Original article

A retrospective pilot study examining the effect of inhalation anesthesia after delivery on intraoperative blood loss in emergency cesarean section

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緊急帝王切開の術中出血量におよぼす吸入麻酔薬の影響：後方視的観察研究

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Abstract

Inhalation anesthetic agents inhibit uterine muscle contractility in laboratory experiments; therefore, intravenous anesthetic use is recommended to avoid the atonic effects of inhalation anesthetics after cesarean section delivery of a fetus. However, the clinical impact of inhalation anesthetic use remains unclear. This study aimed to examine the effects of inhalation anesthetic agents used after delivery on intraoperative blood loss in cesarean section. A single-center retrospective study was performed using clinical data from patients who underwent emergency cesarean section during a 7-year period. A total of 511 patients were analyzed. General anesthesia was performed in 147 patients, and the remaining 364 patients received cesarean section under spinal anesthesia. For general anesthesia, propofol and inhalation anesthesia (sevoflurane and desflurane) were used after cesarean delivery in 125 and 22 patients, respectively. Multivariate regression analysis showed that intraoperative blood loss after delivery was comparable to propofol (−155 mL; 95%CI, −344 to 35 mL). Inhalation anesthetic agents used after delivery were not associated with increased blood loss during cesarean section. Prospective large studies are needed to support these findings.

和文要旨

吸入麻酔薬は基礎研究において子宮平滑筋の弛緩作用が示されている。しかし，臨床において吸入麻酔薬の使用が子宮の弛緩におよぼす影響はほとんど分かっていない。そこで本研究では，分娩後に使用する麻酔薬と帝王切開の術中出血量との関連について検討した。当院で7年間の観察期間に緊急帝王切開が行われた511例の症例を後方視的に解析した。全身麻酔が147例および脊椎麻酔が364例あった。全身麻酔のうち，分娩後に使用された麻酔薬はプロポフォールが125例および吸入麻酔が22例（セボフルラン15例，デスフルラン7例）であった。多変量解析の結果，吸入麻酔の使用はプロポフォールの使用と比較してむしろ出血量の減少傾向を示した（−155 mL；95%信頼区間，−344〜35 mL）。分娩後の吸入麻酔薬の使用と帝王切開の術中出血量との関連は認められなかった。これらの知見を支持するためにはさらなる大規模研究が必要である。

Key words: cesarean section, inhalation anesthesia, propofol, spinal anesthesia, intraoperative hemorrhage.

Background

Inhalation anesthetic agents such as sevoflurane and desflurane induce dose-dependent decreases in skeletal and smooth muscle tone[1-3]. There is *ex vivo* evidence that sevoflurane and desflurane can inhibit uterine muscle contractility[1], although propofol in clinically relevant concentrations did not decrease uterine tone[2]. As such, switching from inhalation to intravenous anesthesia after cesarean section delivery is recommended to avoid the potential atonic effects of inhalation anesthetics[3].

(Received 2022.8.31 / Accepted 2022.10.5)

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However, the effects of switching from inhalation anesthetic agents on intraoperative blood loss remain unclear. This pilot study aimed to examine the effects of inhalation anesthetic agents used after delivery on intraoperative blood loss in cesarean section. Because spinal anesthesia is routinely performed in elective cesarean sections at our hospital, we analyzed emergency cesarean cases.

Materials & Methods

Study design and settings

This was a single-center, retrospective, observational study using data from Toyama University Hospital, which is an academic, teaching, and tertiary care center that covers a population of one million people. This study was approved by our hospital's ethics committee (No. R2020170) and conducted in adherence with the principles of the Declaration of Helsinki. The requirement for written informed consent was waived because of the retrospective nature of this study. Instead, opt-out consent documents were presented on our hospital website for patients who did not wish to participate.

Study participants

We retrieved data from all patients who underwent emergency cesarean section at our hospital during a 7-year period from July 1, 2013 to June 30, 2020. We excluded patients with planned spinal anesthesia who incidentally converted to general anesthesia.

Data collection and measurements

We extracted age, body mass index at delivery, gestational age, and other characteristics from electronic medical records. Preoperative laboratory values were measured within 4 weeks before surgery. Intraoperative blood loss was calculated from the increased weight of surgical gauzes used for blood collection and the suction fluid volume excluding the amount of amniotic fluid. Potential confounding factors for intraoperative hemorrhage include placental previa/abruption, prematurity, previous cesarean surgery, hypertension, diabetes[4], uterine myomas[5], obesity[6], thrombocytopenia[7], and assisted reproductive technology (ART)[8]. Because uterine contractions can influence the amount of intraoperative blood loss, we also included pre-labor rupture of the membranes as a confounding factor in our study. Furthermore, we included increased uterine contents, such as large for gestational age newborns and multiple births, as a potential confounding factor. Category-1 cesarean section was defined as ≤30 min of the decision-to-birth interval[9]. Obstetrical disseminated intravascular coagulation (DIC) was diagnosed by ≥8 points of the scoring system[10]. Endovascular balloons were placed routinely in the bilateral common iliac artery at our hospital. Preoperative antiplatelet use was defined as administered within 1 week before surgery. Preoperative heparin, oxytocic, or tocolytic use were counted until the day of surgery.

Outcomes

The main outcome was intraoperative blood loss in patients with inhalation anesthesia or propofol after delivery. We also analyzed spinal anesthesia as a positive control to determine the absolute difference between inhalation anesthesia and propofol.

Statistical analysis

Continuous variables are presented as mean ± standard deviation. Univariate and multivariate regression analyses were performed to determine the differences in intraoperative blood loss between inhalation anesthesia and propofol after delivery. Multivariate regression analysis was used to adjust all confounding characteristics used in the univariate regression analysis. After multivariate analysis, residual distribution was confirmed to be graphically normal by using quantile–quantile plots. The calculated regression coefficients are shown with 95% confidence intervals (CI). A two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed using statistical software (EZR; a graphical user interface for R; The R Foundation for Statistical Computing, Vienna, Austria)[11].

Results

Patient demographics and surgical characteristics

During the observation period, 517 patients underwent emergency cesarean section in our hospital. After exclusion of six patients with planned spinal anesthesia who incidentally converted to general anesthesia, we analyzed a total of 511 patients (Figure). Patients were 33.3 ± 5.4 years old, had a body mass index of 25.1 ± 4.2 kg/m^2, and were 34.8 ± 4.6 weeks of fetal gestational age. One patient had obstetrical DIC, and nine patients had placement of endovascular balloons (Table 1). All of these patients had placenta previa. There were no patients with hemorrhagic diseases such as hemophilia or von Willebrand's disease. The skin incision-to-delivery interval was 8 ± 3 min, and the operative time was 60 ± 22 min. The median blood loss was 580 mL (range, 120–4220 mL).

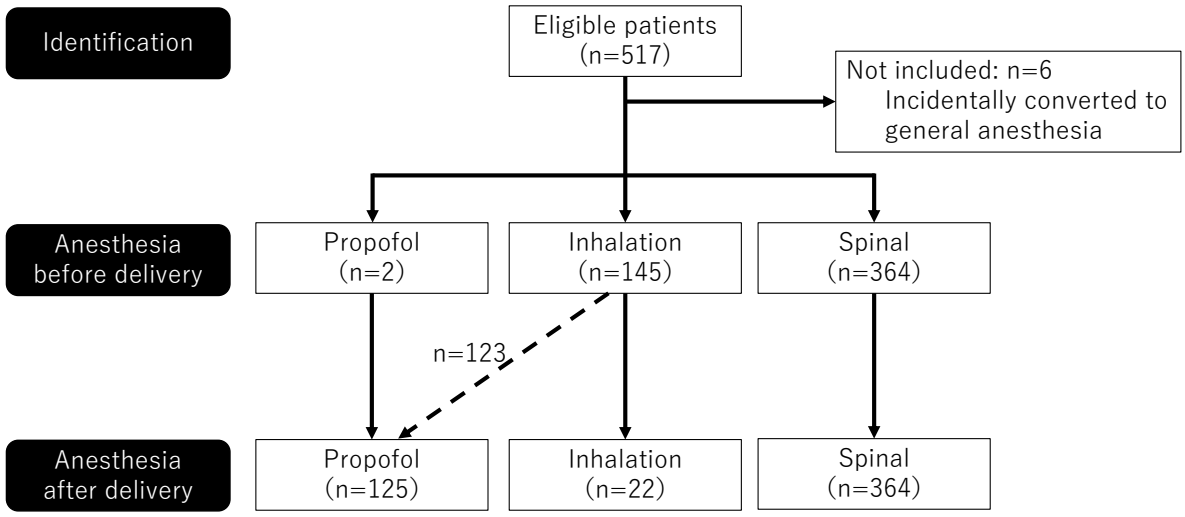

Figure
Anesthetic methods were summarized in this study. A dotted line shows 123 patients who received switching anesthesia from inhalation to propofol.

Table 1: Patient demographics and surgical characteristics

Variables	n=511
Patient	
Age, years	33.3 ± 5.4
BMI at delivery, kg/m^2	25.1 ± 4.2
Gestational age, week	34.8 ± 4.6
Parturition, number	0 (0–6)
Previous cesarean surgery, number	0 (0–3)
Hypertensive disorders	52 (10.2)
Diabetes	39 (7.6)
Uterine myomas	17 (3.3)
Hemoglobin, g/dL	11.1 ± 1.3
Platelet, 10^7/mL	22.8 ± 6.6
ART conception	98 (19.2)
PROM	102 (20)
Placenta previa/Placental abruption	38 (7.4)
Multiple birth/LGA newborn >4000 g	57 (11.2)
Surgery	
Operative time, min	60 ± 22
Blood loss, mL	580 (120–4220)
Category-1	31 (6.1)

Data are presented as number (%), mean ± standard deviation, or median (range). ART, assisted reproductive technology; BMI, body mass index; LGA, large for gestational age; PROM, prelabor rupture of membranes.

Effect of inhalation anesthesia after delivery on intraoperative blood loss

The anesthetics used in this study are shown in Figure. Switching from inhalation anesthesia to propofol after delivery was performed in 123 patients, while 24 patients received no anesthesia switching (two propofol, 22 inhalation anesthesia). Thus, propofol and inhalation anesthesia were used after delivery in 125 and 22 patients, respectively, including 15 patients with sevoflurane and seven with desflurane. The remaining 364 patients received spinal anesthesia. As shown in Table 2, univariate regression analysis showed that inhalation anesthesia use after delivery (n = 22) showed a trend towards reduced blood loss after delivery compared with propofol use (n = 125) (−171 mL; 95%CI, −388 to 46 mL). Multivariate regression analysis, including patients with spinal anesthesia, also showed that intraoperative blood loss using sevoflurane and desflurane af-

ter delivery was similar to that with propofol (−155 mL; 95%CI, −344 to 35 mL). As a positive control, spinal anesthesia use showed a significant reduction in blood loss compared with propofol use (−156 mL; 95%CI, −260 to −53 mL). Multivariate regression analysis also showed that thrombocytopenia, placental diseases, uterine myomas, obesity, ART conception, multiple births and large for gestational age newborns, and oxytocin use were significantly associated with intraoperative blood loss (Table 2).

Discussion

In the present study, we performed a chart-review analysis of the effects of volatile anesthesia on intraoperative blood loss for cesarean section. We found that intraoperative blood loss using sevoflurane and desflurane after delivery was comparable with propofol. In contrast to *ex vivo* studies reporting atonic effects of inhaled anesthetics on the uterus[1], a recent *in vivo* study reported that propofol and sevoflurane had no effects on oxytocin-induced uterine contractions[12]. A small prospective study using univariate analysis also found no differences in intraoperative blood loss between inhalation and propofol anesthesia[13]. These observations suggest that the effects of inhalation anesthesia on the uterus may differ between *ex vivo* and *in vivo*. Nevertheless, the *in vivo* effects of inhalation anesthetics on the uterus remain largely unknown. Thus, prospective studies are required to determine differences in blood loss between inhalation anesthesia and propofol anesthesia.

Critical obstetric hemorrhage is an obstetric emergency and a leading cause of maternal death[14,15]. The high frequency of DIC complications means that prompt hematological interventions, especially fresh frozen plasma and fibrinogen administration, are often required[14,15]. However, there may be insufficient time to prepare transfusion products in emergency surgical

Table 2: Univariate and multivariate regression analyses of intraoperative blood loss

		Univariate		Multivariate	
	Number (%)	Blood loss, mL	*P* value	Blood loss, mL	*P* value
Older age, ≥35 years	225 (44.0)	78 (-8, 165)	0.076	33 (-44, 109)	0.40
Obesity, BMI at delivery ≥25 kg/m^2	223 (43.6)	131 (45, 217)	0.0030	172 (97, 247)	<0.0001
Prematurity	274 (53.6)	110 (25, 196)	0.012	10 (-92, 111)	0.85
Previous parturition	219 (42.9)	62 (9, 115)	0.022	-33 (-124, 58)	0.47
Previous cesarean surgery	98 (19.2)	27 (-51, 104)	0.50	92 (-23, 208)	0.12
Thrombocytopenia, Platelet count < 10 ×10^7/mL	6 (1.2)	1383 (1001, 1764)	<0.0001	1108 (771, 1444)	<0.0001
Placenta previa/Placental abruption	38 (7.4)	829 (682, 977)	<0.0001	728 (563, 895)	<0.0001
Diabetes	39 (7.6)	-94 (-256, 68)	0.25	-122 (-257, 13)	0.077
Hypertensive disorders	52 (10.2)	-49 (-191, 93)	0.50	-47 (-189, 95)	0.51
Uterine myomas	17 (3.3)	339 (100, 577)	0.0054	370 (168, 572)	0.0004
ART conception	98 (19.2)	151 (43, 260)	0.0064	137 (39, 234)	0.0061
Multiple birth/LGA newborn, >4000g	57 (11.2)	121 (-16, 257)	0.083	172 (48, 296)	0.0066
PROM	102 (20.0)	-67 (-174, 41)	0.23	26 (-66, 118)	0.58
Preoperative antiplatelet/heparin use	56 (11.0)	39 (99, 177)	0.58	-62 (-180, 55)	0.30
Preoperative oxytocic use	74 (14.5)	-7 (-129, 115)	0.91	24 (-93, 141)	0.68
Preoperative tocolytic use	174 (34.1)	67 (-24, 158)	0.15	18 (-81, 117)	0.73
Surgery					
Category-1	31 (6.1)	152 (-28, 332)	0.098	-33 (-202, 135)	0.70
Endovascular balloon occlusion use	9 (1.8)	749 (428, 1070)	<0.0001	-52 (-368, 265)	0.75
Oxytocin use	379 (74.2)	23 (18, 29)	<0.0001	101 (16, 188)	0.020
Methylergometrine use	409 (80.0)	-77 (-184, 31)	0.16	-14 (-120, 92)	0.80
Nitroglycerin use	21 (4.1)	-107 (-324, 110)	0.33	-88 (-272, 97)	0.35
Anesthesia					
Propofol (post-delivery anesthesia)	125 (24.5)	Reference		Reference	
Volatile (post-delivery anesthesia)	22 (4.3) (15 sevoflurane, 7 desflurane)	-171 (-388, 46)	0.12	-155 (-344, 35)	0.11
Spinal	364 (71.2)	-311 (-408, -213)	<0.0001	-156 (-260, -53)	0.0032

Regression analyses were performed to examine the confounders in intraoperative blood loss. The calculated regression coefficients are shown with 95% confidence intervals in parentheses. ART, assisted reproductive technology; BMI, body mass index; LGA, large for gestational age; PROM, prelabor rupture of membranes.

cases. Therefore, the prediction of blood loss helps with transfusion decisions. Our findings suggest that intraoperative blood loss can be approximated by known preoperative factors such as thrombocytopenia, placental disease, increased uterine contents, uterine myomas, ART, and obesity[4-8]. A meta-analysis also reported that spinal anesthesia causes less blood loss than general anesthesia[16], which is compatible with our findings. Thus, spinal anesthesia is the preferred choice if time is available, at least with regard to intraoperative blood loss. Even if general anesthesia is used, it may be reasonable to use inhalation anesthesia for the postpartum period without switching to propofol.

There are several limitations of this study. First, this was a retrospective study performed in a single center and included a small number of patients. Second, blood loss was calculated from the suction blood volume and increased gauze weight. Therefore, it was difficult to discriminate blood from amniotic fluid. Third, the anesthetic usage (e.g., the anesthetic drug and concentration) depended on the attending anesthesiologist's preference. Fourth, the use of anesthetic agents before delivery was not analyzed. Finally, postpartum hemorrhage was not considered in this study.

Conclusions

In this pilot study, we examined the effects of inhalation anesthetic agents used after delivery on intraoperative blood loss in cesarean section. Univariate and multivariate regression analyses showed that intraoperative blood loss using sevoflurane and desflurane after delivery was comparable to that with propofol, although this pilot study included a small number of patients. Our findings suggest that sevoflurane and desflurane may be safe for use after cesarean delivery, at least with regard to intraoperative blood loss. Further large studies are needed to support our findings.

Acknowledgment

We thank Dr Eri Noel ARAI for helpful discussions, and Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

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