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Titration of propofol infusion using processed electroencephalogram during combined general and spinal anesthesia

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Abstract

Purpose. To determine the necessary mean infusion rate of propofol during combined nitrous oxide (N_2O) and propofol spinal anesthesia by using the processed electroencephalogram (pEEG).

Methods. Twelve elective gynecological patients were monitored by a Dräger pEEG monitor under N_2O and propofol spinal anesthesia. To make it easier to detect an inadequate depth of anesthesia, muscle relaxants were not given and the patients breathed spontaneously through a laryngeal mask airway. Manual step-down infusion of propofol was employed to provide intraoperative hypnosis. Propofol infusion was titrated to maintain cardiorespiratory parameters within 20% of baseline and the 90th percentile of the spectral edge frequency (SEF 90) of the pEEG between 10 and 13.5 Hz.

Results. The mean (SD) induction dose of propofol was 2.9 (0.4) $mg \cdot kg^{-1}$. The mean (SD) maintenance infusion rate was 4.2 (0.5) $mg \cdot kg^{-1} \cdot h^{-1}$. The mean (SD) time from the end of propofol infusion to the opening of the patient's eyes was 5.4 (2.0) min. No gross movements or intraoperative awareness was recognized. The mean (SD) SEF 90 during the maintenance of anesthesia was 12.2 (1.5) Hz, which increased significantly to 16.2 (1.9) Hz at 1 min before the patients opened their eyes in reponse to verbal commands.

Conclusion. Titration of propofol infusion using SEF during combined general and spinal anesthesia provided a rapid recovery without any clinical signs of inadequate anesthesia.

Key words: Intravenous anesthetics, Propofol, Anesthetic technique, Regional anesthetic, Spinal anesthetic, Monitoring, Electroencephalogram

Introduction

Major regional block combined with propofol infusion is becoming a popular technique of balanced anesthesia. In this technique, analgesia is provided primarily by spinal or epidural anesthesia, while intraoperative hypnosis is achieved by propofol. The technology of target-controlled infusion has now enabled a specific plasma or effect-site concentration of intravenous anesthetics to be achieved and maintained. However, achieving a specific drug concentration does not necessarily ensure an adequate depth of anesthesia in an individual patient, and cases of intraoperative awareness have been reported [1,2]. Consequently, some objective, quantitative measure of the effects of anesthetics is desirable.

The electroencephalogram (EEG) is a measure of the electrical activity of the cerebral cortex. However, conventional EEG monitoring with voluminous data requires an experienced interpreter and thus is not readily applicable in daily practice. Processed EEG (pEEG) analysis produces several numerical descriptors, such as spectral edge frequency (SEF) and median frequency (MF). The SEF 90th percentile (SEF 90) is defined as the frequency below which 90% of the total power of the EEG lies. We used SEF 90 to titrate propofol infusion during gynecological laparotomy under N_2O and propofol spinal anesthesia. This study was performed to determine the necessary mean infusion rate of propofol to maintain SEF 90 within a predefined range.

Materials and methods

After approval from the local ethics committee and written informed consent from the patients had been obtained, 12 patients, ASA physical status I, undergoing elective transabdominal hysterectomy of 60–120 min

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duration, were recruited. Ranitidine 150mg was given by mouth on the night before surgery and again 90min before surgery. Spinal anesthesia was established with 3ml hyperbaric tetracaine 0.4% via L3–4 in the left lateral position. A lumbar epidural catheter was sited via L2–3 for postoperative analgesia. An adequate level of spinal anesthesia extending from T4 to the sacral dermatome was confirmed by checking cold sensation. General anesthesia was induced with 1% propofol infused at a rate of 450ml·h^{-1}, and a laryngeal mask airway (LMA) was placed when appropriate. Patients breathed N_2O in oxygen (FiO_2 0.4) spontaneously through the LMA. Routine monitoring, including electrocardiography, noninvasive blood pressure meassurement, pulse oximetry, and capnometry, was performed. After placement of the LMA, propofol infusion was commenced at a rate of 8mg·kg^{-1}·h^{-1}. If there were no clinical signs of inadequate anesthesia (increase in blood pressure, heart rate, or respiratory rate more than 20% from baseline; gross movement; lacrimation; or pupillary dilatation), the infusion rate was decreased every 5min by 1mg·kg^{-1}·h^{-1} until a rate of 3mg·kg^{-1}·h^{-1} was reached. In case of inadequate anesthesia, 10mg of propofol was given as an intravenous bolus, and the infusion rate was increased by 1mg·kg^{-1}·h^{-1}. Approximately 5min before the end of surgery, propofol and N_2O were discontinued. After completion of the surgical procedure, the patients were repeatedly asked to open their eyes at 30-s intervals. The patients were not stimulated in any other way. The induction dose of propofol was defined as the dose administered before the LMA was placed. This induction dose was subtracted from the total amount infused by the end of the procedure, to determine the amount of propofol used during maintenance. This dose was then divided by the duration of maintenance and body weight to calculate the mean maintenance infusion rate in mg·kg^{-1}·h^{-1}. The interval from the end of propofol infusion to opening of the patient's eyes was recorded. The patients were interviewed 1h after the end of anesthesia and on the following day with regard to recall of any intraoperative events.

Measurement of pEEG

A pEEG monitor (version 3.01, Dräger, Lübeck, Germany) was used to analyze the EEG monitored in the bilateral frontomastoidal configuration. The pEEG data were stored in a PC-compatible computer, and on postoperative replay, raw EEG waveforms were examined to exclude artifactual data due to surgical diathermy. Electrode impedance was kept below 5kOhm throughout the anesthesia. Values of SEF 90 were averaged over 10 consecutive 2-s epochs at each measurement point. SEF 90 was maintained between 10 and 13.5Hz during anesthesia.

Statistics

Statistical analysis was performed using InStat for Macintosh, version 2.03 (GraphPad Software, San Diego, Calif., USA). Comparison of the data of hemodynamics and pEEG variables was performed using repeated-measurement analysis of variance (ANOVA) with post hoc Dunnett's test. A P value less than 0.05 was considered significant.

Table 1. Demographic, anesthetic, and surgical data for patients

					Propofol				
Case no	Age (yr)	Weight (kg)	Height (cm)	Operation	Induction (mg·kg^{-1})	Maintenance (mg·kg^{-1}·h^{-1})	Emergence[a] (min)	Anesthesia (min)	Surgery (min)
1	49	64	157	TAH/SO	3.75	4.25	8	145	94
2	33	43	150	TAH	3.40	5.16	7	86	44
3	23	60	172	TAH/SO	3.33	3.83	9	108	67
4	44	53	162	TAH	2.75	3.45	4	142	102
5	38	55	151	TAH	2.55	4.33	5	99	63
6	48	53	150	TAH	2.70	4.54	5	145	106
7	45	47	145	TAH	2.36	4.22	4	87	58
8	43	60	146	TAH	3.10	3.48	7	135	94
9	45	52	150	TAH	2.88	3.95	3	127	90
10	35	68	161	TAH/SO	2.40	3.71	4	104	60
11	65	54	155	TAH/SO	2.85	4.88	6	95	55
12	41	55	157	TAH	2.51	4.07	3	137	100
Mean	42	55	155		2.88	4.16	5.4	118	78
SD	10	7	8		0.43	0.52	2.0	23	22
95% CI					2.61 to 3.16	3.82 to 4.49	4.2 to 6.7		

TAH, Total abdominal hysterectomy; SO, salpingo-oophorectomy.
[a] Emergence is defined as the interval from stopping propofol infusion to opening of the eyes.

Results

The demographic and anesthetic data for each patient are shown in Table 1. The mean, standard deviation, and 95% confidence interval of the induction dose of propofol were 2.88, 0.43, and 2.61 to 3.16 mg·kg^{-1}, respectively. The mean, SD, and 95% Cl of the maintenance infusion rate were 4.16, 0.52, and 3.82 to 4.49 mg·kg^{-1}·h^{-1}, respectively.

The hemodynamic data are shown in Table 2. There were no significant changes in systolic blood pressure and heart rate throughout anesthesia.

The respiratory data are shown in Table 3.

Figure 1 shows the intraoperative changes in SEF 90 and median frequency (MF) of pEEG. MF is the 50th percentile of the EEG power versus frequency distribution. The values of both SEF 90 and MF at 1 min before opening of the eyes were significantly higher than the values during the maintenance period ($P < 0.001$). After the patients opened their eyes, SEF 90 and MF further increased compared with the values at 1 min before opening of the eyes ($P < 0.001$). The mean and SD of the interval from the end of propofol infusion to opening of the eyes were 5.4 and 2.0 min, respectively. There were no gross movements during anesthesia, and no patients reported explicit intraoperative recall.

Discussion

Since propofol is not an analgesic, it must be given with analgesic agents in most, if not all, surgery. An opioid, nitrous oxide, and regional block have been used with propofol to provide perioperative analgesia. In total intravenous anesthesia (TIVA), anesthetists are often left in a difficult position to judge which component of anesthesia, the analgesic or the hypnotic, needs to be adjusted in response to varying surgical stimuli. In contrast to TIVA, the combination of regional block and propofol infusion offers several theoretical advantages. First, continuous regional block provides a pain-free state without significant ventilatory depression in the postoperative period. Second, the incidence of postop-

Table 2. Intraoperative hemodynamics. Values are mean (SD)

Point	SBP (% baseline)	HR (% baseline)
LMA placement	86 (11)	97 (16)
Incision	78 (12)	91 (14)
15 min after incision	72 (12)	99 (16)
30 min after incision	78 (11)	95 (13)
Propofol infusion off	85 (13)	89 (13)
Eyes open	94 (13)	91 (13)

SBP, Systolic blood pressure; HR, heart rate, LMA, laryngeal mask airway.

Table 3. Intraoperative respiratory data

	Mean (SD)	Range
Intraoperative RR		
Minimum (min^{-1})	19 (3)	15–24
Maximum (min^{-1})	24 (4)	18–29
Intraoperative $EtCO_2$		
Minimum (mmHg)	38 (3)	32–42
Maximum (mmHg)	45 (4)	36–49

RR, Respiratory rate; $EtCO_2$, end-tidal carbon dioxide.

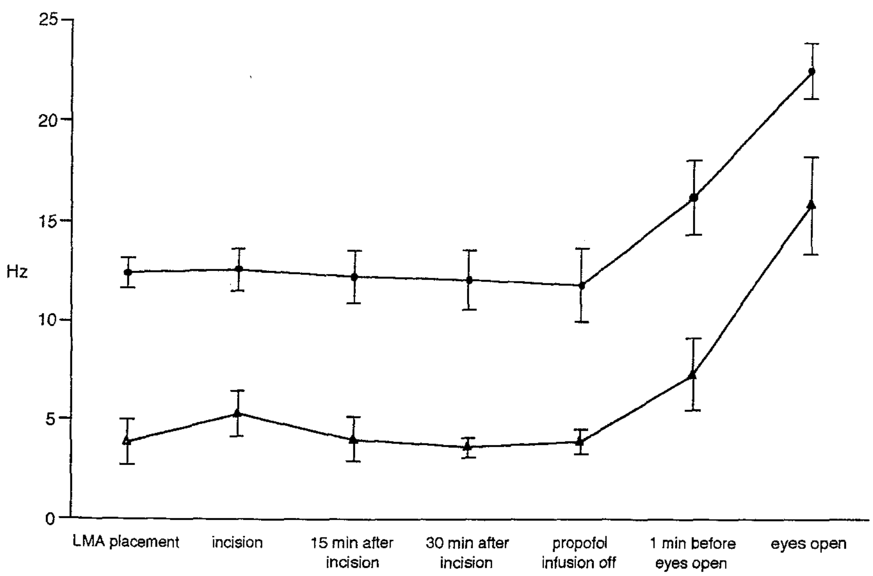

Fig. 1. Intraoperative spectral edge frequency 90th percentile (SEF 90) and median frequency (MF). Values are mean (SD). *Filled circles*, SEF 90; *open triangles*, MF; *LMA*, laryngeal mask airway

erative nausea or vomiting may be lowered by not using a potent opioid. Third, once an adequate level of regional block is confirmed before the start of surgery and the duration of its effect is controlled by choosing appropriate local anesthetics or a catheter technique, then anesthetists need to adjust only hypnosis intraoperatively. However, adjusting propofol infusion according to varying surgical stimuli is not necessarily straightforward, because autonomic responses may be attenuated by sympathetic block due to spinal and/or epidural anesthesia. The pattern of spontaneous respiration and gross movements in unparalyzed patients may provide additional information with regard to the depth of anesthesia. Nevertheless, these valuable signs cannot be used in patients undergoing major surgery, in which the use of neuromuscular block is almost routine. In this study, spinal anesthesia in lieu of epidural block was chosen because the former can provide more reliable sensory and motor block. Tetracaine is a long-acting local anesthetic, and the duration of its effect far exceeded the duration of surgery in these gynecological patients. Spontaneous respiration could be maintained throughout the anesthesia, making assessment of the adequacy of anesthesia easier than in paralyzed patients.

Analysis by pEEG transforms information in the original raw EEG waveforms into several numerical descriptors, such as SEF, MF, delta ratio, and absolute and relative power of the conventional EEG bands. It may be easier to interpret and to follow the trend of these numerical values during anesthesia than the raw EEG waveforms. The choice of these numerical descriptors is controversial. One group titrated propofol infusion to achieve a burst suppressive EEG pattern in neurosurgical patients [3]. However, the time to awakening was significantly longer in these patients than in those who received a standard balanced anesthesia. The authors concluded that burst suppression was not a suitable end point for titration of propofol infusion when a rapid recovery was desirable. On the other hand, many investigators used SEF successfully to predict movement during propofol anesthesia [4], to compare two different kinds of anesthetics [5], or to assess drug effects during the induction of anesthesia [6] and emergence from anesthesia [7,8]. Previous study has confirmed that if SEF 90 is maintained between 10 and 13.5Hz, it is likely that patients are unconscious during general anesthesia [9]. In the present study, SEF 90 was maintained at approximately 12Hz. Not only SEF 90, but also other parameters, indicated adequate depth of anesthesia. All patients breathed spontaneously without any gross movements, and there were no significant hemodynamic or respiratory fluctuations during anesthesia.

In most patients, the final maintenance infusion rate was reached approximately half an hour after infusion was started. It might have been possible to reduce the rate of infusion much more rapidly than we actually did. However, to prevent sudden, potentially dangerous movements, we employed a gradual step-down infusion. One of the theoretical advantages of propofol anesthesia is that the plasma concentration of drug can be increased rapidly by intravenous bolus administration. This allowed us to gradually decrease the rate of maintenance infusion while being vigilant for signs of inadequate anesthesia. In the present study, no patients showed gross movements that hindered surgery. Therefore, it cannot be concluded that monitoring of SEF is useful to detect impending intraoperative movements. A previous study reported a threshold value of SEF 90 of 14Hz to predict movements during anesthesia, with a sensitivity of 72% and a specificity of 82% [10]. To date, an optimal device to monitor the depth of anesthesia has not been developed, and anesthetists still rely on hemodynamic observation to assess the adequacy of anesthesia in patients undergoing major surgery. Monitoring of SEF may provide additional information with regard to hypnosis and help anesthetists titrate propofol infusion during combined general and spinal anesthesia.

References

1. Sandin R, Nordström O (1993) Awareness during total i.v. anaesthesia. Br J Anaesth 71:782–787
2. Kelly JS, Roy RC (1992) Intraoperative awareness with propofol-oxygen total intravenous anesthesia for microlaryngeal surgery. Anesthesiology 77:207–209
3. Van Hemelrijck J, Tempelhoff R, White PF, Jellish WS (1992) EEG-assisted titration of propofol infusion during neuroanesthesia: effect of nitrous oxide. J Neurosurg Anesthesiol 4:11–20
4. Leslie K, Sessler DI, Smith WD, Larson MD, Ozaki M, Blanchard D, Crankshaw DP (1996) Prediction of movement during propofol/nitrous oxide anesthesia. Performance of concentration, electroencephalographic, pupillary, and hemodynamic indicators. Anesthesiology 84:52–63
5. Gurman GM, Fajer S, Porat A, Schily M, Pearlman A (1994) Use of EEG spectral edge as index of equipotency in a comparison of propofol and isoflurane for maintenance of general anaesthesia. Eur J Anaesthesiol 11:443–448
6. Sareen J, Hudson RJ, Rosenbloom M, Thomson IR (1997) Dose-response to anaesthetic induction with sufentanil: haemodynamic and electroencephalographic effects. Can J Anaesth 44:19–25
7. Doi M, Gajraj RJ, Mantzaridis H, Kenny GNC (1997) Relationship between calculated blood concentration of propofol and electrophysiological variables during emergence from anaesthesia: comparison of bispectral index, spectral edge frequency, median frequency and auditory evoked potential index. Br J Anaesth 78:180–184
8. Traast HS, Kalkman CJ (1995) Electroencephalographic characteristics of emergence from propofol/sufentanil total intravenous anesthesia. Anesth Analg 81:366–371

9. Arndt VM, Hofmockel R, Benad G (1995) EEG Veränderungen unter Propofol-Alfentanil-Lachgas-Narkose. [Changing in EEG during propofol-alfentanil-nitrous oxide anesthesia]. Anaesth Reanim 20:126–133

10. Schwender D, Daunderer M, Mulzer S, Klasing S, Finsterer U, Peter K (1996) Spectral edge frequency of the electroencephalogram to monitor "depth" of anaesthesia with isoflurane or propofol. Br J Anaesth 77:179–184