Propofol *vs* Isoflurane for Neurosurgical Anesthesia in Thai Patients

WICHAI ITTICHAIKULTHOL, M.D.*, SOMSRI PAUSAWASDI, M.D.*,
PRAPAPARN SRICHINTAI, M.D.*, PRASERT SARNVIVAD, M.D.**

Abstract

Sixty Thai patients, ASA class I-II, Glasgow coma score of 15 undergoing elective intracranial surgery were randomly assigned to 2 groups. In group I, 30 patients were induced with thiopental 3-5 mg/kg, intubation with succinylcholine 1-2 mg/kg and then maintained with 60 per cent N_2O in O_2, isoflurane and vecuronium as a muscle relaxant. In group II, 30 patients received fentanyl 50 μg, propofol 1.0-2.5 mg/kg for induction and vecuronium 0.08 mg/kg for intubation then maintained with 60 per cent N_2O in O_2, continuous infusion of propofol 2-12 mg/kg/h and vecuronium as a muscle relaxant. Controlled ventilation in both groups was set to maintain PET CO_2 in the range of 28-35 mmHg. 3 patients (1 in group I and 2 in group II) were excluded from the study due to surgical problems. There was no statistical difference in age, sex, ASA status, weight, duration of anesthesia. Group II had a more stable systolic BP, Diastolic BP and Pulse rate than Group I during induction and emergence from anesthesia. Glasgow coma scores in the recovery period, Group II had higher scores than Group I at 5 and 15 minutes but not at 30 minutes. Mean recovery times (eye opening) was 14.03±4.85 minutes in group I which is significantly different from 10±5.17 minutes in group II. The cost of anesthesia in group II was 1.3 times that of group I. In conclusion, although neurosurgical anesthesia for Thai patients with fentanyl-propofol technique produces more stable blood pressure during intubation and emergence, rapid recovery from anesthesia and a higher Glasgow coma score, the cost of anesthesia is more expensive. Furthermore, this technique is more difficult and needs more experience.

The use of thiopental-isoflurane for neurosurgical patients has been widely accepted. Isoflurane is frequently used due to its rapid onset of action and recovery. However, isoflurane increases cerebral blood flow *via* cerebral vasodilatation which is dose dependent[1,2]. This effect elevates intracranial pressure. The increase of intracranial pressure can be compensated by hyperventilation to keep PCO_2 between 25-35 mmHg. Nevertheless, hyperventilation can cause cerebral

* Department of Anesthesiology,
** Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

ischemia from excessive cerebral vasoconstriction[3]. In addition, respiratory alkalosis from hyperventilation may cause coronary vasoconstriction, cardiac arrhythmia, decrease in ionized plasma calcium ion and shift to the left of Hb-O_2 dissociation curve.

Intravenous anesthetic agents except ketamine decrease cerebral O_2 consumption which appear to be beneficial for neurosurgical patients. However, there is the disadvantage of prolonged recovery from most intravenous anesthetic agents. Propofol, the relatively new intravenous sedative - hypnotic agent seems to be promising. It has rapid onset of action and recovery. Furthermore, propofol dose-dependently reduces cerebral blood flow and cerebral metabolic rate and may thus reduce intracranial pressure while cerebral autoregulation and vascular response to PCO_2 are still maintained. Therefore, it should be appropriate for neuroanesthesia.

The purpose of this study was to compare the use of propofol - fentanyl with thiopental - isoflurane for neurosurgical anesthesia in Thai patients at Ramathibodi Hospital in terms of hemodynamics, recovery and cost of anesthesia.

METHOD

After approval of the study protocol by the institutional ethics committee at Ramathibodi Hospital, we studied 60 consenting adult patients undergoing neurosurgery. All patients had ASA physical status I or II, aged between 15-60 years old. These patients had no history of diabetes mellitus, hypertension, heart disease, asthma, chronic obstructive pulmonary disease, liver or kidney diseases. They had a Glasgow coma score of 15 and were randomly allocated into 2 groups.

Group I

In 30 patients, with each patient breathing 100 per cent O_2 by mask for 3-5 minutes, anesthesia was induced with thiopental 3-5 mg/kg intravenously titrated till the patient had lost eyelash reflex. The patient was then intubated with succinylcholine 1-2 mg/kg and anesthesia was maintained with $N_2O : O_2 = 2 : 1$ and isoflurane. Blood pressure was controlled to maintain the change within ± 20 per cent of baseline values. Vecuronium 6 mg was given intravenously then 1-2 mg was given intermittently as needed by using peripheral nerve stimulator.

Group II

In 30 patients, following preoxygenation, anesthesia was induced with propofol 1-2.5 mg/kg and fentanyl 50 ug until loss of eyelash reflex was achieved. A continuous infusion of propofol 7 mg/kg/h was started and adjusted to maintain the change in blood pressure within 20 per cent of baseline. The patient was intubated with vecuronium 0.8 mg/kg and additional 1-2 mg as needed intermittently by the use of a nerve stimulator.

The patients in both groups had not received premedication. All patients had controlled ventilation to keep end tidal CO_2 between 28-36 mmHg.

Intravenous fluids such as 5 per cent D/N/2, 0.9 per cent NSS, RLS, acetar, colloid and blood were given as required. After the end of surgery 1.2 mg atropine and 2.5 mg neostigmine were given for the reversal of muscle relaxant.

During maintenance of anesthesia, if mean arterial pressure was less than 50 mmHg ; metaraminol (Aramine) 0.5 - 1 mg would be given to maintain blood pressure. Conversely, if mean arterial pressure and pulse rate persistently increased > 20 per cent of baseline value despite the administration of isoflurane higher than 2.5 per cent or propofol infusion more than 12 mg/kg/h ; incremental 1-2 mg doses of intravenous propanolol or sublingual nifedipine (Adalat) 5-10 mg or intravenous hydralazine (Nepresol) 5 mg dose was given as appropriate.

Monitoring

Monitoring during anesthesia included non-invasive blood pressure (Dinamap), pulse oximeter, end tidal CO_2 (ET CO_2), ECG, direct arterial pressure at radial artery or dorsalis pedis artery and nerve stimulator at ulnar nerve. Pulse rate and blood pressure were recorded every 5 minutes and were assessed at preinduction, postintubation and at the end of surgery.

Recovery period (starting from the end of surgery till the time patients opened their eyes as commanded) was recorded. Glasgow coma score was assessed at 5, 15 and 30 minutes after surgery.

Statistical analysis

Unpaired *t* tests were utilized to compare demographic (age, weight, duration of surgery, recovery period and volume of intraoperative fluid) data between groups.

X^2 test was used to compare ASA physical status and sex. Data for systolic and diastolic blood pressure, heart rate, Glasgow coma score (GCS) were analyzed by analysis of variance (ANOVA) with Tukey test for multiple comparisons.

All values were considered significantly different if $P < 0.05$

RESULTS

We excluded one patient in Group I (isoflurane) and two patients in Group II (propofol - fentanyl) since they had surgical problems (one patient with intraoperative rupture of aneurysm and two patients with bleeding tumors). Those three patients had mechanical ventilatory support postoperatively. Indication for intracranial surgery is shown in Table 1.

There was no significant difference in age, sex, weight, ASA physical status and duration of anesthesia. However, fluid replacement in the propofol-fentanyl group was significantly higher than the Isoflurane group (Table 2) ($P<0.05$).

Prior to induction, no significant difference in baseline pulse rate was found between the two groups. During induction and emergence of anesthesia, pulse rates increased significantly in Group I patients compared to preinduction. The patients in Group II had a significantly elevated pulse rate during intubation compared to preinduction but we found no elevation of pulse rate during emergence. (Fig 1)

Systolic and diastolic blood pressure in Group I patients increased significantly during intubation and emergence from anesthesia but not in Group II patients. (Fig. 1)

Table 1. Indication for intracranial surgery.

Diagnosis	Group I (cases)	Group II (cases)
Tumor	23	23
Aneurysm	1	3
AVM	1	-
Trigeminal neuralgia	1	2
Hemifacial spasm	4	2

Table 2. Demographic datas and duration of anesthesia (Mean±S.D).

	Group I (Isoflurane)	Group II (Propofol)
Age (year)	42.75±14.53	45.00±14.62
Weight (kg)	58.60±11.57	56.28±07.13
Physical status (I/II)	8/21	10/18
Sex (F/M)	15/14	15/13
Duration (min)	259.10±89.29	219.73±81.12
Fluid (ml)	1437.91± 665.27 *	2325.35± 1228.17 *

* $P < 0.05$

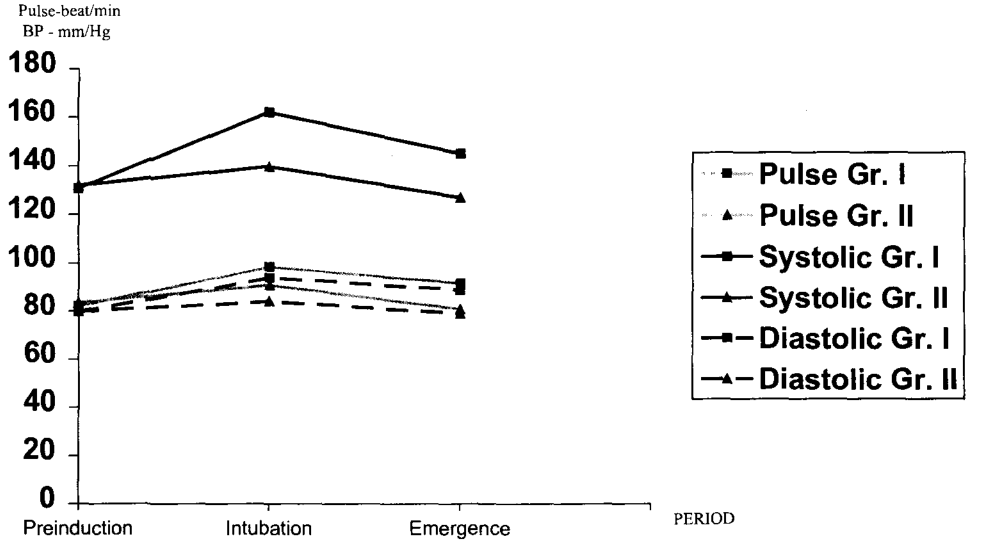

Fig. 1. Pulse rate, systolic, diastolic B.P. (mmHg) at preinduction, intubation and emergence.

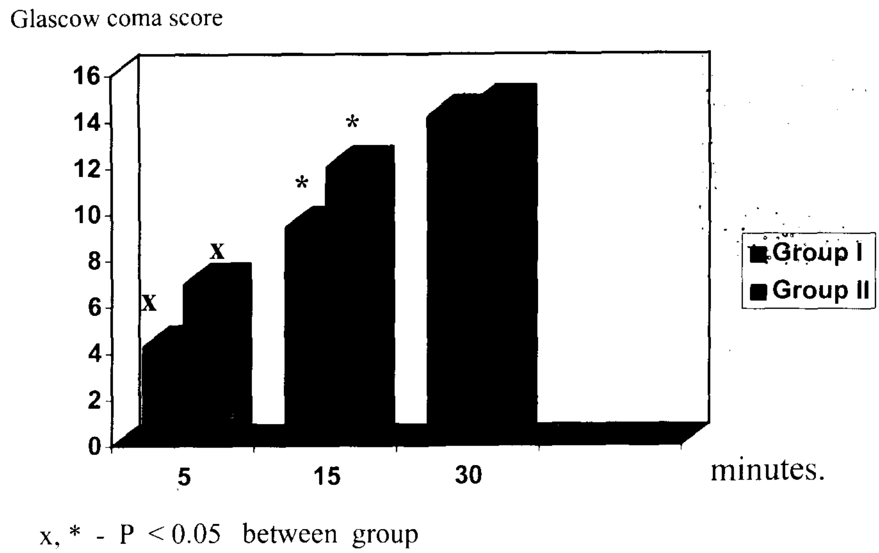

Fig. 2. Glasgow coma score at 5, 15, 30 minutes after the end of surgery.

Times to eye opening was significantly faster in Group II (10.00±5.17 min) than in Group I (14.03 ±4.85 min). Similarly, GCS was significantly higher in Group II (propofol - fentanyl) compared to Group I (isoflurane) at 5 and 15 minutes after surgery but there was no difference at 30 minutes after surgery (Fig. 2).

In view of anesthetic cost ; our hospital retail price for

Isoflurane	10 ml	is	300 Baht.
Fentanyl	2 ml/ampule	is	50 Baht.
Propofol	20 ml/ampule	is	303 Baht.

If we calculate the cost of anesthesia only in the maintenance phase ; the patient weighs 60 kgs and the mean duration of anesthesia is 4 hours ; Group I consumed isoflurane 12 ml/hour, so it would cost 1,440 baht (US $ 56.92) and group II infused propofol 5.11±4.95 mg/kg/min combination with fentanyl 1 ampule. The anesthetic cost of Group II was 1,868 baht (US $ 73.83). Group II costed about 1.3 times of Group I.

DISCUSSION

The aims of neuroanesthesia are to maintain cardiovascular stability, to provide optimal conditions for surgery and to have rapid recovery so that neurological changes can be detected early. In addition, anesthetic agents should not decrease cerebral perfusion or increase cerebral blood volume which would cause an elevation of intracranial pressure.

Standard anesthetic agents for neurosurgery presently are inhalation agents which would increase cerebral blood volume and intracranial pressure dose dependently. With this limitation, propofol has been introduced for use in neuroanesthesia. Propofol does not increase intracranial pressure, has rapid recovery and does not disturb cerebral autoregulation[4,5]. In addition, it gives more stable hemodynamic than inhalation agents[6].

In our study, we found that patients in group II (propofol group) had a more stable pulse rate and blood pressure during intubation and emergence from anesthesia than group I (isoflurane group). This finding was similar to the study of Ravussin in neurosurgical patients[7,8] and the study of Doze in general surgical patients[6]. But Glass[9], Killian[10] and Bayer-berger[11] found no difference in cardiovascular change between the two groups which is probably due to different drug dosage and patient selection.

For the average surgical time of 4 h, Group II patients had a faster recovery time (10.00± 5.17 min) than Group I (14.03±4.85 min). The difference was statistically significant ($p < 0.05$). This finding shows that intravenous anesthesia provides a more rapid recovery than volatile agents which was similar to the previous studies in general surgical patients[12-21]. The rapid recovery in neurosurgical patients is very useful to evaluate neurological status after the surgery. However, Glass[9] and Killian[10] found no difference in recovery period between intravenous anesthesia and inhalation anesthesia. In addition, the study of Todd[22] found that isoflurane produced faster recovery than propofol. Also Larsen[23] found that the patients who received isoflurane had better psychomotor recovery than propofol. The difference might reflect different drug dosage and study methods.

In our study Glasgow coma scores of the propofol group were higher than the isoflurane group at 5 and 15 minutes which related to recovery characteristics. The patients who received propofol-fentanyl had faster recovery of cerebral function.

In view of anesthetic cost, maintenance with propofol-fantanyl (Group II) was more expensive than isoflurane (Group I). Nevertheless we think it is worth using, considering its rapid recovery. A previous study by Aitken[24] also found this similar finding. Killian[10] found that propofol use was three times more expensive than the use of isoflurane. However, the study of Bolt[25] found no difference in the expense between the 2 groups. For the study of Gasagli[26], the expense in the propofol group was lower than the isoflurane group. These variations were probably due to the cost of drug in each hospital, duration of surgery and other anesthetic agents used for maintenance.

SUMMARY

The use of propofol for intracranial surgery in Thai patients produced more stable blood pressure, pulse rate during intubation and emergence from anesthesia; faster recovery time and a better Glasgow coma score (GCS) at 5 and 15 minutes than the use of isoflurane. However, the expense of the propofol group was slightly higher than the inhalation group. Moreover, intravenous anesthesia needs careful drug titration to avoid overdosage ; special equipment for drug administration and experienced anesthesia personnel are also required.

ACKNOWLEDGEMENT

The authors wish to thank Miss Ammarin Thakkinsatian, M.Sc. for her comments and statistical advice.

(Received for publication on October 2, 1996)

REFERENCE

1. Grosslight K, Foster R, Colohan A, et al. Isoflurane for neuroanesthesia : Risk factors for increases in intracranial pressure. Anesthesiology 1985; 63: 533-6.
2. Madsen JB, Cold GE, Hansen ES, et al. The effect of isoflurane on cerebral blood flow and metabolism in humans during craniotomy for small supratentorial cerebral tumors. Anesthesiology 1987; 66: 332-6.
3. Warters R, Allen SJ. Hyperventilation : New concepts for an old tool. Current Opinion in Anesthesiology 1994; 7: 391-3.
4. Fox J, Gelb AW, Enns J, et al. The responsiveness of cerebral blood flow to changes in arterial carbon dioxide is maintained during propofol nitrous oxide anesthesia in humans. Anesthesiology 1992; 77: 453-5.
5. Enns J, Gelb AW, Manninen PH, et al. Cerebral autoregulation is maintained during propofol - nitrous oxide anesthesia in humans. Can J Anaesth. 1992; 39: A43.
6. Doze VA, Shafer A, White PF. Propofol - nitrous oxide versus thiopental-isoflurane - nitrous oxide for general anesthesia. Anesthesiology 1988; 69: 63-71.
7. Ravussin P, Tempelhof TR, Modica PA, et al. Propofol vs thiopental - isoflurane for neurosurgical anesthesia : comparison of hemodynamics, CSF pressure, and recovery. J Neurosurg Anesthesiology 1991; 3: 85-95.
8. Ravussin P, Berger - Bayer MM, Nydegger M, et al. Thiopentone-isoflurane vs propofol in neuroanesthesia for intracranial surgery. Anesthesiology 1988; 69 (3A): A 577.
9. Glass P, Ginsberg B, Hawkins ED, et al. Comparison of sodium thiopental / isoflurane to propofol (delivered by means of a pharmacokinetic model - driven device) for the induction, maintenance and recovery from anesthesia. Anesthesiology 1988; 69 (3A): A575.
10. Killian A, Hamilton P, Tierney M. Propofol versus thiopental - isoflurane in outpatient surgical pro-

cedure. Can J Hosp Pharm 1992; 45: 139-44.

11. Bayer - Berger MM, Ravussin P, Fankhauser H, et al. Effect of 3 pretreatment techniques on CSFP and hemodynamic responses to skull-pin head-holder application during isoflurane or propofol anesthesia. Anesthesiology 1989; 71: A 1134.
12. Motsch J, Breitbarth J, Salzmann R, et al. Recovery of mental and psychomotor skills following general anesthesia. A comparison of isoflurane, midazolam / alfentanil and propofol. Anesthesist 1992; 41: 185-91.
13. Nightingale JJ, Lewis IH. Recovery from day - case anaesthesia : comparison of total I.V. Anesthesia using propofol with an inhalation technique. Br J Anaesthesiology 1992; 68: 356-9.
14. Korttila K, Ostman P, Faure E, et al. Randomized comparison of recovery after propofol - nitrous oxide versus thiopentone - isoflurane - nitrous oxide anaesthesia in patients undergoing ambulatory surgery. Acta Anaesthesiology Scand 1990; 34: 400-3.
15. Siavi C. Propofol with and without nitrous oxide versus thiopentone & isoflurane for the surgery of supratentorial (cerebral) tumours. Min. Anesthesiology 1990; 56: 835-7.
16. Valanne J. Recovery and discharge of patients after long propofol infusion vs isoflurane anesthesia for ambulatory surgery. Acta Anesthesiology Scand 1992; 36: 530-3.
17. Millar JM, Jewkes CF. Recovery and morbidity after day case anaesthesia. A comparison of propofol and thiopentone - enflurane with and without alfentanil. Anesthesia 1988; 43: 738-43.
18. Wetchler BV, Alexander CD, Kondragunta RD. Recovery from the use of propofol for maintenance of anesthesia during short ambulatory procedures. Semin Anesth 1992; 11 (Suppl): 20-2.
19. Ledderose H, Rester P, Carlsson P, et al. Recovery times and side effects after propofol infusion and after isoflurane during ear surgery with additional infiltration anaesthesia. Anaesthesia 1988; 43 (Suppl) : 89-91.
20. Raeder JC, Hole A, Arnul FV, et al. Total intravenous anesthesia with midazolam and flumazenil in outpatient clinics. A comparison with isoflurane or thiopentone. Acta Anaesthesiology Scand 1987; 31: 634-41.
21. Sung YF, Reiss N, Tillette T. The differential cost of anesthesia and recovery with propofol-nitrous oxide anesthesia versus thiopental sodium - isoflurane - nitrous oxide anesthesia. JCHN Anesth 1991; 31: 391-4.
22. Todd MM, Warner DS, Sokoll M, et al. A randomized trial of three anesthetics for neurosurgery. Anesthesiology 1992; 77: A 217.
23. Larsen LE, Gupta A, Ledin T, et al. Psychomotor recovery following propofol or isoflurane anaesthesia for day care surgery. Acta Anaesthesiolgy Scand 1992; 36: 276-82.
24. Aitken HA, Farling PA. The cost of propofol infusion in neurosurgery. Anaesthesia 1991; 46: 329.
25. Bolt ML, Brache EJD, Gopmny H. Total intravenous or balanced inhalation anesthesia for day surgery (comparison of cost and recovery nausea) J One - Day Surgery 1992: 19-20.
26. Gasagi S, Giuntoli M, Chiara M, et al. Economic comparison between a mainly inhalational and a mainly intravenous anaesthetic technique for abdominal surgery in an open circuit system. Gazz Med Ital Arch Sci Med 1991; 150: 361-5.

ศึกษาการให้ยาระงับความรู้สึกในผู้ป่วยผ่าตัดสมองด้วยโปรโปฟอล เปรียบเทียบกับการใช้ไอโสฟลูเรน†

วิชัย อิทธิชัยกุลฑล, พ.บ., สมศรี เผ่าสวัสดิ์, พ.บ.*,*
ประภาพรรณ ศรีจินไตย, พ.บ., ประเสริฐ ศัลย์วิวรรธน์***

ได้ทำการศึกษาผู้ป่วยที่มารับการให้ยาระงับความรู้สึกผ่าตัดสมองจำนวน 60 ราย โดยแบ่งผู้ป่วยเป็น 2 กลุ่ม กลุ่มละ 30 ราย กลุ่มที่ 1 ได้รับยาระงับความรู้สึกด้วยโปรโปฟอล และกลุ่มที่ 2 ได้รับยาไอโสฟลูเรน โดยเปรียบเทียบระบบหัวใจและหลอดเลือด ระยะเวลาที่ฟื้นจากยาระงับความรู้สึก และราคาของการให้ยาระงับความรู้สึกทั้ง 2 วิธี

ผลของการศึกษาพบว่าผู้ป่วยกลุ่มโปรโปฟอล มีอัตราการเต้นของชีพจร ความดันเลือดหลังใส่ท่อหายใจและขณะฟื้นจากยาระงับความรู้สึกเปลี่ยนแปลงน้อยกว่ากลุ่มไอโสฟลูเรน อย่างมีนัยสำคัญทางสถิติ ($P < 0.05$) และผู้ป่วยกลุ่มโปรโปฟอล ฟื้นจากยาระงับความรู้สึกเร็วกว่าไอโสฟลูเรน อย่างมีนัยสำคัญ (10.00 ± 5.17 นาที *vs* 14.03 ± 4.85 นาที) Glasgow coma score ที่ 5 และ 15 นาที หลังผ่าตัดของกลุ่มโปรโปฟอล สูงกว่ากลุ่มไอโสฟลูเรน เช่นกัน แต่จะไม่ต่างกันที่ 30 นาทีหลังผ่าตัด อย่างไรก็ตามค่าใช้จ่ายขณะ maintenance of anesthesia ของผู้ป่วยกลุ่มโปรโปฟอล คิดเป็น 1.3 เท่าของกลุ่มไอโสฟลูเรน

สรุปได้ว่าโปรโปฟอล เป็นยาระงับความรู้สึกที่เหมาะสมสำหรับการผ่าตัดสมอง แต่ผู้ให้ยาระงับความรู้สึกจะต้องมีความรู้และความชำนาญในการใช้เป็นอย่างดี และควรต้องคำนึงถึงเศรษฐกิจและความจำเป็นของผู้ป่วยด้วย

* ภาควิชาวิสัญญีวิทยา,

** ภาควิชาศัลยศาสตร์, คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10400

† รายงานในที่ประชุม 11th World Congress of Anesthesiologists. Sydney, Australia. 14–20 April 1996.