BIS lower than 60) of sevoflurane to be 1.22% and recommended use of 1.2-1.3% in cesarean section⁽¹⁾. Because BIS under 60 does not reliably guarantee that awareness is abolished in terms of implicit memory⁽⁶⁾, and also nitrous oxide might reduce BIS during sevoflurane anesthesia⁽⁷⁾. Since 0.75 MAC of sevoflurane or 1.5% indeed ensures adequate depth of anesthesia, the authors chose to study 2% or even 3% of sevoflurane in cesarean section with the tradeoff of more cardiovascular depression. Induction and intubation took place after skin preparation and draping, so that hemodynamic changes of sevoflurane might be masked by hypertensive response from tracheal intubation as shown in Fig. 1. However, the half-life of brain-alveolar equilibration for this inhalation agent is 2.1 min and the induction-delivery time averaged 12.72 ± 5.66 min ranging from 3 to 28 min, the authors could still see its cardiovascular effect. Hall et al compared 3% and 8% sevoflurane in terms of second stage duration on inhalation induction and found that cardiovascular stability was equal⁽⁸⁾. The presented patients did not need any vasoactive agents to counteract intraoperative hypotension; predelivery systolic pressure was 130, diastolic 80 and heart rate 90 (Fig. 1). This was according to less cardiovascular depression of sevoflurane than halo-

thane and isoflurane, even at high concentrations. Sevoflurane reduces blood pressure mainly by reduction of systemic vascular resistance and sympathetic nerve activity; it does not depress myocardial contractility to the same extent as halothane or enflurane. The baroreflex is not significantly attenuated nor is flow-mediated shear stress-induced dilatation of vascular smooth muscle, although it appears to prolong the period of isovolemic relaxation⁽⁹⁾. The authors concluded that over half MAC sevoflurane could be administered for predelivery period safely in aspect of hemodynamic stability.

Intracellular ionized calcium (Ca^{++}) concentration has been suggested to play an essential role in the regulation of spontaneous contractions of myometrium. Volatile anesthetics reduce this concentration by decreasing the trans-sarcolemmal Ca^{++} influx in uterine muscles and depleting intracellular Ca^{++} stores by increasing Ca^{++} release or by decreasing Ca^{++} uptake into the sarcoplasmic reticulum, thus depressing uterine contraction⁽¹⁰⁾. Sevoflurane inhibits the amplitude and frequency of spontaneous uterine contraction in a concentration-dependent manner. At higher concentrations, there is a decrease in uterine tone and an increase in uterine blood loss⁽¹¹⁾. 2 MAC of sevoflurane was reported to inhibit 58.9% amplitude

and 49.3% frequency to the maximum, and also to reduce the oxytocin-induced contraction of gravid myometrium similarly to isoflurane⁽¹²⁾. Oxytocin at low concentration (~10 nM) only one dose of significantly increased the amplitude, frequency and duration of myometrial contractions⁽¹³⁾. In every patient, the uterine contraction was well accepted by the obstetricians with only one dose of 10 units oxytocin infusion and IV bolus of 0.2 mg methylergometrine maleate (Methergin) after placental delivery. Methergin might potentiate contractions by changing the pattern of action potentials⁽¹⁴⁾. Intraoperative blood loss was 500 ml and amounted to 1,200 ml as a maximum from placenta previa totalis. The patient was not so severely hypotensive to need any vasoactive medication. Most of the time, the uterus still responds appropriately to oxytocin stimulation⁽¹¹⁾. Sevoflurane concentrations in the “up and down” method for analgesia in labor were studied as a mixture between 50% oxygen and air via face mask to be 2-3% and it was administered approximately 1 minute before each uterine contraction with the end-point of end-tidal concentration of 1-1.5%; it relieved pain effectively but did not result in further blood loss nor fetal abnormalities. Only one from 50 cases had dysfunctional labor while the other one underwent cesarean section due to CPD⁽¹⁵⁾. Increasing number of pregnant patients are receiving calcium channel blockers like isradipine to decrease myometrial contractions in case of threatened abortion or premature labor; non-steroidal anti-inflammatory agents (NSAID) like indomethacin are also used to prevent preterm delivery. Both medications could potentiate the inhibitory effect on myometrium of sevoflurane⁽¹⁰⁾. Maternal blood loss did not differ between sevoflurane, isoflurane and spinal anesthesia for cesarean section but during therapeutic abortion, it was associated with higher blood loss than propofol⁽¹⁶⁾. In order to produce significant uterine relaxation for therapeutic purposes such as manual removal of retained placenta, complicated breech extraction, multiple gestation delivery, treatment of uterine inversion and so forth, it might be prudent to use the agent at concentration of 1-1.5 MAC, especially during the wash-in period.

The authors used 2L/min of oxygen and nitrous oxide as 1:1 throughout the operative period and after delivery midazolam and morphine were supplemented. The authors did not monitor end-tidal concentration of sevoflurane and in some cases, the inspired concentration was even up to 3% for a short periods to control the blood pressure in PIH patients.

The addition of nitrous oxide significantly reduces MAC, for example 63.5% N₂O could reduce MAC sevoflurane by 61%⁽¹⁷⁾. For minimal-flow anesthesia (0.5 L/min), the vaporizer dial setting could be lowered down when used with nitrous oxide than with oxygen alone to still maintain constant end-tidal concentration⁽¹⁸⁾. The vapor output concentration is almost the same with dial setting with Penlon in the range of 2-6 L/min fresh gas flow⁽¹⁹⁾.

Due to the low blood solubility, its pharmacokinetics and pleasant odor, sevoflurane alone is feasible for induction. For the parturient undergoing cesarean section with general anesthesia, rapid sequence induction and intubation of the trachea is the standard technique because of impaired gastric emptying associated with pregnancy and the risk of aspiration⁽²⁰⁾. This induction obviously needs intravenous catheter which sometimes is hard to accomplish in an emergency situation. Sevoflurane was reported with good outcome for both mother and child in inhalation induction for emergency cesarean sections like double footling, umbilical cord prolapse, severe tracheal stenosis and status asthmaticus without intravenous access. It was compared to ether, chloroform and cyclopropane use without tracheal intubation in the past.

The present study was one to attest that over half MAC sevoflurane could be safely used in cesarean section, considering its stable hemodynamic effects even at high concentrations in some patients. Somehow, the authors cautioned the dose-dependent inhibitory effect on uterine contractions which could be counteracted with oxytocin and methylergometrine maleate, eventhough no patients in the present study had postpartum hemorrhage. On the other hand, this effect is good for therapeutic uterine relaxations.

Conclusion

Sixty-five parturients were enrolled for a prospective descriptive study on over half MAC sevoflurane in cesarean section. Intraoperative awareness was the first issue of the present study and found that more than 1% sevoflurane before neonatal delivery could abolish this complication. Data on hemodynamic depression, neonatal outcome and intraoperative blood loss were analyzed. Due to less attenuation on cardiovascular functions than other volatile agents, it was safe enough even to 3% concentration. But the tradeoff was dose-dependent inhibitory effect on uterine contractions which could be preserved with oxytocin and methylergometrine maleate. No adverse

fetal effects were revealed nor a higher amount of blood loss related to its direct effect reported. Therefore, the authors concluded that over half MAC or more than 1% sevoflurane was safe in the pre-delivery period during general anesthesia for cesarean section.

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การใช้ยาดมสลบ Sevoflurane ขนาดมากกว่าครึ่ง MAC สำหรับการผ่าตัดคลอดทางหน้าท้อง

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บทนำ: การผ่าตัดคลอดทางหน้าท้องภายใต้การระงับความรู้สึกชนิดทั่วไปนั้น นิยมใช้ยาดมสลบในขนาดที่ต่ำกว่าครึ่ง MAC (minimal alveolar concentration) ร่วมกับการให้ในตรัสออกไซด์และออกซิเจน โดยมักเปิดออกซิเจนในช่วงก่อนทารกคลอดไม่ต่ำกว่าร้อยละ 50 ทำให้มารดาอาจอยู่ในภาวะรู้ตัว (awareness) ขณะผ่าตัดได้ การศึกษานี้จึงมีวัตถุประสงค์ที่จะศึกษาผลของการใช้ยาดมสลบ sevoflurane ซึ่งเป็นยาดมสลบชนิดใหม่ ในขนาดที่มากกว่าครึ่ง MAC สำหรับระงับความรู้สึกในผู้ป่วยที่มารับการผ่าตัดคลอดทางหน้าท้องว่าสามารถลดหรือป้องกันการเกิดภาวะรู้ตัวขณะผ่าตัดได้หรือไม่ มีผลต่อการหดตัวของมดลูก และผลต่อ Apgar score ของทารกมากน้อยเพียงใด

วัตถุประสงค์และวิธีการ: ได้ทำการศึกษาผู้ป่วยที่มารับการผ่าตัดคลอดทางหน้าท้องจำนวน 65 ราย อายุเฉลี่ย 31.00 ± 5.67 ปี น้ำหนักร่างกาย 72.37 ± 10.51 กิโลกรัม ASA physical status 1 ร้อยละ 52 ในการผ่าตัดที่หน้าท้องหน้าและร้อยละ 73 ในการผ่าตัดคลอดฉุกเฉิน ผู้ป่วยส่วนใหญ่มารับการผ่าตัดคลอดเนื่องจากภาวะ cephalopelvic disproportion เคยผ่าตัดคลอดมาแล้ว และภาวะ fetal distress ระยะเวลาการระงับความรู้สึก 59.19 ± 17.35 นาที ระยะเวลาตั้งแต่เริ่มนำสลบจนถึงเด็กคลอด 12.72 ± 5.66 นาที การนำสลบจะใช้วิธี rapid sequence ด้วย thiopental หรือ propofol ใส่ท่อหายใจด้วยยา succinylcholine พร้อมกับทำการกด cricoid ยาสลบหลักหลังการใส่ท่อหายใจคือ sevoflurane ขนาด 1.5-3% และยาหย่อนกล้ามเนื้อชนิด non-depolarizing เมื่อทารกคลอดแล้วจะลดยาดมสลบ sevoflurane ลงเหลือ 0.4-1% ตามการตอบสนองของผู้ป่วยต่อการผ่าตัด และให้ยา midazolam 1.5-2 มก. และ morphine ขนาด 0.1-0.15 มก./กก. บันทึกการเปลี่ยนแปลงทางระบบไหลเวียนโลหิตของผู้ป่วย, Apgar score, ระยะเวลาที่ทารกร้องหลังจากคลอด ปริมาณเลือดที่เสียขณะผ่าตัด และประเมินภาวะการรู้ตัวขณะผ่าตัด เมื่อผู้ป่วยฟื้นคืนสติ และใน 24 ชั่วโมงต่อมา

สรุปผลการศึกษา: การศึกษานี้พบว่า sevoflurane ขนาดมากกว่า 1% (มากกว่าครึ่ง MAC) สามารถนำมาใช้ระงับความรู้สึกสำหรับผู้ป่วยที่มารับการผ่าตัดคลอดทางหน้าท้องได้อย่างปลอดภัย โดยพบว่าผู้ป่วยทั้ง 65 ราย ไม่มีภาวะการรู้ตัวขณะผ่าตัด ไม่มีผลต่อ Apgar score และระยะเวลาที่ทารกเริ่มร้องหลังคลอด รวมทั้งปริมาณเลือดขณะผ่าตัดไม่ได้เพิ่มมากขึ้นจากการผ่าตัดคลอดที่ได้มีรายงานไว้