

Awareness under TIVA

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[Chin Med J \(Engl\)](#). 2011 Nov;124(22):3664-9.

Bispectral index monitoring prevent awareness during total intravenous anesthesia: a prospective, randomized, double-blinded, multi-center controlled trial.

[Zhang C](#), [Xu L](#), [Ma YQ](#), [Sun YX](#), [Li YH](#), [Zhang L](#), [Feng CS](#), [Luo B](#), [Zhao ZL](#), [Guo JR](#), [Jin YJ](#), [Wu G](#), [Yuan W](#), [Yuan ZG](#), [Yue Y](#).

Source

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Abstract

BACKGROUND:

Awareness is a serious complication of general anesthesia. In China, the incidence of intraoperative awareness was 1% in patients undergoing total intravenous anesthesia (TIVA). In this study, we compared the incidence of awareness between Bispectral index (BIS)-guided and routine TIVA protocol and evaluated the effect of BIS on preventing awareness.

METHODS:

A prospective, randomized, double-blinded, multicenter controlled trial was performed. Patients (≥ 18 years of age) undergoing TIVA were randomly divided into BIS-guided group (Group A, BIS was monitored and recommended to maintain between 40 - 60) and control group (Group B, BIS was monitored but the screen was covered). The intraoperative BIS values were downloaded and the BIS trends of confirmed awareness cases were analyzed to determine whether light anesthesia existed.

RESULTS:

Of the total 5228 patients, 2919 patients were assigned to Group A and 2309 to Group B. Four cases of confirmed awareness (0.14%) were reported in the BIS-guided group and 15 (0.65%) in the control group ($P = 0.002$, $OR = 0.21$, 95% confidence intervals: 0.07 - 0.63). The incidence of possible awareness (0.14% vs. 0.26%, $P = 0.485$) and dreaming (3.1% vs. 3.1%, $P = 0.986$) was comparable between BIS-guided group and the control group. Among the 19 confirmed awareness cases, intraoperative BIS trends of six cases were downloaded and identified. Five of them showed signs of light anesthesia as $BIS > 60$ and lasted 19 - 106 minutes, whereas one case had a stable BIS trend and the values were within 60 during the operation. Another five awareness cases were reviewed for anesthesia procedures, of which improper light anesthesia were confirmed.

CONCLUSIONS:

BIS-guided TIVA (BIS was recommended to maintain between 40 - 60) decreased the risk of awareness compared with routine TIVA. The main reason for awareness was light anesthesia.

[J Anesth](#). 2011 Feb;25(1):72-7. doi: 10.1007/s00540-010-1050-y. Epub 2010 Dec 14.

Awareness during anesthesia: the results of a questionnaire survey in Japan.

[Morimoto Y](#), [Nogami Y](#), [Harada K](#), [Tsubokawa T](#), [Masui K](#).

Source

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Abstract

PURPOSE:

We planned a survey to evaluate the current incidence and risk factors of intraoperative awareness.

METHODS:

A questionnaire survey was conducted via the Internet. The survey was designed to obtain information regarding cases involving intraoperative awareness in 2008.

RESULTS:

A total of 172 anesthesiologists answered the survey. The total number of reported anesthetic cases was 85,156. Twenty-four cases of definite or possible awareness were reported by 21 anesthesiologists, of which 14 were cases of definite awareness and ten of possible awareness. The incidence of awareness, including possible awareness, was 0.028%. Propofol was used in 21 cases, sevoflurane in two, and a high dose of fentanyl in one. Bispectral index (BIS) monitoring was used in seven cases (29%). Sixteen patients (67%) were <50 years old, six (26%) were men, and 17 (74%) were women. As the type of surgery, three cases (13%) involved gynecological surgeries and seven (30%) involved cervicofacial surgeries. During surgery, the memory at postural change was preserved in two cases.

CONCLUSION:

The most surprising finding of this study is that total intravenous anesthesia (TIVA) was used in 21 of the 24 (88%) cases of definite and possible awareness. Although the incidence of intraoperative awareness was compatible with the previous studies, meticulous care should be taken when anesthesia is performed by TIVA for high-risk patients. The results of this survey should be verified, as well as further continuous survey and prospective study, because this study was performed by an anonymous questionnaire survey conducted over only 1-year period.

[Br J Anaesth](#). 2008 Aug;101(2):178-85. doi: 10.1093/bja/aen144. Epub 2008 May 30.

Awareness with recall during general anaesthesia: a prospective observational evaluation of 4001 patients.

[Errando CL](#), [Sigü JC](#), [Robles M](#), [Calabuig E](#), [García J](#), [Arocas F](#), [Higuera R](#), [Del Rosario E](#), [López D](#), [Peiró CM](#), [Soriano JL](#), [Chaves S](#), [Gil F](#), [García-Aguado R](#).

Source

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Abstract

BACKGROUND:

We have prospectively evaluated the incidence and characteristics of awareness with recall (AWR) during general anaesthesia in a tertiary care hospital.

METHODS:

This study involves a prospective observational investigation of AWR in patients undergoing general anaesthesia. Blinded structured interviews were conducted in the postanesthesia care unit, on postoperative day 7 and day 30. Definition of AWR was 'when the patient stated or remembered that he or she had been awake at a time when consciousness was not intended'. Patient characteristics, perioperative, and drug-related factors were investigated. Patients were classified as not awake during surgery, AWR, AWR-possible, AWR-not evaluable. The perceived quality of the awareness episode, intraoperative dreaming, and sequelae were investigated. The anaesthetic records were reviewed to search for data that might explain the awareness episode.

RESULTS:

The study included 4001 patients. Incidence of AWR was 1.0% (39/3921 patients). If high risk for AWR patients were excluded, the incidence was 0.8%. After the interview on the seventh day, six patients denied having been conscious during anaesthesia; hence, the incidence of AWR in elective surgery was 0.6%. Factors associated with AWR were: anaesthetic technique incidence of 1.1% TIVA-propofol vs 0.59% balanced anaesthesia vs 5.0% O₂/N₂O-based anaesthesia vs 0.9% other anaesthetic techniques (mainly propofol boluses for short procedures), P=0.008; age (AWR 42.3 yr old vs 50.6 yr old, P=0.041), absence of i.v. benzodiazepine premedication (P=0.001), Caesarean section (C-section) (P=0.019), and surgery performed at night (P=0.013). More than 50% of patients reported intraoperative dreaming in the early interview, mainly pleasant. Avoidable human factors were detected from the anaesthetic records of most patients. Subjective auditory perceptions prevailed, together with trying to move or communicate, and touch or pain perception.

CONCLUSIONS:

A relatively high incidence of AWR and dreams during general anaesthesia was found. Techniques without halogenated drugs showed more patients. The use of benzodiazepine premedication was associated with a lower incidence of AWR. Age, C-section with general anaesthesia, and surgery performed at night are risk factors.

[Masui](#). 2002 Feb;51(2):157-61.

[The changes in hemodynamics and dose requirements in total intravenous anesthesia using propofol and buprenorphine].

[Article in Japanese]

[Tabuchi Y.](#)

Source

Division of Anesthesia, Nagahama City Hospital, Nagahama 526-8580.

Abstract

A retrospective study was performed to evaluate the changes in hemodynamics and dose requirements in total intravenous anesthesia (TIVA) using propofol and buprenorphine without (Group S: spinal surgery (3-6 h), n = 8, 28-79 Y) or with (Group A: abdominal surgery (5-10 h), n = 15, 36-83 Y) epidural anesthesia. All patients were premedicated with midazolam i.m. (2-5 mg). Anesthesia was maintained with a single dose of buprenorphine (Group S: 1.9 +/- 0.4 micrograms.kg⁻¹, Group A: 2.0 +/- 0.5 micrograms.kg⁻¹), propofol infusion and vecuronium with 40% oxygen in air. Group A was supplemented with continuous epidural anesthesia using 2% mepivacaine. In Group A, mean arterial pressure (MAP) and heart rate remained stable after the start of surgery. However, in Group S, 2 hours after the start of surgery MAP increased (P < 0.05) and remained elevated (P < 0.05) at higher levels than those in Group A. The maintenance dose of propofol in Group A (4.0 +/- 1.1 mg.kg⁻¹.h⁻¹) was

significantly smaller than in Group S (6.5 +/- 0.9 mg.kg⁻¹.h⁻¹). In both groups, infusion rates of propofol were unchanged from 1 hour after the start to the end of surgery. Infusion rates of mepivacaine (5.2 +/- 0.9 ml.h⁻¹) were unchanged following the increase 2 hours after the start of surgery. Awakening times were within 25 min (Group S 11.3 +/- 7.2 min vs Group A 14.7 +/- 7.3 min). There was no awareness during anesthesia in either group. The results suggest that additional continuous epidural anesthesia in TIVA would be useful to reduce propofol dose, to stabilize hemodynamic state and to obtain rapid recovery in anesthesia of long duration.

[Acta Anaesthesiol Scand.](#) 1997 Sep;41(8):978-84.

Incidence of awareness in total i.v. anaesthesia based on propofol, alfentanil and neuromuscular blockade.

[Nordström O](#), [Engström AM](#), [Persson S](#), [Sandin R](#).

Source

Department of Anaesthesia, Länssjukhuset, Kalmar, Sweden.

Abstract

BACKGROUND:

There is no reliable technique for monitoring drug concentrations in total i.v. anaesthesia (TIVA) with muscle relaxation. An increased risk of awareness with TIVA has been stated as a possible drawback. The present study was conducted in order to assess the incidence of conscious awareness in TIVA based on propofol, alfentanil and neuromuscular blockade.

METHODS:

One thousand patients anaesthetized with TIVA based on propofol, alfentanil, and neuromuscular blockade were subjected postoperatively to a structured interview for conscious awareness on two separate occasions: on discharge from the post-anaesthesia care unit, and the day after anaesthesia. Five hundred of these patients were also interviewed a third time, approximately 1 week later.

RESULTS:

Two cases of awareness were detected (0.2%). One of these was identified immediately after extubation. The second patient had no memory of intraoperative events or dreams at the first interview, recalled a bad dream on the day after, and had explicit recall of intraoperative events at the interview 8 days later. In both cases, haemodynamic signs of inadequate anaesthesia were present. The incidence of conscious awareness in this study is similar to the lowest previously reported incidence of awareness following general anaesthesia in patients who had been paralyzed and thereafter subjected to a structured postanesthesia interview.

CONCLUSIONS:

If the true incidence of conscious awareness is to be determined, interviews must be extended beyond the first postoperative day. Our study indicates that if appropriate dosing of propofol and alfentanil are adhered to, and proper action is taken in case of haemodynamic alterations suggestive of inadequate anaesthesia, the incidence of conscious awareness in non-cardiac TIVA with neuromuscular blockade is low.

[Can J Anaesth](#). 1996 Sep;43(9):946-53.

Midazolam and awareness with recall during total intravenous anaesthesia.

[Miller DR](#), [Blew PG](#), [Martineau RJ](#), [Hull KA](#).

Source

Department of Anaesthesia, Ottawa General Hospital, Ontario.

Abstract

PURPOSE:

A double-blind study was undertaken to evaluate the influence of graded doses of midazolam on propofol infusion requirements, recovery characteristics and the quality of recovery, associated with propofol/alfentanil/O₂ total intravenous anaesthesia (TIVA).

METHODS:

Ninety ASA Class I and II subjects scheduled for arthroscopic knee surgery were randomly allocated to receive either placebo (Group PLAC), or midazolam doses of 15, 30 or 45 micrograms.kg⁻¹ (Groups M-15, M-30 and M-45, respectively). Anaesthesia was induced and maintained with propofol (infused initially at 100 micrograms.kg⁻¹.min⁻¹, and adjusted thereafter according to anaesthetic depth) and alfentanil (loading dose of 20 micrograms.kg⁻¹, followed by infusion at 0.5 microgram.kg⁻¹. min⁻¹). Postoperatively, times to awakening, recovery, and discharge were evaluated, in addition to psychometric evaluations using the Trieger Dot Test (TDT).

RESULTS:

The study was discontinued prematurely, as six patients unexpectedly experienced intraoperative awareness with recall (4/21 = 19.1% of patients with PLAC vs 2/69 = 2.9% of patients in the midazolam groups, $P < 0.04$). Induction requirements of propofol were found to be lower in the M-30 and M-45 groups when compared with PLAC ($P < 0.05$), whereas propofol infusion requirements were similar among groups. Times to awakening and discharge from the Recovery Room and Day Care Unit, as well as TDT scores, were no greater in any midazolam group than in PLAC.

CONCLUSIONS:

Midazolam 30-45 micrograms.kg⁻¹ decreases the amount of propofol required for anaesthetic induction, without influencing recovery profiles or patient discharge times from the Day Care Unit. Despite careful modulation of the propofol infusion rate, six patients unexpectedly experienced intraoperative awareness with recall, with the lowest incidence occurring in those groups where patients had received midazolam.

[J Anesth](#). 1995 Dec;9(4):311-7. doi: 10.1007/BF02479943.

Total intravenous anesthesia combined with epidural eptazocine.

[Aida S](#), [Tomiyama T](#), [Shimoji K](#).

Source

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Abstract

To reduce the doses of intravenous anesthetics (ketamine, diazepam, droperidol, and vecuronium) used in total intravenous anesthesia (TIVA), epidural administration of a κ -stimulating opioid, eptazocine, was combined with TIVA in 115 patients. Surgical procedures were uneventful under TIVA plus epidural eptazocine; significant depression of EEG and somatosensory-evoked potentials during anesthesia were observed without delay in recovery. The circulatory response and blood glucose level during and after anesthesia and surgery were stable, and there was no postanesthetic respiratory depression. On the other hand, in 46 patients given TIVA only, hypertension, tachycardia, and elevated blood glucose during and after anesthesia were observed: in 25 (54.3%) patients, a vasodepressor was required, and in 18 (39.1%) patients, nitrous oxide was needed. Therefore, epidural eptazocine may make it possible to use lower doses of anesthesia in TIVA, thus reducing the adverse effects associated with TIVA such as hypertension during surgery, intraoperative awareness, postanesthetic respiratory depression, delayed recovery from anesthesia, and neurological signs after anesthesia. This may be due to the κ -stimulating action of epidural eptazocine on the spinal cord and its σ -blocking action, as well as its lack of μ -action on the brain.

[J Clin Anesth.](#) 1995 Feb;7(1):63-70.

A random trial comparing recovery after midazolam-alfentanil anesthesia with and without reversal with flumazenil, and standardized neurolept anesthesia for major gynecologic surgery.

[Jensen AG](#), [Møller JT](#), [Lybecker H](#), [Hansen PA](#).

Source

Department of Anaesthesia, Esbjerg Central Hospital, Denmark.

Abstract

STUDY OBJECTIVE:

To compare the recovery characteristics of total intravenous anesthesia (TIVA) using midazolam-alfentanil, with or without reversal with flumazenil to a standardized neurolept anesthesia with nitrous oxide (N₂O).

DESIGN:

Randomized, double-blinded clinical study.

SETTING:

University medical center.

PATIENTS:

80 ASA physical status I and II women scheduled for major elective gynecologic surgery.

INTERVENTIONS:

Patients were anesthetized with one of three different anesthetic techniques. Patients in the TIVA group with reversal received midazolam-alfentanil reversed with flumazenil (Group 1), the TIVA group without reversal received midazolam-alfentanil reversed with placebo (Group 2), and patients in the neurolept group received anesthesia using thiopental sodium, droperidol, fentanyl, and N₂O (Group 3).

MEASUREMENTS AND MAIN RESULTS:

Recovery was assessed by an observer blinded to the treatment allocation, using a Modified Steward Recovery Score and judgment of orientation and comprehension, collaboration and degree of sedation for the first 4 hours after extubation. Arterial blood gases were measured

30 minutes after extubation. A questionnaire regarding the degree of perioperative amnesia was presented to the patients 4 and 24 hours after surgery. The recovery scores were better in the TIVA group with reversal than in the other two groups from 0 to 30 minutes postoperatively. No difference between the groups could be found thereafter, although after 30 minutes some re-sedation occurred in the TIVA group with reversal. The median injected amount of flumazenil in Group 1 was 0.5 mg. Respiratory depression (breathing frequency below 10 breaths/min) was reversed with naloxone in one patient in the TIVA group with reversal, five patients in the TIVA group without reversal, and no patient in the neurolept group ($p < 0.001$). On blood gas analysis, there was no evidence of hypoxemia or carbon dioxide retention. No difference was seen between the groups regarding consumption of analgesics, degree of amnesia, or patient rating of the quality of anesthesia. One patient in Group 2, however, recorded awareness at skin incision when questioned 4 hours after the operation, but could not recall this 20 hours later.

CONCLUSIONS:

TIVA with midazolam and alfentanil can be used for major gynecologic surgery. Recovery in the neurolept group was equal to recovery in the TIVA group without reversal, and flumazenil improves the recovery after midazolam anesthesia. Overall, in comparison with the neurolept technique no major advantage could be demonstrated using TIVA with midazolam-alfentanil.

[J Cardiothorac Vasc Anesth.](#) 1994 Jun;8(3):284-8.

Total intravenous anesthesia using propofol and alfentanil for coronary artery bypass surgery.

[Gordon PC](#), [Morrell DF](#), [Pamm JD](#).

Source

Department of Anaesthesia, Groote Schuur Hospital, Cape Town, South Africa.

Abstract

Total intravenous anesthesia (TIVA) using alfentanil and propofol was used in 10 patients undergoing coronary artery bypass grafting. In an attempt to diminish unwanted side effects, lower doses were chosen than if either drug had been used alone. Anesthesia was induced with alfentanil, 75 micrograms/kg, followed by a sleep dose of propofol (mean dose 0.5 mg/kg). Maintenance in the precardiopulmonary bypass (CPB) period was achieved by infusions of propofol (6 mg/kg/h) and alfentanil (100 micrograms/kg/h). These were decreased by two thirds on commencement of CPB, and increased to half the initial rate on rewarming to 32 degrees C. Additional boluses of alfentanil were used to control breakthrough hypertension. The mean arterial pressure (MAP) and left ventricular stroke work index (LVSWI) fell significantly on induction. MAP but not LVSWI returned to baseline levels at skin incision. The cardiac index (CI) was maintained. A degree of myocardial depression was suggested by a fall in LVSWI despite maintaining preload, and by the failure of CI to increase in the presence of a reduced SVR. Anesthesia was satisfactory in all but one patient who developed breakthrough hypertension on sternotomy with transient ST segment depression, and awareness after CPB despite a plasma alfentanil concentration of 450 ng/mL. Mean time to waking was 55 minutes. The study indicated that TIVA using propofol and alfentanil in the dosages described provides satisfactory basal anesthesia for coronary artery bypass surgery in patients with good left ventricular function, but requires additional pharmacologic manipulation, particularly with boluses of alfentanil, to control breakthrough hypertension.

[Anaesthesist](#). 1994 Feb;43(2):92-100.

[Total i.v. anesthesia with S-(+)-ketamine in orthopedic geriatric surgery. Endocrine stress reaction, hemodynamics and recovery].

[Article in German]

[Adams HA](#), [Bauer R](#), [Gebhardt B](#), [Menke W](#), [Baltès-Götz B](#).

Source

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Abstract

Clinically-used ketamine is a racemic mixture of two isomers, S-(+)- and R(-)-ketamine. Previous investigations showed the anaesthetic potency of S(+)-ketamine to be three times higher than that of R(-)-ketamine. It was the aim of this study to compare the effects of S-(+)-ketamine and racemic ketamine on endocrine and cardiovascular parameters, recovery, and side effects in geriatric patients during total intravenous anaesthesia (TIVA) for orthopaedic surgery.

METHODS:

Forty patients over 60 years of age scheduled for elective hip or knee replacement were investigated in a double-blind, randomised design. For induction of TIVA, patients received 0.1 mg midazolam, 0.5 mg atropine, 1 mg/kg S(+)-ketamine or 2 mg/kg racemic ketamine, respectively, 2 mg vecuronium, and 1.5 mg/kg suxamethonium. After intubation and relaxation with a total dose of 0.1 mg/kg vecuronium, a continuous infusion of 2 mg/kg per hour S-(+)- or 4 mg/kg per hour racemic ketamine was administered throughout surgery. Blood samples were taken through a central venous catheter at seven time-points, before induction as well during and after surgery, until the 1st postoperative morning for analysis of adrenaline, noradrenaline (by high-pressure liquid chromatography with electrochemical detection), anti-diuretic hormone (ADH), adrenocorticotrophic hormone (ACTH), cortisol (by radioimmunoassay), glucose, and lactate. In addition, systolic arterial pressure (SAP), heart rate (HR), and arterial oxygen saturation were measured, and the time intervals between the end of ketamine infusion and the return of consciousness and orientation were protocolled. The incidence and assessment of dreams and other side effects were reported by the patients.

RESULTS:

Biometric data of the groups were comparable, the mean age of both groups being 68 years. Plasma adrenaline, noradrenaline, ADH, ACTH, cortisol, and glucose as well as SAP and HR increased significantly ($P < 0.05$) during the course of anaesthesia. The influence on lactate levels was not significant. There were no differences between S(+)- and racemic ketamine with respect to these parameters. Three patients in the ketamine-racemate group showed severe arterial hypertension and were withdrawn from the study. Recovery clearly improved after administration of S(+)-ketamine compared to the racemate. Simple orders were followed after 2.0 +/- 3.4 versus 4.9 +/- 6.8 min ($P = 0.07$), orientation with respect to person returned after 5.7 +/- 4.0 versus 14.6 +/- 10.0 min ($P < 0.001$) and spatial orientation after 8.2 +/- 5.4 versus 17.4 +/- 9.7 min ($P < 0.001$). After racemic ketamine, 1 patient remembered a negative dream and 1 patient a positive dream. In the S(+)-group, 1 positive dream was reported. No intraoperative awareness was reported, and all patients would accept the same anaesthesia again.

CONCLUSIONS:

Increases in cardiovascular parameters and insufficient reduction of the stress response with respect to ADH, ACTH, and cortisol seem to require a more potent hypnotic element

during TIVA with ketamine. With regard to endocrine and cardiovascular parameters, the pharmacodynamic effects of racemic and S-(+)-ketamine were comparable. Because of the significant improvement in recovery and the reduced quantitative drug load, S-(+)-ketamine offers a clinical advantage compared with currently used racemic ketamine.