

Original Article

Total intravenous anaesthesia with propofol and remifentanyl for elective neurosurgical procedures: an audit of early postoperative complications

A. Y. C. Wong, A. M. O'Regan, M. G. Irwin

University of Hong Kong, Queen Mary Hospital, Department of Anaesthesiology, Hong Kong

Summary

Background and objectives: This was a prospective audit to assess the incidence and characteristics of early postoperative complications in the recovery room in extubated patients after elective neurosurgical procedures using propofol and remifentanyl-based total intravenous anaesthesia. **Methods:** Vital signs (temperature, conscious level, respiratory rate, oxygen saturation, pulse and blood pressure) and postoperative complications (shivering, nausea, vomiting and cardiorespiratory) were analysed in 145 adult patients over a 1-yr period. **Results:** The overall shivering, postoperative nausea and vomiting and postoperative hypertension (systolic blood pressure more than 25% of the preoperative value) incidences were 30.3%, 16.6% and 35.2%, respectively. Fifty-one percent of the patients had at least one of the above complications. The complication rates were found to be widely different among various types of neurosurgery. The surgical procedures were divided into five groups: supratentorial craniotomy, posterior fossa craniotomy, intracranial vascular procedures, transphenoidal hypophysectomy and extracranial procedures. Median extubation time was similar in all groups and patients were fully conscious with no hypoxia in the recovery room. The intracranial vascular group had the highest shivering and postoperative nausea and vomiting rates (58.8% and 29.4%, respectively). In the supratentorial craniotomy group, 46% of the patients had hypertension. The overall complication rate (presence of any complications) was highest in the supratentorial craniotomy (55.4%), posterior fossa craniotomy (75%) and intracranial vascular (76.5%) groups. Shivering and overall complication rate was significantly related to the anaesthetic time ($P \leq 0.001$ and 0.02 , respectively). **Conclusions:** Despite the potential advantages of total intravenous anaesthesia in titratability, rapid return of consciousness and reduced respiratory complications, making it suitable for planned extubation at the end of neurosurgery, the postoperative complications of shivering, postoperative nausea and vomiting and hypertension were still high.

Keywords: ANAESTHESIA INTRAVENOUS; INTRAVENOUS ANAESTHETICS, propofol; ANALGESICS OPIOID, remifentanyl; NEUROSURGICAL PROCEDURES, craniotomy, supratentorial, posterior fossa, extracranial, intracranial vascular, transphenoidal hypophysectomy; COMPLICATIONS POSTOPERATIVE, shivering, nausea, vomiting, hypertension.

Introduction

The incidence of postoperative complications in the recovery room is reported to be as high as 30% [1–4].

These are mostly connected with nausea and vomiting, shivering, respiratory and cardiovascular derangements. The overall incidence of early postoperative complications in the neurosurgical patients has been reported to be higher [5] but the actual anaesthetic choice was not specified. In our institution total intravenous anaesthesia (TIVA) has become the standard anaesthetic technique. The purpose of this prospective single institution audit was to assess the incidence and

Correspondence to: Andrew Y. C. Wong, Department of Anaesthesiology, University of Hongkong, F2, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. E-mail: wongyca@netvigator.com; Tel: +852 2855 5791; Fax: +852 2855 3384

Accepted for publication 16 January 2006 EJA 3579

characteristics of early postoperative complications in adult patients following elective neurosurgical procedures using propofol and remifentanyl-based TIVA.

Methods

The study was approved by our local institutional ethics review board. It was prospective and all elective adult neurosurgical patients from December 2002 to November 2003 who had received TIVA with propofol and remifentanyl and immediate postoperative extubation were included. Anaesthesia was induced with a target-controlled infusion (TCI) of propofol (Diprifuor™; Astrazeneca, UK) and a remifentanyl infusion ($0.3 \mu\text{g kg}^{-1} \text{min}^{-1}$). Muscle paralysis was achieved with rocuronium prior to tracheal intubation. Anaesthesia was maintained with propofol TCI and a remifentanyl infusion ($0.15\text{--}0.3 \mu\text{g kg}^{-1} \text{min}^{-1}$) with an atracurium or cisatracurium infusion titrated to maintain muscle relaxation (one twitch, train of four (Innervator; Fisher & Paykel Electronics Ltd, Auckland, New Zealand)). Neostigmine and atropine were used to reverse paralysis at the end of surgery. Overall administration and adjustment of TIVA was left to the discretion of the attending anaesthesiologist according to the usual clinical parameters without neurophysiological depth of anaesthesia monitoring. Due to the rapid offset of remifentanyl, in some patients a transition analgesic was administered close to the end of surgery for initial postoperative pain relief. Transition analgesics used were meperidine, fentanyl or morphine ($n = 68, 42$ and 9 , respectively) administered at the discretion of the attending anaesthesiologist. A standard form was completed by a trained recovery room nurse and was used to collate patient information for the first hour or until discharge from the recovery room, should this be sooner. Tympanic membrane temperature (ThermoScan, B Braun, Germany) was measured on admission. The following data was recorded on recovery room admission and every 15 min thereafter: direct arterial pressure, pulse oximeter oxygen saturation (SaO_2) and respiratory rate (Viridia physiological monitor; Hewlett Packard, USA), Glasgow coma score (GCS and power in all limbs), shivering (yes or no) and postoperative nausea and/or vomiting (postoperative nausea and vomiting; yes or no) every 15 min. Other information on the data sheet included patient characteristics data, pre-existing medical disease such as hypertension, surgical pathology and operation, preoperative assessment (including physiological information and neurological assessment), anaesthetic time and extubation time (defined as the time from application of head dressing to safe extubation when the patient had opened his or her eyes, obeyed commands and resumed adequate respiration of more than $8 \text{ breaths min}^{-1}$).

Statistical analysis was performed using Microsoft Excel 2002 and SPSS Version 11 (SPSS Inc., Chicago, IL, USA). For parametric data, t -test (e.g. anaesthetic time, extubation time, respiratory rate, blood pressure (BP), temperature), analysis of variance (ANOVA) (e.g. BP among different groups) and Tukey's test for *post hoc* comparisons were used. For non-parametric data, χ^2 -test with continuity correction (e.g. PONV, shivering) for initial and *post hoc* comparisons and Kruskal–Wallis test (e.g. GCS and oxygen saturation among different groups) were used. Logistic regression was used to test for correlation between two parametric samples. $P < 0.05$ was considered significant.

Results

During the study period, 148 adult elective patients were scheduled for neurosurgery. They all received TIVA for their neurosurgical operation. On emergence, one patient convulsed and two had decreased limb power. They were re-anaesthetized, kept intubated, sent to the computed tomography (CT) suite and excluded from the study. One hundred and fifty patients were included in the review. Thirteen (9%) had pre-existing hypertension. The overall shivering, PONV and postoperative hypertension (systolic blood pressure (SBP) more than 25% of the preoperative value) were 30.3%, 16.6% and 35.2%, respectively. Fifty-one percent of the patients had at least one of the above complications. The complication rates were found to be widely different among various types of neurosurgery. In order to further analyse the characteristics of the postoperative complications, the neurosurgical procedures were divided into five groups: supratentorial craniotomy (SC), posterior fossa craniotomy (PC), transphenoidal hypophysectomy (TH), intracranial vascular (IV) and extracranial (EC) (Table 1). There was no significant patient characteristic difference among the five groups. All the patients had normal temperature, GCS (median 14–15), respiratory rate (median respiratory rate of up to 21 min^{-1}) and SaO_2 (median SaO_2 99–100%) in the recovery room. The anaesthetic time, time to extubation and change in SBP from baseline collected in the recovery room are shown in Table 2. PC and TH groups took the most and least anaesthetic time, respectively. Median extubation time was up to 12 min. All groups showed an increase in SBP from baseline. Using logistic regression, the extubation time was found to be significantly correlated and directly proportional with age ($P = 0.02$) and anaesthetic time ($P = 0.05$).

Throughout the recovery room stay, the number of patients with shivering, PONV, SBP 25% and 30% greater than the preoperative value in each surgical group is shown in Table 3. The rates of PONV ranged from 7.1% in group EC to 29.4% in group IV but

Table 1. Neurosurgical groups (number of patients).

Groups	<i>n</i>	Diagnosis	Known hypertension	ASA (mode)
SC	74	Tumour (73), abscess (1)	9	2
PC	20	Tumour (16), syringomyelia (2), cyst (1), CSF leak (1)	1	2
IV	17	AVM (13), aneurysm (2), trigeminal neuralgia (2)	1	2
TH	20	Pituitary tumour (20)	0	3
EC	14	Skull defect (6), skull osteoma (1), spine tumour (5), spine AVM (2)	2	1
<i>P</i>			0.60	0.06

SC: supratentorial craniotomy; PC: Posterior fossa craniotomy; IV; intracranial vascular; TH: transphenoidal hypophysectomy; EC: extracranial.

Table 2. Duration of anaesthesia, time to extubation and SBP difference (SBPd) on arrival in the recovery room, in each surgical group. SBPd is the change in SBP from the preoperative value in percentage.

Groups	Anaesthesia time (min)	Extubation time (min)	SBPd (%)
SC	309.5 ± 99.4	5–11	20.5 ± 19.4
PC	385.6 ± 164	4–9	18.6 ± 13.5
IV	346.2 ± 98	5–9	14.2 ± 13.4
TH	220.6 ± 61.4	6–12	13.5 ± 12.8
EC	262.4 ± 163.1	5–12	9.7 ± 12.3
<i>P</i>	<0.01	0.50	0.11

SC: supratentorial craniotomy; PC: posterior fossa craniotomy; IV: intracranial vascular; TH: transphenoidal hypophysectomy; EC: extracranial.

Values are mean ± SD or interquartile range. SBPi is the percentage increase in SBP from baseline.

no significant difference was detected. *Post hoc* comparisons always showed significantly lower complication rates in TH and EC groups. With all surgical groups combined, shivering in the recovery room was more common after long anaesthesia ($P < 0.01$) and was not affected by the choice of transition analgesic. The overall complication rate (presence of any complications) was also found to be significantly correlated to duration of anaesthesia ($P = 0.02$).

Discussion

TIVA with propofol and remifentanyl allows rapid and predictable titration of anaesthesia, with swift recovery of consciousness and respiration even after prolonged administration. Propofol also has the additional benefits of reducing PONV, cerebral metabolic oxygen consumption, IV pressure and increasing cerebral perfusion pressure [6–9]. TIVA with propofol and remifentanyl is commonly used in neuroanaesthesia and has become the standard anaesthetic technique for elective neurosurgery in our institution.

The main complications observed were PONV, shivering and hypertension (SBP 25% greater than the baseline value). Of the 145 patients, 74 had at least one of these three complications, giving rise to

an early postoperative overall complication rate of 51% which is close to the 54.4% reported by Manninen and colleagues in 1999, in which the anaesthetic technique was not stated [5]. Studies comparing TIVA with inhalational opioid anaesthesia are warranted.

Patients after neurosurgery are prone to PONV [10]. In a review of early postoperative complications following neurosurgical procedures, PONV was the commonest complication (38.7%), although the anaesthesia technique was not mentioned in that study [5]. In Fabling and colleagues study on neurosurgical patients anaesthetized with fentanyl and isoflurane, 48% and 74% of the patients in the ondansetron and placebo groups, respectively, reported nausea during the first hour postoperatively [11]. TIVA with propofol has been found to produce less PONV compared to inhalational anaesthesia [12–15] in non-neurosurgical patients. This may explain the lower incidence in our study, but in the IV group, the rate is relatively high (29.4%). Retching and vomiting in such patients may cause devastating haemorrhagic complications and a vigorous antiemetic regime should, therefore, be adopted in this group. A high shivering rate was apparent in most groups, even though the patients arriving in the recovery room were normothermic (normal tympanic core temperature). The peripheral or skin temperature was, however, not measured in the study. Both core and skin temperatures contribute to thermoregulatory control [16]. The skin temperature was not measured and may have a more important contribution than core temperature to postoperative shivering. Shivering was related to the type of surgery ($P = 0.02$), with the highest rate (58.5%) in the IV group. Longer anaesthetic time was associated with a higher shivering rate ($P < 0.01$). This may be due to inadequate insulation of the patient's limbs, particularly the hand with the pulse oximeter and intravenous lines. Frequent exposure of the limb to allow inspection of the lines is important to detect loose connections and to make sure that TIVA is being delivered properly. Although meperidine has been reported to be more effective

Table 3. Number of patients with complications during the recovery room stay (%).

Groups	Shivering	PONV	SBPd > 25%	>30%	≥1 complication
SC	24 (32.4%)	11 (14.9%)	34 (46%)	28 (37.8%)	41 (55.4%)
PC	6 (30%)	4 (20%)	8 (14%)	7 (35%)	15 (75%)
IV	10 (58.8%)	5 (29.4%)	6 (35.3%)	3 (17.6%)	13 (76.5%)
TH	1 (5%)	3 (15%)	4 (20%)	3 (15%)	7 (35%)
EC	3 (21.4%)	1 (7.1%)	1 (7.1%)	1 (7.1%)	3 (21.4%)
<i>P</i>	0.02	0.53	0.05	0.08	<0.01

SC: supratentorial craniotomy; PC: posterior fossa craniotomy; IV: intracranial vascular; TH: transphenoidal hypophysectomy; EC: extracranial. SBPd is the percentage increase in SBP from baseline.

than other opioids at reducing postoperative shivering, it was not found to be associated with a lower shivering rate than fentanyl or morphine in the present study [17,18].

Postoperative hypertension is frequent after neurosurgery [19]. In one study, more than 90% of patients in the recovery room had a BP exceeding the preoperative value by 20% [20]. A propofol and remifentanyl combination facilitates rapid titration of anaesthesia and stable intraoperative haemodynamics. However, in the recovery room 46% of the patients in the SC group had hypertension. Hypertension has been associated with an increased risk of postoperative intracranial haemorrhage and cerebral hyperaemia [21,22]. Anaesthesiologists using a TIVA technique should consider employing antihypertensive therapy more liberally during emergence from anaesthesia and in the recovery room, particularly in this subgroup. Postoperative hypertension is significantly more common in the SC group than in the TH and EC groups ($P = 0.03$ and <0.01 , respectively), suggesting a relationship between intracranial surgery and postoperative hypertension.

Our results showed that patients undergoing IV procedures such as PC and IV always produced higher complication rates than the EC ones. The mechanisms leading to increased complications after IV procedures warrant further research. Overall, long anaesthetic time was positively correlated to an increased incidence of postoperative complications ($P = 0.02$). This may be reflected in the IV group which had the second longest anaesthetic time, high shivering and hypertension rates.

Due to perceived pharmacokinetic and dynamic advantages, TIVA with propofol and remifentanyl has become the standard anaesthetic technique in neurosurgery in our institution. We did not include a control group and do not know our complication rates should a different anaesthetic technique (e.g. inhalational) be used, all other factors being equal. Consequently we have had to rely on previously published data for comparison. We feel, however, that this study does help to elucidate the early recovery

characteristics and complications that may be associated with this technique. Another limitation with our study is that the results are from a single-centre study. A multi-centre study on this topic is warranted.

To summarize, the principal early postoperative complications found in our study were PONV, shivering and hypertension. There was an overall complication rate of 51%, but a significant difference among the groups. Complications are more common in intracranial procedures than EC ones: highest in IV surgery (76.5%), and lowest in EC surgery (21.4%). Although the findings with our TIVA technique are similar to previous reports in non-neurosurgical patients in terms of recovery, absence of respiratory complications and reduced PONV, the incidence of other complications, especially hypertension, remains high. Further research into the mechanisms contributing to a high postoperative complication rate in intracranial procedures especially IV surgery is warranted.

References

1. Kluger MT, Bullock MFM. Recovery room incidents: a review of 419 reports from the anaesthetic incident monitoring study (AIMS). *Anaesth Intens Care* 2002; 57: 1060–1066.
2. Zelcer J, Wells DG. Anaesthetic-related recovery room complications. *Anaesth Intens Care* 1987; 15: 168–174.
3. Hines R, Barash PG, Watrous G, O'Connor T. Complications occurring in the postanesthesia care unit: a survey. *Anesth Analg* 1992; 74: 503–509.
4. Rose DK. Recovery room problems or problems in the PACU. *Can J Anesth* 1996; 43: 116–122.
5. Manninen PH, Raman SK, Boyle K, El-Beheiry H. Early postoperative complications following neurosurgical procedures. *Can J Anesth* 1999; 46: 7–14.
6. Petersen KD, Landsfeldt U, Cold GE *et al.* Intracranial pressure and cerebral hemodynamic in patients with cerebral tumours: a randomised prospective study of patients subjected to craniotomy in propofol-fentanyl, isoflurane-fentanyl, or sevoflurane-fentanyl anesthesia. *Anesthesiology* 2003; 98: 329–336.
7. Todd MM, Warner DS, Sokoll MD *et al.* A prospective, comparative trial of three anesthetics for elective supratentorial

- craniotomy. Propofol/fentanyl, isoflurane/nitrous oxide, and fentanyl/nitrous oxide. *Anesthesiology* 1993; 78: 1005–1020.
8. Kahveci FS, Kahveci N, Alkan T, Goren B, Korfali E, Ozluk K. Propofol versus isoflurane anesthesia under hypothermic conditions: effects on intracranial pressure and local cerebral blood flow after diffuse traumatic brain injury in the rat. *Surg Neurol* 2001; 56: 206–214.
 9. Cenic A, Craen RA, Lee TY, Gelb AW. Cerebral blood volume and blood flow responses to hyperventilation in brain tumors during isoflurane or propofol anesthesia. *Anesth Analg* 2002; 94: 661–666.
 10. Gan TJ, Meyer T, Apfel C, Chung F *et al.* Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 2003; 97(1): 62–71.
 11. Fabling JM, Gan TJ, El-Moalem HE, Warner DS, Borel CO. A randomised, double-blind comparison of ondansetron versus placebo for prevention of nausea and vomiting after infratentorial craniotomy. *J Neurosurg Anesth* 2002; 14: 102–107.
 12. Gupta A, Stierer T, Zuckerman R *et al.* Comparison of recovery profile after ambulatory anesthesia with propofol, isoflurane, sevoflurane and desflurane: a systematic review. *Anesth Analg* 2004; 98(3): 632–641.
 13. Hofer CK, Zollinger A, Buchi R *et al.* Patient well-being after general anaesthesia: a prospective, randomized, controlled multi-centre trial comparing intravenous and inhalation anaesthesia. *Brit J Anaesth* 2003; 91(5): 631–637.
 14. Raftery S, Sherry E. Total intravenous anesthesia with propofol and alfentanil protects against postoperative nausea and vomiting. *Can J Anaesth* 1992; 39: 37–40.
 15. Chittleborough MC, Osborne FA, Rudkin GE *et al.* Double-blind comparison of patient recovery after induction with propofol or thiopentone for day-case relaxant general anesthesia. *Anaesth Intens Care* 1992; 20: 169–173.
 16. Cheng C, Matsukawa T, Sessler DI *et al.* Increasing mean skin temperature linearly reduces the core-temperature thresholds for vasoconstriction and shivering in humans. *Anesthesiology* 1995; 82: 1160–1168.
 17. Pauca AL, Savage RT, Simpson S, Roy RC. Effect of pethidine, fentanyl and morphine on postoperative shivering in man. *Acta Anaesth Scand* 1984; 28: 138–143.
 18. Alfonsi P, Sessler D, Du Manoir *et al.* The effects of meperidine and sufentanil on shivering threshold in postoperative patients. *Anesthesiology* 1998; 89: 43–48.
 19. Olsen KS, Pedersen CB, Madsen JB, Ravn LI, Schifter S. Vasoactive modulators during and after craniotomy: relation to postoperative hypertension. *J Neurosurg Anesth* 2002; 14: 171–179.
 20. Gibson BE, Black S, Maass L, Cucchiara RF. Esmolol for the control of hypertension after neurologic surgery. *Clin Pharmacol Ther* 1988; 44: 650–653.
 21. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. *Anesthesiology* 2000; 93: 48–53.
 22. Bruder N, Pellissier D, Grillot P, Gouin F. Cerebral hyperemia during recovery from general anesthesia in neurosurgical patients. *Anesth Analg* 2002; 94: 650–654.