

Effects on the Bispectral Index during Elective Caesarean Section: A Comparison of Propofol and Isoflurane

Pei-Shan Tsai, Chun-Jen Huang, Yu-Chun Hung, Ching-Rong Cheng

Department of Anesthesiology, Mackay Memorial Hospital, Taipei, Taiwan, R.O.C.

Background: Awareness during general anesthesia has been a particular problem during caesarean section. About 7 percent of patients undergoing elective caesarean section have reported dreaming or recall of voices during the procedure. The bispectral index (BIS), a value derived from the electroencephalogram (EEG), has been shown to be useful in monitoring the depth of anesthesia. Supplementation of propofol or isoflurane for maintenance of anesthesia has been shown to effectively reduce the incidence of awareness. However, the effects of propofol or isoflurane on the BIS index have not been fully investigated. We therefore designed this study to compare the effects of isoflurane or propofol supplementation on the BIS index in 24 healthy parturients undergoing elective caesarean section.

Methods: All patients had induction of anesthesia and orotracheal intubation in rapid sequence made possible by 1 MAC isoflurane with 50% N₂O-50% O₂ as conveyer and atracurium. After delivery, patients were randomly assigned to either of two groups (isoflurane or propofol). Patients in the Isoflurane group (n = 12) received 0.5 MAC isoflurane in 67% N₂O-33% O₂ and fentanyl + droperidol. Patients in the propofol group (n = 12) received propofol (8 mg/kg/h) infusion combined with 67% N₂O-33% O₂ and fentanyl + droperidol.

Results: There was no difference between the two groups in total operation time, maternal blood loss, fetal Apgar scores. No differences between the two groups in heart rate, blood pressure or BIS index values were found throughout the surgery. No patient from either group reported recall of the operative procedure. However, 25% of patients (3 of 12) in the isoflurane group had poor uterine contraction, suggestive of doubtful appropriateness of the use of isoflurane for maintenance of anesthesia in delivery.

Conclusions: We therefore concluded that supplementation of isoflurane or propofol for maintenance of anesthesia can satisfactorily decrease the BIS index and minimize the incidence of awareness in patients undergoing caesarean section under general anesthesia. The BIS index is a reliable monitor of the hypnotic component of anesthesia.

Key words: *Caesarean section. Isoflurane. Propofol. Electroencephalography. Awareness.*

Awareness during general anesthesia is a problem that has been increasingly recognized since the introduction of muscle relaxant as a component of anesthetic. The spectrum of awareness ranges from dreaming, recall of specific events, to the rare but very

serious complication of full consciousness with total paralysis.¹ It has long been recognized that this is a particular problem during caesarean section, where the lack of sedative premedication, low inspired concentrations of nitrous oxide and other volatile agents, and withholding of opioids until after delivery, all of which contribute to the risk of awareness.¹ An incidence of about 0.9% in recalling something or 7% of dreaming has been reported in a survey of some 3,000 patients who underwent caesarean section under general anesthesia.²

The bispectral index (BIS), a variable derived from electroencephalography (EEG), has been shown to be a reliable indicator of the level of consciousness³ and thus

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*Address correspondence and reprint requests: Dr. Chun-Jen Huang, Department of Anesthesiology, Mackay Memorial Hospital, 92 Sec.2 Chung San North Road, Chung San, Taipei, Taiwan 10449
Tel.: 886-2-25433535#3009, Fax: 886-2-25433642.*

E-mail: sean@ms2.mmh.org.tw

it is useful in measuring the hypnotic component of the anesthetic state.⁴⁻⁷ A good correlation between BIS and patient movement in response to skin incision has also been reported.⁸⁻¹⁰ Titrating propofol in accordance with BIS monitoring during balanced anesthesia has resulted in decreased propofol use and significantly improved recovery.¹¹ The BIS index has also been shown to be a good method for monitoring awareness during caesarean section.¹²

Propofol infusion coupled with nitrous oxide appears to be a satisfactory technique for caesarean section.¹³ Previous research indicated that supplementation with propofol significantly attenuates the incidence of awareness during caesarean section.¹⁴ Isoflurane has been shown to be a good alternative to halothane in anesthesia for caesarean section¹⁵ and can also effectively reduce the incidence of awareness.¹⁶ Abboud *et al.* demonstrated that propofol is comparable to isoflurane in maintenance of anesthesia for term parturients undergoing caesarean section.¹⁴ However, data regarding the effects of propofol or isoflurane on the BIS index during caesarean section remain lacking. Preliminary data from our institution indicate that supplementation with propofol or isoflurane for maintenance of anesthesia for caesarean section significantly decreases the BIS index. We therefore designed this study to evaluate the effects of propofol infusion or isoflurane supplementation on the BIS index in term parturients undergoing caesarean section under general anesthesia.

Methods and Materials

Patients

The study was approved by the ethics committee at Mackay Memorial Hospital. Informed consent was obtained from 24 parturients (ASA I-II), with age between 22 to 46 years, scheduled for elective caesarean section. The sample size analysis was performed using Sigma Stat (V 2.03) Student's *t*-test sample size prediction algorithm with a power of 0.8. Patients were excluded from the study if they had a history of neurologic or psychiatric disorders, or if they were taking anticonvulsant medication. Patients were also excluded if difficult intubation was expected or if intubation was successful after more than one attempt.

Protocols

After arriving at the operation theater, every patient received 500 mL infusion of lactated Ringer's solution given over 30 min before the operation. Pure oxygen via a face mask was given to each patient for 5 min before in-

duction. After receiving glycopyrrolate (0.005 mg/kg) as premedication, all patients had orotracheal intubation in rapid sequence induction under general anesthesia made possible by pentothal (4 mg/kg) and succinylcholine (1 mg/kg) with cricoid pressure applied by a helper during the act of laryngoscopy and intubation. Following orotracheal intubation, atracurium (0.5 mg/kg) and isoflurane (at an end-tidal concentration of 1.15% ultimately) in 50% N₂O-50% O₂ were given to each patient before delivery. All patients were then mechanically ventilated (10 mL/kg BW × 10 beats/min) to maintain an end-tidal CO₂ concentration within 30–40 mmHg. Body temperature was maintained with a warm blanket and a heating lamp. After delivery of the baby, each patient was given fentanyl (3 µg/kg) and droperidol (5 mg) combined with 67% N₂O in O₂ for maintenance of anesthesia. An oxytocin infusion was then given to promote uterine contraction. Each patient was then randomly assigned to either the isoflurane or propofol group. Patients in the isoflurane group received isoflurane at an end-tidal concentration of 0.5 throughout the rest of the procedure. Patients in the propofol group received continuous propofol infusion (8 mg/kg/h) instead.

Monitoring

The hypnotic effects of isoflurane or propofol supplementation in each group were detected using BIS index values (Aspect A1000 monitor, BIS version 3.12, Medical Systems Inc., Natick, MA, USA) every minute prior to delivery and every 5 min post delivery by a helper who was blinded to the anesthetic given. If BIS index values reached 75 or more for longer than 5 min during the procedure, the concentration of isoflurane or the propofol infusion rate should be increased. Along with BIS index values, heart rate and blood pressure were recorded. If the mean blood pressure (MAP) was less than 65 mmHg for more than 3 min, a bolus of 200 mL of lactated Ringer's solution was given. If the MAP remained less than 65 mmHg for more than 3 min even after lactated Ringer's solution bolus, a decrease in isoflurane concentration or propofol infusion rate was then applied accordingly. If poor uterine contraction was diagnosed by the surgeons, an increase in the oxytocin infusion rate and/or direct uterine massage were applied. Pre- and post-op temperature, total maternal blood loss and total operation time in both groups were also recorded. The newborn was evaluated with Apgar score at 1- and 5-min after delivery. We followed up each patient the next day to ask her about recall during anesthesia.

Statistical Analysis

Data are presented as mean ± SEM. Statistical

analysis of the results was accomplished using Student's *t*-test (two-tailed) for continuous data and Chi-square test for categorical data. The significance level was set at 0.05. Data were processed using SigmaStat for Windows, Version 2.03 (SPSS Inc., Chicago, IL).

Results

Demographic Data

There were 12 patients in each group, and there were no statistically significant differences between the groups in age, height, weight, pre-op hematocrits, mean arterial pressure (MAP), heart rate (HR) and pre-induction BIS index (Table 1). No difficult intubation was encountered in all 24 patients. Therefore, there was no exclusion of patients who were initially included in the study.

BIS index

Both groups had a similar mean BIS index before induction (97.58 ± 0.29 and 97.33 ± 0.22). In the isoflurane group, induction with pentothal significantly decreased the mean BIS index to 39.19 ± 1.78 within 1 min (Fig. 1). A similar trend was observed in the propofol group (38.00 ± 2.22). Oral tracheal intubation then in-

creased the mean BIS index to 45.25 ± 5.05 (isoflurane group) and 44.58 ± 2.23 (propofol group). Prior to delivery, the mean BIS index was 52.35 ± 2.51 and 52.96 ± 3.58 in the isoflurane and propofol groups under isoflurane (1 MAC) in 50% N₂O-50% O₂ respectively. After delivery, partial replacement of isoflurane by fentanyl

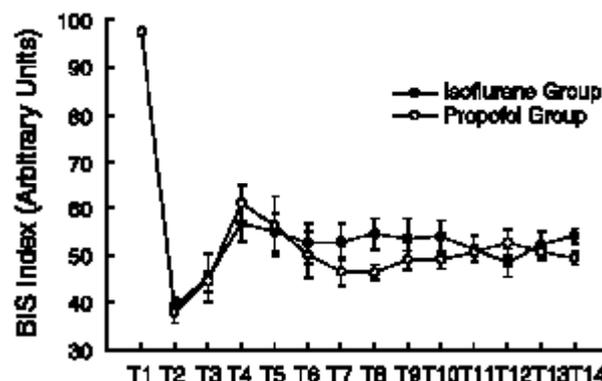


Fig. 1. Mean BIS index changes over time. T1: 1 min before induction. T2: 1 min before intubation. T3: 1 min after intubation. T4: 1 min after incision. T5: 5 min after incision. T6: 1 min after delivery. T7: 5 min after delivery. T8: 10 min after delivery. T9: 15 min after delivery. T10: 20 min after delivery. T11: 25 min after delivery. T12: 30 min after delivery. T13: 35 min after delivery. T14: 40 min after delivery. No difference was noted between these two groups.

Table 1. Demographic, Surgical and Fetal Apgar Scores Data

	Isoflurane	Propofol
Number of Patients Included	12	12
Age (yr)	33.46 ± 1.33	33.42 ± 1.79
Body Weight (kg)	73.88 ± 3.57	70.48 ± 2.62
Height (cm)	158.58 ± 1.22	159.29 ± 1.90
Hct (Pre-op) (%)	36.40 ± 1.09	35.95 ± 1.23
Hct (Post-op) (%)	29.45 ± 1.72	30.77 ± 3.25
MAP (Pre-op) (mmHg)	93.91 ± 3.03	87.42 ± 3.93
Heart Rate (Pre-op) (beats/min)	88.40 ± 4.89	83.80 ± 5.54
Pre-induction BIS Index (Arbitrary Units)	97.58 ± 0.29	97.33 ± 0.22
BIS Index (5 min post-extubation)	79.23 ± 1.63	80.67 ± 1.45
BIS Index (10 min post-extubation)	95.75 ± 0.85	96.03 ± 1.08
Time for Induction (min)	1.79 ± 0.29	2.09 ± 0.29
Induction to delivery interval (min)	7.32 ± 0.73	7.06 ± 0.60
Total Operation Time (min)	53.17 ± 4.15	53.92 ± 3.12
Total Blood Loss (dl)	47.50 ± 6.64	40.91 ± 4.99
Body Temp (Pre-op, °C)	36.93 ± 0.45	36.53 ± 0.78
Body Temp (Post-op, °C)	36.17 ± 0.09	36.26 ± 0.09
Apgar Score (1-min, Arbitrary Units)	8.65 ± 0.27	8.26 ± 0.34
Apgar Score (5-min, Arbitrary Units)	9.23 ± 0.26	9.50 ± 0.17

Data are shown as mean ± SEM. Isoflurane: isoflurane group. Propofol: propofol group. Hct: hematocrit. BIS Index: bispectral index. No difference was found between these two groups.

and droperidol yielded a mean BIS index of 52.60 ± 0.70 with a range of 32 to 74 in the isoflurane group for the rest of the procedure (Fig. 1). By the same token, total replacement of isoflurane by propofol, in the propofol group yielded a similar mean BIS index of 49.32 ± 0.74 (ranging from 32 to 75). There were 3 out of 12 patients in isoflurane group and 2 out of 12 patients in propofol group found to have the mean BIS index values higher than 75 right before baby delivery. Five and 10 min after extubation the mean BIS index in isoflurane group was 79.23 ± 1.63 and 95.75 ± 0.85 respectively and in the propofol group mean index was 80.67 ± 1.45 and 96.03 ± 1.08 respectively (Table 1). There was no statistical difference in mean BIS index values between the two groups throughout the entire procedure (Fig. 1) except for the cumulative mean BIS index after delivery (52.60 ± 0.70 in the isoflurane group vs. 49.32 ± 0.74 in the propofol group ($P = 0.006$) (Fig. 2).

Hemodynamic Data

No statistically significant differences were observed in mean arterial pressure (Fig. 3) or heart rate (Fig. 4). Neither were there statistically significant differences in the time required for induction, time until delivery, total operation time, total blood loss, end maternal temperature, nor 1- and 5-min neonatal Apgar scores (Table 1). None of the patients in either group subsequently reported recall of events during the entire course of delivery.

However, 3 out of 12 patients (25%) in the isoflurane group were reported to have poor uterine contraction which required further management including uterine massage and/or intravenous methylergonovine maleate

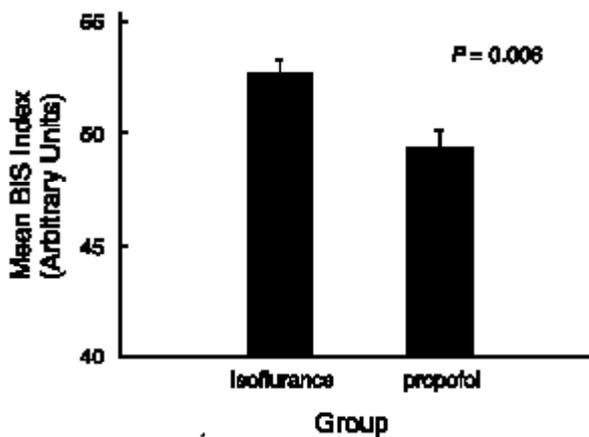


Fig. 2. Cumulated mean BIS index during the maintenance of general anesthesia. Patients in the Isoflurane Group had higher cumulated mean BIS index values than the patients in the Propofol Group during the maintenance of general anesthesia.

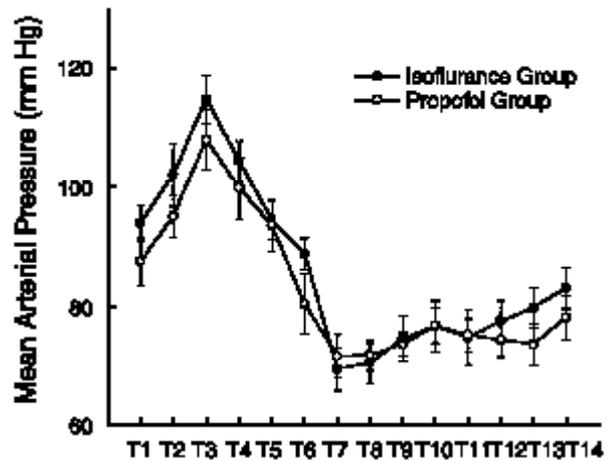


Fig. 3. Mean blood pressure (MAP) changes over time. T1 to T14 are as of Fig. 1. No difference was noted between these two groups.

in addition to the routinely used oxytocin infusion. One of these 3 patients required intravenous ephedrine to maintain blood pressure. None of the patients in the propofol group had poor uterine contraction, but one did require intravenous ephedrine to maintain blood pressure. No other adverse effects were noted in any of the patients.

Discussion

This is the first study to report the effects of supplementation with isoflurane or propofol on the BIS index in patients undergoing elective caesarean section under general anesthesia. Our data indicate that supplementation with isoflurane or propofol provides satisfactory hypnosis in these patients. Previous research by Glass PS *et al.*, has indicated that memory function remains intact

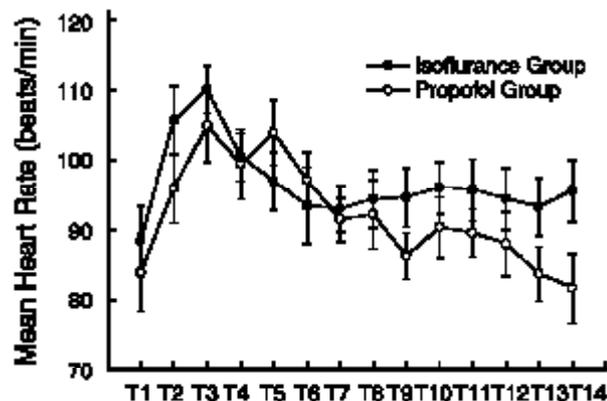


Fig. 4. Mean heart rate (HR) changes over time. T1 to T14 are as of Fig. 1. No difference was noted in these two groups.

at higher BIS index values of 93 ± 5 (mean \pm SD), while recall is absent at lower BIS index values of 70 ± 18 (mean \pm SD),⁷ which was consistent with the results reported by Liu *et al.*¹⁷ Gajraj *et al.* further indicated that a BIS index value of 55 is the threshold value for a state of unconsciousness, with a specificity of 100%.⁴ The mean BIS index values in our patients after induction and after delivery were less than 55. Our observation that none of our patients reported recall of events during delivery further confirms that maintaining a mean BIS index value of less than 55 can satisfactorily prevent awareness. This observation also confirms that the BIS index is a good tool for monitoring the hypnotic components of the anesthetic state.

Conflicting data have been noted regarding the effects of propofol *vs.* thiopental for induction in caesarean section.^{18,19} However, most researchers agree that thiopental remains a good drug for induction^{19,20} and propofol is a good agent for maintenance.^{13,14,21} We therefore designed this study using these two intravenous agents respectively for induction and maintenance of anesthesia afterwards in one of the groups. Celleno *et al.* indicated that thiopental is a good induction drug for caesarean section.¹⁹ Our data confirmed that thiopental offers a hypnotic component of good quality during induction. Propofol has also been demonstrated to provide an anesthesia of good quality.^{13,14} Our data also indicated that propofol infusion with fentanyl is a satisfactory technique for caesarean section. Our observation that propofol was not associated with poor uterine contraction further indicates that this is a safer regimen.

The use of isoflurane for maintenance has been demonstrated to be a good alternative to halothane.²² Our data also confirm that isoflurane offers a good quality anesthesia. New inhalation agents, such as sevoflurane and desflurane, have been widely used lately due to their low blood/gas solubility. Faster emergence and better recovery have been reported using sevoflurane or desflurane for maintenance of anesthesia.^{23,24} Previous studies have indicated that these 2 agents also offer satisfactory anesthesia for caesarean section.^{25,26} However, their effects on BIS index values in caesarean section have not yet reported. Furthermore, our observation that 25% of patients in the isoflurane group had poor uterine contractions suggests that caution should be taken in the use of inhalation agents for caesarean section. Further evaluation is needed to clarify this concern.

We conclude that supplementation with isoflurane or propofol provides a good hypnotic component of anesthesia in parturients undergoing elective caesarean section. Propofol appeared to be a better agent than isoflurane for maintenance due to a high incidence (25%) of poor uterine contraction following the use of isoflurane.

References

1. Bogod DG, Orton JK, Yau HM, Oh TE: Detecting awareness during general anaesthetic caesarean section. An evaluation of two methods. *Anaesthesia* 45:279-284, 1990.
2. Lyons G, Macdonald R: Awareness during caesarean section. *Anaesthesia* 46:62-64, 1991.
3. Sigl JC, Chamoun NG: An introduction to bispectral analysis for the electroencephalogram. *J Clin Monit* 10:392-404, 1994.
4. Gajraj RJ, Doi M, Mantzaridis H, Kenny GN: Analysis of the EEG bispectrum, auditory evoked potentials and the EEG power spectrum during repeated transitions from consciousness to unconsciousness. *Br J Anaesth* 80:46-52, 1998.
5. Sebel PS, Bowles SM, Saini V, Chamoun N: EEG bispectrum predicts movement during thiopental/isoflurane anesthesia. *J Clin Monit* 11:83-91, 1995.
6. Singh H: Bispectral index (BIS) monitoring during propofol-induced sedation and anaesthesia. *Eur J Anaesthesiol* 16:31-36, 1999.
7. Glass PS, Bloom M, Kears L, Rosow C, Sebel P, Manberg P: Bispectral analysis measures sedation and memory effects of propofol, midazolam, isoflurane, and alfentanil in healthy volunteers. *Anesthesiology* 86:836-847, 1997.
8. Kears LAJ, Manberg P, Chamoun N, deBros F, Zaslavsky A: Bispectral analysis of the electroencephalogram correlates with patient movement to skin incision during propofol/nitrous oxide anesthesia. *Anesthesiology* 81:1365-1370, 1994.
9. Sebel PS, Lang E, Rampil IJ, White PF, Cork R, Jopling M, Smith NT, Glass PS, Manberg P: A multicenter study of bispectral electroencephalogram analysis for monitoring anesthetic effect. *Anesth Analg* 84:891-899, 1997.
10. Vernon JM, Lang E, Sebel PS, Manberg P: Prediction of movement using bispectral electroencephalographic analysis during propofol/alfentanil or isoflurane/alfentanil anesthesia. *Anesth Analg* 80:780-785, 1995.
11. Gan TJ, Glass PS, Windsor A, Payne F, Rosow C, Sebel P, Manberg P: Bispectral index monitoring allows faster emergence and improved recovery from propofol, alfentanil, and nitrous oxide anesthesia. BIS Utility Study Group. *Anesthesiology* 87:808-815, 1997.
12. Lubke GH, Kerssens C, Gershon RY, Sebel PS: Memory formation during general anesthesia for emergency cesarean sections. *Anesthesiology* 92:1029-1034, 2000.
13. Gregory MA, Gin T, Yau G, Leung RK, Chan K, Oh TE: Propofol infusion anaesthesia for caesarean section. *Can J Anaesth* 37:514-520, 1990.
14. Abboud TK, Zhu J, Richardson M, Peres DS, Donovan M: Intravenous propofol *vs.* thiethylal-isoflurane for caesarean section, comparative maternal and neonatal effects. *Acta Anaesth Scand* 39:205-209, 1995.
15. Ghaly RG, Flynn RJ, Moore J: Isoflurane as an alternative to halothane for caesarean section. *Anaesthesia* 43:5-7, 1988.
16. Tunstall ME, Sheikh A: Comparison of 1.5% enflurane with 1.25% isoflurane in oxygen for caesarean section: Avoidance of awareness without nitrous oxide. *Br J Anaesth* 62:138-143, 1989.
17. Liu J, Singh H, White PF: Electroencephalographic bispectral index correlates with intraoperative recall and depth of propofol-induced sedation. *Anesth Analg* 84:185-189, 1997.

18. Yau G, Gin T, Ewart MC, Kotur CF, Leung RK, Oh TE: Propofol for induction and maintenance of anaesthesia at caesarean section. A comparison with thiopentone/enflurane. *Anaesthesia* 46:20-23, 1991.
19. Celleno D, Capogna G, Emanuelli M, Varrassi G, Muratori F, Costantino P, Sebastiani M: Which induction drug for caesarean section? A comparison of thiopental sodium, propofol, and midazolam. *J Clin Anesth* 5:284-288, 1993.
20. Schultetus RR, Hill CR, Dharamraj CM, Banner TE, Berman LS: Wakefulness during caesarean section after anesthetic induction with ketamine, thiopental, or ketamine and thiopental combined. *Anesth Analg* 65:723-728, 1986.
21. Gin T, Gregory MA, Chan K, Oh TE: Maternal and fetal levels of propofol at caesarean section. *Anaesth Intens Care* 18:180-184, 1990.
22. Abboud TK, D'Onofrio L, Reyes A, Mosaad P, Zhu J, Mantilla M, Gangolly J, Crowell D, Cheung M, Afrasiabi A: Isoflurane or halothane for caesarean section: Comparative maternal and neonatal effects. *Acta Anaesth Scand* 33:578-581, 1989.
23. Peduto VA, Mezzetti D, Properzi M, Giorgini C: Sevoflurane provides better recovery than propofol plus fentanyl in anaesthesia for day-care surgery. *Eur J Anaesth* 17:138-143, 2000.
24. Dupont J, Tavernier B, Ghosez Y, Durinck L, Thevenot A, Moktadir-Chalons N, Ruyffelaere-Moises L, Declerck N, Scherpereel P: Recovery after anaesthesia for pulmonary surgery: Desflurane, sevoflurane and isoflurane. *Br J Anaesth* 82:355-359, 1999.
25. Gambling DR, Sharma SK, White PF, Van Beveren T, Bala AS, Gouldson R: Use of sevoflurane during elective caesarean birth: A comparison with isoflurane and spinal anaesthesia. *Anesth Analg* 81:90-95, 1995.
26. Abboud TK, Zhu J, Richardson M, Peres DS, Donovan M: Desflurane: A new volatile anesthetic for caesarean section. Maternal and neonatal effects. *Acta Anaesth Scand* 39:723-726, 1995.

應用畢氏腦波指數監測，比較 Propofol 與 Isoflurane 在選擇性剖腹產婦身上之差異

蔡佩珊，黃俊仁，洪育均，鄭清榮

背景：全身麻醉在剖腹產手術，常因其手術的特殊性，使得甦醒機率較其他手術為高。畢氏腦波監測器，是利用數位化腦波分析，來量化病人的意識狀態。

方法：報告中收集 24 位進行選擇性剖腹產手術的產婦，給與全身麻醉。所有產婦在胎兒娩出前，所給予的處置皆相同；胎兒娩出後，將產婦隨機分成兩組，一組給予 propofol 8 mg/kg/h，一組給予 isoflurane 0.5 最低有效肺泡濃度 (MAC)，來維持麻醉深度。整個麻醉過程皆用畢氏腦波監測器監測，藉以比較兩者在鎮靜效果上，是否有臨床應用的價值；再者，比較兩者在統計上或臨床上，是否有效果上的差異。

結果：Isoflurane 與 propofol 這兩組，在畢氏腦波指數監測下，發現皆有良好效果，甦醒機率低。

結論：雖然兩組在臨床上或統計學上皆無明顯差異，但 isoflurane 這組因宮縮不佳而需處理的機率，較 propofol 這組為高。

關鍵詞：剖腹生產。Isoflurane。Propofol。腦波監測儀。甦醒。