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Original Article

Cost-effectiveness of different regimens of anesthesia for day surgery in China

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Abstract: Objectives: To compare the cost-effectiveness of inhalation of sevoflurane, target-controlled infusion (TCI) of propofol, intravenous (IV) propofol for induction-inhalation of sevoflurane, and IV propofol for induction-inhalation of desoflurane for anesthesia maintenance in day surgery. Methods: 240 patients, scheduled for elective day surgery, were randomly divided into 4 groups (n = 60 each): inhalation of sevoflurane anesthesia group (group S); TCI of propofol anesthesia (group P); and intravenous propofol for induction of anesthesia-inhalation of sevoflurane for maintenance of anesthesia group (group PS); and intravenous propofol for induction of anesthesia-inhalation of desoflurane for maintenance of anesthesia group (group PD). Results: Group S was associated with less time to loss of consciousness, as well as the other three groups were associated with less time to recovery ($P < 0.05$). Group P was associated with a higher anesthetic agents cost than other 3 groups ($P < 0.05$), and group S was associated with a higher anesthetic agents costs than group PS and PD ($P < 0.05$). Conclusion: Induction with intravenous injection of propofol and maintenance with inhalation of desoflurane is the most cost-effective method of anesthesia for day surgery.

Keywords: Anesthesia, sevoflurane, desfulrane, propofol, cost-benefit analysis, day surgery

Introduction

Day surgery shows a rising tend in the proportion of in modern surgeries and requires utmost safety, rapid recovery and minimal side effect of the anesthesia [1]. General anesthesia is widely applied, and the regimens of drug combination are changing [2]. Building on the premise of relatively limited medical resources in China, it is increasingly concerned by anesthesiologists how to reduce the cost of anesthetics and improve the recovery quality of patients. In other countries, anesthetic drugs for day surgery usually include propofol, isoflurane, sevoflurane or desflurane. Although there have been studies to compare the cost-effectiveness of these drugs [3-5], the results are different due to different observation indicators, objects and drug prices [1].

For the advantages of rapid response and quick elimination, sevoflurane and desflurance have been widely applied in day surgery in China [6]. The present study aimed to observe the different combination methods of propofol, sevoflurance, desflurane and other anesthetics in induction and maintenance phase, evaluate the efficacy and cost of the combinations of many drugs in clinical practice and assess the post-anesthesia recovery quality of patients by pharmacoeconomics method in order to find a most cost-effective drug combination for day surgery anesthesia.

Materials and methods

Ethics

This study has been approved by the ethics committee of Luwan Branch of Ruijin Hospital, and informed consent form has been signed by the patients or their families.

Methods

Two hundred and forty female or male ASA I or II patients (aged 18-60, body mass index: 16~30 kg/m^2) who underwent laparoscopic surgery under general anesthesia with endotracheal intubation were included. In accordance with random number table, all the patients were divided into four groups (n = 60): sevoflurane inhalation group (group S), propofol target-controlled infusion group (group P), iv propofol for induction of anesthesia-inhalation of sevoflurane for anesthesia maintenance group (group PS) and iv propofol for anesthesia induction-inhalation of desoflurane for anesthesia maintenance group (group PD). Exclusion criteria: surgical patients with known or suspected allergy or abnormal reaction to halogen anesthetics identified or suspected malignant hyperthermia history or family history and emergency surgery or complex regional anesthesia, pregnant and lactating women. The expected operation time was 45-75 min. In all the patients without premedication, venous access was established after they entered the room, and then Lactated Ringer's Solution was infused. Routine monitoring of respiratory rate, heart rate, noninvasive blood pressure and saturation of pulse oximetry was performed. Narcotrend (Monitor Technik, Bad Bramstedt, Germany) for anesthesia and consciousness depth monitoring was connected to measure NT indexes, and muscle relaxation monitor was connected for muscle relaxation monitoring.

Anesthesia induction

Group S was given inhalation of 8% sevoflurane with oxygen flow rate of 8 L/min. Group P received target-controlled infusion of propofol with the target plasma concentration of 4 μg/ml. Group PS and PD was administered with intravenous injection of 2 mg/kg propofol. After the consciousness of the patients disappeared, all the four groups were given intravenous injection of 2 μg/kg fentanyl and 0.6 mg/kg rocuronium bromide when NT index measured by Narcotrend was less than 46, and all underwent endotracheal intubation and anesthetic equipment connection for mechanical ventilation with oxygen flow rate of 2 L/min to maintain PETCO2 at 30~40 mm Hg (1 mm Hg = 0.133 kPa).

Maintenance of anesthesia

Group S and PS received inhalation of sevoflurane (Baxter in U.S., lot number: A098L319). Group PD underwent desflurane inhalation (Baxter in U.S., lot number: H067D322) and the end-tidal concentration was maintained at 1MAC~1.5MAC. Group P received target-controlled infusion of propofol (AstraZeneca, 500 mg/vial (lot number: KN141), 200 mg/vial (lot number: X14060A)) with the target plasma concentration of 3-6 μg/ml. In the process of anesthesia, the mean arterial pressures in the patients of the four groups were maintained at less than 20% of the baseline value. If necessary, fentanyl was added additionally during the operation (the maximum dose was not more than 6 μg/kg). During the operation, the patients in whom the spontaneous breathing recovered were given additionally 0.3 mg/kg Rocuronium bromide, and the depth of anesthesia was controlled at NT index 22-46. Vecuronium bromide and fentanyl were not administered within 30 min before the expected end of the surgery, and end-tidal sevoflurane and propofol target concentration were minimized to improve palinesthesia speed. At the end of surgery, propofol, sevoflurane and desflurane were discontinued. Meanwhile, the oxygen flow rate was increased to 5 L/min, and the ventilation parameters remained unchanged. When T1 measured by TOF for muscle relaxation monitoring recovered to 15%, 40 μg/kg neostigmine and 1 mg atropine were intravenously injected. The patients who opened their eyes when they were called upon and with TOF > 0.9, tidal volume > 5 ml/kg, respiratory rate > 10 breaths/min and PetCO: < 45 mmHg were given removal of tracheal catheter and then were sent to postanesthesia care unit (PACU). The patients who can maintain stable vital signs for ≥ 30 min, had no significant postoperative bleeding and can state their name can leave PACU. During the postoperative follow-up, the patients should be injected intravenously with 3 mg Granisetron Hydrochloride Injection in case of nausea and vomiting; and 30 mg ketorolac tromethamine were injected intravenously into the patients who complained of pain with VAS > 4 (this medicine can be repeatedly added).

Record content

1). The occurrence of adverse reactions of bradycardia, hypertension and hypotension during operation. 2). The time of loss of consciousness (from the beginning of medication to the patient's unresponsiveness to oral instruction, and the NT index is < 46 by Narcotrend); spon-

Table 1. General condition of the patients of the four groups

	P	S	PS	PD
N	60	60	60	60
Female/male	38/22	39/21	40/20	37/13
Age (years)	47.45 ± 12.33	45.35 ± 10.63	48.03 ± 13.73	46.09 ± 14.72
Body weight (Kg)	61.41 ± 11.79	60.14 ± 12.58	59.2 ± 10.87	58.77 ± 12.43
Operation time (min)	60.27 ± 17.55	56.53 ± 15.69	57.44 ± 16.34	58.02 ± 15.56
ASA1 patients (%)	70%	67%	67%	65%
ASA2 patients (%)	30%	33%	33%	35%
Operative types				
Department of gynecology	33	31	31	33
Urological department	12	13	14	13
Department of plastic surgery	8	7	7	7
General surgery department	7	8	8	7

Table 2. Comparison of the patient number exhibiting adverse reactions in the four groups

Groups	P	S	PS	PD
Bradycardia	0	1	1	2
Hypertension	1	2	1	1
Hypotension	1	1	2	1

taneous breathing recovery time (from withdrawal to spontaneous breathing recovery); awakening time (from withdrawal to eye opening); orientation recovery time (from withdrawal to correctly answering the name and birth date). 3). The dosage of anesthetics, analgesics and muscle relaxation agents during the anesthesia process. 4). The number of nausea and vomiting and the cost of medicines and the cost of pain medication through the postoperation follow-up visits.

In PONV (post operation nausea and vomiting) classification, class I: no PONV within 24 hours; II: light nausea without vomiting within 24 hours; III: obvious and unbearable nausea within 24 hours (drug control is needed on occasion); IV: vomiting within 24 hours, and the vomit is gastric content, drug control is required.

Calculation method for the anesthetic cost

The cost of intravenous medication was calculated on the basis of the number of ampoule opened. Group P used propofol (AstraZeneca, specification: 500 mg/50 ml) both during anesthesia induction and anesthesia maintenance and group PS used propofol (AstraZeneca, specification: 200 mg/20 ml) during anesthesia induction. The dosage of sevoflurane was 250 ml/bottle (Baxter) and desflurane 240 ml/bottle (Baxter).

We calculated the consumption with the following formula: $V = (P \times F \times T \times M) \div (2412 \times d)$: V: the consumption of sevoflurane or desflurane (ml), P: the volatilization pot concentration set of sevoflurane or desflurane, F: oxygen flow rate (L/min), T: time (min), M: the molecular weight of sevoflurane 200.06, the molecular weight of desflurane 168.04, d: the density of sevoflurane (1.525 g/ml), the density of desflurane (1.465 g/ml). Sevoflurane/mL RMB10.61, desflurane/mL RMB3.55, propofol (500 mg/50 ml) RMB256, propofol (200 mg/20 ml) RMB98, fentanyl during anesthesia 0.1 mg/2 ml RMB4.88, Rocuronium Bromide 50 mg/5 ml RMB92, granisetron hydrochloride 3 mg/vial RMB50, ketorolac tromethamine 30 mg/vial RMB37.

Statistical analysis

SPSS 19.0 was used for analysis. Measurement data were expressed as means ± standard deviation, chi-square was adopted for comparison of data in the table, and one-way analysis of variance was used for intergroup comparison. $P < 0.05$ was considered statistically significant.

Results

The operation was finished within 75 minutes for all 240 patients. The operation types included laparoscopic ovarian cystectomy, laparo-

Table 3. Comparison of anesthesia induction and awakening among the four groups

Groups	P	S	PS	PD
Consciousness loss time (s)	110 ± 44	52 ± 32a	65 ± 27	66 ± 34
Respiration recover time (min)	7.02 ± 2.76	5.5 ± 2.87	5.17 ± 2.90	5.09 ± 2.65
Awakening time (min)	12.67 ± 6.56	9.2 ± 4.4*	9.37 ± 4.65*	8.76 ± 4.22*
Orientation recover time (min)	17.33 ± 5.13**	15.67 ± 6.11**	15.89 ± 7.22**	12.34 ± 5.91**

Note: *$P < 0.05$ compared to group P; **$P < 0.05$ compared to group PD.

Table 4. Nausea and vomiting in the four groups

Group	N	Grade I	II	III	IV
P	60	14	8	16	22
S	60	12	6	17	25
PS	60	12	7	18	23
PD	60	11	9	17	23

scopic inguinal herniorhaphy, percutaneous nephroscopic lithotripsy, unilateral thyroid resection and parotid tumor removal. 1). No significant difference was found in general information, anesthesia time and operating time among the four groups (*P* > *0.05*). See **Table 1**. No significant difference was found in the occurrence of anesthesia-induced adverse reactions among the four groups (*P* > *0.05*). See **Table 2**. The time-to-loss of consciousness of group P was longer than that of group S (*P* < *0.05*). Compared with group P, the awakening time of the other three groups was shorter (*P* < *0.05*). Compared with group PD, the orientation recovery time of group P, S and PS was longer (*P* < *0.05*). See **Table 3**. No significant difference existed in the occurrence rate of postanesthesia nausea and vomiting and the cost of medicines among the four groups (*P* > *0.05*) (See **Tables 4**, **5**). The cost of intravenous anesthetics of group P was significantly higher than the other three groups (*P* < *0.05*). The cost of inhaled anesthetics of group S was obviously higher than that of group PS and PD (*P* < *0.05*). There were not obvious differences in the cost of analgesics and muscle relaxation agents during anesthesia, the incident rate of postanesthesia pain and the cost of medicines among the four groups (*P* > *0.05*). See **Table 5**.

Discussion

Day surgery requires the utmost safety, rapid recovery and minimal side effect from anesthesia. It has been thought that the key of the economic problem of clinical anesthesia was fewer side effects after anesthesia, i.e. the postoperation pain reduced and there are no such complications as nausea and vomiting [4, 7, 8]. Therefore, the treatment for complications is the key factor to ensure a smooth day surgery. That the life of the patient is not affected and the patient can quickly return to the society is of crucial importance. By evaluating the combination of general anesthesia drugs through the method of pharmacoeconomics, this study aims to find the optimal combination of anesthetic.

The results of the paper showed that the time-to-loss of consciousness of group S was shorter (*P* < 0.05) than that of group P, indicating that the sevoflurane inhalation for anesthesia induction can bring a good effect. This may be due to the low blood/gas partition coefficient of sevoflurane so that it can achieve a blood/gas balance [9, 10] within a short time. Compared with group PD, the orientation recovery time of group P, S and PS extended (*P* < *0.05*), This likewise suggested that desflurane has a low blood/gas partition coefficient and can rapidly wash out the medicines, which was supported by the literature [11-13].

The total expense of anesthetic of group P is obviously higher than that of the other three groups, while group PS and PD require the lowest expense (P < 0.05). It is worth noting that the calculated quantity of 500mg propofol Prefilled Syringes would be more than its actual quantity in most operations and while such a problem exists in all intravenous anesthetics, Thereby, the anesthesia cost increases [10] of group P to some extent. The amount of inhalation anesthetics in this article has referred to the calculation method of Dion [14] to avoid wasting anesthetics. The dosage of sevoflurane and desflurane per hour in this study is slightly higher than that by Weinberg et al [1], for which the reason is that the concentration by Weinberg is controlled within 1MAC while the concentration of inhalation anesthetics in this

Table 5. Cost of anesthetic and the medicines for processing the complications

Group	Dose of propofol and/or inhaled anesthetic per hour (mg/ml)	Cost of propofol and/or inhaled anesthetic per hour	All-in cost of intravenously injected/inhaled anesthetic	Cost of analgesics and muscle relaxant	Cost for processing post-anesthesia nausea and vomiting	Cost for processing post-anesthesia pain
P	865.46 ± 131.27	507.19 ± 118.95	605 ± 99.30	104.45 ± 2.47	53.95 ± 13.66	41.93 ± 13.02
S	24.96 ± 3.71	264.83 ± 39.36	384.15 ± 13.61*	104.28 ± 2.48	56.25 ± 16.75	39.06 ± 13.66
PS	13.85 ± 2.35	242.94 ± 24.93	341.7 ± 18.43*,**	103.98 ± 2.47	57.32 ± 17.89	41.63 ± 12.68
PD	39.25 ± 3.28	237.34 ± 11.64	338.15 ± 21*,**	103.78 ± 2.44	56.25 ± 16.75	41.35 ± 12.28

Note: *$P < 0.05$, compared to group P; **$P < 0.05$, compared to group S.

study is larger than 1MAC. In order to reduce the potential renal toxicity of sevoflurane, the oxygen flow rate is controlled within 2 L/min.

The total expense of anesthetic of group P was much higher than that of the other three groups ($P < 0.5$). According to foreign literature [15, 16], the cost of propofol used for anesthesia is high, but it can cause lower restlessness after extubation and the postanesthesia nausea and vomiting rate can be reduced by 25% by means of propofol induction/maintenance compared with inhalation anesthetics. Postoperative nausea and vomiting are the most common complications after anesthesia and the important issues which affect the patient's recovery in perioperative period and extend the discharge time [16, 17]. In this study, the occurrence rate of postanesthesia nausea and vomiting and the cost of medicines are of no significance differences among the four groups ($P > 0.05$). Such results were supported by the study of Terry [2]. However, in the study of Elliott et al, the sevoflurane induction/maintenance group required lower cost but had higher occurrence rate of nausea and vomiting which needed more costs for treatment compared to this study. It may be caused by laughing gas mixed while inhaling anesthetics in Elliott study. Laughing gas may increase the post-anesthesia nausea and vomiting [7, 17]. The incidences of pain in the four groups in this study were close to those in previously reported [4, 18], and there were not obviously differences among the four groups.

The aim of this study was to evaluate the cost-effectiveness of the anesthetic combination without considering the environmental pollution caused by anesthetic inhalation. The results of this study showed that the expense of the desflurane group (group PD) was close to that of the sevoflurane group (group PS) in day surgery. The reason may be that the unit price of sevoflurane in China was higher than that in Australia while the unit price of desflurane was closer [1]. However, the volume of the consumed desflurane is considerably larger than that of sevoflurane, which may indicate that the desflurane would cause more pollution to environment than sevoflurane. Low flow anesthesia can reduce the consumption of inhaled anesthetics, and the consumption of sevoflurane and desflurane lowered by 1/4 under the oxygen flow of 0.5 L compared with that under the oxygen flow of 2 L. Low flow anesthesia would decrease the environmental pollution by inhaled anesthetics [1]. Meanwhile, the human cost of medical staff is not taken into account as well.

To sum up, intravenous injection of propofol for induction and desflurane inhalation for maintenance is the most cost-effective medicine combination method in day surgery.

Disclosure of conflict of interest

None.

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