Bispectral Index in Assessment of 3% and 4.5% Desflurane in 50% N_2O for Caesarean Section

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Background: *To prevent awareness and uterine atony among parturients during general anesthesia for caesarean section, volatile anesthetic agents have been limited to 0.5 MAC in 50% N_2O. This technique appeared to be inadequate to produce BIS values less than 60 in isoflurane and sevoflurane.*
Objective: *To assess BIS value during general anesthesia with 3% and 4.5% desflurane in 50% N_2O before delivery.*
Material and Method: *The parturients were blinded and randomized in opaque envelopes to one of the two study groups. Seventy-two elective caesarean section ASA I - II parturients were induced and intubated with thiopental 4 mg/kg, succinylcholine 1.5 mg/kg and were received either 3% or 4.5% desflurane in 50% N_2O to maintain general anesthesia. Both groups received rocuronium 0.6 mg/kg for muscle relaxation. Morphine 0.1 mg/kg and midazolam 0.06 mg/kg were administered after delivery.*
Results: *There were no differences in demographic data in both groups. The incidences of patients with a satisfactory BIS score (< 60) in the 4.5% desflurane group was 81% that was significantly more than 42% in the 3% desflurane group ($p < 0.000$). Mean BIS values at neonatal delivery were 62 $\pm$ 8 in the 3% desflurane group, versus 49 $\pm$ 12 in the 4.5% desflurane group. Indices of maternal and neonatal outcome were similar between the two groups.*
Conclusion: *General anesthesia for caesarean section with 4.5% desflurane in 50% N_2O maintained BIS < 60 more significantly than 3% of desflurane in 50% N_2O without maternal and neonatal adverse effects in healthy paturients.*

Keywords: *BIS, Bispectal index, Caesarean section, Desflurane*

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The incidence of the awareness in general anesthesia with 50% N_2O without inhalation anesthetic agents for caesarean section is 12-26%[1-3].The prevalence was less than 1% when the technique was supplemented with 0.5 MAC of inhalation anesthetic agents[4-7]. Anesthetic technique has been modified with many regimens to reduce risk of awareness without adverse effect on neonatal outcome or maternal blood loss. Lyon et al increased the dose of thiopentone (5-7 mg/kg) and concentration of volatile anesthetic agents and reported the incidence of awareness to be 0.4%[8]. Jirasiritham et al[9] concluded that over half MAC sevoflurane could be used pre-delivery in caesarean sections on the issue of awareness, hemodynamics, and fetal conditions. Abboud used 6% desflurane for caesarean section and reported no adverse effect on maternal blood loss and neonatal outcome[10].

The Bispectral index(BIS) is a monitor of anesthetic depth with 40-60 being associated with adequate surgical anesthesia[11] and a low incidence of intra-operative awareness[12-14].Using 1% sevoflurane before delivery achieved BIS value < 60 without adverse effect on maternal blood loss and neonatal outcome[14]. However, many reports concluded that 0.5 MAC of inhalational anesthetic agents in 50% N_2O did not satisfactorily achieve BIS values < 60 in caesarean section[13,15-17]. The objective of the present study was

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to assess the BIS value during general anesthesia with 3% and 4.5% desflurane in 50% N_2O for caesarean section.

Material and Method

The protocol of the present study was approved by the Clinical Research Ethics Committee of Ramathibodi Hospital, Mahidol University. Written informed consent was obtained from 72 ASA I - II full-term parturients underwent elective caesarean section under general anesthesia. Patients with pre-term or multiple gestations, pre-operative non-reassuring fetal status or with any medical condition that required modification of the anesthetic protocol were excluded from the present study. The parturients were blinded and randomized in opaque envelopes to one of the two study groups. Standard monitoring included non-invasive arterial pressure measurement, electrocardiography and pulse oximetry were applied. End tidal concentration (ET) (Datex Ohmeda; Capnomac ultima: ULT-SVI®) of desflurane was monitored at y-piece of the circle absorber circuit. A BIS A-2000 monitor (Aspect Medical Systems) was used to continuously measure and display the BIS value.

The baseline BIS values and hemodynamic variables were obtained. The parturients were pre-hydrated with 500 ml of Ringer lactate solution, rapid-sequence induction of anesthesia and endotracheal intubation were performed using IV sodium thiopental 4 mg /kg and succinylcholine 1.5 mg /kg with the application of cricoid pressure. Anesthesia was maintained with desflurane at an ET of either 3% or 4.5% with N_2O 3 l/min and O_2 3 l/min. The target ET of desflurane was achieved within 3 min by gas analyzer in all parturients. Muscle relaxation was maintained with 0.6mg/kg intravenous rocuronium in an initial bolus dose and additional 5-10 mg as necessary. The parturients were mechanically ventilated to maintain an ET CO_2 of 30-35 mmHg. Surgical incision was done after induction.

After delivery of the neonate and umbilical cord was clamped, routine oxytocin and methylergometrine maleate were administered intravenously. 0.1-0.2 mg/kg of morphine and 0.05-0.2 mg/kg of midazolam were given IV bolus. Fresh gas flow was reduced to 2 l/min of N_2O and 1 l/min of O_2 without inhalation anesthetic agents. Intra-operative hypotension was treated with Ringer Lactate Solution and with 3-6 mg ephedrine IV bolus as needed. Additional oxytocin infusion and second dose of methylergometrine maleate were used as indicated. Blood transfusion was administered if needed. The parturients were ventilated with 100% O_2 at 5 l/min at the end of the surgery. Neostigmine of 0.05 mg/kg and atropine of 0.025 mg/kg were used to reverse paralysis from muscle relaxant. The parturients were extubated when they were awake.

BIS values, arterial blood pressure, and heart rate were recorded after intubation, skin incision, and delivery of the neonate. Neonatal Apgar scores, additional oxytocin, methylergometrine maleate and ephedrine requirements, estimated blood loss and duration of skin incision to delivery time were also recorded by a blinded person to the patient groups. Paturients were interviewed regarding intra-operative awareness 24 hour post operatively.

Sample size was calculated by basic formula for contingency tables from the present pilot study. Probability of BIS < 60 in patients who were maintained with desflurane at an ET of 3% or 4.5% were 0.5 or 0.8 respectively. Total 36 patients in each group would be necessary to find and absolute differences in the incidence of BIS < 60 of 30% ($\alpha = 0.05$ and $\beta = 0.8$).

The results were expressed as number of patients with BIS < 60 (satisfy) or > 60 (unsatisfy) when maintained with desflurane at an ET of 3% or 4.5%. Nonparametric data were analyzed by the Mann-Whitney-U test and Chi-square test. Where a significant difference was detected, post hoc inter-group comparisons were made using the LSD test. The p-values of < 0.05 were considered statistically significant.

Results

The two groups were comparable with respect to age, weight, ASA physical status, the time between induction to delivery of the neonate, the time from skin incision to delivery of the neonate, estimate blood loss and the duration of surgery (Table 1). The neonatal apgar scores, the hemodynamic variables were not different between the two groups.

The number of patients with satisfactory BIS score (< 60) in the 4.5% desflurane group was significantly more than those in the 3% desflurane group ($p < 0.000$) (Table 2). The incidence of BIS < 60 in the 3% desflurane group was 42% and 81% in the 4.5% desflurane group.

The BIS value was done at intubation, skin incision and the delivery time. The highest BIS value was at the delivery time. The mean of BIS value at delivery time of the 3% desflurane group (62 ± 8) was significantly different from the 4.5% desflurane group (49 ± 12) ($p < 0.000$).

There were no instances of intrao-perative awareness. Three parturients receiving 3% desflurane

Table 1. Demographic and surgical characteristic

	3% Desflurane (n = 36) (mean ± SD)	4.5% Desflurane (n = 36) (mean ± SD)
Age (yr)	31 ± 5	32 ± 5
Weight (kg)	68 ± 12	71 ± 14
ASA (1/2)	28 / 8	27 / 9
Estimated blood loss (ml)	625 ± 278	697 ± 256
Induction to delivery time (min)	8.6 ± 4.3	8.6 ± 4.2
Duration of surgery (min)	56.4 ± 15.6	59.2 ± 17.5

Table 2. Number of parturients with BIS value < 60 or > 60 at the time of neonatal delivery

	Number (%)	
	BIS < 60	BIS > 60
Desflurane 3%	15 (42)	21 (58)
Desflurane 4.5%	29 (81)	7 (19)

and four parturients receiving 4.5% desflurane required an additional oxytocin and methylergometrine maleate for augmentation of uterine tone. No parturient in each group required an IV ephedrine to treat hypotension. All of the parturients had no clinical awareness intraoperatively and were satisfied with the surgery.

Discussion

The general anesthetic technique for caesarian section is to balance risk of maternal awareness with uterine atony and neonatal depression. The critical period of awareness is the time from skin incision to delivery. So the present study limited to the time from induction to the delivery period. The use of 0.5 MAC of inhalation anesthetic agents such as halothane[3,7,15], isoflurane[6], enflurane[3], sevoflurane, and desflurane[10] in 50% N_2O significantly reduced the maternal awareness without the risk of uterine atony or hemorrhage.

Using 1% isoflurane prior to delivery was not a problem with neonatal depression[8].Chin and Yeo[16,17]also reported using 1.22% and 1.5% sevoflurane in 50% N_2O had no effect on the neonate.

Turner et al[18]reported that both sevoflurane and desflurane had dose-related depression of the contractility of isolated pregnant human myometrium with a similar degree at concentrations of 0.5, 1 and 1.5 MAC. Yildiz et al[19]also reported dose dependent inhibiting effect of desflurane and sevoflurane on oxytocin induced contractions of isolated pregnant human myometrium.

Desflurane showed less inhibition than sevoflurane and suggested that 0.5 MAC of sevoflurane and 0.5-1 MAC of desflurane may be safely used in the presence of oxytocin following delivery of the infant and placenta during caesarean section without fear of uterine atony and hemorrhage. Abboud[10] used 6% desflurane for caesarean section and reported no adverse effect on maternal blood loss and neonatal outcome. The present study used 4.5% desflurane for caesarean section safely by supporting of these data. The results show no difference in maternal hypotension, IV ephedrine, oxytocin, methylergometrine maleate, blood loss, and apgar score in both groups.

BIS has allowed recent investigators to address the adequate depth of anesthesia for caesarean section. There are evidences to suggest that 0.5 MAC of volatile anesthetic agent may not provide adequate anesthetic depth. Chin and Yeo[17] found that 1% sevoflurane in 50% N_2O did not reliably produce BIS value of < 60. Yeo and Lo[13] reported the same result with isoflurane.

Chin and Yeo[16,17] also reported that 1.22% and 1.5% sevoflurane in 50% N_2O were required to maintain BIS < 60 and < 42 respectively in the period between skin incision and delivery of the neonate. The mean BIS value of 3% desflurane in 50%N_2O in the present study was 62 + 8 (95% confidence interval, 59.7-65.1) which was significantly different from 49 + 12 (95% confidence interval, 45.1-53.5) in the 4.5% desflurane group.

The limitation of this paper was that the study was done in a clinical situation, therefore the target end tidal concentration of desflurane was not achieved at the induction period so the BIS value was not correlated with desflurane end tidal concentration at that time. However, the highest BIS was at delivery time, when the target endtidal concentration was already achieved.

Conclusion

General anesthesia for caesarean section with 4.5% desflurane in 50% N_2O was maintained BIS < 60 more significantly than 3% of desflurane in 50% N_2O without maternal and neonatal adverse effects in healthy paturients.

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การศึกษาค่า bispectral index ในการให้ยาระงับความรู้สึกผ่าท้องคลอดด้วย 3%และ 4.5% desflurane ใน 50% N_2O

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ภูมิหลัง: *เพื่อป้องกันภาวะความรู้สึกตัวในระหว่างให้ยาระงับความรู้สึกผ่าท้องคลอด ในขณะเดียวกันมดลูกยังสามารถหดรัดตัวได้ดี การให้ยาดมสลบ เช่น 0.5 MAC ของhalothane, isoflurane และ sevoflurane ร่วมกับ 50% nitrous oxide โดยไม่ให้ยากลุ่ม opioids จนกว่าจะคลอดบุตร พบว่า end-tidal concentrations ของ 0.5% - isoflurane, 1% sevoflurane (0.5 MAC)ใน 50% N_2O ไม่สามารถทำให้หญิงตั้งครรภ์ที่มาทำการผ่าท้องคลอดมีค่า BIS น้อยกว่า 60 แต่ 1.5% sevoflurane (0.75 MAC) สามารถลดค่า BIS ได้น้อยกว่า 60*

วัตถุประสงค์: *เพื่อติดตามภาวะความรู้สึกตัวหญิงตั้งครรภ์ที่มาผ่าท้องคลอด เปรียบเทียบระหว่าง 3% desflurane และ 4.5% desflurane ใน 50% N_2O โดยใช้ bispectral Index (BIS)*

วัสดุและวิธีการ: *ทำการศึกษาในผู้ตั้งครรภ์จำนวน 72 รายที่มาผ่าท้องคลอด เฝ้าติดตามผู้ตั้งครรภ์ด้วย pulse rate ความดันเลือด คลื่นหัวใจ ความอิ่มตัวของออกซิเจนในเลือด ความเข้มข้นของ desflurane และ BIS monitor ผู้ป่วยได้รับการนำสลบด้วยวิธี rapid sequence intubation โดยใช้ sodium thiopental ขนาด 4 มก./กก. และใส่ท่อหายใจด้วย succinylcholine ขนาด 1.5 มก./กก. จากนั้น maintained $N_2O:O_2$ = 3:3 ร่วมกับ 3% desflurane หรือ 4.5% desflurane ใน50% N_2O ยาหย่อนกล้ามเนื้อใช้ rocuronium ช่วยหายใจให้ end tidal CO_2 มีค่า 35 มม.ปรอท หลังจากคลอดบุตรแล้ว ให้ oxytocin 10 IU ในน้ำเกลือ 1,000 มล. และ 0.2 มก. methylergometrine maleate 0.1 – 0.15 มก./กก. ของมอร์ฟีน เปลี่ยน $N_2O:O_2$ = 2:1 ร่วมกับ 0.05 มก./กก. ของ midazolam ถ้ามีความดันเลือดต่ำให้สารน้ำ หรือ ephedrine ครั้งละ3 – 6 มก. เมื่อผ่าตัดเสร็จ หยุด N_2O และ desflurane ให้ออกซิเจน 5 ลิตร/นาที และแก้ฤทธิ์ยา หย่อนกล้ามเนื้อด้วย neostigmine และ atropine*

ผลการศึกษา: *ไม่มีความแตกต่างในอายุ น้ำหนัก ASA physical status ในผู้ป่วยทั้ง 2 กลุ่ม อุบัติการณ์ผู้ป่วยในกลุ่ม 4.5% desflurane ใน 50% N_2O ที่มีค่า BIS < 60 คิดเป็นร้อยละ 81 มากกว่าร้อยละ 42 ซึ่งเป็นอุบัติการณ์ในกลุ่มที่ได้ 3% desflurane ใน 50% N_2O อย่างมีนัยสำคัญทางสถิติ ($p < 0.000$) ในกลุ่ม3% desflurane มีค่าเฉลี่ยของ BIS เท่ากับ 62 $\pm$ 8 เทียบกับ 49 $\pm$ 12 ในกลุ่ม 4.5% desflurane ไม่พบภาวะความรู้ตัวในระหว่างผ่าตัดในผู้ป่วย 2 กลุ่ม ปริมาณสารน้ำ oxytocin และจำนวนผู้ตั้งครรภ์ที่ได้รับ methylergometrine maleate และ ephedrine ไม่มีความแตกต่างกัน*

สรุป: *การให้ยาระงับความรู้สึก ในผู้ตั้งครรภ์ที่มาผ่าท้องคลอดด้วย 4.5% desflurane ใน 50% N_2O สามารถลด BIS < 60 ได้มากกว่าในกลุ่ม 3% desflurane ใน 50% N_2O อย่างมีนัยสำคัญทางสถิติ โดยไม่มีภาวะแทรกซ้อนในมารดาและทารก*