Use of a remifentanil and propofol combination in outpatients to facilitate rapid discharge home

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The goal of our study was to evaluate whether the combination of remifentanil and propofol facilitated shorter recovery time and decreased charges compared with conventional balanced anesthesia. We studied 49 patients, aged 13 to 75 years, who underwent elective outpatient surgery.

All data were analyzed using the Pearson χ^2 and the Student t test; results were considered statistically significant at a P value of .05 or less. Group 1 received a remifentanil-propofol combination and group 2, a conventional balanced anesthetic. Group 1 had decreased mean operating room ($280.83 vs $337.42; P = .05) and operating room plus postanesthesia care unit (PACU) ($442.67 vs $544.62) charges (P = .02). Group 1 had less PACU time (48.26 vs 59.62 minutes) and 2 group 1 patients bypassed the PACU.

We conclude that a remifentanil-propofol combination is more cost effective than conventional balanced anesthetics and enables some patients to bypass the PACU, resulting in quicker discharge. Our findings have important implications for ambulatory surgery centers and office-based practices.

Key words: **Ambulatory surgery, outpatient surgery, propofol, remifentanil.**

Rapid recovery from anesthesia and return of cognitive function are universal goals during outpatient surgery. Combinations of medications are used to provide anesthesia because no single drug is able to provide all components of anesthesia without seriously compromising hemodynamic and/or respiratory function, impairing operating conditions, or delaying postoperative recovery. Ideal combination dosing facilitates optimal therapeutic effect without producing significant side effects.

Literature documents that the interaction of propofol and remifentanil results in decreased propofol doses required for anesthesia.[1] In addition, postanesthesia cognitive recovery occurs more quickly when propofol is combined with opioid medications.

Remifentanil hydrochloride is a phenyl piperidine derivative with μ-opioid agonist effects and unique pharmacokinetic properties. It has a rapid onset and an ultra-short duration of action. The methyl-propionic acid ester side chain of remifentanil is hydrolyzed by plasma and tissue esterase to a less potent (1/4,600 potency of the parent compound) carboxylic acid derivative.[2] Remifentanil has a rapid effect. Its blood-brain equilibration time is 1 minute. It has a small central volume of distribution, rapid clearance, and rapid offset of effect with a context-sensitive half-life of 3 minutes and a terminal elimination half-life of about 10 minutes. The carboxylic acid metabolite of remifentanil undergoes primarily renal elimination with an elimination half-life of 80 to 137 minutes. The pharmacodynamic and pharmacokinetic profiles of remifentanil suggest that the drug would be clinically useful when a rapidly titratable and potent opioid effect is desirable with concomitant predictable offset of action that minimizes time of respiratory depression.

Propofol is described chemically as 2,6-diisopropylphenol. It is highly lipophilic and is 98% bound to protein. The half-life of propofol is 2 to 4 minutes. Clearance from the central compartment ranges from 23 to 50 mL/kg per minute. In addition to the active component, propofol, the mixture also contains soybean oil, glycerol, egg lecithin, disodium edelate, and sodium hydroxite to adjust the pH. The injectable emulsion is isotonic and has a pH of 7 to 8.5.[3,4] Propofol undergoes glucuronide conjugation in the liver. Intraoperatively, propofol is potentiated by opioids.[5]

The purpose of this study was to examine the combination of remifentanil and propofol to determine whether patients were discharged home earlier, the cost-effectiveness of the combination, and the complications of using the combination.

Methods

This study involved an institutional review board–approved, retrospective review of 49 outpatient charts for patients with ASA physical status I through IV.

Approximately half of the cases were to be included in each of the 2 groups (group 1, remifentanil-propofol combination; group 2, conventional balanced anesthesia). Inclusion criteria were age 12 years or older, ASA physical status I through IV (systemic disease had to be well controlled for patients with ASA physical status III or IV), and undergoing outpatient elective surgery. Charts of males and females were reviewed. Exclusion criteria included unstable medical conditions; long-term use of benzodiazepines, clonidine, or opioids; opioid use within 12 hours of surgery; history of substance abuse; psychiatric illness; pregnancy or lactation; hypersensitivity to opioid or propofol lipid emulsion; and participation in an investigational drug trial within 8 weeks before surgery.

Patients received all of their regular medications on the morning of surgery. After arrival in the operating room (OR), intravenous access was established with lactated Ringer's solution, and patients received general anesthesia via an endotracheal tube. Further agents used for anesthesia were specific to the groups studied and are described subsequently.

Group 1 received a mixture starting at 50 µg/mL of remifentanil and 10 mg/mL of propofol, resulting in a final syringe admixture of a 20-mL solution containing 25 µg/mL of remifentanil and 5 mg/mL of propofol. The diluent used was 5% dextrose and water, which is compatible with both drugs.[6,7] Admixtures always were checked for visual stability and to verify that they showed no evidence of precipitation or separation. Inductions were accomplished using slow intravenous administration of 1.0 to 1.5 mg/kg of propofol from the mixture. The maintenance infusion was 25 to 75 µg/kg per minute of propofol using the remifentanil-propofol mixture.

Nitrous oxide and oxygen were used in a 50/50 concentration for maintenance. Rocuronium, a short- to intermediate-term muscle relaxant, was used as needed for intubation. The rocuronium loading dose was 0.5 mg/kg, and maintenance doses were 0.2 mg/kg boluses as needed. Postoperative pain was controlled with a field block intraoperatively or intravenous or intramuscular ketorolac, 30 to 60 mg, before the end of anesthesia.

Group 2 received a conventional balanced anesthetic. Patients were induced with propofol, 1 to 2 mg/kg, and fentanyl, 2 to 5 µg/kg, via intravenous boluses. In addition, these patients received inhalation with a 50/50 concentration of nitrous oxide and oxygen. As in group 1, group 2 received rocuronium, 0.5 mg/kg, and maintenance doses of 0.2 to mg/kg boluses as needed for intubation. Finally, group 2 received titrated doses of isoflurane or sevoflurane inhalation agents because propofol was not used after induction in this group. Group 2 did not receive a field block or ketorolac but received analgesia as needed in the postanesthesia care unit (PACU).

We retrospectively reviewed OR and anesthesia records for all cases. Cost information was obtained from the resource center. Specific variables collected included the preoperative characteristics, age, sex, and ASA physical status; OR characteristics, including total surgery time, OR + PACU time, OR charges, and OR + PACU charges; PACU characteristics, including total PACU time, PACU stay, and PACU charges; intraoperative characteristics, including OR total discharge score (total score, 1-10 for each patient based on movement, respiration, blood pressure level, consciousness, and pulse oximetry reading), OR discharge activity score, OR discharge respiratory score, OR discharge consciousness score, and OR discharge pulse oximetry score; intraoperative complications, including hypotension, bradycardia, prolonged awakening, nausea, and emesis; and PACU complications, including hypotension, bradycardia, prolonged awakening, nausea, emesis, and hallucinations.

Comparison of time to discharge from the endpoint of surgery was compared between groups. Also, any anesthesia-related side effects were noted. All statistical procedures for the study were conducted using SPSS version 10.0 (SPSS, Inc, Chicago, Ill). Counts within categories were compared with the Pearson χ^2. Quantitative data factors such as OR, PACU, and total OR and PACU time and charges and OR discharge activity scores were analyzed by application of the Student *t* test to the difference of means for the study groups. Differences were considered statistically significant at a *P* value of .05 or less.

Results

A total of 49 cases were studied. Group 1 (n = 23) included patients who had received the remifentanil-propofol combination, and group 2 (n = 26) included patients who had received conventional balanced anesthetics. There were no significant differences between groups in age, sex, or ASA physical status. The average age for group 1 was 29.7 years (range, 13-58 years; SD, 14.20 years); there were 11 males (48%) and 12 females (52%). The average age for group 2 was 36.0 years (range, 14-75 years; SD, 18.09 years); there were 12 males (46%) and 14 females (54%). ASA physical status was as follows: group 1: I, 10 (44%); II, 10 (43%); and III, 3 (13%); group 2: I, 6 (23%); II, 14 (54%); III, 5 (19%); and IV, 1 (4%).

The charts reviewed had dissimilar diagnoses and procedures. There were 10 ear, nose, and throat cases,

7 dental cases, 1 plastic surgery case, 1 urology case, 2 obstetrical cases, and 2 orthopedic cases in group 1. Group 2 consisted of 20 ear, nose, and throat cases, 5 dental cases, and 1 obstetrical case.

The OR charges and OR + PACU charges for group 1 were significantly less than for group 2. Drug charges for group 1 patients included the cost of remifentanil and propofol only, whereas group 2 patients were charged for the cost of propofol, fentanyl, and the inhalation agent. The mean charges were $280.83 (SD, $80.86) for group 1 and $337.42 (SD, $112.08) for group 2.

Findings were similar for the OR + PACU charges: group 1 had a mean of $442.67 (SD, $130.05) and group 2 a mean of $544.62 (SD, $174.85). Although the difference was not statistically significant, the mean PACU charges for group 1 (mean, $171.80; SD, $90.24) was less than for group 2 (mean, $207.20; SD, $93.93). PACU charges were based on the length of stay in the unit by charging for the first hour and every half hour thereafter.

Although the differences were not statistically significant, group 1 had shorter times for total surgery, OR + PACU, and total PACU than group 2. Group 1 had a mean total surgery time of 26.78 minutes (SD, 13.51 minutes), and group 2 had a mean surgery time of 34.23 minutes (SD, 23.14 minutes). For OR + PACU time, group 1 had less combined time (mean, 75.04 minutes; SD, 30.59 minutes) than group 2 (mean, 93.85 minutes; SD, 49.20 minutes). The mean total PACU time for group 1 was 48.26 minutes (SD, 28.27 minutes) and for group 2 was 59.62 minutes (SD, 35.69 minutes).

The intraoperative characteristics reviewed were OR total discharge score, activity score, respiratory score, circulatory score, consciousness score, and pulse oximetry score. Group 1 had significantly higher OR total discharge scores (1-10) than group 2 (Table 1). Patients in group 1 had a higher level of consciousness than patients in group 2, which shows clinical significance (Table 2). Otherwise, intraoperative characteristics between groups were similar. One additional intraoperative finding in group 1 was that no individuals who received the remifentani-propofol mixture reported pain with injection.

Intraoperative complications reviewed were hypotension, bradycardia, prolonged awakening, nausea, and emesis. Patients in group 2 had significantly fewer overall intraoperative complications (4 [15%]) than patients in group 1 (10 [44%]) (P = 0.03). This was because bradycardia occurred in 7 group 1 patients (30%). However, the bradycardia observed in these 7 cases was not associated with hypotension and resolved without treatment in PACU. Otherwise, intraoperative complications between groups were similar.

Group 1 had fewer PACU complications than group 2 (2 [10%] in group 1 and 6 [23%] in group 2). Bradycardia was the only complication that occurred in group 1 (2 [9%]). Bradycardia also occurred in group 2 (3 [(12%]). Additionally, group 2 experienced hypotension (1 [4%]), nausea (1 [4%]), and emesis (2 [8%]).

Two patients in group 1 bypassed the PACU, which is not statistically significant but may be clinically significant. The PACU complications reviewed were hypotension, bradycardia, prolonged awakening, nausea, emesis, and hallucinations. The groups were similar, and there were no statistically significant differences.

Discussion

The groups showed no statistically significant differences in age, sex, or ASA physical status. The average total surgery time was approximately 27 minutes in group 1 compared with 34 minutes in group 2. The total PACU time was less in group 1. In fact, 2 patients bypassed the PACU after the anesthetic. Actual OR

Table 1. Summary of operating room total discharge scores (possible scores, 1-10)*

	Group 1 (n = 23)	Group 2 (n = 26)
Total Score	No. (%)	No. (%)
10	15 (65)†	6 (23)
9	8 (35)	17 (65)
8	0 (0)	1 (4)
6	0 (0)	2 (8)

* Group 1 received a remifentanil-propofol combination; group 2, a conventional balanced anesthetic.
† P = .02; significance was set at ≤ .05.

Table 2. Summary of operating room discharge consciousness scores*

	Group 1 (n = 23)	Group 2 (n = 26)
Description	No. (%)	No. (%)
Fully awake	10 (43)	7 (27)
Arouses to voice	13 (57)	16 (62)
Not arousable	0 (0)	3 (12)

* Group 1 received a remifentanil-propofol combination; group 2, a conventional balanced anesthetic. Percentages for group 2 do not total 100 because of rounding. P = .16 (not statistically significant but clinically significant).

drug charges and actual OR and PACU charges were almost 20% less in group 1. Although not statistically significant, PACU complications occurred less frequently in group 1, which may have contributed to group 1 incurring less total PACU time and fewer OR and PACU charges.

The use of propofol and remifentanil for outpatient surgery has been well-researched, and use is common. Combination and simultaneous administration of the drugs allows synergism, cost savings, and ease of use.[8] Because the context-sensitive half-life is approximately 3 minutes,[9] the analgesia dissipates quickly; therefore, to enable rapid patient discharge, local anesthesia or a nonsteroidal anti-inflammatory drug must be used for postoperative pain control. Compared with anesthesia with propofol alone, the combination reduced propofol and remifentanil requirements. The distribution half-life of propofol is 2 to 10 minutes, and the second-phase half-life is 26 to 56 minutes. The terminal elimination half-life is 1.5 to almost 30 hours but would not apply to anesthetics lasting less than 1 hour. Another advantage of the remifentanil-propofol mixture was that it seemed to eliminate the reported 70% incidence of pain on injection.[10]

The remifentanil-propofol mixture contained in 1 syringe is easy to use, cost-effective, and suited to a busy ambulatory surgery center or office practice. We recommend mixing just before use. After giving the initial bolus induction and securing the airway, 1 infusion pump can be used for the case. Our experience with the mixture suggests that it may be feasible for many patients to bypass the recovery room and be discharged directly home from the OR. This technique would be an asset to busy office and ambulatory surgery practices performing general anesthesia.

Limitations to this study included the small sample, duration of surgery, and the various types of surgeries included for analysis. Increasing the sample size, having a homogeneous surgery sample, using liquid chromatography for drug compatibility testing and evaluation, and designing a prospective, randomized, double-blind study based on our small retrospective study are suggestions for future studies.

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