General Anesthesia

Desflurane improves the throughput of patients in the PACU. A cost-effectiveness comparison with isoflurane

[L'usage du desflurane permet de réduire l'occupation de la SDR : étude de rentabilité comparée avec l'isoflurane]

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Purpose: In a pharmacoeconomic approach of anesthesia, postanesthesia care unit (PACU) occupancy can be chosen as a criteria of effectiveness to compare two anesthetic drugs with different rates of elimination and different costs of administration. Our objective was to develop a cost-effectiveness approach for the comparison of isoflurane (I) and desflurane (D).

Method: In this prospective observational study, 68 patients aged 18–70 received either D or I for maintenance of anesthesia for inpatient abdominal procedures. Length of stay (LOS) in PACU was collected by a blinded observer. After the relationship between duration of surgery and LOS in PACU had been established in the 68 observed patients, we estimated the PACU occupancy according to duration of surgery and time of admission in PACU using a computer model of 204 consecutive patients, based on the hypothesis of an exclusive use of either D or I. Outcome measures were direct costs of the anesthesia procedure and occupancy of the PACU.

Results: The direct cost of the anesthetic was significantly higher with D than with I. This represents an increase of CAN\$ 2 708 for the 204 patients. PACU occupancy was reduced by at least one patient (out of five beds) during 26.1% of the time with D ($P < 0.01$).

Discussion: Improving the throughput of patients in PACU by using new halogenated anesthetic agents with faster rates of elimination may outweigh the incremental cost of this strategy. This becomes particularly meaningful in operating theatres experiencing frequent overcrowded periods.

Objectif : L'occupation de la salle de réveil (SDR) peut être choisie comme critère pour réaliser une étude coût-efficacité entre deux agents d'anesthésie de coûts d'administration différents. Le but du présent travail est de réaliser une comparaison coût-efficacité entre l'isoflurane (I) et le desflurane (D).

Méthode : Dans cette étude prospective observationnelle, 68 patients de 18 à 70 ans, hospitalisés pour une intervention chirurgicale abdominale, ont reçu soit I, soit D pour le maintien de l'anesthésie. La durée de séjour (DDS) en SDR était mesurée par un observateur indépendant. Après avoir établi la relation liant la durée opératoire et la DDS en SDR pour les 68 patients observés, nous avons bâti un modèle permettant de prédire l'occupation en SDR en fonction de la durée d'opération et de l'heure d'arrivée en SDR pour 204 patients consécutifs avec l'hypothèse d'une utilisation exclusive soit de I, soit de D. Les paramètres évalués ont été le coût d'administration et l'occupation de la SDR.

Résultats : Pour les 204 patients du modèle, le surcoût lié à l'utilisation de D a été de 2 708 \$ CAN. Avec le D, l'occupation de SDR a été réduite d'au moins un patient (sur cinq postes) durant 26 % du temps d'ouverture de la SDR ($P < 0,01$).

Conclusion : La réduction de l'occupation de la SDR peut compenser le surcoût entraîné par l'usage de D par rapport à I. Cela est particulièrement intéressant dans les SDR où il existe des périodes de saturation.

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OPTIMIZING the organization of the operating room (OR) may have important economic implications.¹ Among the factors influencing the organization of the OR, length of stay (LOS) in the postanesthesia care unit (PACU) could determine the throughput of the patients² and may have direct economic repercussions mainly related to staffing workload and organizational outcomes.³⁻⁵ Thus, in a pharmacoeconomic approach of anesthesia, the LOS in the PACU, by influencing the occupancy of the PACU, can be chosen as a criteria of effectiveness to compare two anesthetic drugs associated with different direct costs.

New halogenated anesthetics with faster rates of elimination, like desflurane (D), allow for faster recovery from anesthesia than older agents like isoflurane (I).⁶ The benefit of this faster recovery increased with increased duration of anesthesia.⁷ None of these controlled studies demonstrated that faster recovery from anesthesia may reduce the LOS of the patients in PACU, thereby reducing the patients' occupancy in the PACU.

After pharmacologic differences between drugs have been clearly established by randomized-controlled trials, it has been advocated to evaluate drugs with observational studies in the wider and more realistic conditions of clinical practice.^{8,9} Observational (also labelled effectiveness or pragmatic) studies offer the advantage of taking into account numerous factors affecting drug handling, related to practitioner experience, clinical habits, and the complex interactions between the patient, the physician and the healthcare system. Such studies sacrifice some internal validity in order to improve the generalizability and the clinical significance of the conclusions. Under observational conditions, when physicians are free to select the delivered concentration and the time of agent discontinuation prior to the expected end of the procedure, D still leads to a faster recovery than I after surgical procedures lasting more than 100 min.¹⁰ Among the numerous variables influencing the LOS in PACU,^{11,12} we hypothesized that the choice of halogenated agent might have some influence. The organizational impact of this hypothesis remains to be established.

This observational study, based on clinical daily practice, was undertaken to establish the differential cost-effectiveness ratio of two different halogenated anesthetic drugs with different rates of elimination. The occupancy of the PACU was considered as the main outcome measure. We hypothesized that use of D would result in lesser patient occupancy of the PACU.

Methods

Study conditions

After Ethical Committee approval and patient informed consent, the study was initiated in patients aged 18–70, ASA physical status I or II, scheduled for abdominal inpatient surgeries of various durations. Subjects received either D (group D) or I (group I) for the maintenance of anesthesia with alternative allocation, i.e., when an agent was used, the next patient anesthetized by the same practitioner received the other. This was done to avoid a specific inclusion selection of the halogenated agent by a particular practitioner involved in the study.

Forty patients in each group were planned. *A priori* exclusion criteria were patients ASA physical status III or IV and patients requiring prolonged postoperative sedation or ventilatory support for surgical reasons (esophageal resection and major liver surgery). *A posteriori* exclusion criteria were unplanned need for postoperative sedation, incomplete data collection (i.e., the exact time of completion of wound closure or the delivered concentration of volatile agent throughout the procedure), or deviation from the protocol (i.e., use of another induction agent than thiopental or another opiate than sufentanil during the course of anesthesia or modification of fresh gas flow). Patients withdrawn from the final analysis were not replaced.

The study was purely observational. Physicians were free to use the inhaled agents as they wished. Ability for the patient to be discharged from PACU was evaluated by an anesthesiologist blinded to the inhaled agent administered. All variables were collected by a resident in pharmacy unaware of the treatment group.

The PACU under consideration is in a surgery unit of 120 beds in a University Hospital. Approximately 4,000 operations are performed each year. The operating theatre includes four operating rooms and five PACU beds. The PACU is open from 9 a.m. to 8 p.m. and is staffed by nurses. One nurse supervises the PACU from 9 a.m. to 4 p.m. and another one from 12 a.m. to 8 p.m. Thus, there is an overlap of two nurses caring for the patients in the PACU between 12 a.m. to 4 p.m., which corresponds to the most active work period.

The study started at the induction of anesthesia and ended at the departure of the patient from the PACU.

Evaluation was performed after implementation of a quality assurance program associated with the reorganization of patient's flow and standardization of our anesthetic practices.

Anesthetic procedure

The study protocol corresponded to usual clinical practice in the institution. All practitioners had exten-

sive experience with the use of the inhaled agents under investigation.

After premedication with oral hydroxyzine 1.5 mg·kg⁻¹ one hour before surgery, anesthesia was induced with thiopental 3–5 mg·kg⁻¹, sufentanil 0.2–0.3 µg·kg⁻¹ and atracurium 0.5 mg·kg⁻¹ and maintained with a continuous infusion of atracurium, repetitive boluses of sufentanil of 0.1 µg·kg⁻¹ and halogenated agents. D or I was delivered in a mixture of O₂/N₂O (50%–50%) at 1 L·min⁻¹ fresh gas flow. Fresh gas flow was maintained constant during the course of anesthetic administration. If fresh gas flow was modified patients were withdrawn from the final analysis. No specific recommendations were given to practitioners regarding the administration of anesthetic agents. Physicians were free to select the delivered concentration and the time of agent discontinuation prior to the expected end of the procedure.

The continuous infusion of atracurium was stopped 30 min before the expected end of the procedure. The last bolus of sufentanil was injected at least 30 min before the expected end of the procedure.

At the end of the procedure, fresh gas flow was increased to 6 L·min⁻¹ oxygen 100%. Residual neuromuscular blockade was antagonized with neostigmine (40 µg·kg⁻¹), and atropine (15 µg·kg⁻¹).

Intraoperative hypothermia was prevented with hot air warming system (Bair Hugger®, Augustine Mediale, Minneapolis, MN, USA).

Postoperative analgesia was implemented in the PACU with propacetamol (2 g) and *iv* morphine titration (2 mg bolus every five minutes) until adequate pain relief. Postoperative nausea and vomiting (PONV) were treated with metoclopramide 10 mg intravenously. If PONV still persisted 30 min later, ondansetron 4 mg was administered intravenously.

Patients were considered fit for discharge from the PACU after the following criteria were reached :

- Aldrete score of 10¹³
- Adequate pain relief (visual analog scale < 3/10)
- Absence of nausea and/or vomiting
- Absence of surgical complication (bleeding...)

The end of the surgery was selected as the baseline of our evaluation (T0).

Study variables

RESOURCE CONSUMPTION

All medications and supplies to anesthetize each patient were recorded. Anesthetic drugs other than halogenated agents included nitrous oxide, thiopentone, sufentanil and atracurium. All open vials were considered as fully consumed. Non-anesthetic drugs included antibiotics, *iv* fluids, analgesics, antiemetics and myorelaxant antagonists (Table I).

TABLE I Drug costs (quantity; price list AP-HP 1999)

		Cost (CAN\$)
<i>Halogenated agents</i>	Desflurane (100 mL)	33.4
	Isoflurane (100 mL)	25.6
<i>Other anesthetic drugs</i>	Thiopental (0.5 g)	1.2
	Sufentanil (50 µg)	2.1
	Atracurium (50 mg)	5.6
	Nitrous oxide (1 m ³)	3.85
<i>Non-anesthetic drugs</i>	Atropine sulfate (0.5 mg)	0.07
	Ephedrine (30 mg)	0.27
	Saline (500 mL)	1.04
	Gelatin (500 mL)	4.76
	Hydroxyethyl-starch (500 mL)	10.60
	Glucose 5% (500 mL)	1.13
	Neostigmine (2.5 mg)	1.19
	Metoclopramide (10 mg)	0.08
	Propacetamol (2 g)	1.73
	Morphine (10 mg)	0.77
	Amoxicilline (2 g)	0.53
	Netilmicine (150 mg)	3.51
	Ornidazole (1 g)	3.19
	Cefamandol (0.75 g)	2.54
	Cefotaxime (1 g)	4.34
	Oxygen (1 m ³)	0.54

The costs of volatile anesthetic agents were calculated using the formula described in detail elsewhere.¹⁴ Concentrations on the vaporizer were recorded throughout the procedure.

Costs were derived from the unit costs of the drug and price lists at AP-HP (Assistance Publique des Hôpitaux de Paris; Table 1). One CAN\$ was considered equivalent to 4.86 French Francs.

Collection of the cost data started on arrival in the OR and ended at the departure from the PACU. Costs of equipment used during anesthesia, indirect costs and non-medical costs were not included in our measurements.

MEASUREMENT OF PACU OCCUPANCY

In this study, effectiveness is represented by PACU occupancy for patients anesthetized with either D or I.

In a first step, we constructed two regression lines derived from the observed data (68 patients), linking the duration of surgery and the LOS in PACU for each halogenated agent.

In a second step, these regression equations were applied to determine the theoretical LOS in PACU according to the duration of the procedure and the halogenated agent in 204 consecutive surgical patients (corresponding to 26 operating days). Regarding these

204 patients, truly recorded variables were duration of the procedure and time to admission in the PACU. Thereafter, the LOS in PACU (and consequently the time when the patients left the PACU) were calculated using the regression equation previously derived from the observed population. We hypothesized these 204 patients received either I or D, exclusively. At this stage, a computer modelization, taking into account the arrival and departure times from the PACU, allowed us to simulate the number of patients present in the PACU at any time during the day, according to the halogenated agent of interest. PACU occupancy was assessed for intervals of 15 min. The number of patients present within a period was then divided by 26 days in order to obtain the average occupancy in the PACU during this period of observation. The number of patients was assessed at the end of a 15-min period. The difference of occupancy in the PACU according to the volatile agent used is expressed as average occupancy (number of patients present at a definite period) and percentage of total occupancy during the 26 operating days.

STATISTICAL ANALYSIS

The linear regression between the duration of the procedure and the LOS in the PACU according to the halogenated agent used was validated with a Bootstrapping technique (SPSS v. 9.0).¹⁵ Briefly, the Bootstrap technique consisted of multiple resampling with random samples of 30 patients in each group. Regression equations were recalculated for these new samples and pooled to derive a new value for the slope and for the correlation coefficient. The Bootstrap technique is intended to provide an accurate estimate of the uncertainty associated with study parameters especially in studies with small sample size and where normal distribution is questionable. In our study, the Bootstrap technique was used to improve the validity of the slope of the regression equation between the duration of the procedure and the LOS of the patients in the PACU, according to the halogenated agent delivered. The simulated PACU occupancy, based on 204 consecutive patients and the hypothesis of exclusive use of either D or I, was thereafter compared with ANOVA analysis.

To test the robustness of our conclusions on PACU occupancy, a sensitivity analysis was performed. For this purpose, the theoretical LOS in PACU were increased and thereafter decreased by 10% for each agent (D and I). Simulated occupancy in PACU was calculated again with these new values in order to determine if the differences between the two groups persisted after these changes.

Demographic data, duration of the procedure and costs were compared with Student's unpaired t test.

Demographic data and duration of the procedures are presented as medians and interquartiles in order to show the distribution of the values. Other results are given in means $\pm$ SD.

The threshold for statistical significance was considered as $P < 0.05$.

Results

Demographic data

Surgical procedures included herniorrhaphies, cholecystectomies, colonic segmental resections and partial pancreatectomies. Distribution of the type of procedures was similar between the two groups.

A total of 68 patients was studied. Thirty-six patients received I and thirty-two received D. Twelve patients were withdrawn from the final analysis (eight in the D and four in the I group). Reasons for withdrawal were unplanned need for postoperative prolongation of sedation (one in the D group), incomplete data collection (five in the D group and three in the I group) or deviation from the protocol (two in the D group and one in the I group).

Demographic data of the 68 observed patients are presented in Table II and did not differ between groups. Doses of thiopental (370 ± 68 and 347 ± 78 mg for D and I respectively), sufentanil (51 ± 27 and 48 ± 32 μ g for D and I respectively) and atracurium (128 ± 85 and 112 ± 64 mg for D and I respectively) did not differ between groups.

Demographic data and duration of surgery did not differ between the observed patients and the 204 consecutive patients in whom the model was applied.

Costs

Administration of D was CAN\$ $0.063 \cdot \text{min}^{-1}$ more costly than I (respectively CAN\$ $0.087 \cdot \text{min}^{-1}$ and CAN\$ $0.024 \cdot \text{min}^{-1}$; $P < 0.05$; Table III).

The cost of non-halogenated anesthetic drugs, non-anesthetic drugs and supplies did not differ between the two groups (Table III).

When applied to the 204 consecutive patients, the exclusive use of D would have increased the cost by CAN\$ 2 708 (CAN\$ 13.28 per patient) as compared with I.

Cost effectiveness analysis

OBSERVED PATIENTS

Time to reach an Aldrete score of 10, incidence of PONV and mean LOS in PACU after I or D anesthesia are presented in Table IV. LOS in the PACU was significantly shortened after D anesthesia as compared with I. The relationship between duration of the procedure and LOS in PACU after D or I anesthesia is

TABLE II Demographic data of patients in groups D and I

	I	D
<i>n</i>	36	32
Age (yr)	56 [40–64]	48 [32–64]
Sex (M / F)	20 / 16	21 / 11
Weight (kg)	70 [61–76]	66 [57–74]
ASA status (I / II)	25 / 11	26 / 6
Procedure duration (min)	151 [105–293]	174 [112–292]

D=desflurane; I=isoflurane. Results presented as median [interquartile range]. No differences between groups.

TABLE III Comparison of costs related to anesthesia with D or I

	I	D
Halogenated agents	3.4 ± 1.9	15.8 ± 10.1*
Other anesthetic drugs	21.1 ± 7.8	23.5 ± 10.0
Non-anesthetic drugs	19.2 ± 14.2	20.5 ± 18.2
Supplies	9.4 ± 3.6	10.9 ± 3.9
Total	53.7 ± 22.4	70.8 ± 34.8*

I=isoflurane; D=desflurane.

Results in CAN\$. Mean ± standard deviation. **P* < 0.05.

TABLE IV PACU data according to volatile agent in the observed patients

	I	D
<i>n</i>	36	32
Aldrete score of 10 (min)	46 [32–60]	30 [20–32]*
Patients receiving morphine (<i>n</i>)	34	28
Morphine titration (mg)	6 [3–8]	8 [3–10]
Incidence of PONV (<i>n</i>)	16	15
Length of stay in PACU (min)	137 [110–172]	111 [88–134]*

I=isoflurane; D=desflurane; PONV=postoperative nausea and vomiting. PACU=postanesthesia care unit.

Results presented as median [interquartile range]. **P* < 0.05.

presented in Figure 1. During D anesthesia, the LOS in PACU was not correlated with the duration of surgery ($r^2=0.10$; $P > 0.05$) whereas it was with I ($r^2=0.31$; $P < 0.01$).

MODEL OF OCCUPANCY IN THE PACU

When the model was applied subsequently to 204 patients, occupancy in the PACU was reduced in the D group as compared with I ($P < 0.01$; Figure 2).

PACU occupancy was reduced by one or more patients 26.1% of the time with D as compared with I. Similarly, periods where the PACU was empty increased by 6.5% with D.

Analysis of sensitivity

When the theoretical LOS in the PACU for the 204 patients was increased by 10% when patients received

FIGURE 1 Relationship between duration of the procedure and length of stay in postanesthesia care unit (PACU) according to the inhaled agent used for the maintenance of anesthesia. Dots=desflurane; Squares= isoflurane.

FIGURE 2 Average occupancy in the postanesthesia care unit (PACU) according to the halogenated agent administered in 204 simulated patients within a period of observation of 26 days. Average occupancy is reduced after desflurane anesthesia ($P < 0.01$).

D hypothetically, and simultaneously decreased by 10% for those hypothetically receiving I, the average difference in PACU occupancy still remained less after D anesthesia ($P=0.024$).

Discussion

This observational evaluation shows that maintenance of anesthesia with D allows for a reduction of the LOS

of patients in the PACU as compared with I. The faster discharge of patients from the PACU leads to a reduction of PACU occupancy, particularly during crowded periods, thereby potentially improving the overall organizational process in the operating theatre.

D has the lowest blood solubility among the available halogenated agents, allowing for a faster rate of elimination after discontinuation.¹⁶ Numerous trials have demonstrated previously that recovery after D anesthesia is more rapid than after I anesthesia, especially after long lasting procedures.^{6,7} Aside from safety and patient well-being, this faster recovery from anesthesia may have a significant effect in reducing LOS in the PACU. However, the relationship between faster recovery and reduction of the LOS in the PACU has not been well established and remains controversial.^{11,12} Anesthetic technique and the duration of the surgery have been identified as potential factors affecting discharge time. Moreover, the incidence of pain, drowsiness and PONV are the most common medical causes of delay for patients to be discharged from the PACU. Furthermore, many extra-anesthetic factors can influence LOS in the PACU (e.g., lack of ancillary personnel, availability of beds in the ward...).

LOS in the PACU influences the number of patients present in the PACU, thereby affecting the level of activity of the personnel in the PACU and/or turnover. In this perspective, PACU occupancy may be chosen as a parameter of economic evaluation since it influences personnel labour costs, the major determinant of overall charges.⁴ Potential benefits of optimization of the PACU turnover have been estimated with computer simulations of patient flow. In a previous study by Tiby-Lévy *et al.* it was shown that reducing LOS of patients would enable PACU's to treat the same number of patients with lower costs or, conversely, to increase the number of patients admitted.³ These authors emphasize that, even without restructuring the anesthesia team, the benefit of such programs would be translated in quality of delivered care, and reduction of the risk of postanesthesia hazards. In an analysis of the strategies to decrease PACU costs, Dexter *et al.*, using a computer simulation, investigated the influence of anesthetic drugs on occupancy in PACU. They determined that a combination of propofol for induction and D for the maintenance of anesthesia, rather than thiopental and I, could decrease PACU costs by 14%, allowing an earlier discharge of the last patient admitted in PACU.⁴ In their hypothetical model that arbitrarily considers one admission per hour, decreasing time to discharge by at least 10% allowed a decrease of the peak number of

patients present in the PACU by 20%. As pointed out by these authors, it should be noted that it is difficult to put a strict monetary value on a reduction in PACU occupancy. Especially in our French health organization, PACU nurses are full-time employees and a minimum number of nurses is required whatever the number of patients present. Thus, any reduction in PACU occupancy does not necessarily translate into decrease in labour costs. We chose to perform a cost-effectiveness analysis examining the costs associated with a reduction in PACU occupancy, considered as a unit of success without placing a monetary value on the success.¹⁷ The organizational impact of the reduction of PACU occupancy becomes meaningful when surgical activity is growing continuously, leading to an increase of overcrowded periods. Thus, the additional cost of D may avoid or delay structural investments to increase the capacity of the PACU. Furthermore, the LOS in PACU after D anesthesia remains independent of the duration of surgery, enabling a better predictability of PACU occupancy. Such data should help an anesthesia department to develop an algorithm to optimize the use of halogenated agents, taking into account the foreseeable patient flow within the day.

In the current period of health care cost containment, many studies advocate considering a rational use of pharmaceutical resources.¹⁸⁻²⁰ The present study is in accordance with this perspective. In Europe, new anesthetic agents like D and sevoflurane have a higher cost of acquisition than older compounds like I. In our study, the only significant cost differences between the two groups (pharmaceutical products and medical devices) was related to the differential cost of halogenated agent administration. In the present cost-effectiveness analysis, the increased cost of D has to be linked with the organizational and economical benefits of a decrease in the PACU occupancy. However, it should be noted that the additional cost of D is only a small part of the overall cost of the surgical process.²¹

The limitations of the observational nature of the study deserve discussion. Recent reviews have recommended validation of the conclusions drawn from controlled trials by observational evaluations. This recommendation has been made to ensure that the observed differences between two drugs or two different strategies remain significant in the context of clinical daily practice.^{8,9} Observational evaluations are considered as a useful adjunct to controlled studies, especially in pharmacoeconomic investigations.⁹ Although designed in a different manner than controlled trials, observational studies should be performed in accordance with guidelines.^{8,9} In particular, prospec-

tive assessment, homogeneity of the demographic data (checked in the final analysis), and blinded observers are mandatory. These criteria were fulfilled in the present study. This approach has been presented recently and discussed in a publication from our group, based on the same observed population, focussing on the rate of awakening.¹⁰ Our model was based on observed cases, set in routine conditions, therefore integrating many confounding environmental factors in the final result. However, in an attempt to reduce the extent of several of these confounding factors, potentially influencing the patients' LOS in PACU, we chose objective eligibility criteria for discharge. Incidence of PONV, and occurrence of pain requiring specific treatment were similar between the two groups. Patients judged able to be discharged from the PACU were transferred to the ward without delay. Even so, it is noteworthy that the lack of randomization runs the risk of selection bias. Demographic data and duration of surgical procedures were similar between groups, suggesting an homogeneous assignment of patients to the study groups. Although several effectiveness trials have included random assignment to treatment, randomization infringes somewhat on natural practices (i.e., limitation of study enrollment, practitioners more prone to demonstrate the interest in a new drug...).⁹ Finally, observational studies run the risk of poor data collection. We paid a particular attention to keep only patients with high quality data collection in the final analysis.

It should be noted that, because the LOS in PACU was dependent on the duration of anesthesia with I and because the observed difference between both agents were more pronounced after lengthy procedures, a different ratio between long and short procedures would have modified the results. Extrapolation of our results to other institutions with different case loads would, thus, be limited.

Our observational evaluation shows that PACU occupancy is likely to be reduced when using D rather than I for the maintenance of anesthesia. This could have major implications in the organization of operating theatres, especially in structures with high levels of activity and when overcrowding of the PACU occurs. In these circumstances, the higher acquisition cost of D could be offset.

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