Pharmacoeconomics of Propofol Versus Thiopental for Induction of Anaesthesia in Short Procedures

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ABSTRACT

This study compared the costs and benefits of using propofol/fentanyl versus thiopental/fentanyl for induction of anaesthesia in short procedures. A prospective, cohort trial was conducted in conjunction with a patient survey. The study population included a consecutive sample of American Society of Anaesthesiologists. Class I or II patients who underwent short operative procedures and who were given one of the studied anaesthetic regimens. Insoflurane/N_2O was used for maintenance of anaesthesia in all cases. Propofol patients showed a significantly shorter time to eye opening ($p=0.0025$); orientation to date of birth, place, and day of week ($p=0.0002$); time to consciousness ($p=0.0019$); and time in recovery room ($p=0.013$); but not time to tolerating 50 mL of oral fluid ($p=0.06$). Nausea and vomiting occurred in 41% of thiopental patients and 19% of propofol patients (difference 22%; 95% C.I., -1% to 44%). Based on survey results, propofol patients subjectively reported fewer side effects upon returning home and were able to resume daily activities earlier than thiopental patients. With the current staffing and patient load at our institution, an estimated 4.8 hours of nursing time per day would be made available if propofol were used in place of thiopental for induction of anaesthesia in these procedures. If propofol were used for all daycare surgery patients in our institution, the annual acquisition cost is projected to be $60,331.28 versus $8,079.68 for thiopental. In conclusion, the use of propofol for induction of anaesthesia in short procedures is more expensive than thiopental but may yield qualitative advantages including more rapid recovery, less nausea and vomiting, and less burden on recovery room nursing staff.

Key Words: *pharmacoeconomics, propofol, thiopental.*

Can J Hosp Pharm 1995; 48:208-213

RÉSUMÉ

On a comparé, au cours de cette étude prospective avec cohorte qui a été menée conjointement à un sondage auprès des mêmes patients, les coûts et les avantages de l'association propofol/fentanyl à ceux de l'association thiopental/fentanyl pour l'induction de l'anesthésie dans les interventions de courte durée. La population de l'étude comprenait un échantillon consécutif de patients de classe I ou II de l'American Society of Anesthesiologists qui ont subi une brève opération et reçu l'un des deux régimes anesthésiques àl'étude. Le maintien de l'anesthésie était assuré dans tous les cas par l'isoflurane et le N_2O. On a noté une diminution du temps d'ouverture des yeux ($p = 0,0025$), du temps d'orientation; évocation de la date de naissance, des lieux et du jour de la semaine ($p = 0,0002$), du temps de reprise de conscience ($0 = 0,0019$) et du temps en salle de réveil ($p = 0,013$), mais non du temps pour garder 50 mL de liquide ($p = 0,06$), chez les patients qui ont reçu du propofol comparativement à ceux qui ont reçu du thiopental. Ces derniers ont éprouvé des nausées et des vomissements dans 41 % des cas, comparativement à 19 % chez ceux qui avaient reçu du propofol (différence de 22 %, intervalle de confiance de 95 %, écart - 1 % à 44 %). Selon les résultats du sondage, l'évaluation subjective des patients qui ont reçu du propofol montre qu'ils ont eu moins d'effets secondaires à leur retour à la maison et qu'ils étaient capables de reprendre leurs activités quotidiennes plus rapidement que ceux qui avaient reçu du thiopental. Avec le personnel actuel et le nombre de patients par infirmier(ère) à notre établissement, nous pourrions consacrer 4,8 heures du plus en temps de soins par jour si le propofol était utilisé à la place du thiopental pour l'induction de l'anesthésie dans les interventions de courte durée. Le coût d'achat annuel du propofol pour toutes les chirurgies d'un jour dans notre établissement s'élèverait à 60 331,28 $ comparativement à 8 079,68 $ pour le thiopental. Le recours au propofol serait certes plus cher que l'usage du thiopental, mais il concéderait des avantages qualitatifs comme un réveil plus rapide, moins de nausées et de vomissements et moins d'heures affectées en salle de réveil pour le personnel infirmier.

Mots clés : *pharmacoéconomie, propofol, thiopental.*

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Acknowledgments: The authors would like to acknowledge Linne Storey, Head Nurse of PAR and Daycare Surgery at Lions Gate Hospital, and her whole nursing staff for patiently preparing the charts and monitoring the patients. Ruth Milner of U.B.C. Hospital Shaughnessy Site Research Centre for her statistical work. Dr. Francis C. Ping, Head of Anaesthesia at Lions Gate Hospital, for his help and suggestions. Dr. Bruce Carlton of the Pharmacy Department at B.C. Children's Hospital for his advice on our protocol.

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INTRODUCTION

Propofol's rapid onset of action, short duration of effect, and low incidence of side effects make it well suited for anaesthesia in short surgical procedures. While many studies have demonstrated advantages of propofol for total anaesthesia,[1-11] propofol has also been shown to reduce recovery time and adverse effects when used strictly for induction.[12-21] The high acquisition cost of propofol compared to that of traditional anaesthetic agents raises questions about its cost-effectiveness. Several authors have examined this issue;[8-11] however, these studies have all utilized regimens in which propofol was used for both induction and maintenance. We designed this study to compare the costs and benefits of propofol and thiopental for induction of anaesthesia in short procedures. Specifically we looked at recovery times, incidence of nausea and vomiting, and nursing hours per patient. Through a patient survey we also assessed side effects after discharge and the ability to resume daily activities.

METHODS

Propofol was compared to thiopental for induction of anaesthesia in short daycare procedures in a prospective, cohort study. The study included a consecutive sample of patients undergoing short procedures between September 21 and December 24, 1992. Patients were included in the study if they were classified as ASA I or II (as per the American Society of Anaesthesiologists guidelines[22]); underwent cystoscopy $\pm$ pyelogram, laparoscopic tubal ligation, dilation and curettage, or termination of pregnancy; were given propofol/fentanyl or thiopental/fentanyl for induction of isoflurane/N_2O maintained anaesthesia; and were older than 19 years. Patients were excluded if they did not meet the criteria listed above. The choice of the anaesthetic was at the discretion of the anaesthetist.

After the procedure, patients were discharged to the post anaesthetic recovery unit (PAR) where nursing staff, who were unaware of the anaesthetic agents used (anaesthetic records were not available in PAR), recorded the patient's recovery time from the end of surgery in terms of: time to spontaneous eye opening; orientation to date of birth, place, and day of week; time when the patient could tolerate 50 mL of clear oral fluid; time to consciousness defined as achieving a Steward scale[23] of 6, and total time spent in recovery. The number of nausea and vomiting episodes experienced in PAR was also recorded. Patients were requested to complete a questionnaire at approximately 24 hours after their procedure to document side effects experienced at home including nausea, vomiting, difficulty sleeping, headache, and weakness. The survey also included patients' estimates of when they were able to eat, resume leisure activities, and return to work. Finally, the questionnaire asked whether the patient had undergone previous surgery, whether they would choose the same anaesthetic if they required subsequent surgery, and asked for any additional comments.

A minimum required sample size of 14 patients per group was estimated to detect a 15% difference in time to eye opening ($\alpha = 0.05$, $\beta = 0.20$) based on recovery results from previous studies where propofol and thiopental were used for induction.[3,6,7,12,19,24] The group comparability and length of recovery times calculated from the end of the procedure were analyzed statistically using descriptive statistics and multiple regression analysis, where appropriate. Each nausea and vomiting episode was estimated, based on nursing experience, to consume five minutes of nursing time to account for patient monitoring, clean up, and medication administration. Comments on the returned patient questionnaires were summarized to identify patients' subjective opinions regarding the agent they received. Cost calculations were based on a propofol acquisition cost of $8.88/200mg ampoule and $7.88/2.5g vial of thiopental. All costs are in Canadian dollars. Annual cost projections assume 8726 patients per year which was the number of daycare operations done at our institution from April 1, 1992 to March 31, 1993.

RESULTS

Fifty-two propofol and 22 thiopental patients were included over the three-month study period. All patients enrolled in the study were used in the data analysis. Patients received an average dose $\pm$ SD of 2.29 $\pm$ 0.45 mg/kg of propofol or 4.32 $\pm$ 0.73 mg/kg of thiopental for induction, and nitrous oxide in oxygen with isoflurane 0 to 4% for maintenance. Patients also received succinylcholine, vecuronium, and/or d-tubocurarine. Twenty-seven patients received 20 to 50 mg of lidocaine prior to the propofol to reduce pain on injection.

The differences in patient age, weight, sex, ASA grouping, fentanyl dose, and length of procedure are listed in Table I along with 95% confidence intervals. When these group comparability parameters were included as independent variables in multiple regression analysis, none were associated with outcome (i.e., recovery times studied). The proportion of patients in the two study groups undergoing each procedure is also listed in Table I.

Propofol patients showed a significantly shorter time to eye opening, orientation, time to consciousness, and time spent in recovery room, but not time to tolerating 50 mL of oral fluid (Table II).

Based on the average doses of propofol and thiopental quoted above, a mean patient weight of 68 kg (Table I), and the annual daycare surgery patient load at our institution, the annual drug acquisition cost for

Table I: Group Comparability

	Propofol n=52	Thiopental n=22	Difference (95% C.I.)
Mean age, yrs (SD)	43.7 (15.94)	50.4 (18.94)	6.7 (-2.3 to 15.7)
Sex, % male	25.0	13.6	-11.4 (-29.9 to 7.2)
Mean weight, kg (SD)	67.63 (14.05)	67.97 (14.22)	0.34 (-6.72 to 7.40)
ASA I/II	37/15	13/9	
Mean length of surgery, min (SD)	8.83 (6.019)	13.86 (8.061)	5.03 (1.28 to 8.77)
Mean fentanyl dose, mcg/kg (SD)	1.12 (0.499)	0.87 (0.260)	-0.25 (-0.42 to -0.08)
Procedures:			
laporoscopic tubal ligation	1 (2%)	3 (14%)	
pregnancy termination	12 (23%)	2 (9%)	
dilatation and curettage	19 (36%)	7 (32%)	
cystoscopy	3 (6%)	3 (14%)	
cystoscopy and pyelogram	17 (33%)	7 (32%)	

Table II: Recovery Outcomes

	Propofol Mean (min)	SD	Thiopental Mean (min)	SD	p
	(n = 52)		(n = 22)		
Time to eye opening	7.00	4.30	10.91	4.83	0.0025
Time to consciousness	8.25	4.64	13.32	6.03	0.0019
Time spent in recovery room	111.46	26.36	142.55	49.95	0.013
	(n = 52)		(n = 13)		
Time to orientation	9.30	6.01	14.5	6.91	0.0002
	(n = 43)		(n = 14)		
Time to tolerating 50 mL of oral fluid	53.79	26.61	76.07	30.49	0.06

all daycare patients to be induced with propofol would be $60,331.28 versus $8,079.68 for thiopental. This does not take into account wastage from discarding partly used vials or ampoules. Quantification of wastage was not possible; however, it was assumed to be small since anaesthetists involved in the cases studied generally save part vials for subsequent cases.

Nausea and vomiting occurred in 41% (9/22) of thiopental patients and 19% (10/52) of propofol patients (difference 22%; 95% C.I., -1% to 44%). This included 12 episodes in the thiopental group versus 11 episodes in the propofol group. Antiemetics (dimenhydrinate or prochlorperazine) were used in five thiopental and seven propofol patients.

An estimate of nursing time required to attend to patients recovering from propofol induction versus thiopental induction was calculated. Using an estimate of five minutes of nursing time to attend to each nausea and vomiting episode, nurses spent 2.7 minutes for this activity in each thiopental patient and 1.1 minutes for each propofol patient, representing a difference of 1.6 minutes per patient. The mean difference in time spent in the recovery room was 31.09 minutes (Table II). Given our institution's standard of one nurse to three patients, this would free 10.36 minutes of nursing time per patient. Therefore, nursing time would be reduced by 11.96 minutes to attend to a patient recovering from propofol induction. At our institution, this translates to an average of 4.8 hours per day if all surgical daycare patients were induced with propofol versus thiopental.

Fifty percent (11/22) of thiopental patients and 33% (17/52) of propofol patients returned their questionnaires (Table III). In the 24 hours following their procedure, a higher percentage of thiopental patients reported side effects and a higher percentage of propofol patients were able to eat, resume leisure activities, and return to work. It should be noted that a higher percentage of thiopental patients indicated they were retired and thus could not be assessed with respect to the timing of their return to work. Side effects listed as "other" for propofol included neck- or backache (two patients), perspiring (one patient), pain of injection (one patient), cramps (two patients), tongue quivering (one patient), and dizziness (one patient), while those listed for thiopental included sore throat (one patient), neck- or backache (two patients), chest pain (one patient), and tiredness (two patients).

DISCUSSION

Propofol has been used for induction and maintenance of anaesthesia in a large number of trials investigating its impact on recovery and side effect profile.[1-11] Most of these studies have shown shorter recovery times[1-11] and fewer side effects[3-11] compared to traditional anaesthetics. Investigators have also compared propofol to traditional induction agents when inhalation anaesthetics are used for maintenace.[12-21,25,26] While the majority of these trials have demonstrated a reduced recovery period,[12-21] the observations

Table III: Response to Patient Survey

	Propofol (%) n = 52	Thiopental (%) n = 22
Response	17 (33)	11 (50)
Nausea	3 (18)	4 (36)
Vomiting	2 (12)	2 (18)
Difficulty sleeping	1 (6)	1 (9)
Headache	6 (35)	3 (27)
Weakness	3 (18)	4 (36)
Other	9 (53)	6 (55)
Able to eat:		
right away	2 (12)	0
same day	13 (76)	7 (64)
next day	1 (6)	2 (18)
more than 24 hours	0	1 (9)
survey incomplete	1 (6)	1 (9)
Resume leisure activities:		
right away	1 (6)	0
same day	13 (76)	5 (45)
next day	3 (18)	1 (9)
more than 24 hours	0	1 (9)
survey incomplete	0	1 (9)
Return to work:		
same day	0	0
next day	6 (35)	1 (9)
more than 24 hours	4 (24)	3 (27)
retired	2 (12)	4 (36)
survey incomplete	5 (29)	3 (27)
Previous surgery:		
yes	15 (88)	9 (82)
no	2 (12)	1 (9)
survey incomplete	0	1 (9)
Would you choose the same anaesthetic?		
yes	14 (82)	6 (55)
no	3 (18)	4 (36)
survey incomplete	0	1 (9)

regarding adverse effects have not been as consistent.

All of the published trials which have investigated propofol's cost-effectiveness compare regimens utilizing propofol for both induction and maintenance to more traditional regimens involving an injectable induction agent and inhalation anaesthetics for maintenance.[8-11] While most of these studies showed benefits through a varied reduction in recovery time and adverse effects,[8,9,11] one author concluded that the routine use of propofol for day-surgery patients was not justified.[10]

Our study is the first to investigate the cost-benefit of propofol versus thiopental when used strictly for induction of anaesthesia in short procedures. Propofol patients showed significantly shorter recovery than thiopental patients. We believe the induction agent was primarily responsible for the differences in the measured recovery times based on the results of multiple regression analysis which indicated that age, sex, weight, ASA class, length of surgery and fentanyl dose did not influence recovery times. The proportion of patients undergoing each procedure was similar between the two study groups (Table I). Our results also suggest that the use of propofol is associated with less nausea and vomiting than thiopental.

It is difficult to draw conclusions about the cost advantages of propofol as its benefits do not correspond to a direct dollar value. The reduced nursing time to attend to propofol patients cannot be projected to a cost-savings since staffing levels are predetermined and cannot fluctuate in small increments to adjust for reduced workload. In order to take advantage of the potential 4.8 hours per day of nursing time made available with the exclusive use of propofol for induction in the studied procedures, significant changes in the PAR staffing system would have to be implemented. Without such changes, this advantage would be limited to increasing the amount of nursing time available per patient. It may increase the capacity of the PAR; however, the number of operations performed per day also depends on the number of surgeons and the operating room capacity.

The results of the patient survey show that a higher percentage of propofol patients indicated that they would choose the same anaesthetic if they had another surgery. The decreased incidence of nausea and vomiting in this group probably contributed to this. It should be noted that the majority of patients in both groups had undergone previous surgery allowing an informed assessment of their anaesthetic experience. The patient survey results also indicate that propofol patients were able to resume leisure activities and return to work sooner than thiopental patients which would presumably hasten their return to normal productivity. The fact that more thiopental patients were retired may have influenced this result.

Our results should be interpreted with caution for several reasons. First, this was not a randomized trial and

the choice of anaesthetic agents used was at the discretion of the anaesthetist. Of the five anaesthetists involved in the cases studied, one was involved in a single case (thiopental was used), one used thiopental exclusively, and two used propofol exclusively. Only one anaesthetist selected between the two agents for these procedures. He tended to use thiopental for cystoscopy and pyelograms, while propofol was used for gynecological procedures. Despite this tendency, the overall proportion of urological versus gynecological procedures was similar between the groups (39% versus 61% for propofol, 45% versus 55% for thiopental). We tried to account for potential bias associated with the anaesthetists' selection of the induction agent through multiple regression analysis of group comparability parameters. The results indicate that none of the comparability parameters studied were associated with the measured differences in recovery times.

Another point worthy of comment was the incomplete documentation for two of our recovery time parameters: orientation (13/22 thiopental) and time to tolerating 50 mL of oral fluid (43/52 propofol, 14/22 thiopental). This could indicate serious bias. However, even if these results are ignored, there is still a statistically significant difference for three commonly measured recovery parameters. As well, the 95% confidence interval for nausea and vomiting included zero, which suggests the possibility of no difference between the groups for this parameter. On the other hand, the interval was very much skewed in favour of propofol and there was a large absolute difference (22%). Finally, the nature of the patient survey precluded statistical analysis and; therefore, no definite conclusions should be drawn from this information.

One should keep in mind that the procedures studied were very brief and may not represent a typical case load in all institutions which utilize propofol for induction of anaesthesia. At many institutions, longer and more diverse cases are being treated as outpatient procedures. The doses of propofol and thiopental used in this study were comparable to previous studies.[12-21,25]

The results of this study suggest that there may be advantages associated with the use of propofol in place of thiopental for induction of anaesthesia in short procedures, but these results should be validated with a randomized, blinded, prospective study. Whether these advantages justify the added expense of propofol should be an institution-specific decision including consideration of the quality of the patients' experience and the amount of nursing care required in the recovery room.

REFERENCES

1. Cork RC, Scipone P, Vonesh MJ, et al. Propofol infusion vs. thiopental/ isoflurane for outpatient anesthesia. *Anesthesiology* 1988; 69(suppl 3A):A563.
2. Gold MI, Sacks DJ, Grosnoff DB, et al. Comparison of propofol with thiopental and isoflurane for induction and maintenance of general anesthesia. *J Clin Anesth* 1989; 1:272-6.
3. Korttila K, Nuotto EJ, Lichtor JL, et al. Clinical recovery and psychomotor function after brief anesthesia with propofol or thiopental. *Anesthesiology* 1992; 76:676-81.
4. Sanders LD, Clyburn PA, Rosen M, et al. Propofol in short gynaecological procedures. *Anaesthesia* 1991; 46:451-5.
5. Kashtan H, Edelist G, Mallon J, et al. Comparative evaluation of propofol and thiopentone for total intravenous anaesthesia. *Can J Anaesth* 1990; 37:170-6.
6. Boysen K, Sanchez R, Krintel JJ, et al. Induction and recovery characteristics of propofol, thiopental and etomidate. *Acta Anaesthesiol Scand* 1989; 33:689-92.
7. DeGrood PMRM, Harbers BM, vanEgmond J, et al. Anaesthesia for laparoscopy: a comparison of five techniques including propofol, etomidate, thiopentone and isoflurane. *Anaesthesia* 1987; 42:815-23.
8. Sung YF, Reiss N, Tillette T. The differential cost of anesthesia and recovery with propofol-nitrous oxide anesthesia versus thiopental sodium-isoflurane-nitrous oxide anesthesia. *J Clin Anesth* 1991; 3:391-4.
9. Killian A, Hamilton P, Tierney M. Propofol versus thiopental-isoflurane in outpatient surgical procedures. *Can J Hosp Pharm* 1992; 45:139-44.
10. Cade L, Morley PT, Ross AW. Is propofol cost-effective for day-surgery patients. *Anaesth Intensive Care* 1991; 19-201-4.
11. Marais ML, Maher MW, Wetchler BV, et al. Reduced demands on recovery room resources with propofol (Diprivan) compared to thiopental-isoflurane. *Anesthesiol Rev* 1989; 16:29-40.
12. Gold MI, Abraham EC, Herrington C. A controlled investigation of propofol, thiopentone and methohexitone. *Can J Anaesth* 1987; 34:478-81.
13. MacKenzie N, Grant IS. Comparison of the new emulsion formulation of propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. *Br J Anaesth* 1985; 57:725-31.
14. Rolly G, Verichelen L. Comparison of propofol and thiopentone for induction of anaesthesia in premedicated patients. *Anaesthesia* 1985; 40:945-8.
15. Raeder JC, Misvaer G. Comparison of propofol induction with thiopentone or methohexitone in short outpatient general anaesthesia. *Acta Anaesthesiol Scand* 1988; 32:607-13.
16. Heath PJ, Kennedy DJ, Ogg TW, et al. Which intravenous induction agent for day surgery? *Anaesthesia* 1988; 43:365-8.
17. Edelist G. A comparison of propofol and thiopentone as induction agents in outpatient surgery. *Can J Anaesth* 1987; 34:110-6.
18. O'Toole DP, Milligan KR, Howe JP, et al. A comparison of propofol and methohexitone as induction agents for day case isoflurane anaesthesia. *Anaesthesia* 1987; 42:373-6.
19. Valtonen M, Kanto J, Rosenbert P. Comparison of propofol and thiopentone for induction of anaesthesia for elective Caesarean section. *Anaesthesia* 1989; 44:758-62.
20. Morison DH, Dunn GL. A comparative study of Diprivan and thiopental as induction agents in dental patients (abstract). *Anesth Analg* 1987; 66:S123.
21. Chittleborough MC, Osborne GA, Rudkin GE, et al. Double-blind comparison of patient recovery after induction with propofol or thiopentone

for day-case relaxant general anaesthesia. *Anaesth Intensive Care* 1992; 20:169-73.
22. Schneider AJL. Assessment of risk factors and surgical outcome. *Surg Clin North Am* 1983; 63:1113-26.
23. Steward DJ. A simplified scoring system for the post-operative recovery room. *Can Anaesth Soc J* 1975; 22:111-2.
24. Dunn GL, Morison DH. Diprivan (propofol) and thiopental as induction agents in dental outpatients. *Semin Anesth* 1988; 7:(Suppl 1)26-8.
25. Moore J, Bill KM, Flynn RJ, et al. A comparison between propofol and thiopentone as induction agents in obstetric anaesthesia. *Anaesthesia* 1989; 44:753-7.
26. Sanders LD, Isaac PA, Yeomans WA, et al. Propofol-induced anaesthesia: double-blind comparison of recovery after anaesthesia induced by propofol or thiopentone. *Anaesthesia* 1989; 44:200-4.