

Original Article

Recovery from Anesthesia: Comparison of Propofol and Isoflurane for General Anesthesia with or without Nitrous Oxide

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Abstract: Objective: The present study was designed to assess the recovery from propofol compared with isoflurane anesthesia.

Methods: Patients were randomly divided into 6 groups according to the anesthetic technique as follows: with or without nitrous oxide, maintenance agents (propofol, isoflurane), and induction agents (propofol, thiamylal). The recovery times, postoperative pain, nausea and vomiting (PONV) and mood were evaluated after operation.

Results: The measured times in isoflurane groups with epidural anesthesia were significantly shorter than those in groups with nitrous oxide. However, only the oriented times in the propofol group with epidural anesthesia were significantly shorter than those in the propofol group with nitrous oxide. In addition, there were no significant differences in any of the times among the groups without epidural anesthesia. In groups with epidural anesthesia, the recovery times in the propofol group were significantly longer than those in the propofol-induction and isoflurane-maintenance group. The subjective pain scale score in the propofol with nitrous oxide group was greater than that in all epidural groups. Significant differences were not found in emesis and feeling among the groups.

Conclusion: Propofol could not provide for a rapid emergence with less PONV when compared with isoflurane. Propofol as an induction agent did not show better results than thiamylal after isoflurane anesthesia. Nitrous oxide did not increase the incidence of PONV after propofol or isoflurane anesthesia.

Key words: Anesthetics, Isoflurane, Propofol, Recovery times, PONV

INTRODUCTION

There are many studies indicating that propofol is a better induction agent than thiopental¹⁻³⁾ and provides better recovery from anesthesia than inhalation techniques⁴⁻¹⁰⁾. However, some studies have reported a lack of efficacy of propofol compared with isoflurane anesthesia¹¹⁻¹³⁾. This discrepancy seems to be due to the differences between anesthetic techniques employed. For example, whether or not anes-

thetic techniques include nitrous oxide, whether or not propofol is used only for induction, whether narcotics are being used for supplement of anesthesia, and so on. There has been no systematic study examining these factors. The present study was designed to assess 1) recovery from propofol compared with isoflurane anesthesia, 2) recovery following induction with either propofol or thiamylal during isoflurane anesthesia, and 3) whether nitrous oxide influences recovery from propofol or isoflurane anesthesia.

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PATIENTS AND METHODS

With the approval of the Ethics Committee at Yamanashi Medical University we conducted a prospective study of 102 adult ASA physical status I and II patients, from whom informed consent was obtained. Patients were scheduled for superficial, extremities or lower abdominal surgical procedures. No patient had a history of allergy to medications or evidence of hepatic, renal, hematological or cardiovascular disease. Patients were premedicated with or without atropine 0.3–0.5 mg intramuscularly given 30–45 min prior to induction of anesthesia. None was taking any medication which might affect recovery from anesthesia. Monitoring included automated non-invasive pressure cuff, pulse oximetry, ECG, pulse and respiratory rate.

Forty-two patients presenting for non-major (e.g., superficial or extremities) surgical procedures were randomly allocated to one of three groups as follows:

I. GOPp group ($n = 14$). Propofol was used as the induction agent at a dose of 1.5–2.0 mg·kg⁻¹. Patients were then maintained on 6–12 mg kg⁻¹h⁻¹ propofol with nitrous oxide 66 % in oxygen.

II. GOIp group ($n = 14$). Propofol was used as the induction agent at a dose of 1.5–2.0 mg·kg⁻¹. Patients were then maintained on 1–3 vol % isoflurane (inspired concentration) with nitrous oxide 66 % in oxygen.

III. GOIt group ($n = 14$). Thiamylal was used as the induction agent at a dose of 4.0–5.0 mg·kg⁻¹. Patients were then maintained on 1–3 vol % isoflurane (inspired concentration) with nitrous oxide 66 % in oxygen.

Sixty patients scheduled to undergo lower abdominal operations or mastectomy had epidural and general anesthesia. An epidural catheter was inserted into appropriate interver-

tebral space before general anesthesia. They were randomly assigned to one of three groups as follows:

IV. AOPp group ($n = 20$). Propofol was used as the induction agent at a dose of 1.5–2.0 mg·kg⁻¹. Patients were then maintained on 4–6 mg·kg⁻¹h⁻¹ propofol. Ventilation was maintained with oxygen and air so that the FiO₂ was 0.33–0.50. Epidural anesthesia was maintained with 1–2 % mepivacaine hydrochloride.

V. AOIp group ($n = 20$). Propofol was used as the induction agent at a dose of 1.5–2.0 mg·kg⁻¹. Patients were then maintained on 0.5–1 vol % isoflurane (inspired concentration) with oxygen and air so that the FiO₂ was 0.33–0.50. Epidural anesthesia was maintained with 1–2 % mepivacaine hydrochloride.

VI. AOIt group ($n = 20$). Thiamylal was used as the induction agent at a dose of 1.5–2.0 mg·kg⁻¹. Patients were then maintained on 0.5–1 vol % isoflurane (inspired concentration) with oxygen and air so that the FiO₂ was 0.33–0.50. Epidural anesthesia was maintained with 1–2 % mepivacaine hydrochloride.

Muscle relaxation for all groups of patients was obtained by an intravenous bolus of vecuronium bromide 0.1–0.15 mg·kg⁻¹ before intubation and supplementary dose of 1–3 mg if required. All patients were ventilated to maintain PaCO₂ with 33–40 mmHg. Ephedrine and nicardipine were administered, if necessary. No other drugs were given during surgery. We did not use any narcotic drugs during anesthesia that might affect the recovery from anesthesia. The inspired concentration of isoflurane and infusion rate of propofol were unchanged from 30 min before the end of surgery. At the end of the operation, residual neuromuscular blockade was reversed with a combination of neostigmine 2–4 mg and atropine sulfate 1–2 mg, and maintenance agents were discontinued. Extuba-

tion was performed when spontaneous respiration was well established. Early postoperative recovery times were evaluated as follows: (1) extubation time (elapsed time from termination of the maintenance agents until the patients were extubated), (2) awakening time (time from discontinuation of the maintenance agents until the patients could open their eyes on verbal command), (3) time to squeeze hand (time until the patients could squeeze the observer's hand on command), (4) time to show tongue (time until the patients could show their tongues on command), and (5) orientation time (time until the patients were oriented to date and place). Rectal temperature was determined at the times of intubation and extubation. Anesthesia time was calculated as the time from the start of induction until discontinuance of the maintenance agents. Operation time was noted.

The patients were interviewed by the anesthetist for complications of anesthesia and surgery such as nausea, vomiting, postoperative pain and mood right after they awakened. Postoperative pain was assessed by patients as absent, mild, moderate or severe. Analgesic (e.g., flurbiprofen) was then given intravenously for pain if required. Mood was also rated as excellent, good, ordinary, bad or worst.

On the next day following surgery, the patients were interviewed again for side effects of anesthesia and surgery such as nausea, vomiting and mood.

The groups were compared statistically by the chi-squared test for categorical variables, and the Kruskal-Wallis test and one-way ANOVA followed by Student-Newman-Keuls test for continuous variables. The data are presented as mean \pm S.D. A probability of less than 0.05 was regarded as statistically significant.

RESULTS

There were no significant differences among the groups in age, weight, anesthesia and operation times, and body temperature at intubation. However, the sex ratio in the GOPp group was significantly different from the GOIt and epidural (AOPp, AOIp, AOIt) groups. Mean delivered doses of propofol and isoflurane in the groups without epidural anesthesia (GOPp, GOIp, GOIt) were significantly greater than those in the isoflurane groups without nitrous oxide (AOPp, AOIp, AOIt). Rectal temperature at extubation in the AOIp and AOIt groups was significantly lower than that in the AOPp group (Table 1).

The times to initial clinical recovery and extubation are presented in Table 2. All measured times in the isoflurane groups with epidural anesthesia (AOIp, AOIt) were significantly shorter than those in the groups with nitrous oxide (without epidural anesthesia) (GOIp, GOIt). However, only the oriented times in the AOPp group were significantly shorter than those in the GOPp group. In addition, there were no significant differences in all measured times between the groups without epidural anesthesia (with nitrous oxide). In the groups with epidural anesthesia, there were significant differences in the recovery times between AOPp and AOIp groups.

Postoperative pain, emesis and feelings are shown in Table 3 and Figure 1–3. Postoperative pain in the GOPp group was more severe than that in the epidural groups (AOPp, AOIp, AOIt). Significant differences were not found in other terms of those results.

DISCUSSION

These results indicate that the recovery times

Table 1 . Clinical characteristics

	GOPp(n=14)	GOIp(n=14)	GOIt(n=14)	AOPp(n=20)	AOIp(n=20)	AOIt(n=20)
Age (yr)	41.6±16.0	43.1±15.7	47.9±15.9	50.3±14.4	47.1±11.2	48.2±7.1
Sex (male: female)	10:4	6:8	3:11*	5:15*	5:15*	3:17*
Weight (kg)	63.0±12.1	56.0±8.8	58.6±12.6	53.4±8.6	53.0±7.4	54.5±10.3
Anesthesia time (min)	209±100	236±90	214±105	219±97	196±72	193±68
Operation time (min)	174±101	197±85	173±100	175±93	158±68	153±64
Rectal temperature at intubation (°C)	36.6±0.29	36.7±0.29	36.6±0.43	36.6±0.34	36.4±0.46	36.4±0.36
Rectal temperature at extubation (°C)	36.6±0.42	36.7±0.51	36.8±0.46	36.7±0.37	36.3±0.68 ⁺	36.2±0.44 ⁺
Mean concentration of isoflurane (Vol %)		1.13±0.19 [†]	1.01±0.05 [†]		0.68±0.18	0.72±0.22
Mean infusion rate of propofol (mg · kg ⁻¹ · h ⁻¹)	6.32±0.72			4.49±0.76*		

Values are means ± SD or numbers.

*p<0.05 vs GOPp group

⁺p<0.05 vs AOPp group

[†]p<0.05 vs AOIp, or AOIt group

Table 2 . Time to initial clinical recovery and extubation

	GOPp(n=14)	GOIp(n=14)	GOIt(n=14)	AOPp(n=20)	AOIp(n=20)	AOIt(n=20)
Extubating time (min)	13.3±5.7	13.6±6.1	14.6±4.2	10.1±4.7	7.3±3.7*	8.1±5.2*
Awakening time (min)	11.4±5.4	11.6±4.2	12.8±4.7	8.1±5.1 [†]	4.8±3.1*	6.7±5.2*
Time to squeeze hand (min)	12.8±5.3	14.4±6.2	15.6±5.4	9.7±4.5 [†]	6.5±3.5*	7.0±4.8*
Time to show tongue (min)	14.8±5.0	15.8±7.0	16.5±4.6	11.9±5.2 [†]	8.2±4.5*	8.8±6.2*
Date oriented time (min)	19.0±6.4	23.1±8.2	19.7±6.7	14.3±5.9 [†]	10.3±4.6*	12.8±5.9*
Place oriented time (min)	20.1±7.8	22.9±8.1	19.6±7.0	14.2±5.8 [†]	10.4±4.5*	12.7±5.8*

Values are means ± SD.

*p<0.05 vs GOIp, or GOIt group

[†]p<0.05 vs GOPp group

[‡]p<0.05 vs AOIp group

Table 3 . Postoperative emesis

	GOPp(n=14)	GOIp(n=14)	GOIt(n=14)	AOPp(n=20)	AOIp(n=20)	AOIt(n=20)
Nausea (at operating theater)	0	2	2	1	2	3
Nausea (after leaving operating theater)	1	2	3	2	5	6
Vomiting (at operating theater)	0	1	0	1	0	1
Vomiting (after leaving operating theater)	0	1	1	1	1	4

Values are numbers.

No significant differences were found.

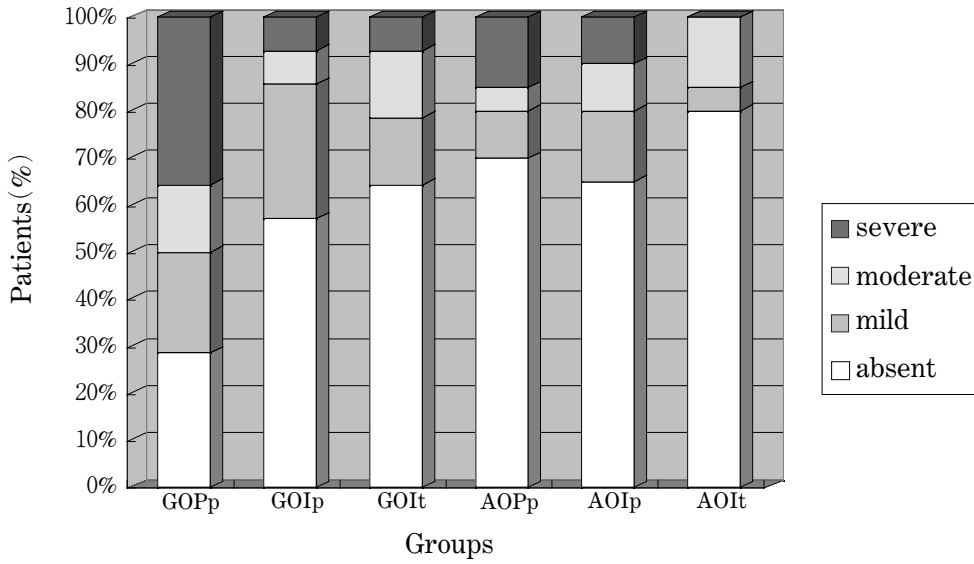


Fig. 1. Postoperative pain assessed by patients as absent, mild, moderate, or severe when interviewed by an anesthetist right after awakening. Postoperative pain in the GOPp group was severer than that in the epidural groups (AOPp, AOIp, AOIt).

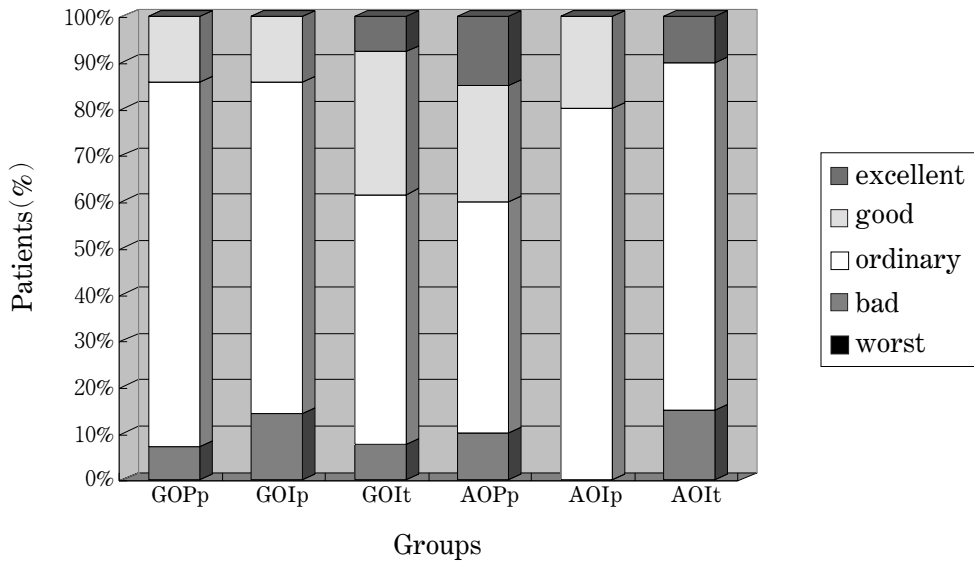


Fig. 2. Postoperative mood rated by patients as excellent, good, ordinary, bad, or worst when interviewed by an anesthetist right after awakening. There were no significant differences among the six groups.

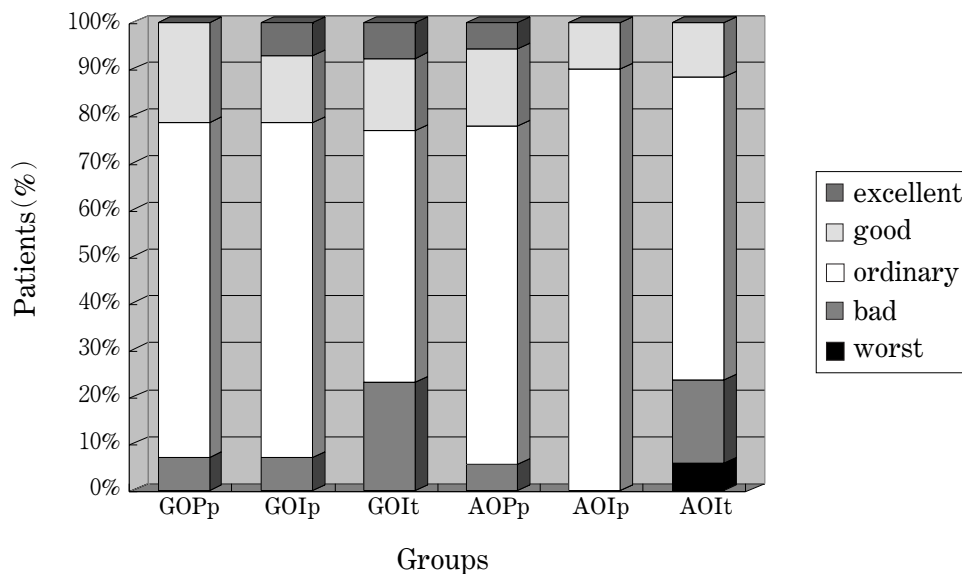


Fig. 3. Postoperative mood rated by patients as excellent, good, ordinary, bad, or worst when interviewed by an anesthetist on the next day following surgery. There were no significant differences among the six groups.

in patients with isoflurane and epidural anesthesia (AOIt, AOIp) were shorter than those in patients with isoflurane and nitrous oxide (GOIt, GOIp). This was probably due to the differences in anesthetic depth, although nitrous oxide might have influenced the recovery. However, shorter recovery of patients with propofol and epidural anesthesia (AOPp) was only seen in the date and place oriented times when compared with patients with propofol and nitrous oxide (GOPp). In addition, the recovery times in patients with propofol and epidural anesthesia (AOPp) were significantly longer than those in patients with bolus administration of propofol followed by isoflurane and epidural anesthesia (AOIp). These results are not in agreement with previous studies showing that propofol promotes faster clinical recovery than isoflurane anesthesia⁵⁻¹⁰). However, Zuurmond *et al.*¹¹) have reported that recovery tests showed no differences between isoflurane and propofol accom-

panied with nitrous oxide (GOIp vs. GOPp). This is compatible with our results. Kirvelä *et al.*¹³) also indicated that the recovery parameters were similar for both total intravenous anesthesia with propofol (AOPp) and isoflurane with nitrous oxide (GOIt). This represents a slight difference from our case. We cannot simply compare the GOIt group with the AOPp group because we used an epidural technique in the AOPp group, we did not use narcotics such as fentanyl or alfentanil, and the anesthetic depth might be totally different. When comparing the AOPp and AOIp groups, the recovery times from propofol anesthesia were longer than those from isoflurane, despite of the body temperature being higher. This may possibly have been due to the difference in anesthetic depth at the end of operation between propofol and isoflurane anesthesia.

Doze *et al.*¹⁴) have reported that for non-major surgeries, the times to awakening, responsive-

ness, orientation, and ambulation were significantly shorter with propofol (GOPp) than with isoflurane (GOIt), but for major abdominal operations, recovery characteristics did not differ between the propofol and isoflurane groups. This is consistent with the results of Kalman *et al.*¹⁵⁾ that the early and late recoveries of psychomotor function from major abdominal surgery were similar among AOPp, GOPp and GOIt groups. On the other hand, for non-major surgery such as elective termination of pregnancy, it was reported that initial recovery is more rapid in the propofol group (GOPp) than in the isoflurane group (GOIp)¹⁶⁾. These facts suggest that after major surgery the influence of operation would be so great that differences in anesthetic technique may be negligible.

Thiamylal is a commonly used ultra short-acting barbiturate with a potency 1.1 times that of thiopental and clinical properties virtually identical to those of thiopental. We used thiamylal as an induction agent for comparison with propofol. Previous studies have suggested that propofol is a better induction agent than thiopental¹⁻³⁾. However, in this study there were no significant differences in the recovery times, incidence of postoperative nausea and vomiting (PONV) or mood between the GOIp and GOIt groups or between the AOIp and AOIt groups. As the above studies^{2,3)} except reference 1¹⁾ are short procedures, anesthesia time may be an important factor in recovery when compared with different anesthetic techniques. In fact, the faster recovery and less PONV give propofol an advantage over thiamylal or thiopental in outpatient anesthesia^{17,18)}.

Postoperative pain in the GOPp group was severer than that in the epidural groups (AOPp, AOIp, AOIt). As we interviewed the patients immediately after they awoke, the conscious state in the GOPp group might have been clear-

er than in the GOIp and GOIt groups although there were no significant differences in awakening times among the groups. However, it is interesting to note that there were no significant differences among all groups in the incidence of PONV and mood on the operation day or the next day. In addition, the combination of nitrous oxide with propofol or isoflurane did not change the degree of symptoms. Many studies have shown that propofol causes less emesis and better mood than isoflurane^{4,6,8-10,15)} or thiopental^{3,17)} despite the presence of nitrous oxide. Although we do not know the exact reason why there were no differences in the post-operative conditions, we found that nitrous oxide did not increase the incidence of PONV after propofol or isoflurane anesthesia. The latter event is consistent with Korttila's report¹⁹⁾. Recently, Harper *et al.*²⁰⁾ and Bree *et al.*²¹⁾ denied the efficacy of propofol in the treatment of PONV. However, Gan suggested the importance of therapeutic dose ranges of propofol for antiemetic effects^{22,23)}.

There are limitations in our study. The study was not double-blinded; because of limited staff numbers, the recovery was not judged by a second anesthetist unaware of the anesthetic technique used. There was also a significant difference in sex ratio among the groups. This would have affected the results of our study. The reason for the higher numbers of females in the epidural groups results from the fact that lower abdominal surgery consisted mostly of gynecological procedures. We could not compare patients with nitrous oxide and those without nitrous oxide for the same anesthetic and surgical levels, that is to say, one with epidural anesthesia and one without. This stems from the considerable variation in the types of surgery; patients scheduled for allocation to nitrous oxide groups differed from those scheduled to

epidural groups. It may not be therefore reasonable to undertake statistical comparison between these two subsets of patients. However, our study has an advantage over other studies; it should not have been affected by the premedicated drugs and narcotics.

In conclusion, propofol could not provide a rapid emergence with less PONV when compared with isoflurane. Propofol as an induction agent did not show better results than thiamylal after isoflurane anesthesia. Nitrous oxide did not increase the incidence of PONV after propofol or isoflurane anesthesia.

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