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ORIGINAL ARTICLE

Comparison of cognitive, ambulatory, and psychomotor recovery profiles after day care anesthesia with propofol and sevoflurane

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Abstract
Purpose We compared the recovery profile of propofol and sevoflurane when used for maintenance of anesthesia in elective day care operative procedures.
Methods One hundred ASA physical status I and II patients, aged between 18 and 50 years, were randomly assigned to receive either propofol–nitrous oxide or sevoflurane–nitrous oxide maintenance of anesthesia. Early and intermediate recovery in terms of cognitive and ambulatory functions was recorded. Psychomotor testing, in the form of Trieger dot test and digit symbol substitution test, were performed before surgery and in the post-anesthesia care unit at 15 min, 30 min, 1 h, 2 h, and 4 h following nitrous oxide switch-off to evaluate intermediate recovery.
Results There were no significant differences in recovery of early cognitive functions between the two groups, except that patients in the sevoflurane group were more responsive at around 10 min following nitrous oxide switch-off and "recalled address" earlier than patients in the propofol group. There was no significant difference in between the two groups with regard to "home-readiness."
Conclusions Recovery from sevoflurane anesthesia, especially with regard to cognitive functions, may be slightly faster than from propofol, but the difference is not sufficiently significant to affect the time to "home-readiness" in patients undergoing day care surgery.

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Introduction

Propofol and sevoflurane have become the drugs of choice for induction and maintenance of anesthesia in the outpatient setting because of the ideal anesthetic characteristics of smooth and rapid induction and recovery profile with few postoperative side effects [1, 2]. We designed this randomized trial to compare the quality of anesthetic emergence, specifically, the cognitive, ambulatory, and psychomotor recovery, after sevoflurane or propofol maintenance of anesthesia in patients undergoing day care surgery.

Materials and methods

The study was started after approval by the ethics committee and registration with the Clinical Trials Registry India (http://ctri.nic.in; REF/2012/03/003412). Patients signed an informed, written consent before enrollment in the study. An anesthesiologist conducted a preoperative evaluation to assess the suitability of patients for enrollment. One hundred healthy male and female patients, aged 18–50 years, of ASA physical status I and II, who were undergoing day care surgery of <1 h duration were enrolled. Exclusion criteria for potential subjects were (a) a history of significant cardiovascular, pulmonary, hepatic, or renal disease, (b) hypersensitivity to anesthetics or familial history of malignant hyperthermia, (c) disabling neuropsychiatric disorders, (d) chronic drug or alcohol abuse, (e) morbid obesity, (f) women who were pregnant or

breast-feeding, and (g) patients who refused to give consent.

The assignment of patients to propofol or sevoflurane anesthesia groups was randomized by a sealed envelope technique. The propofol group received fentanyl/propofol/nitrous oxide for maintenance of anesthesia and the sevoflurane group received fentanyl/sevoflurane/nitrous oxide for maintenance. The anesthesiologist administering the anesthesia remained blinded to recovery recordings. All subjects were asked to refrain from alcohol, sedatives, and tobacco for 24 h before surgery. They were also told not to drive a car or operate machinery for 24 h after anesthesia and were also asked to have an escort to their home.

During preoperative evaluation, psychomotor state [Trieger dot test (TDT) and digit symbol substitution test (DSST)] was assessed. After three attempts, a final attempt was taken as baseline. The tests were performed in sitting position with the dominant hand after baseline hemodynamic variables (pulse rate, systolic, mean, and diastolic arterial blood pressure) were recorded. In the evening, all patients received diazepam 5–10 mg orally. The usual monitors were used, and a 20 G intravenous cannula was secured on the nondominant hand. A modified lactated Ringer's solution was started at a rate of 3 ml/kg/h. Analgesic fentanyl 2 μg/kg was given intravenously. Patients were induced with propofol 2 mg/kg intravenously slowly over 30 s until loss of eyelash reflex and central fixation of eyeballs; this was followed by placement of a laryngeal mask airway (LMA). Anesthesia was maintained in the propofol group with nitrous oxide 60–65 %, oxygen 30–35 %, and a propofol infusion at 4–6 mg/kg/h to maintain mean arterial pressure (MAP) within 20 % of baseline values. In the sevoflurane group, maintenance of anesthesia was provided with sevoflurane [0.85 minimum alveolar concentration (MAC)] with nitrous oxide 60–65 % in oxygen, with the inspired concentration being adjusted to maintain MAP within 20 % of baseline values. Ventilation was controlled via the circular system. Blood pressure, heart rate, O_2 saturation, and end-tidal CO_2 concentration were measured and recorded before the induction of anesthesia, every minute during induction, and every 5 min thereafter. Any tachycardia occurring from surgical stimulation prompted the administration of a top-up of fentanyl 0.5 μg/kg. Because laparoscopic sterilizations constituted a substantial number of the surgeries done, one dose of succinylcholine 0.5 mg/kg was used before Verres' needle insertion to ensure adequate muscle relaxation during this time. In both groups the study drugs were stopped, without tapering, at initiation of skin closure, although nitrous oxide was continued up to the end of skin closure. Emergence times (min) from nitrous oxide shut-off to the time of response to painful stimuli, spontaneous opening of eyes, response to verbal commands, and address recall were measured. When a patient responded to verbal commands and had stable hemodynamics, the patient was transferred to the recovery room. In the recovery room each patient was assisted to sit up every 5 min. After a patient could sit unaided, he/she was asked to stand with support and subsequently without support by the blinded observer anesthesiologist. Once a patient stood without support, he/she was assisted to walk with and without support. Times at which sitting and standing with and without support occurred were recorded. Walking with and without swaying to one side and climbing stairs up and down a two-step wooden block of stairs was recorded.

DSST and TDT were repeated in the post-anesthesia care unit at 15 and 30 min, and at 1, 2, 3, and 4 h after discontinuation of nitrous oxide by the same observer who was blinded to the anesthesia the patients had received.

In the TDT, patients were asked to connect dots within 1 min. The number of missed dots was noted. In the DSST, patients were given 90 s to replace digits with appropriate symbols located in a legend at the top of the page. The test measured recoding skills and recognition of sensory (visual) information, mental concentration, fine muscular coordination, and ability to alter eye fixation. To avoid practice factor obscuring results in this test, a new set of arrangement of 30 digits was given to the patient.

Post-anesthesia adverse events or experiences such as headache, confusion, nausea, vomiting, giddiness, and pain at injection site were assessed and recorded. In the evening during the post-anesthesia visit, all patients were asked to evaluate their satisfaction with the anesthesia by a grade of excellent, good, fair, or poor, respectively.

Statistical analysis

Before the beginning of the study, an a priori power analysis suggested a sample size of 41 patients for each group to provide 80 % power at $\alpha = 0.05$. We chose 50 patients in each group assuming a 20 % dropout rate because of difficulty in properly performing the psychomotor tests. All parameters of early recovery and psychomotor recovery tests are presented as mean ± SD unless otherwise stated, and SPSS 16.0 was used for analysis. Distribution of patients with respect to age, sex, weight, duration of surgery, and duration of anesthesia was compared with the unpaired t test. Incidence of postoperative complications was studied and compared between the two groups using Chi square analysis. To assess impairment within each group as compared to baseline, the paired t test was used. Impairment of cognitive, ambulatory, and psychomotor recovery with respect to baseline of one group was compared to impairment with respect to baseline of the other group using independent-samples unpaired t test. P values < 0.05 were considered statistically significant.

Table 1 Demographic characteristics for the two anesthetic treatment groups

	Propofol	Sevoflurane
Number (*n*)	50	50
Age (years)	40 ± 13	39 ± 13
Weight (kg)	67 ± 16	69 ± 16
Sex (male/female)	14/36	18/32
ASA physical status (I/II)	38/12	36/14
Surgery time (min)	52 ± 29	56 ± 29
Anesthesia time (min)	67 ± 27	71 ± 26
Procedures (*n*)		
Laparoscopic sterilization	25	24
Hernia surgeries	18	19
Breast surgeries	7	6
Cone biopsy	0	1

Values are mean ± SD or numbers

Table 2 Use of adjunctive drugs and post-anesthesia adverse events or experiences in the two treatment groups

	Propofol	Sevoflurane
Number (*n*)	50	50
Adjunctive intraoperative drugs		
Fentanyl (μg)	176 ± 63	185 ± 54
Propofol (mg)	626 ± 372	144 ± 37
Succinylcholine (mg)	28 ± 13	28 ± 12
Post-anesthesia adverse events or experiences (*n*)		
Headache	0	0
Confusion	4	5
Nausea	12	13
Vomiting	5	10*
Giddiness	8	5
Pain at injection site	1	0
Patient satisfaction with anesthesia (*n*)		
Excellent	49	48
Good	1	2
Fair	0	0
Poor	0	0

Values are mean ± SD or numbers

* Significantly different from propofol group, $P < 0.05$

Results

The two study groups were comparable with respect to age, weight, ASA physical status, type and duration of surgical procedure, and duration of anesthesia (Table 1), as well as the total doses of adjunctive drugs such as fentanyl (Table 2).

The emergence times from discontinuation of nitrous oxide to response to pain, spontaneous eye opening, and response to commands were similar in the two treatment groups (Fig. 1). However, the time to recalling address was quicker in the sevoflurane group (11 min) as compared to the propofol group (16 min) after switching off nitrous oxide (Fig. 1). This difference was found to be statistically significant. There was a trend toward earlier recovery of parameters studied for response to pain and spontaneous eye opening in the propofol group, whereas for the response to commands and recalling address, these trends were reversed, although it reached statistical significance only for the last parameter (Fig. 1).

No significant difference was found in the variables of home-readiness, including the patient's ability to sit, stand, walk, and climb without support (Fig. 2), dress themselves, and tolerate oral fluids, between the anesthetics. However, the actual time to home discharge was earlier in the propofol compared with the sevoflurane group (data not reported). However, when we analyzed the reasons for this, we found it was related more to issues of arranging an attendant to accompany the patient home, rather than an effect of the anesthetic regimen used; thus, we did not present those data here.

A higher incidence of postoperative emesis was reported in the sevoflurane group (Table 2). No differences were found in the incidence or severity of other post-anesthesia adverse events or experiences in the recovery room (Table 2).

Similarly, no intergroup differences were found during psychomotor testing in the form of TDT and DSST scores (Figs. 3, 4). Impairment in both groups lasted for around 2 h, by which time the performance recovered to baseline. Impairment at each time interval was also identical between the two groups. The performance at psychomotor tests is detailed in Figs. 3 and 4.

Finally, the levels of satisfaction achieved in patients by both anesthetic regimens were found to be identical.

Discussion

In this study, we found that certain aspects of early recovery were quicker with sevoflurane compared to the propofol group.

Recovery of ambulatory parameters to assess home-readiness was identical between the two groups. However, postoperative vomiting was significantly less frequent in the propofol group. Although the actual time to discharge from the hospital was shorter in the propofol group as compared to the sevoflurane group, the causes were not related to the anesthetic regimen. No significant statistical difference in three of the early recovery parameters (response to pain, spontaneous eye opening, and response to commands) was found between groups. However, Fig. 1

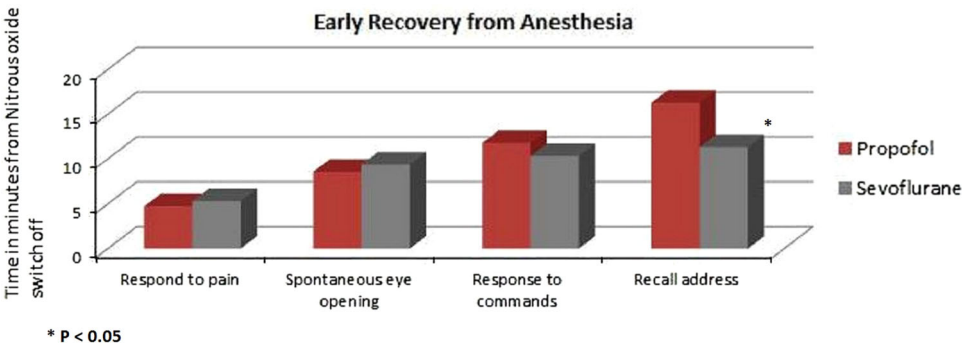

Fig. 1 Early recovery from anesthesia

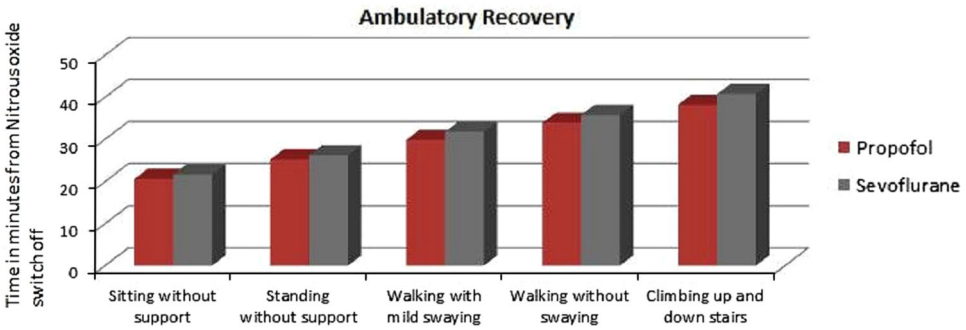

Fig. 2 Ambulatory recovery

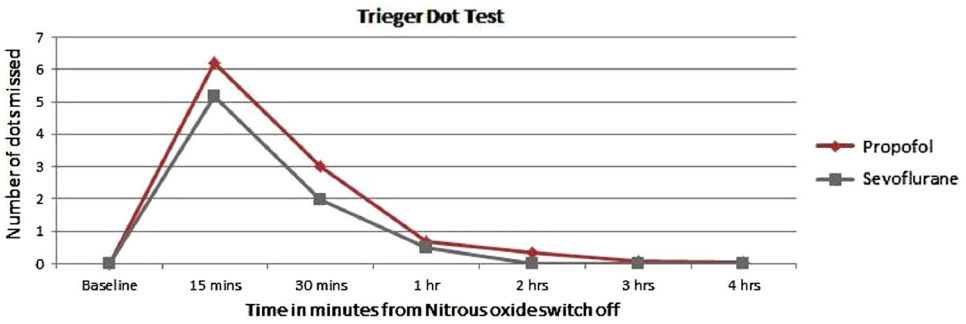

Fig. 3 Trieger dot test

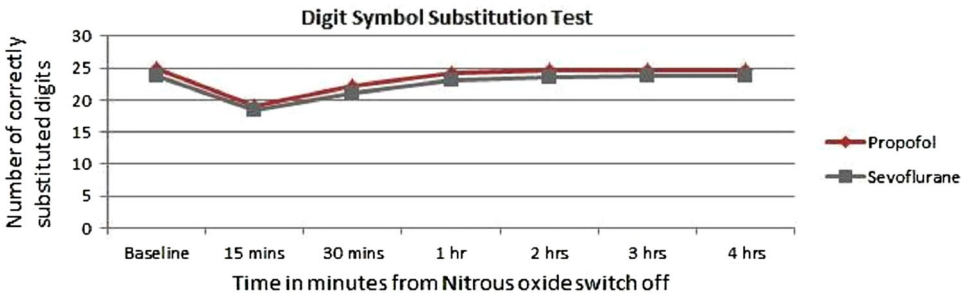

Fig. 4 Digit symbol substitution test

does show that the first two parameters of early recovery, response to pain and spontaneous eye opening, were marginally although not significantly faster in the propofol group as compared to sevoflurane. This trend was then reversed when the other two parameters were studied, i.e., the response to commands and recalling address, which were faster in the sevoflurane group, although the difference attained statistical significance only for the fourth parameter (recalling address). Drugs such as propofol have a relatively short context-sensitive half-time, despite the fact that a large amount remains present in the less well perfused compartments of the body. The slow return of propofol from these compartments generally contributes little to the concentration of drug in the central

compartment, from which it is rapidly cleared. Therefore, the concentration in the central compartment rapidly declines below the hypnotic threshold after discontinuation of the infusion, contributing to short emergence times, despite the fact that a substantial quantity of propofol might remain in the body. Thus, this propofol that comes back into the central compartment at a slower rate would seem to have little significance in daily clinical practice. However, when compared to another "rapid-offset" drug such as sevoflurane, this amount of residual drug might result in greater sedation, which could be the phenomenon that we encountered in terms of a more significant prolongation of "time to recall address" in the propofol group. For a low-solubility volatile agent such as sevoflurane, the effect of reservoirs of anesthetic relative to duration of anesthesia is almost absent. However, given that the difference between the groups in terms of minutes for the time to recall address was still only 5 min, its clinical relevance would be of doubtful value. Hence, the choice of maintenance anesthetics would be guided more by economic factors.

One factor that could have influenced our results was that the depth of anesthesia at "nitrous oxide switch-off" was not known. We used clinical assessment of anesthetic depth based on hemodynamic responses to pain during surgery and therefore could have erred into maintaining patients at different depths of anesthesia, which in turn would affect recovery. It is of course well known that utilizing depth of anesthesia monitors such as the bispectral index (BIS) results in much faster recovery as compared to conventional anesthetic maintenance [3]. However, a few other studies have not shown any notable correlation between the last-noted BIS value before stopping infusions of propofol and emergence time [4]. Our trial further suggests no difference between propofol and sevoflurane with respect to time to home-readiness. However, actual home discharge was faster by about 15–20 min in the propofol group owing to factors unrelated to the anesthetic drug used.

Psychomotor testing in the immediate postoperative period may be affected by several other variables including pain and postoperative nausea and vomiting (PONV). However, Korttila and Seppala [5] had suggested that acute pain did not adversely influence psychomotor functions. Although the incidence of nausea was identical between the two groups, a significantly greater proportion of patients in the sevoflurane group did experience vomiting, and we are not entirely sure whether that could have influenced psychomotor performance postoperatively. Several psychomotor tests have been used and found to be sensitive in assessing residual effects of alcohol [6], intravenous sedatives, and anesthetics [7, 8] as well as after analgesics [9] and sedative/analgesic [10] combinations. The tests that we used, the DSST and the TDT, have been employed in similar scenarios previously [11]. The recovery pattern of psychomotor functions was identical for both groups and was rapid enough that by 2 h after the discontinuation of nitrous oxide no difference from baseline was evident.

In the TDT we noticed that performance was impaired in both groups, only until the end of the first hour, although the propofol group demonstrated a better grip on the pen with smoother writing on paper as compared to the sevoflurane group. The practice factor that might have crept into this test could have been avoided by altering different geometric figures instead of a single figure every time. Another limitation of the way we conducted this test was that we could have measured the distance (in mm) from dots missed to increase the sensitivity of the test. The DSST test measured recoding skills and recognition of sensory (visual) information, mental concentration, fine muscular coordination, and ability to alter eye fixation. Performance in both groups was impaired for DSST only up to 1 h.

Postoperative nausea and vomiting were significantly more common with sevoflurane compared with propofol, and the use of antiemetics was consequently more common in the sevoflurane group. Tramer et al. [12], in a meta-analysis, found that maintenance of anesthesia with propofol has an advantage compared with other anesthetics when the incidence of complications is in the range of 20–60 %, with numbers needed to treat (NNT) of <5. The incidence of postoperative vomiting in the sevoflurane group was 20 % in our present analysis, which would support the use of propofol infusion. However, the efficacy of propofol alone for reducing PONV would be small compared to its use along with antiemetic prophylaxis in patients at risk.

Clearly, at least certain aspects of early recovery were faster in the sevoflurane group as compared to the propofol group. However, in actual clinical practice, the magnitude of this difference should not be reason enough to recommend one anesthetic regimen over the other. Furthermore, propofol scores over sevoflurane with its antiemetic properties. There was little to choose between the two groups with regard to other important aspects of day care surgery such as time to "home-readiness" and patient satisfaction with the anesthetic regimen followed. The psychomotor tests assessed also did not seem to recommend one anesthetic protocol over the other. In conclusion, the anesthetic regimen for maintenance of anesthesia between propofol and sevoflurane needs to be guided by the training and experience of the anesthesiologist, the practices of and equipment available in the hospital, and economic considerations, because the choice of anesthetic drugs appears to play an insignificant role in outcome after day care surgery.

Conflict of interest None.

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