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Original Research Article

Evaluation of Prolonged Propofol Infusion on Recovery Profile and Cognitive Function in Daycare Surgical Patients

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Abstract

Background: Propofol is a commonly used anesthetic for daycare surgery due to its rapid onset and good recovery profile, but in ambulatory surgical patients, prolonged infusion can delay psychomotor and cognitive recovery. This prospective comparative study compared the recovery profile and early cognitive function following short and prolonged propofol infusion in daycare surgery in adults.

Materials and Methods: Ninety ASA physical status I-II patients aged 18-60 years who were scheduled for elective daycare procedures under total intravenous anesthesia (TIVA) were randomly divided into two groups: short infusion (Group S, <=60 minutes, n=45) and prolonged infusion (Group P, 61-120 minutes, n=45). The recovery endpoints were time to eye opening, orientation, modified Aldrete score >=9, ambulation, discharge readiness, postoperative nausea-vomiting, and rescue analgesia.

Results: The cognitive function was evaluated preoperatively and at 30 minutes, 2 hours, and 24 hours postoperatively with the digit-symbol substitution test, trail-making test A, and Mini-Mental State Examination. Demographic variables were similar. Group P showed longer time to eye opening (9.8 ± 3.1 vs 6.2 ± 2.4 min), orientation (13.6 ± 4.2 vs 9.1 ± 3.5 min), Aldrete score >=9 (20.4 ± 6.8 vs 14.2 ± 5.9 min), and discharge readiness (169.5 ± 31.6 vs 134.8 ± 26.9 min; $p < 0.001$).

Conclusion: At 30 minutes, digit-symbol scores were lower and trail-making time was longer in Group P, but scores returned to baseline at 2 hours and were similar at 24 hours. Early recovery and transient cognitive performance were delayed by prolonged propofol infusion, but not impaired.

Keywords: Propofol; Daycare Surgery; Recovery Profile; Cognitive Function; Total Intravenous Anesthesia; Ambulatory Anesthesia.

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Introduction

Anesthetic techniques for daycare surgery must ensure adequate hypnosis and analgesia, with rapid recovery, minimal postoperative nausea-vomiting, and safe discharge. Propofol is a widely used agent for induction and maintenance of anaesthesia in ambulatory surgery due to its rapid redistribution, short context sensitive half-life following short infusion, antiemetic effects and smooth recovery characteristics [1].

Many studies have examined the use of total intravenous anesthesia (TIVA) with propofol compared to volatile anesthesia, and some have found that the early recovery or postoperative nausea is superior, depending on the procedure, opioid regimen, duration of infusion and recovery endpoint [2-4]. Post-anesthetic recovery is multi-dimensional. Early recovery involves awakening, airway management, orientation and stable vital signs. Intermediate recovery is ambulation, oral intake, pain control, no nausea, and prepared for discharge. Late recovery involves returning of psychomotor function, memory, attention and ability to carry out daily activities.

In day care surgery, cognitive function is especially important because the patient is sent home on the same day and needs to be able to understand the postoperative instructions, avoid unsafe activities, and be aware of warning signs. There are

differences in cognitive recovery within the first hour after surgery between propofol and inhalational anesthesia, despite comparable recovery later on [5,6]. Because of the increase in tissue distribution and cumulative dose with longer infusion, the duration of propofol infusion may impact recovery. Propofol has good pharmacokinetics but may cause delayed emergence, psychomotor speed and discharge readiness, particularly when used with opioids or sedatives during prolonged infusion. Recovery of cognitive flexibility has been demonstrated to be earlier than reaction time or psychomotor speed following propofol sedation, both by computerized and paper-based cognitive tests [7,8]. Ambulatory surgery can be important even if the patient's cognition slows for a short time, since discharge decisions are made within 1-3 hours of anesthesia.

The literature on the use of prolonged propofol infusion in routine daycare surgical patients is scarce. Numerous studies have compared anesthetic agents, rather than the duration of the infusion, or have included elderly patients or inpatient surgery, or have studied postoperative cognitive dysfunction after 24 hours. Although recent reviews indicate that TIVA may be associated with a decrease in EPOC, there is still significant heterogeneity in cognitive tests and timing [9,10]. Thus, targeted assessment of short versus long duration of propofol infusion in daycare patients may be useful to further optimize recovery strategies. The purpose of the present study was to assess the impact of the long-term use of propofol infusion on recovery profile and early cognitive function in reproductive-age and middle-aged adult daycare surgical patients. The main aim was to compare the discharge readiness time of the short and prolonged infusion groups. Secondary goals included comparing early recovery milestones, postoperative adverse effects, and cognitive test performance up to 24 hours.

Materials and Methods

The study was a prospective comparative study carried out in a day care surgical unit of a tertiary care hospital for six months. Adult patients (18-60 years old) ASA physical status I-II scheduled for elective daycare procedures under TIVA with propofol were screened. The procedures performed were minor general surgery, gynecological day procedures, short-term diagnostic laparoscopy, and orthopedic soft-tissue procedures. Patients were all given routine preoperative evaluation and were instructed to follow standard fasting guidelines.

Discharge readiness time was chosen as the primary outcome and the sample size was determined accordingly. With a mean difference of 20 minutes, a SD of 30 minutes, 80% power and 5% alpha error, 41 patients were needed in each group. Forty-five patients were included in each group to provide for the exclusion of patients. Patients were randomized based on the actual infusion duration of propofol that was recorded intraoperatively: Group S (infusion duration <=60 minutes) and Group P (infusion duration 61-120 minutes). Exclusion criteria were neurological disease, psychiatric illness, cognitive impairment, chronic sedative use, alcohol dependence, and difficult airway requiring prolonged airway manipulation, conversion to inpatient admission for surgical reasons, intraoperative hemodynamic instability, and inability to complete cognitive tests.

Standard monitoring included electrocardiography, noninvasive blood pressure, pulse oximetry, capnography, and bispectral index (BI) if available, for all patients. Fentanyl 1-2 microgram/kg and propofol 1.5-2 mg/kg were used to induce anesthesia, and the infusion of propofol was adjusted to 75-150 microgram/kg/min to maintain the appropriate depth of anesthesia. Airway management was done with a supraglottic airway or endotracheal tube as per procedure. Where appropriate, non-opioid analgesics and local infiltration were used. Ondansetron 4mg was given close to the end of surgery. The infusion of propofol was discontinued at skin closure, and the total dose and duration were noted.

An observer blind to the study objective assessed recovery outcomes. Early endpoints were time to eye opening after stopping propofol, response to verbal command, orientation to name/place, and modified Aldrete score >=9. Intermediate endpoints were time to oral intake, ambulation, pain score, nausea-vomiting, requirement for rescue analgesics and readiness for discharge based on institutional criteria. The digit-symbol substitution test, trail-making test A and Mini-Mental State Examination were used to assess cognitive function preoperatively and at 30 minutes, 2 hours and 24 hours postoperatively. Independent t test or Mann-Whitney U test was used for continuous variables, chi-square test was used for categorical variables, repeated-measures ANOVA was used for cognitive scores, and linear regression was used for predictors of discharge readiness. A p value < 0.05 was taken as statistically significant.

Results

Ninety patients completed the study, with 45 in each group. Demographic variables, ASA status, baseline cognitive scores, and type of airway device were comparable. As expected, duration of anesthesia and total propofol dose were significantly higher in Group P. Hemodynamic variables remained within acceptable range in both groups. No patient required unplanned postoperative ventilation, and no case was converted to inpatient admission because of

anesthesia-related complications. Recovery milestones were significantly delayed in the prolonged infusion group. Time to eye opening, response to command, orientation, Aldrete score >=9, ambulation, and discharge readiness were all longer in Group P. The mean discharge readiness time was 169.5 ± 31.6 minutes in Group P compared with 134.8 ± 26.9 minutes in Group S ($p < 0.001$).

Pain scores and rescue analgesic requirements were similar, indicating that discharge delay was more related to sedation and psychomotor recovery than pain. Postoperative nausea-vomiting was low in both groups, consistent with the antiemetic profile of propofol and routine ondansetron prophylaxis. Cognitive outcomes showed transient impairment after prolonged infusion. At 30 minutes, Group P had lower digit-symbol substitution scores and longer trail-making test A time than Group S. Mini-Mental State Examination scores showed a small decline at 30 minutes in Group P but remained within normal range. By 2 hours, cognitive scores in both groups improved substantially and were not significantly different for MMSE, although digit-symbol scores remained slightly lower in Group P.

At 24 hours, all cognitive test scores were comparable with baseline in both groups. Regression analysis showed that propofol infusion duration and total dose independently predicted discharge readiness time after adjustment for age, sex, procedure duration, fentanyl dose, and pain score.

Table 1: Demographic and intraoperative characteristics

Variable	Short infusion <=60 min (n=45)	Prolonged infusion 61-120 min (n=45)	p value
Age (years)	38.6 ± 11.4	40.2 ± 10.9	0.49
Female, n (%)	24 (53.3)	26 (57.8)	0.67
BMI (kg/m2)	24.8 ± 3.6	25.2 ± 3.8	0.61
ASA I/II	26/19	24/21	0.67
Infusion duration (min)	46.8 ± 9.1	86.4 ± 17.6	<0.001
Total propofol dose (mg)	426 ± 112	742 ± 186	<0.001

Table 2: Recovery profile after stopping propofol infusion

Recovery parameter	Short infusion	Prolonged infusion	p value
Eye opening (min)	6.2 ± 2.4	9.8 ± 3.1	<0.001
Orientation (min)	9.1 ± 3.5	13.6 ± 4.2	<0.001
Aldrete score >=9 (min)	14.2 ± 5.9	20.4 ± 6.8	<0.001
Ambulation (min)	93.6 ± 21.8	118.7 ± 25.4	<0.001
Discharge readiness (min)	134.8 ± 26.9	169.5 ± 31.6	<0.001
PONV, n (%)	3 (6.7)	5 (11.1)	0.46

Table 3: Cognitive test scores over time

Test and time point	Short infusion	Prolonged infusion	p value
DSST baseline	61.4 ± 8.6	60.8 ± 8.9	0.74
DSST 30 min	52.9 ± 9.2	45.6 ± 10.1	<0.001
DSST 2 h	58.7 ± 8.8	56.1 ± 9.4	0.18
Trail-making A 30 min (s)	48.6 ± 12.5	62.4 ± 15.8	<0.001
MMSE 30 min	28.6 ± 1.1	27.8 ± 1.4	0.004
MMSE 24 h	29.1 ± 0.8	29.0 ± 0.9	0.58

Discussion

This study revealed that in day care surgery, the recovery of early and intermediate recovery milestones was delayed and there was transient impairment in psychomotor cognitive tests with the use of prolonged propofol infusion. Patients who had infusion for 61-120 minutes took longer to open their eyes, orient, achieve Aldrete score, walk and be ready for discharge than those who had shorter infusion. Cognitive differences were most pronounced at 30 minutes and mostly normalized by 2 hours, and were not seen at 24 hours. The results are consistent with the pharmacological prediction that prolonged infusion and higher cumulative doses will result in longer redistribution and early psychomotor recovery without necessarily leading to permanent cognitive dysfunction in healthy adults.

Propofol is still a good choice for ambulatory anesthesia due to its smooth induction and low incidence of nausea-vomiting [1]. Propofol-based techniques have been compared to other methods and recovery has been found to be faster or similar, depending on the comparator and the time of recovery [2-4]. The present study, however, focuses on the fact that the length of infusion is

important in propofol anesthesia. The context-sensitive half-time of propofol is good for moderate infusion times, but cumulative doses may cause a delay in the discharge related functions. Awakening is not the only criteria used for ambulatory discharge; orientation, ambulation, pain control, nausea control, and cognitive ability to follow instructions are all factors.

The cognitive results are of interest. Processing speed, attention, visuomotor coordination and executive function are sensitive to digit-symbol substitution and trail-making tests. The prolonged-infusion group had poorer performance at 30 minutes and the MMSE had only small changes. This confirms previous findings that global screening tests might not be as sensitive as timed psychomotor tests to identify early recovery differences [7,8]. There are also studies that have compared the effects of propofol with volatile anesthesia, and found that while cognitive function later in recovery may be similar, there are differences in the immediate postoperative period [5,6]. Thus, the recovery program for day care operations should not be solely based on orientation or MMSE-type screening if rapid discharge is intended following longer anesthetics.

The low nausea and vomiting rate in both groups is clinically useful. Propofol is also antiemetic and may help to decrease postoperative nausea when used in ambulatory surgery in certain settings. The prolonged group in this study did not report nausea or pain as a factor in their discharge delay, but rather recovery time and transient psychomotor slowing. This distinction is relevant as it may be possible to optimize the analgesic and antiemetic without reducing the length of discharge if there is residual sedation. Dose titration, depth monitoring (if available), multimodal analgesia to decrease opioid needs, and scheduling procedures to ensure sufficient recovery time after longer infusions may enhance efficiency.

The advantages of this study are that it was prospective, used a standardized anesthetic protocol, objective recovery endpoints, and repeated cognitive assessment up to 24 hours. There are some limitations such as non-random allocation based on infusion duration, surgical procedure heterogeneity, lack of plasma propofol concentration measurement, and limited use of advanced cognitive batteries. This study was conducted in relatively healthy adults; results may not be applicable to elderly patients, patients with neurological disease, or procedures longer than 2 hours. Randomized trials with dose adjusted propofol strategies, target-controlled infusion, volatile anesthesia and adjuncts (dexmedetomidine or remifentanil) should be compared to standardised outcome of neurocognitive function in the future. The results have implications for ambulatory anesthesia discharge planning. A patient can be awake and oriented, but with slower psychomotor speed or diminished attention or delayed coordination. This distinction is crucial as it means that the instructions for discharge, timing of medication, wound care and warning signs need to be understood correctly. Timed tests like digit-symbol substitution and trail-making are more sensitive to early impairment than are broad cognitive screening tests. The current study confirms the use of sufficient observation time following longer propofol infusions instead of a fixed time for all daycare cases.

The dose of propofol and duration of infusion were independent predictors of discharge readiness even when controlling for procedure duration and fentanyl dose. This indicates that exposure to anesthetic is a direct cause of recovery variability. Dose-sparing approaches can thus be more efficient. These include local anesthetic infiltration, multimodal non-opioid analgesia, avoiding unnecessary benzodiazepines, careful titration to a clinical endpoint or processed EEG target (if available), and stopping infusion at the end of surgical stimulation. These can help to decrease the total amount of propofol and opioids used without compromising patient comfort.

This is reassuring for healthy daycare patients as they do not have persistent cognitive impairment at 24 hours. This is in line with the good recovery profile of propofol and literature indicating that many early cognitive differences following anesthesia are likely to be temporary [7-10]. The findings should, however, not be extrapolated to elderly patients, patients with baseline cognitive impairment, patients with sleep apnea, patients with hepatic or renal dysfunction, or procedures that require longer anesthesia. These groups may be more susceptible to delayed neurocognitive recovery and may need more conservative discharge criteria.

In terms of research, this study emphasizes the importance of having standardized cognitive endpoints in ambulatory anesthesia. Comparisons are difficult because studies employ a variety of tests, time periods, and definitions of recovery. The consensus terminology has led to better classification of the postoperative outcomes of later cognitive disorders, but the same-day psychomotor recovery is less standardized [11,12]. Future trials should include objective recovery scores, patient-reported readiness, psychomotor testing, and home events (dizziness, nausea, pain, and recall of instructions). This would give a more patient-centred insight into the recovery process following daycare anaesthesia with propofol. Clinically, the findings are not in opposition to the use of propofol for daycare surgery. Rather, they facilitate personalized recovery evaluation following

extended infusions. Patients in the prolonged group had a good recovery by 24 hours but their initial psychomotor slowing indicates that discharge teams should give written instructions, have responsible adult escort, and reinforce that patients should not drive, operate machinery, sign important documents or make critical decisions on the day of anesthesia. These precautions are still relevant even if the scores for routine recovery seem to be good [13-15].

Conclusion

Extended propofol infusion during daycare surgery resulted in delayed early recovery and discharge readiness when compared to shorter infusion.

It also resulted in a transient decrease in psychomotor cognitive function at 30 minutes, but returned to baseline levels at 2 hours and was not impaired at 24 hours. When using propofol infusion for more than 60 minutes in the ambulatory patient, careful dose titration and adequate observation time are recommended.

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